TABLE OF CONTENTS

(Please see index after table of contents for cross reference)

Contents

1. Overall Approach and Governance

G1A. MEETING THE INTENT OF THE CLINICAL AND TRANSLATIONAL SCIENCE AWARD (CTSA)

G1A1. Specific Aims

Attain a Shared Vision. The University of Rochester (UR) and NIH share a common vision for clinical and translational science. As envisioned by the NIH in its pre-CTSA application conferences, clinical and translational science can best be advanced by creating an integrated academic home for this discipline. At UR, this shared vision has driven our research planning over the past several years. As evidence of our commitment to this transformation, we have already put into place several components of this plan, described in section G1A3. The CTSA will greatly accelerate our ability to add remaining critical elements and infrastructure, which together will provide a nurturing, academic home for clinical and translational science.

Create a Clinical and Translational Science Institute (CTSI). A major goal of the University of Rochester Medical Center (URMC) is to serve as a national model for an integrated clinical and translational science enterprise that provides reference benchmarks on scientific productivity, innovative approaches for educating and recruiting clinical and translational scientists, and effective ways to nurture cross-disciplinary collaboration. Key components of our strategic plan include: a new 150,000 sq. ft. Clinical and Translational Sciences Building (CTSB); an upgraded, newly renovated 10,500 sq. ft. General Clinical Research Center (GCRC); and enhanced enabling disciplines and resources such as epidemiology, biostatistics, computational biology, imaging and functional genomics. Under the CTSA, these facilities and enabling resources will be integrated and upgraded to become the University of Rochester Clinical and Translational Science Institute (UR CTSI).

Enhance Dynamic Governance. The driving rationale and overarching objective of the UR CTSI is to coordinate and integrate the scientific, educational, administrative and regulatory elements of clinical and translational science. Under a governance structure in which the UR CTSI Program Director has authority over space, faculty and other resources related to the CTSI, and in which our current GCRC budget is redistributed to the pertinent CTSI Key Functions, we plan to augment the ability of our faculty to conduct multidisciplinary clinical and translational research, to stimulate and nurture new investigators to become active in clinical and translational science, and contribute nationally to the transformation of these two distinct research fields into a single new discipline. This new discipline will create new knowledge and techniques to diagnose, prevent and treat human disease, and establish an environment that catalyzes their application to clinical practice in the community.

Our **specific aims**, which are aligned with the CTSA Key Functions, are to:

1. develop novel methodologies for clinical and translational research, including research design, mathematical and statistical modeling, and biomedical laboratory technologies;
2. initiate innovative pilot studies that foster interdisciplinary collaboration in the application of these novel methodologies;
3. enhance biomedical informatics to facilitate data access and sharing, intra- and inter-institutionally, in a manner that safeguards data security and privacy, and ensures best practices;
4. support the design of new clinical and translational studies by drawing on the disciplines of epidemiology, biostatistics and ethics;
5. integrate regulatory resources to assure that interactions between research participants and clinical investigators occur at the highest standards of regulatory compliance and management efficiency;
6. strengthen resources enabling clinical and translational participants and investigators to interact effectively;
7. partner with community organizations to facilitate efficient dissemination of information on the importance, safety and value of clinical and translational science, and to reduce disparities in participation in clinical and translational research;
8. develop new cores for technologies and resources that support clinical and translational science;
9. structure educational and training programs to promote career development in the distinct discipline of Clinical and Translational Science;
10. develop a consortium of research partners consisting of Upstate New York institutions to foster translation of basic science discoveries and sharing of resources on a regional basis; and
11. evaluate the UR CTSI through the measurement of rigorous performance criteria, both for individual Key Functions, as well as the CTSI as a whole.

G1A2. Background and Significance

New Leadership & Vision. For almost a decade, UR leadership has been exploring ways to build on its strong foundation in clinical and translational science so as to complement its ongoing investments in basic research. In 2002, the appointment of David Guzick, MD, PhD as Dean of the School of Medicine and Dentistry inaugurated a specific commitment to clinical and translational science, and a strategic initiative was launched to create an academic home for this combined discipline, as summarized in G1A3. This was indeed timely, as it presaged the launch in 2003-04 of NIH's Roadmap, including the "Re-Engineering of the Clinical Research Enterprise." In July, 2005, UR appointed a new President, Joel Seligman, who commenced a

University-wide strategic planning process, integrating the strategic initiative for clinical and translational research into the University-wide planning process.

New Clinical and Translational Science Building (CTSB). The CTSA would transform clinical and translational science at UR. Creation of the CTSI will bring together heretofore diverse faculty and resources, and supplement these resources with the infrastructure and partnering required for successful clinical and translational research outcomes. At the hub of the UR CTSI will be the CTSB, which will bring together, under one roof: innovative research programs from diverse fields; cross-cutting scientific disciplines such as biostatistics, bioinformatics and epidemiology; and core support functions such as the IRB, grants management, and technology transfer. The resources in this building will directly interface with our GCRC, which itself will be substantially upgraded in renovated space. While the CTSB and GCRC are at the core of the CTSI, other key aspects of current clinical and translational research, such as the functional genomics and proteomics laboratories, will be housed at other locations but coordinated and integrated under the CTSI.

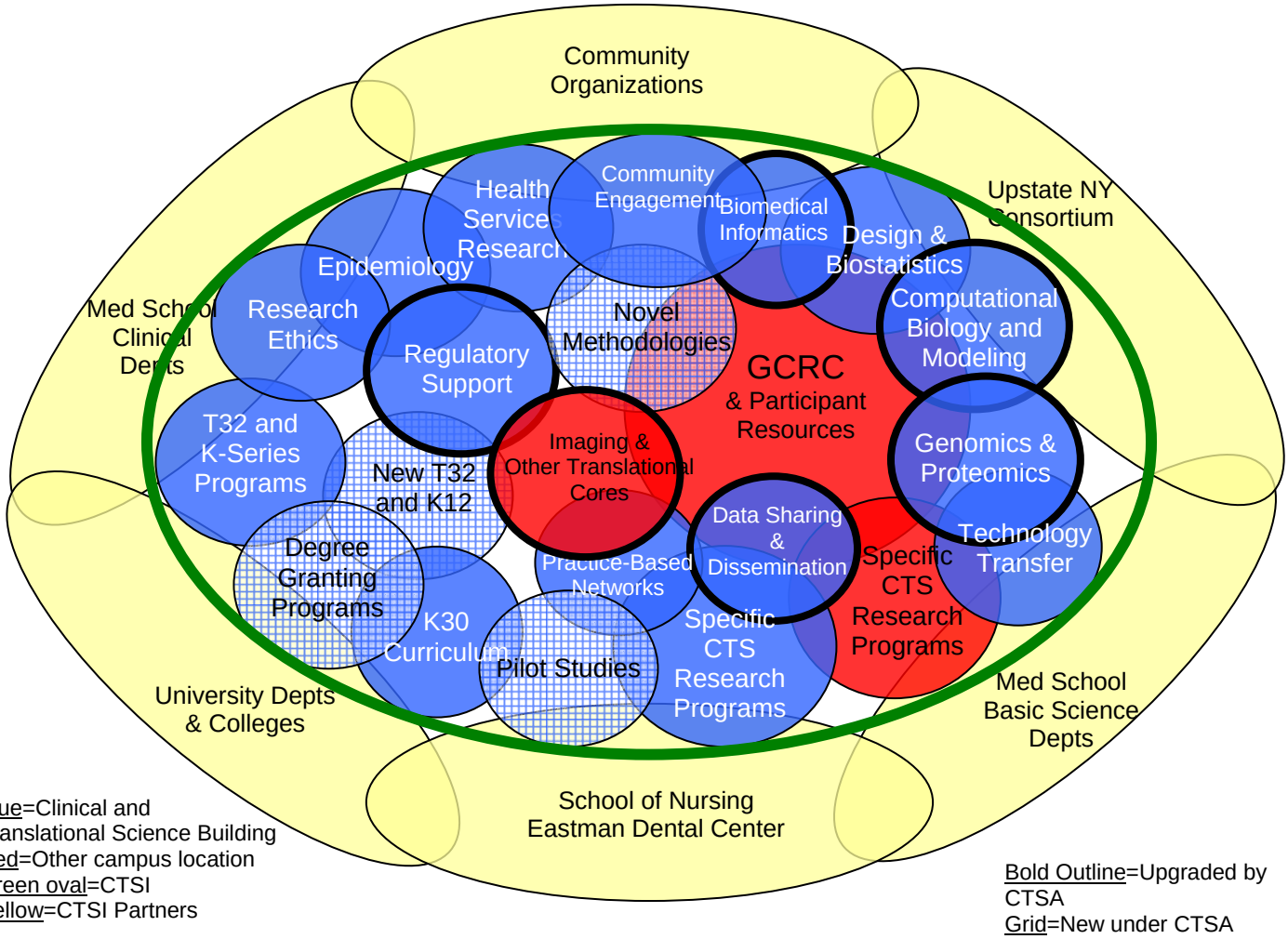
Enhanced Research and Training Environment. The proposed CTSA would foster a more comprehensive clinical and translational science environment by: starting a new PhD Program in Translational Biomedical Science, and 2 new Master's Degree programs, organized and supported by the K12 and T32 mechanisms; establishing or upgrading critical core translational resources; upgrading regulatory and oversight functions; and better enabling existing research programs and disciplines to translate scientific discovery into clinical practice and community dissemination.

Dynamic & Interactive Governance. Figure G1A1, shown on the next page, presents the components of the UR CTSI. This schematic representation is based upon a presentation by NIH Director Elias A. Zerhouni, MD, entitled "A Strong Foundation: Building a Home for Clinical and Translational Sciences" at the National Meeting on Enhancing the Discipline of Clinical and Translational Sciences, held on May 23, 2005 (www.ncrr.nih.gov/clinicaldiscipline.asp). In the first figure, the typical components of clinical and translational research at most academic health centers (GCRC, K30 curriculum, training awards, disease-specific research centers) are seen as disconnected. In the subsequent two figures, using a systems biology framework, a fortified and enabling infrastructure connects these components and thus forges a new, integrated discipline.

Clinical and Translational Science Institute (CTSI). The UR CTSI is depicted in Figure G1A1. Elements to be located in the CTSB are shown as blue circles, while components located in other areas of the campus, to be coordinated under the CTSI, are shown as red circles. Components that will be new under the CTSA are designated by a grid within the circle, while elements that will undergo upgrades under the CTSA are designated by outlining the circle in bold. All of the elements of the CTSI are conceptually collected within an oval outlined in green. CTSI partners are shown as yellow ovals intersecting the CTSI and its components. The areas of overlap are meant to reflect areas of programmatic intersection and collaboration. However, they are not meant to show explicitly all areas of overlap; rather, they are simply illustrative of much more frequent intersections between the various CTSI elements than can be shown in this type of schematic illustration.

Several aspects of Figure G1A1 are noteworthy. First, the Program Director will have authority over resources, space and faculty for all elements within the green oval, with oversight by the Senior Vice President for Academic Affairs of the University and the President. As well, he will have responsibility, in conjunction with Co-Directors and Key Function Directors, for interactions among Key Functions within the CTSI, and between the CTSI and partners elsewhere in the University, community and state. (A detailed description of CTSI governance is provided in section G1E.) Second, consistent with the mandate of the RFA to reorganize and reallocate resources in a manner that fosters an integrated academic home for clinical and translational research, much of the current budget of the GCRC will be distributed to pertinent Key Functions as a base of support for these functions. Third, many core components of the CTSI will be located under the CTSB (blue),yet, we will also take advantage of selected existing research centers in their current locations (red), which will be integrated into the CTSI as important components.

Figure G1A1. University of Rochester Clinical and Translational Sciences Institute (CTSI)



Fourth, the CTSI interacts with partner schools and colleges at the University, including Nursing, Dentistry, and Arts, Science and Engineering. Fifth, the CTSI also interacts with basic science departments and research centers at the medical school. Sixth, many existing clinical and translational research cores will be upgraded by the CTSA (outlined in bold) while others will be new under the CTSA (grid). New initiatives that will be supported by the CTSA are the T32 training program in translational science, the K12 program for training junior faculty in clinical and translational science, new degree granting programs such as a PhD in translational science, new imaging and other translational cores, and infrastructure support for the development of novel methodologies. Seventh, Figure G1A1 conveys the interaction between the UR CTSI and our community and region. In the Rochester community, we have links with the Monroe County Health Department, major employers, the Rochester School District and the Primary Care Practice-Based Network. Across Upstate New York, a particularly innovative aspect of the UR CTSI is the creation of a consortium of universities and other research partners, which might serve as a national model for regional consortia. Eighth, another innovative feature of the UR CTSI is the data sharing and dissemination plan, which might also be informative for a national approach to a logic model for such dissemination. And ninth, it can be seen that the UR CTSI is a trans-University entity. Regulatory support functions such as the Institutional Review Board and the Office of Research and Project Administration are University-wide offices.

Taken as a whole, the new organization illustrated in Figure G1A1 will transform clinical and translational science at UR by creating an academic home with the infrastructure, governance and institutional support needed to forge a new discipline that coalesces the two fields. The UR CTSI will thus accelerate the generation of multidisciplinary clinical and translational science at UR. In addition, the UR CTSI will provide significant contributions to a national consortium of CTSAs by providing innovative models for facilities, governance, regional collaboration and data sharing and dissemination.

G1A3. Strategic Planning for Clinical and Translational Research: Prior Experience and Planning

Our objectives in clinical and translational science are to create new knowledge and techniques that are applicable to improving the diagnosis, prevention or treatment of human disease, to facilitate translation of

such new knowledge to clinical practice in the community, and to stimulate and nurture new investigators to become active in clinical and translational science. Such research is a highly collaborative endeavor, requiring effective interaction and teamwork among faculty, trainees, students and administrative staff.

In 2002, under leadership of the new Dean of the School of Medicine and Dentistry, URMC embarked upon a sequence of strategic steps to exploit its collaborative, cross-disciplinary spirit as the basis for a more integrated and robust clinical and translational research enterprise. As a result, listed here chronologically, we are now poised to create substantial incremental value with the transformational addition of the CTSA.

G1A3a. Reorganize medical school leadership to facilitate clinical and translational research.

Because of the differences in knowledge base and infrastructure between clinical and basic research, Dr. Guzick created two positions in the Dean's Office in 2002, a Senior Associate Dean for Basic Research, and a Senior Associate Dean for Clinical Research. Howard J. Federoff, MD, PhD, and Thomas A. Pearson, MD, MPH, PhD, were appointed to the basic and clinical positions, respectively. Dr. Federoff is also Director of the Center for Aging and Developmental Biology. He does basic research on the development of somatic mosaic mouse technologies, the elucidation of nerve growth factor function in the adult, and translational research on the development of Herpes virus vectors for gene therapy and on environmental and genetic interactions in Parkinson's disease. Dr. Pearson is also Chair of the Department of Community and Preventive Medicine. He directs substantial national and international multidisciplinary research as Principal Investigator of our CDC Prevention Research Center ("National Center for Deaf Health Research") and of a major World Heart Federation study of the prevention of cardiovascular disease in a low-to-middle income country (Grenada). Further, Dr. Pearson is our institutional leader in clinical and translational research training, serving as PI on our K30 program. Both Dr. Pearson and Dr. Federoff work closely with Dr. Guzick in facilitating clinical and translational research efforts across the Medical Center. This is done in collaboration with the School of Nursing and the Eastman Dental Center, with oversight by the Senior Vice President for Health Affairs.

G1A3b. Create and maintain a Research Resource Inventory.

An important early step was to create a Research Resource Inventory that tracked clinical and basic research. This Inventory serves three purposes: 1) it represents an important dimension of the environmental assessment of clinical and basic research at URMC; 2) updates of this Inventory provide "outcome" data needed to evaluate progress in clinical research at URMC—the inventory was first created in 1998 and has been updated in 2003 and 2005; and 3) it is an online resource that provides faculty and trainees with information that directs them to important shared services and opportunities for collaboration and mentorship.

In Table G1A1, the distribution of funding across research categories based on the 2005 survey was reported by each of 585 principal investigators in the web-based survey, using the NIH definition of clinical research. In most cases, an entire project was reported as "basic" or as "clinical." In many cases, however, such as a Program Project with multiple projects, or an individual R01 with several specific aims that traversed animal models and human application, total research effort was divided between basic and clinical based on the distribution of research effort across aims. It can be seen from Table G1A1 that the ratio of basic to clinical research funding overall at the University of Rochester School of Medicine and Dentistry (URSMD) is virtually 50:50. NIH-funded research, however, is 64% basic and 36% clinical, approximating the 2:1 ratio between basic and clinical research that NIH funds across all institutions nationally. The difference can be attributed mainly to industry-sponsored research, which is predominantly clinical in nature. Federally-sponsored research of $151.3 million represents 70% of total sponsored funding. In preparation for this grant application, we reviewed each abstract for the funded NIH research grants (N=362) shown in Table G1A1 and classified them as clinical, translational or basic, using the definition of translational research provided in the RFA for this award. During FY05, we found that the NIH research grants (measured as a count instead of funding level) at URMC was distributed as follows: 64% Basic, 13% Translational, and 23% Clinical.

Table G1A1.Total sponsored research expenditures, FY2005, UR School of Medicine and Dentistry (URSMD)*

	Sponsor Type				
Category	*NIH*	*Federal - Non-NIH*	*Industry*	*Other*	*Grand Total*
Patient-Oriented Translational Research	16,290,620	313,811	2,905,129	2,745,596	22,255,157
Patient-Oriented Experimental Therapeutics	17,189,191	485,155	19,683,216	6,451,129	43,808,692
Population-Based Research	8,678,703	3,261,822	4,875,875	3,376,621	20,193,022
Health Services and Outcomes Research	2,029,002	1,708,179	514,507	2,136,574	6,388,263
Ethics and Health Policy Research	33,303	-	-	142,119	175,422
Subtotal - Clinical Research	44,220,820	5,768,968	27,978,728	14,852,040	92,820,555
Basic Research	78,657,039	4,050,414	2,095,409	11,629,193	96,432,055
Subtotal – Research	122,877,859	9,819,382	30,074,137	26,481,232	189,252,610
Clinical Research Education/Training	3,765,176	959,656	514,174	633,393	5,872,399
Basic Research Education/Training	6,864,657	579,637	35,438	369,627	7,849,360
Clinical Education/Training	298,531	2,369,582	10,289	3,462,867	6,141,269
Subtotal - Education/Training	10,928,364	3,908,876	559,901	4,465,887	19,863,029
Clinical Research Conference	64,025	-	-	141,755	205,780
Basic Research Conference	959,547	20,341	-	60,924	1,040,813
Clinical Conference	-	388,284	-	23,842	412,126
Subtotal – Conference	1,023,573	408,625	-	226,521	1,658,719
Other - Not Research, Education or Training	1,850,760	494,285	67,241	2,943,166	5,355,451
Total	136,680,555	14,631,168	30,701,279	34,116,806	216,129,809

*Data on total NIH funding for UR's FY 2005, reported in Table G1A1, are not identical with the 2005 data reported from NIH because NIH uses a different time frame for the fiscal year.

Table G1A2 shows a frequency tabulation of research projects according to ICD-10 category. Research at URMC encompassed a broad spectrum of diseases foci, the greatest foci on nervous system, mental and behavioral disorders, blood and immune diseases, infectious disease, cancer, and circulatory diseases. The CTSA will therefore support a wide variety of disciplines and disease-oriented programs. Additional tables describing URMC research are provided in Section G5A.

G1A3c. Expand biostatistics and bioinformatics.

In 2002, David Oakes, PhD completed two 5-year terms as Chair of Biostatistics and stepped down from his position. Dr. Oakes remains an active researcher and collaborator in biostatistics, and will serve a major role in Design, Biostatistics and Clinical Research Ethics, as described in G2D. At the time that Dr. Oakes stepped down as Chair, research at URMC was expanding and faculty members in the Department were unable to meet increasing demands for their expertise. In addition, there were few faculty members who could address rapidly developing needs in bioinformatics.

Table G1A2. Distribution of medical conditions in URMC sponsored research, based on the frequency of ICD-10 keywords (total=100%), from 2005 Research Resource Inventory

ICD-10 Keyword	%	ICD-10 Keyword	%
Nervous system	15.6	Pregnancy and perinatal	3.9
Blood and immune system	10.4	Genitourinary	3.0
Infectious	8.2	Eye	2.2
Mental and behavioral	8.2	Congenital	2.1
Circulatory	8.1	Injury and poisoning	2.1
Neoplasms	7.2	Digestive system	1.9
Factors influencing health status	6.3	External causes of morbidity/mortality	1.4
Respiratory system	5.0	Ear and mastoid process	0.8
Endocrine, nutritional, metabolic	4.5	Skin	0.5
Musculoskeletal	4.1	Other	4.5

Under Dr. Guzick's leadership as Dean, the Department was expanded to include bioinformatics and computational biology, was given new research and administrative space created from a shelled floor in a new research building, and acquired a new Chair, Andrei Yakovlev, PhD, with expertise in both classical biostatistics and bioinformatics. Dr. Yakovlev was appointed as Chair in 2002 with a specific plan to recruit faculty jointly with other departments to foster multidisciplinary research and to forge new interdisciplinary methodologies. Under Dr. Yakovlev, the Department of Biostatistics and Computational Biology has grown from 7 to 20 faculty members, with ongoing research in both biostatistics and bioinformatics and with multidisciplinary collaborations involving almost every clinical and basic science department; sponsored research to Department PIs has grown from annual awards of $805,823 in FY02-03 to $5,092,206 in FY05-06.

G1A3d. Identify critical cross-departmental programs within clinical and translational science, and identify faculty leaders in each of these areas.

Clinical and translational science comprises an extremely broad range of research areas. These extend from the translation of basic scientific discoveries into diagnostic tests or therapeutic agents (bench to human); to the development of specific devices or drugs (human to bedside); and to the implementation of new diagnostics, therapeutics, and best practices into the community (bedside to curbside). As a key part of our strategic planning, and as also emphasized in the CTSA RFA, we have recognized the need for a systematic infrastructure that better serves the evolving discipline of clinical and translational science.

To create this infrastructure in our Strategic Plan, we used the NIH Roadmap and its definitions of clinical and translational research as the framework to organize six interdisciplinary subcommittees that were institution-wide, i.e., cross-departmental and cross campus. Under this Plan, interdisciplinary clinical and translational science is supported by core functions, which we call "shared support units," and by specific research disciplines. Faculty whose work related to the multidisciplinary Centers were identified from the School of Medicine, the School of Nursing, the Eastman Dental Center, the College of Arts, Science and Engineering, the Institute of Optics, and community institutions (Monroe County Department of Health and the predominant Rochester health insurance company, Excellus). Faculty leaders in each of these interdisciplinary areas were identified as Chairs of strategic planning subcommittees. Members of these committees produced analyses and summary recommendations, which are now being incorporated into a University of Rochester Strategic Plan. Substantial overlap exists between this framework—in cross-cutting scientific areas, supporting disciplines and shared support units—and that called for by the CTSA. Thus, substantial planning work had been done in advance of the RFA for the CTSA, as captured by Figure G1A1 above.

G1A3e. Improve the process for clinical and translational research review and administration

A common theme that has emerged from committee reports and discussions is the need to improve the process by which clinical and translational research is reviewed, administered and overseen at UR. Investigators must obtain review and approval by the Institutional Review Board, the Office of Human Subject Protection (OHSP), and the Office of Research and Project Administration (ORPA). In addition, many grants interface with the Office of Medical Center Counsel, the Office of Technology Transfer (OTT), the General Clinical Research Center, and the Office of Research Accounting and Costing Standards, as well as many academic departments. Often, these multiple reviews require time and effort from the clinical investigator. Regulatory requirements frequently change and are likely to increase.

To enhance communication and improve efficiency, one key recommendation is that critical support services, such as the IRB, ORPA, and OTT, be more effectively coordinated and co-located in close proximity to clinical research programs. In anticipation of the physical integration of services and programs in the Clinical and Translational Science Building, we have formed a Research Review Process Improvement Team (RPIT) to carry out the functional integration. This team is chaired by the Senior Associate Dean for Clinical Research and includes the leadership of the above offices as well as active investigators. Members of the RPIT represent the institution's offices of research administration, human subject protection, counsel, technology transfer and clinical research. The

group also includes a number of research administrators and faculty members involved in clinical research. Monthly meetings of the RPIT have been held since September 2003, led by Dr. Pearson.

The goals of this Team are to: 1) ensure policies and procedures that effect full compliance, 2) promote an efficient institutional review and oversight process for clinical and translational research, and 3) facilitate collaboration between the administrative departments that are responsible for the review of proposed clinical research projects and post-award administration of approved projects. The ultimate goal is to encourage URMC faculty in their efforts to produce high-quality clinical research by ensuring that necessary research proposal review policies and processes are as efficient and speedy as possible. Among its accomplishments, the RPIT has: designed and conducted a survey of researchers at the Medical Center to obtain input on administrative processes and procedures that affect research; developed or refined University policies related to clinical and translational research; created an intranet site for making these policies available to the Medical Center community; facilitated accreditation of the University's human subjects review process; and reviewed and updated the University's standard clinical trials agreement.

Under the CTSI, if the new discipline of Clinical and Translational Science is to be successfully forged, the institution must serve the investigator and research participants. Toward this end, some of the CTSA resources will be devoted to strengthening the infrastructure provided by the RPIT. As regulatory requirements for clinical and translational research evolve, an enhanced form of this Team will ensure that researchers will be adequately supported to meet evolving needs.

G1A3f. Expand education and training in clinical and translational research

Many faculty members are recruited to clinical departments after completing residencies and fellowships in specific clinical disciplines. Fellowships often provide exposure to research, including clinical research, but new faculty completing these programs are rarely trained adequately to embark on a career of independent investigation. Similarly, faculty members recruited to research positions in basic science, whether directly from postdoctoral fellowships or as more senior independent investigators, typically lack experience and training in the potential translational aspects of their work. These faculty members represent substantial human capital, however, that should and can be invested in the clinical and translational research enterprise. Therefore, a critical strategic priority is to provide these faculty members with additional training in the tools and methods of clinical and translational research. In this manner, junior faculty will more readily transition from trainee to independent investigator, and more senior faculty will think more constructively about the translational aspects of their basic science discoveries. Several steps have been taken to support this strategic priority from the standpoint of clinical research. The CTSA is needed to extend this initiative to translational research.

Prominent among these steps has been the establishment of the Rochester Clinical Research Curriculum (RCRC), initially funded by an NIH K30 award in 1999 and renewed for funding through 2010. As a result of K30 awards, NIH has "raised the bar" for the quantity and quality of training for a clinical research career. The RCRC provides a core of didactic training in the principles and methods of clinical research, as well as a series of skill-building workshops and visits to clinical research facilities and support services at URMC. The culminating experience is a mentored clinical research project. Trainees who complete the program earn a Master's in Public Health with a concentration in Clinical Investigation. Over 130 trainees have been enrolled. A popular and successful component of the RCRC is the "Practical Skills in Grant Writing" course, in which all students complete a grant application. Of 52 RCRC scholars completing the program, 29 are Principal Investigators on their own research grants. RCRC scholars, including those still in the program, account for 148 externally-funded grants, 33 of them from federal sources.

The Medical Center has also promoted the clinical research career development of its faculty through NIH career development awards. Currently, 9 faculty members are supported under clinically-oriented K01 awards, 11 under K08 awards, 19 under K23 awards, and 4 under K24 awards. Of these 43 awards, 16 applications were completed as part of the RCRC grant writing course. (See Table G5C11 for a list of current K Awards.)

Finally, the Medical Center has a concentration of pre- and postdoctoral research training programs that compares favorably to almost any other academic medical center. Many of these are geared specifically toward clinical research: 111 pre-doctoral and 95 postdoctoral trainees participate in 48 different programs, including 32 T32-supported programs, 3 R25 grants and a K12. Twenty-four of these programs have a primary or secondary clinical research focus. Excellent examples of this are the T32 program in "Experimental Therapeutics of Neurologic Disorders," which is now in its 4th multi-year funding cycle, and the T32 Program in "Research Training in Preventive Cardiology" now in its second 5-year funding cycle. (See Table G5C12.) None of these training programs, however, focus specifically on translational research. Under the proposed CTSA, we will use the T32 mechanism to support a PhD in translational biomedical science, and the K12 to train medical, dental and nursing faculty in translational as well as clinical research.

In addition to training investigators, an important strategic component of our education mission is to incorporate the principles and practice of clinical and translational research into the undergraduate medical student curriculum. This occurs throughout the four years of medical school with a series of courses, seminars and elective research experiences. For example, the first four weeks of the curriculum is Mastering Medical Information, in which epidemiology, biostatistics, evidence-based medicine, and informatics precede the traditional anatomy course. In fact, the second lecture in medical school, following the Dean's introduction lecture, is on hypothesis-directed

research.

Of particular note, the Academic Research Track (ART) was initiated in the 2005-06 academic year to enrich the curriculum of the medical school to support students who are interested in pursuing careers in academic medicine. ART provides selected students, who are strongly motivated to pursue an academic career in medicine, with a broad and deep exposure to research that involves both didactic and mentored research experiences and an enriched medical school curriculum. This includes a "year out" for a more intensive research experience and/or a Master's Degree program. Although students may choose to concentrate in basic research, most have chosen to work with faculty engaged in clinical or translational research. Under the CTSA, support for medical students during their "year out" in clinical or translational research is incorporated into the T32 proposal.

G1A3g. Enhance the General Clinical Research Center

The Clinical Research Center at URMC has its origins in a two-bed metabolic unit established in 1946. Early on, it participated in studies of the effects of radiation in humans as part of the Manhattan Project. Much of the original work on the NPH formulation for insulin was completed on this unit. The Center grew to four beds as part of a cancer research unit and established a separate clinical laboratory and metabolic kitchen. This effort formed the critical mass that became one of the original eight NIH-funded GCRCs in November of 1960, and it has been continuously funded since its inception. In 1977, the present space within the new hospital was established. This space has expanded, with support from the URMC, to accommodate an increasing number of outpatient studies.

The GCRC is a combined adult and pediatric unit totaling 8474 sq. ft. in contiguous space. To enhance the GCRC, the Dean increased focus on the availability of GCRC resources for clinical research, encouraged the inclusion of the GCRC in grant applications from both new and established investigators, and greater emphasis on translational research. These initiatives, which were part of the overall efforts to enhance the level of institutional focus and support of clinical research, resulted in substantial growth in new GCRC projects. There were 82 projects approved last year, which represents a 17% increase over the previous year and a 35% increase over the prior year. Last year, there were 46 publications resulting from studies that were supported in part by the GCRC. Over 70% of the projects that flow through the GCRC are funded by NIH. This group of GCRC investigators received over $61,000,000 in federal funds last year.

In March 2005, the GCRC underwent a competitive renewal and site visit. It received a highly competitive score and has been refunded for an additional five years with a recommended annual direct budget of approximately $2,000,000. Strengths found in the summary statement from the site visit include the infrastructure of the GCRC, including Administration and Financial Management, Nursing, Bionutrition, Biostatistics and Informatics. The involvement and leveraging of training grants (e.g. K30) and specific research groups were also considered strengths. Weaknesses, however, were related to the current space in an inpatient hospital unit and its functionality. As part of the strategic planning process at URMC, we have committed to a relocation and substantial upgrade of our GCRC facilities, described in section G1D2.

G1A3h. Enhance the Office of Technology Transfer

At URMC, the Office of Technology Transfer (OTT) was started in July, 2001 with a primary mission of facilitating the transfer of technology arising from URMC research to industry for the benefit of the public good by creating new and useful products and by promoting economic development. While there is a parallel office at the University of Rochester that performs a similar function for its other schools and colleges, it was felt that the focus on biomedical science at URMC dictated a need for an office that specialized in biomedical technology. Following the opening of the OTT, increases in invention disclosures, technology licenses, and patent filings quickly followed. In 2005, there were 94 patent filings and $28.7 million in royalty revenues, which contributed to UR's ranking seventh among U.S. universities in technology transfer revenue.

The OTT function in furthering technology development is consistent with the spirit of the CTSA and with the third mission of the NIH, which is to "expand the knowledge base in medical and associated sciences in order to enhance the Nation's economic well being and ensure a continued return on the public investment in research." Thus, continued institutional funding for the OTT at Rochester will support the overall goals of the CTSA. An additional component of this support is integration with the Key Function pertaining to education and training, including a successful course entitled "Technology Transfer: Working with Industry." Another component is integration of technology transfer expertise with Key Functions pertaining to the development of novel clinical and translational methodologies, to pilot and collaborative translational and clinical studies, and biomedical informatics.

G1A3i. Build a Clinical and Translational Science Building (CTSB) as the URMC academic home for clinical and translational research

Leading up to the RFA for the CTSA, presentations by NIH leadership have identified a compelling need for medical centers to create an academic home for clinical and translational research that will effectively utilize basic science discoveries and the growing field of translational research to meet the health care needs of our communities. For example, according to the Executive Summary of the above-cited May 23, 2005 meeting, it is stated that "The NIH Roadmap provides the bricks but does not build a home…This academic home must include a cadre of well-trained investigators and integrated resources that will advance the new intellectual discipline of clinical and translational sciences. The new home will advance the health of the Nation by transforming patient observations and basic discovery into clinical practice" (accessed on 12-24-05 from www.ncrr.nih.gov/clinicaldiscipline.asp).

The varied research strategic planning subcommittees described above on cross-cutting clinical and translational science virtually all concluded, quite independently of one another and well in advance of the NIH pronouncements on the matter, that a facility should be erected on the URMC campus that would coalesce clinical and translational research programs with pertinent research disciplines, shared support services and regulatory functions. This Clinical and Translational Science Building (CTSB) represents a logical conclusion of the strategic planning process, and is entirely consistent with the CTSA requirement for an academic home for clinical and translational research. The program planning for the CTSB is presented under "Approach." The University's enthusiastic support is described under "Institutional Commitment."

G1A4. Approach

G1A4a. Overall approach

To meet the intent of the CTSA, we will create the University of Rochester Clinical and Translational Research Institute (UR CTSI) that encompasses all components of the Medical Center as well as other relevant Schools and Colleges within the University. Included at the Medical Center are the School of Medicine and Dentistry (including its GCRC), the School of Nursing, and the Eastman Dental Center. Also important is the College of Arts, Science and Engineering, particularly its Departments of Biology, Brain and Cognitive Sciences, Computer Science and Electrical Engineering, as well as the Center for Visual Science.

Consistent with the requirements of the RFA, and further described under "Governance" (Section G1E), the Principal Investigator of the CTSA will direct the UR CTSI. He will have overall authority for all aspects of space, faculty, and budgets that are components of the UR CTSI, with oversight by the Senior Vice President of Health Affairs (SVPHA). In this role, he will report directly to the SVPHA, who has authority over all components of the Medical Center and who in turn reports directly to the President of the University. A letter from the SVPHA confirming his support for this organizational structure, as well as a letter of support from the President of the University of Rochester, is included in Section H.

A new, 150,000 sq ft. building, the Clinical and Translational Sciences Building (CTSB), in conjunction with a new 10,500 sq. ft. General Clinical Research Center (GCRC), will be the academic home of the UR CTSI. As shown in Table G1.4, and as discussed in sections G1D1 and G1D2, the Clinical and Translational Science Building and General Clinical Research Center will contain most of the infrastructure for clinical and translational research, as well as several research programs, although some components of the UR CTSI will remain physically located elsewhere on the URMC campus. (See Figure G1.2) In breaking down administrative and financial barriers to promote clinical and translational science at the University of Rochester, we have distributed much of the current GCRC budget related to matters such as biostatistics, subject advocacy, core laboratories, and other functions to the appropriate Key Function in the CTSI.

G1A4b. Faculty

1) Leadership (Program and Key Function Directors). Large numbers of faculty across numerous UR departments will participate in this CTSA as investigators and mentors. The leadership of the CTSA consists of the Program and Key Function Directors. These are senior investigators who remain actively involved in translational and clinical science, have substantial administrative experience, and have demonstrated considerable collaboration on clinical and translational research projects and training programs.

The governance of the UR CTSI is discussed below in detail (Section G1E). Included in the governance structure is an Executive Committee, which is charged with overall responsibility for achieving the goals of the NIH as stated in the RFA and for achieving the specific aims of this application. The Executive Committee will consist of the following faculty members:

1) Program Director and Principal Investigator—David Guzick, MD, PhD, Dean of the School of Medicine and Dentistry and Professor of Obstetrics and Gynecology. Dr. Guzick is currently PI on the University of Rochester GCRC grant and is an active investigator on his own R01 study of endometriosis-associated pain, as well as co-investigator and mentor on several other grants. Dr. Guzick has developed a mature organizational structure with substantial talent in the Dean's office, in which appropriate authority is delegated, with his oversight, to six Senior Associate Deans and their staff members. He will devote 25% effort to the CTSA, reflecting much of his current focus on coordination of the research enterprise, including clinical and translational research. Dr. Guzick's effort on the CTSA is further discussed by Dr. Mac Evarts, Senior Vice President for Health Affairs, in his letter (Section H).
2) Program Co-Director—Thomas Pearson, MD, MPH, PhD, Senior Associate Dean for Clinical Research and Chair of the Department of Community and Preventive Medicine. Dr. Pearson is currently P.I. on the University of Rochester Clinical Research Curriculum (K30), the University of Rochester CDC Research Prevention Center, and a Preventive Cardiology Training Program (T32), as well as several clinical research projects with bedside-to-community translational implications.
3) Program Co-Director—John Gerich, MD, Program Director of the General Clinical Research Center and Professor of Medicine. Dr. Gerich has 20 years of experience in running the GCRC in two major institutions, and maintains an active research program on insulin dynamics.
4) Co-Director of Translational Resources Key Function—Howard Federoff, MD, PhD, Senior Associate Dean for Basic Science and Director of the Center for Aging and Developmental Biology and Professor of

Neurology. Dr. Federoff is PI on the Parkinson's Disease Gene Therapy Study Group, the Rochester Nathan Shock Center, an Interdepartmental Neuroscience Training grant, and several R01 studies that pertain to bench-to-bedside translation in neuroscience medicine.

In addition to the Executive Committee, the Director and Co-Director of each Key Function will plan important leadership roles in the CTSI. (See Section G1E.) Program and Key Function Directors and Co-Directors are shown below in Table G1A3, which lists their academic appointment, role in the CTSA, and current grants on which they are Principal Investigator. Care has been taken to assure that each of the Program and Key Function directors has committed sufficient time to carry out their appointed roles in the CTSA, and has been given responsibility and authority, along with adequate staff, space and funds, to achieve their respective specific aims.

Table G1A3 Program and Key Function Directors

Name	Academic Title	CTSA Role	Award Title (Principal Investigator)	Sponsor	Annual Project Costs
Guzick, David S.	Dean; School of Medicine and Dentistry; Professor Obstetrics & Gynecology	Program Director and Principal Investigator	General Clinical Research Center	DHHS/PHS/NIH	$ 2,790,470
			Treatment of Endometriosis-Associated Pelvic Pain	DHHS/PHS/NIH	$ 294,989
			Extramural Research Facilities Improvement Program	DHHS/PHS/NIH	$ 541,589
Pearson, Thomas	Professor and Chair, Community and Preventive Medicine	Program Co-Director, Director, Research Education, Training and Career Development Director, Regional Collaboration	The Rochester Prevention Research Center	DHHS/PHS/CDC	$ 666,933
			The Effect of Niacin ER/Lovastatin on Peak Walking Time in Pts.	Kos Pharm., Inc.	$ 66,620
			Radiology Cancer Research Training Curriculum	DHHS/PHS/NIH	$ 293,698
			The Dose Response of Niacin ER/Lovastatin on Peak Walking Time (PWT)	Kos Pharm., Inc.	$ 16,826
			A Randomized, D-B, P-C of MK_0524/Niacin Combination Tablet	Merck & Co.	$ 7,147
			Research Training in Preventive Cardiology	DHHS/PHS/NIH	$ 451,777
			PH3, Multi-SITE,D-B, Rand.on Efficacy, Safety, & Tolerability of Fixed Combo Torcetrapib	Pfizer Inc	$ 14,237
			University of Rochester Clinical Research Curriculum	DHHS/PHS/NIH	$ 312,857
			Grenadian Heart Study	World Heart Federation (WHF)	$ 92,305
Federoff, Howard	Director Ctr Aging & Devel Biology, Professor of Neurology	Program Co-Director Director, Translational Technologies and Resources	Peripheral Leukocyte Biomarkers in Alzheimer's Disease	DHHS/PHS/NIH	$ 196,345
			HSV Amplicon Activation of Innate and Adaptive Immunity	UNIV/Miami	$ 69,220
			Interdepartmental Neuroscience Training	DHHS/PHS/NIH	$ 291,351
			Amplicon BAC Engr. to Discover New Molecules in Neural Regen. & Repair	Johnson & Johnson	$ 659,292
			Proteomic Biomarker Discovery in PD	DHHS/PHS/NIH	$ 203,514
			Rochester Nathan Shock Center	DHHS/PHS/NIH	$ 699,130
			Improved HSV Vectors: Gene Transfer into Nervous System	DHHS/PHS/NIH	$ 483,353
			Parkinson's Disease Gene Therapy Study Group	DHHS/PHS/NIH	$ 1,957,005
			Dev. & Application of Single Chain Antibodies for PD Therapy	DOD/ARMY	$ 536,593
			Ancillary Study to ADCS Valproate Trial	Abbott Laboratories	$ 268,922
			HSV Amplicon-mediated Disruption of Abeta Fibrillogenesis	DHHS/PHS/NIH	$ 418,201
Gerich, John	Professor, Medicine	Program Co-Director, Patient and Clinical Interaction Resources	Eval. of Diabetic Retinopathy Progression in Subjects with Type 2 Diabetes Mellitus	Quintiles, Inc	$ 35,373
			Alpha and Beta Cell Function in Normal and Diabetic Man	DHHS/PHS/NIH	$ 551,832
Bennett, Nancy	Associate Professor, Medicine	Director, Community Engagement	PRICE III:Factors Influencing a Decision to Adopt U.S. Prev. Svcs Task Force Stds.	UNIV/Ca, San Dieg	$ 10,014
			Racial and Ethnic Disparities in Immunization Initiatives	Roch Prim Care Ntwrk	$ 20,055
			Racial and Ethnic Adult Disparities in Immunization Initiative	Excellus Hlth Plan, Inc.	$ 64,035
			Integrated Cancer Services Program	NYS/Health	$ 255,379
			Breast & Cervical Cancer Early Detection Program - Monroe County	Health Research Inc	$ 129,128
			Surveillance for SARS and Severe Pneumonia Syndrome in the EIP Network	Health Research Inc	$ 242,632
Chadwick, Gary	Assoc. Provost & Director, Off. for Hum. Sub. Protection	Co-Director, Regulatory Knowledge and Support			
Fiscella, Kevin	Associate Professor, Family Medicine	Co-Director, Community Engagement	Open-Label Treatment of Subjects on 2.5 mg of Mifepristone	Athenium Pharm, LLC	$ 37,539
			RCT of Primary Care-based Patient Navigation-Activation	DHHS/PHS/NIH	$ 658,558
			The Impact of HMO's on Disparities	DHHS/PHS/AHRQ	$ 150,747
			Randomized Control Trial of Mifepristone for Fibroids	DHHS/PHS/NIH	$ 180,438
			Do Reporting Biases Mitigate Disparity Estimates?	DHHS/PHS/AHRQ	$ 148,844
			The Impact of Racial/Ethnic Disparities in Health Care on Minority Years of Life Lost	R. Wood Johnson Fnd	$ 25,860
Fisher,Susan G	Associate Professor, Community and Preventive Medicine	Co-Director, Design, Biostatistics and Clinical Research Ethics	Chronic Kidney Disease and Anemia: The Importance of Early Detection	Amgen, Inc	$ 16,660
			A Comprehensive Investigation of Viral-induced Lymphomagenesis	DHHS/PHS/NIH	$ 389,612
Holloway, Robert	Associate Professor & Vice Chair, Neurology	K12 Director; Co-Director, Design, Biostatistics and Clinical Research Ethics	Neurology Outcomes Research: Clinical Trials/Training	DHHS/PHS/NIH	$ 111,323
			CALM-PD Cohort Study	Pharmacia & Upjohn	$ 405,346

Table G1A3 Program and Key Function Directors (cont.)

Name	Academic Title	CTSA Role	Award Title (Principal Investigator)	Sponsor	Annual Project Costs
Krusch, David	Associate Professor, Surgical Oncology	Co-Director, Biomedical Informatics			
LaCelle, Paul	Professor, Pharmacology & Physiology, Sr Associate Dean for Graduate Studies	T32 Director			
Liders, Gunta	Assoc VP for Res Admin	Co-Director, Regulatory Knowledge and Support	Discovery Concept Fund	Johnson & Johnson	$ 76,842
			Graduate Research Fellowships Program	NSF	$ 23,787
Moxley, Richard	Professor, Neurology	Co-Director, Pilot and Collaborative Studies	Natl Registry of Myotonic Dystrophy & Facioscapulohumeral Muscular Dystrophy	DHHS/PHS/NIH	$ 535,792
			Muscular Dystrophy Cooperative Research Center	DHHS/PHS/NIH	$ 1,571,158
			MD Cooperative Center Supplement: Rochester	Musc Dystrophy Assoc	$ 488,947
Oakes, David	Professor, Biostats & Comput. Bio.	Co-Director, Design, Biostatistics and Clinical Research Ethics	Coordination and Statistics for CoQ10 in PD in Phase 3	DHHS/PHS/NIH	$ 1,193,432
			Training Environmental Health Biostatistics	DHHS/PHS/NIH	$ 143,049
Rosier, Randy	Professor and Chair, Orthopedics	Co-Director, Pilot and Collaborative Studies	Activation of Chondrocyte Maturation in Osteoarthritis	DHHS/PHS/NIH	$ 288,421
Schwarz, Edward	Assoc. Prof, Ctr Musculoskeletal Research	Co-Director, Novel Methodologies	Biomech. Eval. of Autograft, Allograft, and Revitalized Allograft Healing	DePuy	$ 75,103
Szilagyi, Peter	Professor, General Pediatric	Co-Director, Community Engagement	Rochester Center for Adolescent Immunization Research (RCAIR)	DHHS/PHS/CDC	$ 247,226
			Enhanced Surveillance-Newly Vaccine Preventable Diseases	DHHS/PHS/CDC	$ 495,511
Treanor, John	Professor, Medicine	Director, Novel Methodologies	An Open-Labeled, Single-Arm Trial to Assess FluMist	PPD Development, Inc.	$ -
			Eval. of the Protective Efficacy of Trivalent Recombinant Baculovirus	Prot Sci Corp	$ 99,473
			A Dose-Ranging Study of Merck Bivalent Influenza Peptide Conjugate Vaccine.....	Merck	$ 66,958
			A Non-Inferiority Comparison of Fluviral Influenza Vaccine ..	PharmaNet	$ 122,375
			Evaluation of Control Measures Against Diseases Other Than AIDS	DHHS/PHS/NIH	$ 2,790,850
			A PH I Clin Trial of the Vical Prophylactic Anthrax DNA Intramuscular Vaccine AB01	ViCal, Inc	$ 15,476
Wang, Dongwen	Asst. Prof, Biostatis Comput Bio	Co-Director, Biomedical Informatics			
Welle,Stephen L	Professor, Medicine	Co-Director, Translational Technologies and Resources	AMDeC Genomic Cores Initiative, Microarray Resource Center	AMDeC Foundation, Inc	$ 784,270
Wu, Hulin	Professor, Biostats Comput. Bio.	Co-Director, Biomedical Informatics	University of Rochester Center for Biodefense Immune Modeling	DHHS/PHS/NIH	$ 1,985,135
			Nonparametric Modeling of Long-term HIV/Cell Dynamics	DHHS/PHS/NIH	$ 264,562
			AIDS Clinical Trial Modeling and Stimulation	DHHS/PHS/NIH	$ 423,228
Yakovlev, Andrei	Professor & Chair, Biostats Comput. Bio.	Director, Design, Biostatistics and Clinical Research Ethics	Quantitative Insight into Gene Cooperation	DHHS/PHS/NIH	$ 314,784

2) Education and Training. An exceptionally strong team has been organized to lead an Integrated Clinical and Translational Research Training Program and the Education and Training Key Functions. *Thomas A. Pearson, MD, MPH, PhD,* will serve as Director of this Key Function and will direct the Rochester Clinical and Translational Research Curriculum. As noted above, Dr. Pearson is also a Co-Program Director of the proposed UR CTSI. He has also been Principal Investigator for the K30 Program since its inception in 1999, as well as for the R25 Program sponsored by NCI and a T32 Program sponsored by NHLBI. Dr. Pearson is also Chair of the Department of Community and Preventive Medicine, which will house the new Master's and PhD Degree Programs for the UR CTSI. He has a longstanding record of mentoring and research in cardiovascular epidemiology and preventive cardiology. *Paul LaCelle, MD, PhD,* will direct the T32 Predoctoral Program. Dr. LaCelle is the Senior Associate Dean for Graduate Education in the School of Medicine and Dentistry, and chairs the Committee on Graduate Studies. As such, he has authority for all predoctoral training (Master's and Doctorate). Dr. LaCelle is also Professor of Pharmacology and Physiology, with a distinguished record of graduate student supervision and basic science research. *Robert Holloway, MD, MPH,* will direct the K12 Career Development Program. Dr. Holloway is Associate Professor and Associate Chair for Academic Affairs in the Department of Neurology, with a joint appointment in Community and Preventive Medicine. He is also Associate Director of the Clinical Trials Coordination Center. He is currently supported by a K24 award

from NINDS and is a co-investigator on the K30 award. Dr. Holloway has a distinguished track record of mentoring fellows in experimental therapeutics and in research on clinical trials, cost-effectiveness and research ethics in the field of Parkinson's disease.

3) Administrative Staff. The CTSI will merge two current administrative staffs into an Administrative Core supporting the UR CTSI Executive and Administrative Committees (see Governance, G1E). First, URMC's Office of Clinical Research, supported in part by the K30 award, is managed by Thomas Fogg, MS, who is Senior Planner for Clinical Research. He has had extensive experience in the management and administration of clinical and translational research. He is the administrator responsible for managing the Research Resource Inventory (see section G1A3b), manages the CDC-funded Prevention Research Center, the CDC-funded Cardiovascular Health Intervention Research and Translation Network, and the K30-supported Rochester Clinical Research Curriculum. He has demonstrated expertise in the development of logic models, program planning and evaluation, and project management, and has provided administrative support to the institution's strategic planning efforts in clinical and translational research. Second, the administrative core for the GCRC is headed by Kathleen Jensen, RN, MHSA who has extensive experience in clinical and research administration. After working as an ICU nurse for 8 years, she obtained a Master's degree in Health Services Administration and was Vice President of a 177-bed hospital in Myrtle Beach, South Carolina for 8 years before coming to Rochester. As Administrator of the Rochester GCRC, she has streamlined operations and enhanced throughput to improve investigator access. She successfully worked with the IRB to combine separate IRB and GCRC applications into one convenient electronic application. Last year, she coordinated a successful site visit and competing renewal for the GCRC. Both of these administrators have experienced assistant staffs. The merger of these two staffs into the UR CTSI Administrative Core, which will be located in the Clinical and Translational Science Building, gives the CTSI seasoned administrative support across the wide range of required Key Functions.

G1A4c. Detailed programming of UR CTSI components

The current components of the UR clinical and translational research enterprise include the General Clinical Research Center (GCRC), a number of clinical and translational research programs in specific specialties, pertinent scientific disciplines such as biostatistics and epidemiology, and support and regulatory functions. This enterprise, which has been led by the Dean and the two Senior Associate Deans for Clinical and Basic Research, has been successful in attracting substantial sponsored research support for clinical and translational research as shown in Table G1A1. To achieve a transformative creation of a single discipline of Clinical and Translational Science, however, the CTSA is needed to provide infrastructure elements that fill in the gaps between existing components. The CTSA will also provide the impetus to create a reorganized governance structure that integrates faculty with enabling resources and support services under a single Program Director with authority over space, faculty and resources.

Table G1A4 provides a more specific listing of the elements presented in Figure G1A1. Most of the Key Functions of the UR CTSI will be co-located in the CTSB. In this manner, the CTSB recapitulates a 1996 Strategic Plan for cross-departmental basic research at the University of Rochester Medical Center (URMC) that brought basic scientists from different disciplines together with new facilities, shared cores and other support services. Just as this plan resulted in substantially enhanced multidisciplinary basic research, doubling NIH-funded research over an 8-year time frame, the coalescence of diverse clinical and translational research faculty and enabling resources under one roof will dramatically enhance our ability to determine etiologies of disease, prevent illness, improve diagnostic testing, develop effective treatments, and facilitate the dissemination of best practices in the community.

The CTSB will serve as both the physical and academic home for clinical and translational science, and will bring together a number of major research programs, shared clinical and translational science Key Functions, other shared resources, and administrative support (Table G1A4). Yet, by way of interaction of faculty located at the CTSB with other CTSI faculty at other campus locations, it will also serve as a coordinating hub, linking CTSB functions with other key partners of the CTSI throughout the University. As shown in Table G1A4, these other partners are located at the School of Medicine and Dentistry, the School of Nursing, and the Eastman Dental Center. All are within walking distance of one another, mostly under one roof, and juxtaposed to the new basic science buildings (see Figure G1D4, below).

Table G1A4. Components of the University of Rochester Clinical and Translational Sciences Institute

Line #	Program Component	Net Sq. Ft. (000s)	FY '05-'06 Institutional Support ($ millions)	FY '05-'06 Sponsored Funding ($ millions)	Proposed CTSA Support ($ millions)	Location	CTSA Impact
1	***Clinical and Translational Research Programs***						
2	CDC National Center for Deaf Health Research	1.5		1.1		CTSB	Enabled
3	Neurology Clinical Trials Coordination Center	14.8	1.8	19.6		CTSB	Enabled
4	Heart Research Center	8.1	0.5	8.3		CTSB	Enabled
5	Smoking Cessation Research	1.5		1.0		CTSB	Enabled
6	Family Medicine Research Program	3.7	0.1	2.0		CTSB	Enabled
7	Neuromuscular Disease Center	3.7		4.3		CTSB	Enabled
8	Epidemiology	1.5	0.2	1.2		CTSB	Enabled
9	Health Services and Outcomes Research	0.5	0.1	0.9		CTSB	Enabled
10	Public Health Practice	1.5	0.1	0.4		CTSB	Enabled
11	Classical Biostatistics	4.1	1.0	0.6		CTSB	Enabled
12	Computational Biology and Modeling	4.3	0.3	1.3		CTSB	Enabled
13	Global Health Research	0.5	0.3	1.4		CTSB	Enabled
15	Other SMD Department-Based Clinical Research	46.3		54.8		SMD	Enabled
16	Nursing Research	9.0	1.6	3.0		SON	Enabled
17	Oral Health Research	1.7		1.4		EDC	Enabled
18	***CTSI Key Functions***						
19	Novel Methodologies	0.3			0.4	CTSB	New
20	Pilot and Collaborative Studies	0.3			0.4	CTSB	New
21	Biomedical Informatics	1.0	0.3		0.5	CTSB	Upgraded
22	Design, Biostatistics and Clinical Research Ethics	0.4			0.4	CTSB	Upgraded
23	Regulatory Knowledge and Support	0.3			0.5	CTSB	Upgraded
24	Participant and Clinical Interaction Resources	10.5	0.6	2.2	0.3	SMH	Upgraded
25	Community Engagement/Center for Community Health	2.7	0.5	1.1	0.4	CTSB	Enabled
26	Translational Technologies and Resources						
27	Laboratory Support Center	0.5			0.9	CTSB	New
28	Human Metabolism Laboratory	1.0	0.1	0.2	0.5	SMD	Enabled
29	Research Education, Training and Career Development						
30	Curriculum Development/Program Coordination	1.0		0.3		CTSB	Upgraded
31	K12 Career Development Program	0.5			0.5	CTSB	New
32	T32 Predoctoral Research Training	1.0			0.5	CTSB	New
33	Upstate Academic Consortium	0.5			0.3	CTSB	New
34	***Other Shared Support Services (CTS only)***						
35	Genomics Core	2.8	0.1	0.3		SMD	Enabled
36	Proteomics Core	0.3	0.1			SMD	Enabled
37	Imaging Core	0.2				SMD	Enabled
38	Cell Sorting Resources	0.4	0.1			SMD	Enabled
39	***Administrative Support (CTS only)***						
40	Office of Clinical and Translational Research	1.5			0.3	CTSB	New
41	SMD Senior Associate Dean for Clinical Research	0.5	0.3			CTSB	Enabled
42	SMD Senior Associate Dean for Basic Research	0.5	0.3			CTSB	Enabled
43	Office of Human Subject Protection	2.5	1.4			CTSB	Enabled
44	Research Project Administration Office (satellite)	0.3	0.4			CTSB	Enabled
45	Research Accounting Office (satellite)	0.3	0.4			CTSB	Enabled
46	***Total***	132.0	10.6	105.4	5.9		

Abbreviations
CTS – Clinical and Translational Science; **CTSB** - Clinical and Translational Science Building; **EDC** - Eastman Dental Center; **SMD** - School of Medicine and Dentistry; **SMH** - Strong Memorial Hospital; **SON** - School of Nursing.
Notes
1. Funding includes current and anticipated external funding from all sources for the period July 2005 through June 2006.
2. Space allocated for SMD department-based clinical research programs includes all space associated with research programs whether full-time or part-time.

As noted in the discussion of Figure G1A1, the CTSI—represented by the green oval drawn around key functions and programs—does not exist in isolation. Rather, there is substantial interaction between clinical and translational science at URMC with our community and region. As shown in Figure G1A1, and as described in detail in the section on Community Engagement (G2G), the UR CTSI has links with the Monroe County Health Department, major employers, the Rochester School District and the Primary Care Practice-Based Network. Moreover, across Upstate New York, the CTSI will also relate to a consortium of 10 universities and corporate partners, described below in Section G2J. Also as conceptually depicted in Figure G1A1, faculty in the CTSI will

have ongoing interaction with faculty involved in basic science departments and centers that are involved in clinical and translational research, and with departments in the University of Rochester College of Arts, Science and Engineering.

Based on the data in Table G1A4, current and immediately planned activities in the UR CTSI will occupy 128,300 sq. ft. of research space, mainly in the Clinical and Translational Science Building, but also in nearby facilities in the School of Medicine and Dentistry and the School of Nursing. Based on current year estimates, these programs will be supported by $103.8 million in sponsored funding, not counting the CTSA, and by $10.8 million in institutional funding. Faculty brought together under the UR CTSI, shown in Table G1A4, already provide much of the expertise needed for an integrated academic home for clinical and translational research. They will be enabled by the incremental and upgraded Key Functions of the CTSA to enhance their collaborative scientific efforts and improve their operational efficiency. In this manner, the CTSA will build upon existing resources at the University of Rochester to create an integrated Institute that will significantly contribute to the stated RFA goal of transforming the now distinct fields of clinical and translational science into a single new, integrated discipline.

G1A4d. Achieving the Specific Aims of the UR CTSI

A summary of the strategies we will use to achieve each of the 11 specific aims listed in G1A1 is presented below, including a reference to the associated Key Function. These strategies are further described in Section G2 of this grant application, which presents the Key Functions of the CTSI in Section G4 (Implementation and Milestones).

1) Develop novel methodologies for clinical and translational research. (Key Function G2A) We will accomplish this aim by: supporting pilot projects that foster the development of new methodologies with wide application, particularly in the areas of mathematical and computational modeling, clinical trial designs, imaging methods, internet-based interventions, and biomarker methods; facilitating interactions between clinical and translational investigators and these methodologies; and assessing the methodological needs of clinical and translational science and proactively addressing these needs.

2) Provide resources for innovative pilot studies that foster interdisciplinary collaboration in the application of these novel methodologies. (Key Function G2B) We will accomplish this aim by forming a committee consisting of internal and external reviewers that will prioritize proposed clinical and translational pilot projects relative to overall CTSI goals. Prioritization will take into account the goal of funding pilots at different levels for beginning vs established investigators, and for different categories of clinical and translational research.

3) Support clinical and translational researchers by enhancing biomedical informatics resources. (Key Function G2C) We will accomplish this aim by: developing a local information infrastructure that provides support of all aspects of clinical and translational science through each stage of its life cycle; facilitating the access and sharing of data intra- and inter-institutionally in a manner that safeguards data security and privacy; and improving the research translation process through knowledge dissemination in clinical practice, integration of data management, mathematical and statistical modeling, computer simulation, process control, and behavioral interventions.

4) Provide resources to support the design of new clinical and translational studies by drawing on the disciplines of epidemiology, biostatistics and ethics. (Key Function G2D) We will accomplish this aim by: developing new statistical and epidemiologic design approaches to research questions in clinical and translational science; providing detailed planning support for clinical and translational research related to study populations, establishment of exposure and outcome definitions, management of issues related to bias and confounding and other biostatistical/epidemiologic matters; and contributing to research regarding the ethical perceptions of research stakeholders, and the impact and cost-effectiveness of CTSI discoveries.

5) Integrate regulatory resources with biomedical informatics and participant-clinical interactions in a manner that provides efficient and researcher-focused support for regulatory compliance and management. (Key Function G2E) We will accomplish this aim by: training clinical and translational investigators in the optimization of study design, regulatory review and the informed consent process; conducting quality improvement and good-clinical-practice audits to assess compliance with federal and institutional regulations; developing a computer-assisted program to assist researchers in preparing regulatory review submission documents and informed consent materials; and sharing best practices in support of regulatory knowledge and compliance with the entire University and the National CTSA Consortium.

6) Enhance participant and clinical resources in the conduct of clinical and translational research. (Key Function G2F) We will accomplish this aim by: expanding support for patient-oriented clinical and translational research in terms of space, personnel and ancillaries; facilitating the interaction of basic scientists with clinical investigators; promoting the use of novel research techniques in clinical and translational studies; and facilitating protocol initiation and subject recruitment and participation.

7) Partner with community organizations to facilitate research on the efficient dissemination of best practices and the reduction in disparities. (Key Function G2G) We will accomplish this aim by: establishing core CTSI community engagement activities; ensuring active involvement of the CTSI Community Advisory Board; establishing long-term research partnerships with community organizations; supporting existing practice-based research networks and starting new ones; developing training programs for Clinical and Translational Science researchers to understand and incorporate community perspectives; and increasing the level and diversity of subject participation in clinical and translational research.

8) Develop new cores for technologies and resources that support clinical and translational science. (Key Function G2H) We will accomplish this aim by upgrading the physical infrastructure and personnel in support of selected technologies that are expected to have the broadest applicability for enhancing clinical and translational science. This will include establishment of a laboratory support center to promote productive interactions between clinical and translational investigators and core resources; improved imaging technologies; and creation of a translational technology access subsidy,

9. Structure educational programs to initiate and promote career development in the discipline of Clinical and Translational Science. (Key Function G2I) We will accomplish this aim by: organizing URMC research and training programs within the UR CTSI to promote interaction and integration between existing programs and Key Function groups; creating new curricula leading to a Master's Degree in Translational Research, a Master's Degree in Clinical Investigation, or a PhD Degree in Translational Biomedical Sciences; expanding a mentor development program; developing a predoctoral program (T32) using the new curricula to train graduate and medical students; and initiating a Clinical/Translational Research Career Development (K12) Program tailored to fellows and junior faculty members' needs, leading to Master's or PhD Degrees and independent careers in clinical and translational science.

10) Develop a consortium of institutions and partners across Upstate New York to foster translation of basic and clinical science discoveries. (Additional program component, Section G2J) We will accomplish this aim by: organizing a consortium of at least eight biomedical research institutions in the Upstate New York region into a regional network for translational research; developing inventories of clinical and translational research that is ongoing at member institutions and the research resources accessible for collaborative research; extending the resources of several Key Functions on a regional basis; providing access of consortium members to CTSI and GCRC resources; and providing opportunities for training, career development and continuing education to consortium members.

11) Evaluate the UR CTSI through rigorous performance measurement and feedback. (Section G3) We will accomplish this aim by: development of objectives and measurable outcome measures for each Key Function; creation of a logic model for self-evaluation of the UR CTSI; assessment of activities, outputs and outcomes on a pre-specified basis; correction of deficiencies identified on annual review; and participation in the national CTSA consortium in its evaluation plans.

G1B. PARTICIPATING INSTITUTIONS

Based on direction from the Program Office, participating institutions can be considered those within the academic home of clinical and translational science. In Rochester, the academic home is the CTSI, designated by those components within the green oval in Figure G1A1. All of these are parts of the University of Rochester. However, the CTSI interacts with other entities as shown by the intersecting yellow circles in Figure G1A1. Some of these entities (The School of Nursing, Eastman Dental Center, and the College of Arts, Science and Engineering) are also part of the University of Rochester, but some are outside partners. These outside partners include community organizations and members of the Upstate New York Consortium, which has been coordinated in conjunction with this application.

Letters from partners are included in Section H. All partners agree to follow NIH policies with respect to (1) listing clinical trials at ClinicalTrials.gov; (2) sharing of resources; (3) data sharing and public access and (4) establishing policies in support of investigator academic independence, reporting of patents or patentable concepts, and publication rights.

G1C. INNOVATION

Innovative elements contained in each of the Key Functions contribute to the exciting potential value that the CTSA can add to clinical and translational research at the University of Rochester Medical Center. Highlights of the innovative aspects of each Key Function are as follows:

G2A – *Development of Novel Clinical and Translational Methodologies*. The UR CTSI will actively seek out methodological barriers among faculty, and stimulate research to overcome them. Faculty leaders in these fields, who have demonstrated ability in novel research methodologies, will focus on the development of new approaches specifically targeted at clinical and translational science. This will allow investigators in this CTSA, and in other CTSAs nationally, to benefit from novel approaches to clinical and translational methodologies. A variety of proactive and engaging approaches will be used to disseminate information about novel methods to investigators.

G2B – *Pilot and Collaborative Translational and Clinical Studies*. The pilot studies Key Function within the UR-CTSI will coordinate with other Key Functions to meet programmatic needs identified by the UR CTSI Executive Committee. An important novel feature is pilot study support for a broad range of project types, intending to reflect the varying needs of faculty at different career stages. These would include travel awards ("mini-sabbaticals") to acquire new knowledge and skills, support for non-hypothesis and technology development projects, as well as traditional pilot study funding. Also novel is the use of an RFA mechanism for pilot data deemed important by the UR CTSI Executive and Administrative Committees.

G2C – *Biomedical Informatics*. This Key Function is novel in the way that it integrates a variety of informatics services, such as data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention, to provide context-specific support for clinical and translational sciences at different stages of their lifecycle. In addition, the AllScripts TouchWorks electronic medical record being implemented at the

University of Rochester Medical Center captures, in coded format, all ambulatory patients' medications, problem lists, allergies, and immunization history, as well as documentation of patient visits. This provides UR CTSI an unusual opportunity, from an informatics perspective, to provide access to these data in support of clinical and translational research.

G2D – *Design, Biostatistics and Clinical Research Ethics*. The UR CTSI will bring together expertise in biostatistics, epidemiology and clinical research ethics in a novel, integrated design consulting and collaboration service. Such services were heretofore available at the University of Rochester in an incomplete and nonintegrated fashion. Moreover, faculty at the UR CTSI and at other CTSAs nationally will have access to novel approaches to research design, data analysis and ethics developed by UR faculty in this Key Function. Examples of novel approaches include: the fostering of new disciplines in clinical and translational research decision-making, impact and cost-effectiveness analysis and management of conflict of interest; diagnostic and prognostic molecular signatures of disease, new methods for the design of clinical trials and analysis of results, and new biomathematical methods for the analysis of gene arrays and gene regulatory networks that impact on cancer, genetic conditions and other human diseases.

G2E – *Regulatory Knowledge and Support*. The Regulatory Knowledge and Support Key Function will build upon the UR's nationally-recognized expertise in this area to create a new and vital level of specialized regulatory support specifically aimed at clinical and translational research, such as support for IND and/or IDE filings. This will be innovative in that a dedicated unit of specialists in translational research will be assigned to support investigators in areas that are unique to this type of research. This Key Function will also develop online interactive tools for assistance in developing informed consent forms and preparing documentation for University oversight functions. Developing tools that will improve review submissions, regulatory compliance and human subject safety will have a major impact on this CTSA and, through sharing, on other CTSA-supported programs nationally. Also innovative is the expansion of the investigator-oriented Portal currently used by all faculty participating in the CTSI research education, training, and career development programs noted in Section G2i, as a means of initiating mandatory compliance education for all CTSI investigators and University research faculty.

G2F – *Participant and Clinical Interactions Resources*. The UR CTSI will dedicate a designated senior-level investigator to the promotion of collaborations between basic scientists and clinical researchers. In addition, it will: organize a clinical research coordinator's office; expand the role of the Research Subject Advocate; expand a mentoring program to promote and encourage the career development of translational investigators; and promote research subject participation through the provision of new services such as transportation and child care.

G2G – *Community Engagement*. The Community Engagement Key Function will bring community representatives and local health care providers together to advise the UR CTSI on ways to build community awareness of and support for clinical and translational research. It will also train investigators in the techniques of community-based participatory research, and will design and test novel approaches to research subject recruitment and retention.

G2H – *Translational Technologies and Resources*. The UR CTSI will take a new approach to offering laboratory services by appointing a faculty-level director to identify technological barriers to research and find ways to help investigators succeed in overcoming them. Funding will be available to investigators to defray a share of laboratory service costs; such funds will flow directly to the laboratory in question, an efficient and flexible mechanism of support.

G2I – *Research Education, Training and Career Development*. Under the auspices of the UR CTSI, the University will organize two new master's degree programs, in clinical investigation and translational research, and a new PhD program in translational biomedical sciences. These programs will be available to trainees at a variety of career stages. In addition, the UR-CTSI will expand a mentor development program to ensure that trainees have access to trained mentors capable of guiding their career development.

G2J – *Upstate New York Consortium*. The Upstate New York Translational Network (UNYTRN) brings together nine Upstate organizations involved in health and biomedical research into a powerful consortium organized under a not-for-profit Foundation. This could serve as a national model for sharing and dissemination of clinical and translational science resources on a regional basis, and for providing smaller organizations with access to the national CTSA program.

G3 – *Evaluation and Tracking*. The self-evaluation plan for the UR CTSI has developed a logic model for examining the transformation of research at URMC into an academic home for clinical and translational science. This logic model could be easily scaled to create a national CTSA logic model.

The innovations contained in each of the Key Functions will be brought together in the CTSB, which will serve as the hub of the CTSI at the UR. While not novel *per se*, the CTSB in combination with other features—our strong governance structure, extent of community partnerships, creation of UNYTRN, redistribution of existing funding to the Key Functions, and development of a logic model that may serve as a model for the national CTSA Consortium—constitutes, we believe, an innovative and responsive Clinical and Translational Science Institute.

G1D. INSTITUTIONAL COMMITMENT

Supporting the innovative approach to the UR CTSI's Key Functions and its facility support is a governance structure (G1E) that, while not novel *per se*, reflects the central role of CTS research at URMC. This governance

structure positions the CTSI Program Director with direct reporting to the Senior Vice President for Health Affairs. Through the Program Director, an efficient, functional process for the allocation and distribution of clinical and translational science resources will occur in a seamless fashion, including faculty appointments (and promotion), allocation of space, commitment of resources for equipment, pilot studies, etc., and all other matters pertaining to the CTSI.

Over the next 5 years, as part of an institution-wide overall strategic planning process at UR, we are committed to several additional areas of support for clinical and translational science. These include, independent of the CTSA, several strategic initiatives: the CTSB; expanded and upgraded facilities for the GCRC; enhancement of cross-campus education and research in clinical and translational science; creation of institutional cores in medical informatics, bioinformatics, and statistical modeling; and expansion of our cores in imaging, genomics and proteomics. Addition of the new or upgraded resources provided by the CTSA will greatly accelerate the progress that can be made in our ability to contribute new discoveries and novel methods in the area of clinical and translational science, and to disseminate these clinically-translated discoveries and knowledge about best practices to clinicians in our community, region, and nationally.

Major institutional support for clinical and translational science over the next 5 years is as follows:

G1D1. Clinical and Translational Science Building (CTSB)

Program components of the CTSB are shown in Table G1A4 above, along with allocated space and current funding. Shown in Figure G1D1 is a site map of the URMC campus, with designations for the location of the new GCRC and the CTSB. Blue and red colors are used, as in Figure G1A1, to designate programs inside or outside of the CTSB, respectively. A schematic view of the floor-by-floor location of the various programmatic elements contained in the CTSB can be seen in Figure G1D2, also on the next page.

Figure G1D1 Site Plan for Clinical and Transitional Science Building, University of Rochester

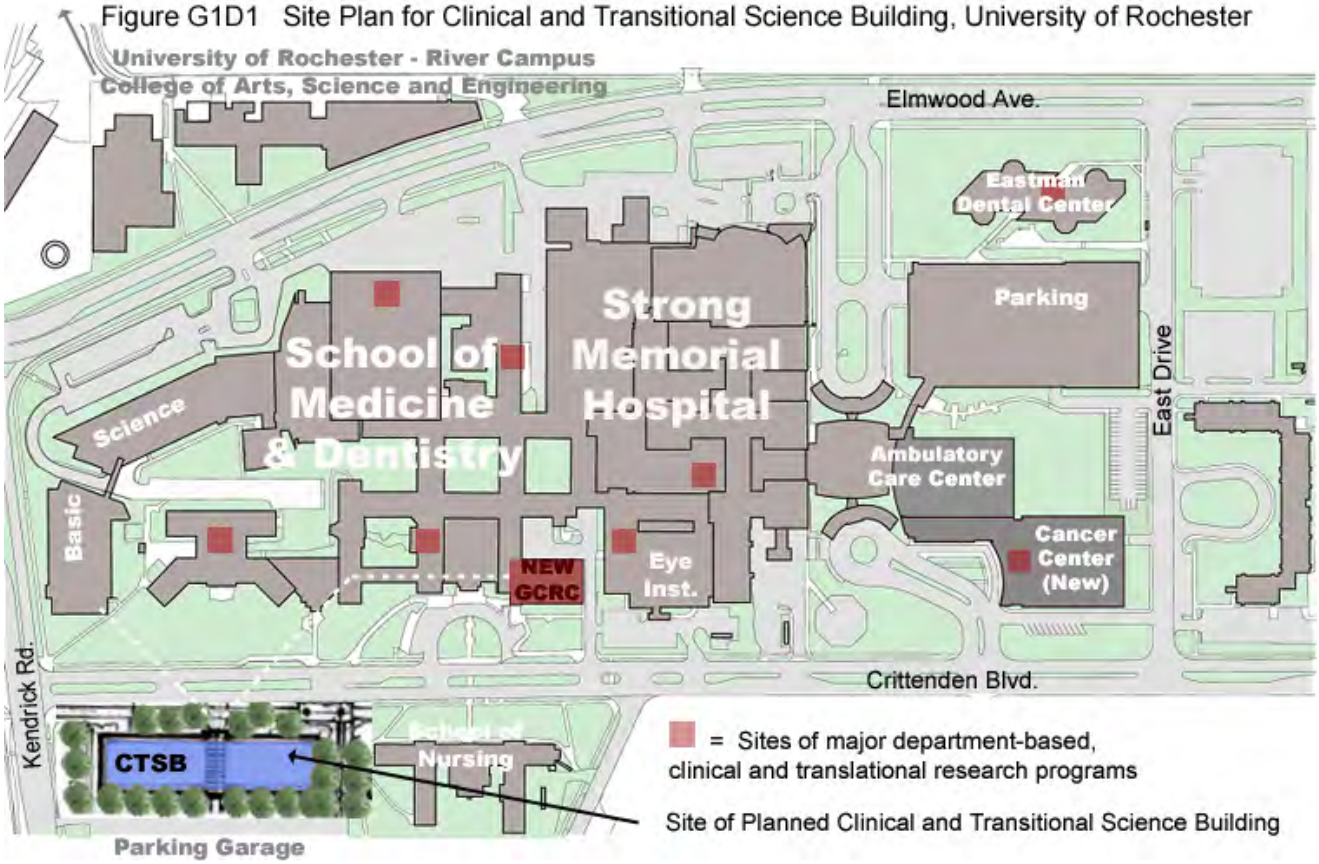
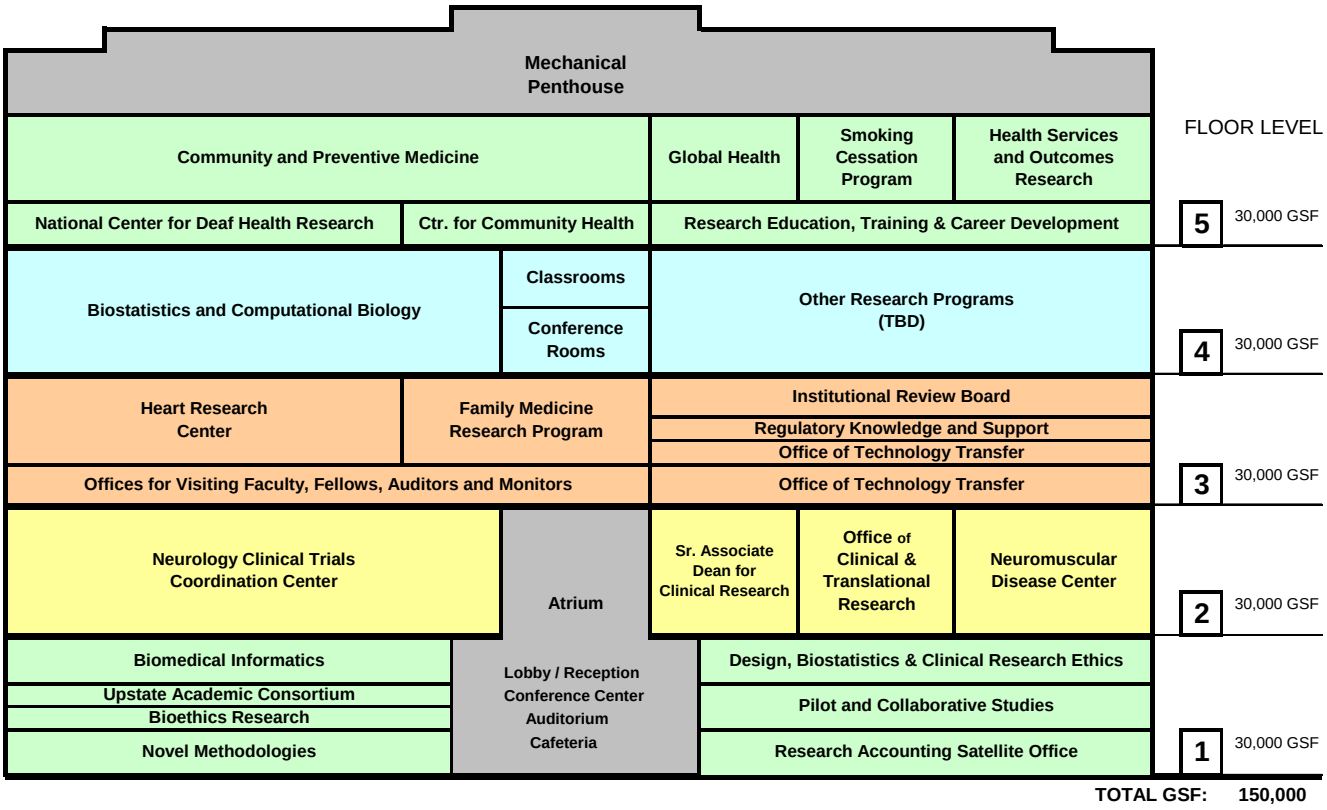


Figure G1D2 Stack Diagram of Clinical and Translational Science Institute (CTSI), University of Rochester



The CTSB facility was the outgrowth of 3 years of strategic planning efforts involving over 140 faculty, 31 Chairs and Center Directors, and the full leadership of URMC, including the Senior Vice President for Health Affairs, the Dean of the School of Medicine and Dentistry, the Senior Associate Dean for Clinical Research and the Senior Associate Dean for Basic Research. The CTSB has the support of the President of the University of Rochester and is part of the current strategic plan, subject to approval by the University Board of Trustees. (See letter from President, section G2H.)

The CTSB will foster a coalescence of clinical research programs, collaborative disciplines, support services, and administrative staff under one roof, creating an integrated home for clinical and translational science. Faculty members who are conducting major studies in clinical and translational science will interact in the same facility with those who work in key enabling disciplines such as biostatistics, epidemiology and outcomes research, and with those who provide critical services such as regulatory support, human subject protection and research ethics. As shown in Figure G1A1, and also conveyed in Table G1A4, although the CTSB will serve as the hub for the CTSI, it will not be the CTSI. In addition to the research programs, disciplines and support functions in the CTSB, the CTSI will coordinate with other clinical and translational research programs and enabling cores that exist throughout the URMC and broader University.

Thus, virtually all components of the CTSI will be collected together in one academic home—the CTSB. The only exceptions are: the GCRC, which requires specialized clinical/investigational facilities, and which will relocate to a newly-renovated facility across the street from the CTSB; laboratory-based translational resources, which require wet-lab space that will not be available in the CTSB; and specific clinical research programs that are currently well situated nearby on the URMC campus (Figure G1D1).

G1D2. Upgraded General Clinical Research Center (GCRC)

As part of the strategic planning process and in conjunction with input from GCRC investigators, it was concluded that the current GCRC space does not currently meet the needs of investigators as well as it has in the past. The GCRC was originally configured as a hospital inpatient unit at a time when overnight studies were more prevalent. Over the years, however, the growth of the outpatient component of the Center has far outpaced inpatient studies, which have declined in volume. The current space and design does not easily provide the flexibility that is needed for outpatient studies while maintaining the current and planned inpatient program. Therefore, a key part of the Strategic Plan for URMC is to upgrade and enhance the GCRC as part of the Clinical and Translational Science Institute.

This Center, as currently conceived, will be located a short distance (across the street) from the new Clinical and Translational Science Building (Figure G1D1). To aid in accomplishing the goals of the CTSA, which entails an expansion and upgrading in clinical and translational research activity and functionality, the GCRC will move to space totaling 10,495 sq. ft., which is 23% larger than the current site. It will be located on the ground floor of the Medical Center, adjacent to a main entrance with immediately adjacent surface parking. This contrasts with its present location as the GCRC, which is on the fourth floor of the hospital some 150 feet away from the elevators and a considerable distance from the nearest parking facility. The new location will facilitate usage by volunteers and investigators, and foster interaction with other Key Functions by virtue of its proximity to the CTSB.

This new space will be extensively renovated and closely located to many of the hospital resources used by our investigators, such as radiology. It will be more readily accessible to subjects, will provide adequate space for anticipated expansion of patient-oriented research, and will facilitate “one-stop-convenience” for investigators and subjects. Thus, the new unit will have satellite space for 1) Research subject advocate activities, 2) Informatics, 3) Biostatistics, 4) IRB personnel, and 4) Regulatory personnel. The design of the patient area will provide enhanced space for subjects, assuring them privacy and comfort, which is critical for longer invasive studies. This new facility will also provide space to accommodate a conference room (which has been cited as a weakness in the current Center), adequate storage for equipment and supplies, and office space for key personnel.

G1D3. Ongoing funding for existing clinical and translational science programs and services

As shown in Table G1A4, cash funding for faculty salaries and other expenses related to a variety of clinical and translational research programs and support functions amounts to $10.5 million in the current fiscal year. This figure does not include core departmental budget allocations, space rental, or other in kind support. The University of Rochester is committed to maintaining this level of support, and increasing it proportionately with expansion in the scale of clinical and translational science.

G1E. GOVERNANCE

G1E1. Overview

As described above, the CTSI will be established as a major administrative entity within the University of Rochester, and substantial institutional support will be provided to the CTSI to assure its success in achieving the goal of fostering novel methodologies, discoveries and applications in the new discipline of Clinical and Translational Science. Toward this end, as depicted in the governance structure of the CTSI (Figure G1E1), the Program Director will have authority over the requisite space and resources under the purview of the CTSI, as well as faculty appointments, protected time and promotion. In this proposal, the Dean of the School of Medicine and Dentistry, a clinical investigator who remains active in research, will serve as the Program Director. He will have authority over the space, resources and faculty affairs related to the components of the CTSI, as indicated in the letter of support

from Mac Evarts, MD, Senior Vice President of Health Affairs. The CTSI Director also has acknowledged support to commit 25% effort in this leadership role (See letter in Section H1). He will also ensure that appropriate institutional credit for academic achievement is given to Key Function Directors in the context of promotion, tenure and compensation.

Under the University of Rochester's Table of Organization, the Dean (CTSI Program Director) reports to the Senior Vice President for Academic Affairs, who in turn reports to the President of the University. This reporting relationship is preserved under the CTSI, ensuring that the interactions between the School of Medicine and Dentistry, and other University entities—such as the School of Nursing, Eastman Dental Center, Strong Memorial Hospital and Highland Hospital, College of Arts, Science and Engineering—will occur at the highest level of authority in the University.

G1E2. UR CTSI Executive Committee

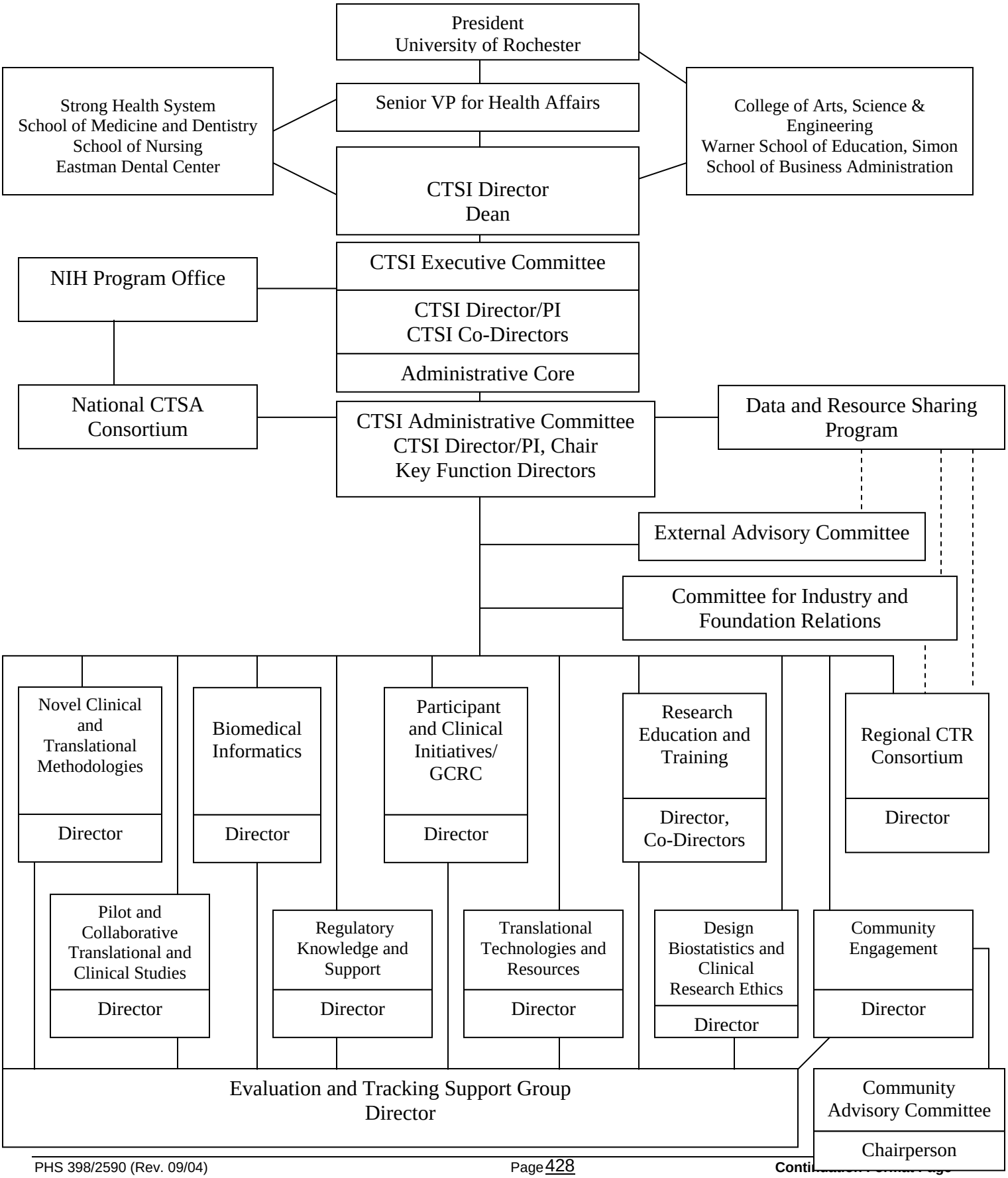
The CTSI Program Director will serve as Chair of the UR CSTI Executive Committee, also shown in Figure G1E1, which will consist of three Program Co-Directors—the Senior Associate Dean for Basic Research, the Senior Associate Dean for Clinical Research, and the Program Director of the GCRC. An administrative core that includes two senior administrators (the current Administrator for the GCRC and the current Senior Planner for the Office of the Senior Associate Dean for Clinical Research) and a secretary will support the Executive Committee. Meetings of the Executive Committee will occur weekly to manage the operational aspects of the CTSI and to ensure that all of the Specific Aims are being advanced in accordance with NIH goals and regulations. In this manner, the Committee's responsibility for the structure, function and budget of the CTSA program will be vigilantly pursued. On a rotating basis, Directors of the Key Functions will give presentations to the Executive Committee regarding progress and operational problems. This will lead to the timely resolution of any concerns that might arise. In this manner, and through the collection of other pertinent data, the Executive Committee will monitor the utilization of resources, appropriateness of their use, and productivity of each Key Function on an ongoing basis, making adjustments to the distribution of resources if warranted. In addition, this Committee will review, on an annual basis, each Key Function Director and the performance of the Key Function. Inadequate performance may result in a recommendation for change of Director. The Committee will be charged with recruitment of the replacement. As shown in Figure G1E1, the Chair of the UR CTSI Executive Committee will interact with the NIH Program Office to seek advice and to report on progress with respect to these responsibilities.

G1E3. UR CTSI Administrative Committee

The Executive Committee will provide oversight to the CTSI Administrative Committee. This Committee, consisting of the Executive Committee members plus the Key Function Directors, will meet monthly, and will be supported by the Administrative Core. Reports of progress and of administrative issues arising in each Key Function will be systematically reviewed. Any significant problems will be referred to the Executive Committee for disposition. If indicated, consultation with the NIH Program Office will take place before a final decision is reached. Since all Key Function Directors and Program Directors/Co-Directors will be included, this Committee is best suited to provide representation to the National CTSA Consortium. It will also receive progress reports from a subcommittee for the Data and Resource Sharing Partnership. Given that data and resources are situated in the Key Functions, this Committee will oversee that activity.

Figure G1E1 also depicts the interactions that are anticipated between the UR CTSI Executive Committee, the UR CTSI Administrative Committee, the NIH Program Office, the national CTSA Consortium, and the Data and Resource Sharing Program. At the interface between the CTSI Executive & Administrative Committees and the UR CTSI Key Functions will be two committees: an External Advisory Committee and a Committee for Industry and Foundation Relations.

Figure G1E1 Organizational Chart for the Rochester Clinical and Translational Science Institute



G1E4. Advisory Committees

1) External Advisory Committee. An External Advisory Committee will be named following funding of the UR CTSI. The K30 Program has had such a Committee consisting of six well-reputed investigators and educators in clinical and translational research, including representatives from industry and regional collaborators. A similar group of 6-8 authorities in clinical and translational research will be named prior to initiation of the UR CTSI. The plan is to convene the group twice a year, once by conference call, to discuss the Annual Progress Report, and a second time face-to-face to have presentations by Key Functions leaders, CTSI research projects, new investigators and trainees. At each meeting, minutes will be kept and recommendations will be developed. These will be addressed by the Executive Committee, which will report back to the External Advisory Committee regarding implementation of the recommendations.

2) Committee on Industry and Foundation Relations. With new paths being championed for accelerating clinical applications of biomedical research, as evidenced by this RFA, correspondingly new paradigms for partnerships of academic health centers with industry and foundations are needed. At the University of Rochester Medical Center, in addition to an active Office of Technology Transfer (92 patent applications filed in FY05, with $38 million in royalty revenues), in 2005 we established an Office of Corporate Alliance, which systematically organizes URMC intellectual property for presentation and review by pharma and biotech industries. A Foundations Office is also engaged in matching faculty research with appropriate Foundations; in FY05, $2.3 million was obtained from Foundations in support of URMC research. We will draw on this experience to create a Committee on Industry and Foundation Relations, which will carry out the functions noted in Section G2K, serving at the interface between the UR CTSI Administrative Committee and the Key Functions. This Committee will also interface with the Regional Consortium. The Committee on Industry and Foundation Relations will have six members from industry and foundations who are knowledgeable about the UR CTSI and will advise us on opportunities in these sectors.

G1E5. Key Function Groups

Sections describing each Key Function in section G2 will review the administrative structure of that Key Function, as well as the interactions with the Administrative Committee and the broader organizational framework. Each Key Function has a Director or Co-Directors, as well as staff to support their initiatives. The Community Engagement Key Function has a Community Advisory Board, described in Section G2G.

G1E6. Evaluation and Tracking Support Group

This group will develop and carry out the Evaluation Plan proposed in Section G3. All Key Function groups and other CTSI Committees will provide data for this function. Each Key Function will have its own evaluation plan and data collected for that purpose. The Evaluation and Tracking Support Group will receive those data and provide evaluation reports for individual Key Functions. Moreover, using a logic model, the Evaluation and Tracking Support Group will provide an overall self-evaluation of the UR CTSI and compliance with the National CTSA Evaluation Plan. See Section G3 for the organization and activities of this group.

G1F. NATIONAL COLLABORATION, SHARING AND DISSEMINATION PLAN

Data sharing at the UR CTSA will be both investigator-specific and center-wide. Data sharing will adhere to all provisions of HIPAA and other regulatory requirements. We will work together with the URMC IRB and Information Security Office to protect personal health information. Two data sharing services will be implemented to provide flexible support to investigators. The first service pertains to the actual publications or documentations about research. For this purpose, we will use DSpace, a digital repository to capture, store, index, distribute, and preserve the intellectual outputs of university faculties, with which UR is one of the major partners. The second service involves the direct sharing of the original research data, which will be based on data encoding standards and data integration protocols.

We describe below (Section G1F2) the use of these standards and protocols for sharing of research data within the UR CTSI. For data sharing with external collaborating organizations, we will develop a service that is based on agreements among the collaborating parties to use a specific set of data encoding standards and data integration protocols. With this agreement, each participating party will provide services to assist others to identify the available data sets at the local site and to handle administrative and regulation issues. Once the agreement is in place, the data at an individual site can be shared with its collaborators using the same mechanism that we will have implemented for data sharing within the UR CTSI. This data sharing effort will: (a) serve the local community to implement the Rochester Health Information Organization (RHIO), within which URMC has played a leadership role to build an area-wide collaboration for continuity of care and other data sharing efforts, (b) serve the Upstate New York Translational Research Network to pool research data; (c) serve federal agencies, such as NIH and FDA, to fulfill data sharing and reporting requirements, and (d) serve other CTSA programs for collaborative informatics efforts.

The informatics service for process knowledge reusing will be based on the standard model for process knowledge representation. For this purpose, we will develop: (a) a process knowledge repository to store clinical and translational science processes in standard format, and (b) a process knowledge execution engine to interpret them. For process knowledge reuse within the UR CTSI (for example, reuse of the process knowledge of a validated clinical trial protocol for clinical trial process monitor and control), the business logic layer of the UR CTSI information infrastructure will handle the request of a specific piece of process knowledge by an informatics service,

retrieve it from the repository, transmit it to the execution engine, and feed the results back to the original requesting service. Reuse of process knowledge across CTSAs will be based on agreements among the collaborating parties to use the standard model for process knowledge representation, similar to the approach used for data sharing.

G1F1. Participation in a National CTSA Consortium

The UR CTSI intends to develop as a national model for clinical and translational science. Toward that end, participation in the National CTSA consortium will be an important means to share best practices and finely hone evaluation strategies. The UR CTSI will be well positioned to network nationally, as we intend to do this regionally through the Upstate New York Translational Research Network (see section G2J). UR CTSI faculty and staff will actively participate in the national CTSA Steering Committee and CTSA subcommittees, organized around the Key Functions.

G1F2. Plan for Data Sharing

Data sharing at the UR CTSI is investigator-specific. Several methods of data sharing may be used, including publication in peer-reviewed journals, documentation of research in public archives, and dissemination of the actual datasets of the research through web services. The nature of the data and the restrictions that may apply to it will guide investigators in their choice of data sharing methods. The UR CTSI encourages investigators to share data and will ensure that appropriate methods are developed and utilized to achieve data sharing in all appropriate situations. Data sharing must adhere to all provisions of HIPAA. The rights and privacy of people who participate in research must be protected at all times. Data for sharing should be free from any identifiers that would link the results to any individual research participants.

The Biomedical Informatics Key Function will implement specific strategies for two data sharing services that would provide investigators with the ease and flexibility required to meet the sharing provision. At the initial stage (first 2 years), we will focus on the archiving service pertaining to the publication and documentation of the research. We will use DSpace for this purpose. Since the UR is one of the six major research universities of the DSpace federation and an early adaptor of the system, we will take this advantage to provide the archiving support for data sharing efforts. Data shared through this mechanism will be primarily based on a text format, such as MS Word or PDF. Other researchers' use of such documentation data is straightforward, and thus no additional documentation and agreement are required.

The second phase of data sharing (from year 3) will be implemented along with the development of standards for data encoding, data integration, and process knowledge representation. At this stage, data sharing will entail the availability of the actual datasets generated from research. Since the dataset by itself is of little value without the knowledge of the study details and the context under which the research operated, we will thus still need to associate the actual datasets with the publication/documentation of the original research. DSpace will continue to be an option for this purpose to store both the publications and the associated datasets. For investigators that desire a more controlled method for sharing their data, Biomedical Informatics will implement web service applications as a solution to support automatic data sharing, integration, and analyses. For this purpose, the datasets need to be in specific formats that can be automatically interpreted by computer systems for further processing and analyses. Therefore, data sharing through this mechanism requires agreements among the parties involved in the data sharing activities. An example of such a format for automatic data sharing is XML, which can be used to wrap up both the metadata about the research (including the publication and documentation) and the actual datasets. The structure of the data represented in the XML format is defined by its schema, which must be agreed among all participating parties in order to correctly interpret the data. These common schemas for data sharing need to be standardized to serve a large research community. Additional technical details to develop standards for data sharing and process knowledge reuse can be found in Section G2C. In addition to the actual datasets and the technical standards, we will also share the software tools (for example, the system for data integration and the execution engine of process knowledge interpretation, see Section G2C) developed from this project with collaborators, such that they can be used in together with the data. It is important to note that sharing of actual datasets will also need to address other non-technical issues, such as regulation requirements and intellectual property rights, which will also be included in the data sharing agreements. We will work with the NIH CTSA Informatics Steering Committee to develop mechanisms to address these issues to ensure the effective dissemination of data and technology.

G1F3. Plan for Sharing Research Resources

With respect to our plan for the sharing of research resources and our management of intellectual property, we will adhere to the NIH Grant Policy on Sharing of Unique Research Resources including the Sharing of Biomedical Research Resources Principles and Guidelines for Recipients of NIH Grants and Contracts issued in December, 1999 http://ott.od.nih.gov/NewPages/RTguide_final.html. We have separately addressed the specific Software Resource sharing plan in Section G1F4, below. All other unique tangible resources generated by this project will either be distributed freely or deposited into a repository/stock center making them available to the broader research community, either before or immediately after publication. If we assume responsibility for distributing any newly generated resources, we will fill requests in a timely fashion. In addition, we will provide relevant protocols and published data upon request (as addressed in the Data Sharing Plan, Section G1F2). Material transfers will be made with no more restrictive terms than in the Simple Letter Agreement (SLA) or the Uniform Biological Materials Transfer Agreement (UBMTA) and without reach through requirements. Should any intellectual property arise which requires a patent, we will ensure that the technology (materials and data) remains widely available to the research

community in accordance with the NIH Principles and Guidelines document. For whole animal resources, we will have the recipient investigators provide written assurance and evidence that the animals will be used solely in accord with their local IACAC review; that animals will not be further distributed by the recipient without consent of our-Program; that animals will not be used for commercial purposes. Requests for resources from for-profit corporations, or for any commercial uses of shared resources, will be negotiated by our institution's technology transfer office. All licensing shall be subject to distribution pursuant to the institution's policies and procedures on royalty income. The technology transfer office will report any invention disclosure submitted to them to the appropriate federal agency.

G1F4. Plan for Sharing Software

The University of Rochester supports and agrees to abide by the software dissemination plan put forth in the proposal, such as sharing of the biomedical informatics standards encoded in computer-interpretable formats (for example, data integration protocols and process knowledge representation model), specific biomedical process knowledge (for example, clinical trial protocol and practice guidelines) represented using these standards, software tools to support the use of standards (for example, software systems for data integration and process knowledge interpretation), and novel programs for bioinformatics research and image processing.

The specific terms for software sharing include:

(1) The software will be freely available to academic institutional biomedical researchers, educators, and other institutions in the non-profit sector, such as institutions of education, institutions of research, and government laboratories.

(2) Commercialization of enhanced or customized versions of the software, or incorporation of the software or pieces of it into other software packages will be permitted at the sole discretion of the University of Rochester and will be subject to agreement by University of Rochester Office of Technology Transfer and the party that will initialize the commercialization or incorporation.

(3) Modification of the software by other researchers and institutions outside the University of Rochester CTSA and the sharing of the modified version of the software are permitted, subject to the terms specified above. All such permitted modifications will then be made freely available both to the University of Rochester, and as specified in the NIH Software Sharing and Dissemination specifications.

G2A. DEVELOPMENT OF NOVEL CLINICAL AND TRANSLATIONAL METHODOLOGIES

Introduction

Original research on novel methodologies and approaches for translational and clinical sciences will be an important component of the University of Rochester Clinical and Translational Science Institute (CTSI). In addition, for novel methodologies to be useful, they must be applied widely. Thus, a second important goal of this program function is to facilitate the use of novel methodologies in new ways by disseminating information and providing access to these advanced techniques to members of the CTSI, others in the University community, and partners in the Upstate Consortium.

G2A1. Specific Aims

G2A1a. Develop new methodologies with wide application.

1) Solicit And Review Proposals For Development Of Novel Methodologies And Approaches
2) Provide Support For Especially Promising Proposals To Develop New Methodologies
3) Establish Travel Grants For Investigators To Travel To Other Institutions To Learn New Methodologies.

G2A1b. Facilitate interactions between available or potentially available methodologies and clinical/translational researchers.

1) Provide Information Regarding Novel Methodologies In Widely Available Sources (Intranet, Newsletters) In Non-Technical Accessible Formats
2) Include Review Of Possible New Technological Approaches As Part Of The Standard Review Of Potential Protocols By The General Clinical Research Center (GCRC) Advisory Committee

G2A1c. Assess research needs and proactively address future needs of Institute members.

1) Conduct Routine Needs Assessments Among Members

G2A2. Background and Significance

As defined by NIH, the overall purpose of the CTSA process is to provide resources and develop methodologies intended to overcome blocks at both the discover (translation between bench and bedside) and implementation (translation between bedside and practice) steps. These steps have been identified as the two major roadblocks that are preventing the explosion of new information in the basic sciences from being translated into new therapeutics for clinical application (1). This crisis has led directly to the effort to reinvent the translational science enterprise (2).

Development of novel methodologies concerns itself predominantly with the first general roadblock, the actual translation from basic science to human clinical studies. The disconnect between basic and clinical sciences has been noted by members of the research community (3). However, the University of Rochester is unique in the close working relationship between workers in the basic and translational sciences. Our CTSI key function of developing novel methodologies will take advantage of this close relationship to develop widely applicable methodologies that will significantly enhance the scope and speed of translational research.

G2A3. Prior Experience

The University of Rochester has been a leader in the development of clinical and translational methodologies, and many of our current General Clinical Research Center (GCRC) research projects utilize such methodologies. Examples of this type of research include:

Development of systems for **large-scale screening of human pathogens for T cell epitopes**, exploiting the remarkable efficiency of micro-bead-based particulate antigen delivery coupled with large-scale sequencing of pathogenic organisms and the subsequent development of directed expression libraries which encompass all of the proteins of an organism (John Frelinger). These approaches are now being translated to the human system using model antigens such as those derived from influenza or CMV. Because this system is much more efficient and less expensive than peptide libraries, it could also potentially be used in the systematic analyses of multiple individual responders.

Development of a **serum biomarker for axonal injury** after concussion, using diffusion tensor imaging and proteomic technology (Jeff Bazarian, GCRC protocol 992). This is a cross-disciplinary project that

involves investigators in emergency medicine, radiology, neuropsychology, and neural sciences. As part of the proteomic component of this approach, these investigators are exploring the association of a variety of serum markers (e.g., S100b, cleaved-tau, and NF-L levels) with abnormal head CT scans and results of neuropsychological studies after head injury.

Several GCRC investigators (Clement Ren, Edward Walsh, Ann Falsey) are using novel techniques for measurement of **inflammatory mediators in exhaled air** condensates, allowing non-invasive sampling of the lower airways. This has become an integral part of asthma clinical research, and is rapidly moving to the forefront of the study of the pathogenesis of a variety of viral respiratory pathogens in humans as well.

Flourispot assays for measurement of cells secreting multiple cytokines simultaneously, and **luminex** methodologies for multiple cytokine determination developed by the Human Immunology Center (HIC) (see below) are being utilized by GCRC investigators (Edward Walsh, Eun–Hyung Lee, GCRC protocol 902) to evaluate primary T cell responses to respiratory syncytial virus in young infants. A great advantage of these methodologies has been that they allow detailed measurements on very small volumes of blood (1-2 mL) suitable for infants.

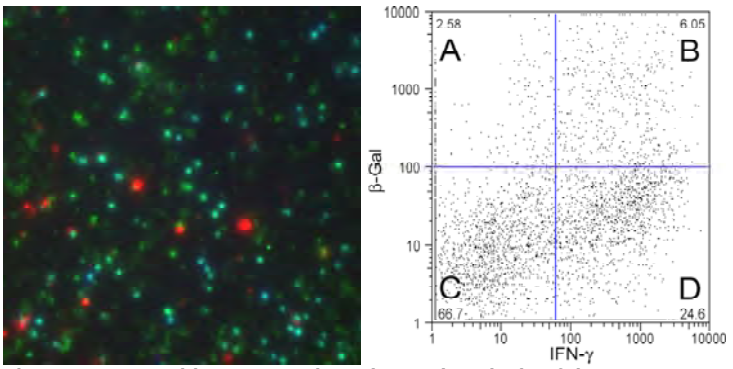


Figure G2A1: Multiparameter detection and analysis of three independent effector functions. Left: Spleen cells from Listeria-infected mice were stimulated with LLO91-99 peptide on beta-gal-transduced P815 target cells. Release of b-Gal (red), and secretion of IFNγ (blue) and MIP1α (green) were detected with Cy3, Cy5, and Cy2, respectively. **Right**: Exploraspot was used to detect and quantify spots in each color. Events gated on MIP1α^+ spots were analyzed in FlowJo for IFNγ secretion and cytotoxicity.

Development of **novel clinical trial designs**, including the so-called "n of 1 trial" design for rare diseases. GCRC investigators based at Highland Hospital (James Cleland), funded by the Muscular Dystrophy Association are currently funded to develop and conduct such trials not only in rare disease research but also to optimize medical therapies for patients with more common diseases. Design of such trials is relatively straightforward compared to larger crossover and other trial designs, and is cheaper, but requires biostatistical expertise as well as pharmacy support available through the GCRC.

Computer software that uses **internet-based behavioral interventions** designed to improve compliance of clinicians with HIV care guidelines (Amneris Luque, Dongwen Wang). These investigators are currently modifying their software approaches to include interventions that can improve compliance of study subjects with protocol interventions, and to be useful in the recruitment of subjects for clinical trials.

Although measurement of pulmonary function in adults is well established, these techniques are not suitable for use in very young infants. Investigators in Pediatric Pulmonary Medicine (Clement Ren) have developed technology suitable for measuring **lung function in preschool- aged** (3-6 y/o) children and are developing an infant pulmonary function laboratory. These techniques can be applied both in the clinic or even in the home, and should greatly facilitate clinical studies of lung development and interventions in prematurity and cystic fibrosis.

"Real-Time" data assessments are being developed by GCRC investigators (Geof Williams, GCRC protocol 804), utilizing hand-held devices that transmit data from home multiple times per day. This is particularly good for medication side effects and psychological scales for motivation, mood, and symptoms, and could be applied more widely for any clinical trial that requires frequent reporting of symptoms normally collected retrospectively through the use of diary cards or memory aids.

In addition to these activities being conducted by the current GCRC, there are several additional centers that are actively engaged in the development of new methodologies directly applicable to translational research.

The University of Rochester has recently been awarded a Center to develop technology for **sophisticated measurements of cellular and innate immunity** (the Human Immunology Center (HIC), Tim Mosmann, Microbiology and Immunology). The goals of this center are to develop novel research methodologies related to human immunology, validate and standardize the methodologies to provide reliable and reproducible results, and collaborate to transfer the methodologies to researchers performing translational research. An important component of the HIC is to provide training and technology resource information to investigators. A training

series, “Working with Human Specimens in the Research Laboratory” consisting of six interactive laboratory and lecture sessions covering topics from safety through technical methods was presented in the spring of 2005 with an attendance of 26 individuals. In addition, seven M.D. fellows and two graduate students rotated through the HIC core lab, receiving training in human immunological techniques including multichromatic flow cytometry, Elispot and isolation of cell populations. Figure: G2A1

The HIC website, http://www.urmc.rochester.edu/aab/vaccbio/hic/, was expanded, providing more technological information for eleven-color multichromatic applications and a 24-hour on-line scheduling calendar to meet the demand for using the HIC BD LSR II eleven-color flow cytometer. Additionally, the Center has continued organizing and sponsoring a seminar series in human immunology research at the URMC, including internal and external speakers.

A large number of valuable new methodologies have been developed by the HIC that are being used collaboratively by translational researchers, both on the GCRC and elsewhere. *Immunofluorescent multi-chromatic flow cytometry:* A fully functional core facility providing assistance with reagents, design, quality control, training and access to multi-chromatic flow cytometry for multiple investigators at URMC has been established, and the number of trained operators/users expanded from 30 in 2004 to 53 in 2005 with about half involved in human research activities. Separate immunophenotyping panels (eleven colors each) have been developed for general immunophenotyping of peripheral blood mononuclear cells, T cell activation/effector/memory analysis, NK cell activation, B cell reconstitution, and lymph node T cell analysis. Panels are currently under design for intracellular staining, T regulatory cell analysis, and dendritic cell analysis from human lymph nodes. Coordination has been initiated with investigators at the Roswell Park Flow Cytometry laboratory in Buffalo, New York and with Dr. Xia Jin, Infectious Diseases Division, in a dengue virus vaccine project. *Enzyme-linked immunospot Assay (ELISPOT):* The HIC core laboratory developed standard operating procedures for several cytokine and immunoglobulin B cell ELISPOT assays. These assays are currently in use in support of translational research in the area of lymphoma (Jonathan Friedberg), SLE (Jennifer Anolik), studies of infection of human infants with human herpesvirus type 6 (Mary Caserta), and malaria vaccine (David Topham). *Fluorispot Assays* for detection of the simultaneous secretion of two to three cytokines per cell in conjunction with automated data acquisition software has also been developed and validated. *Human Tetramer Assays for CD8+ T cells:* These assays will be used by Dr. William Sheehan, Transplantation Center and Dr. Nicholas Crispe, Center for Vaccine Biology, in a clinical study to study HLA-A2 matched and unmatched patients following liver transplants in hepatitis C-infected patients and time to complications. The Center is currently developing techniques for near-infrared reflectance confocal imaging of immune cells *in vivo* in collaboration with Dr. James Zavislan of the Center for Optics.

Novel imaging techniques have been extensively developed by researchers in the Center for Musculoskeletal Research (Edward Schwarz, Regis O’Keefe), including the purchase of a dedicated research 3 Tesla MRI instrument located on site. These investigators have developed advanced software technology for both Computerized Tomographic (CT) as well as MRI scanning that has allowed three-dimensional, high resolution imaging of a variety of bone and joint diseases. Figure: G2A2

Revitalizing structural allografts for large segmental defects of bone are being developed (Edward Schwarz). This tissue engineering technology takes advantage of recombinant adeno-associated viral vectors, which can be freeze-dried directly onto the cortical surface of a massive allograft without loosing infectivity. In addition to the tissue engineering technology, a novel dynamic MRI outcome measure is being developed as the primary outcome measure to quantify vascularity within the medullary cavity of the allograft. Currently, the GCRC is providing advice on IND filings with the FDA and biostatistical expertise.

A rapid diagnostic to assess the presence of active osteomyelitis is being developed to replace highly invasive percutaneous aspiration and culture methods of detecting Staphylococcus (Edward Schwarz). Novel immuno-dominant *S. aureus* antigens have been identified using translational animal models of osteomyelitis. Functional ELISAs have been developed to screen patient sera. Currently, the design of a clinical trial to investigate the sensitivity and specificity of these ELISAs requires biostatistical expertise and support available through the GCRC.

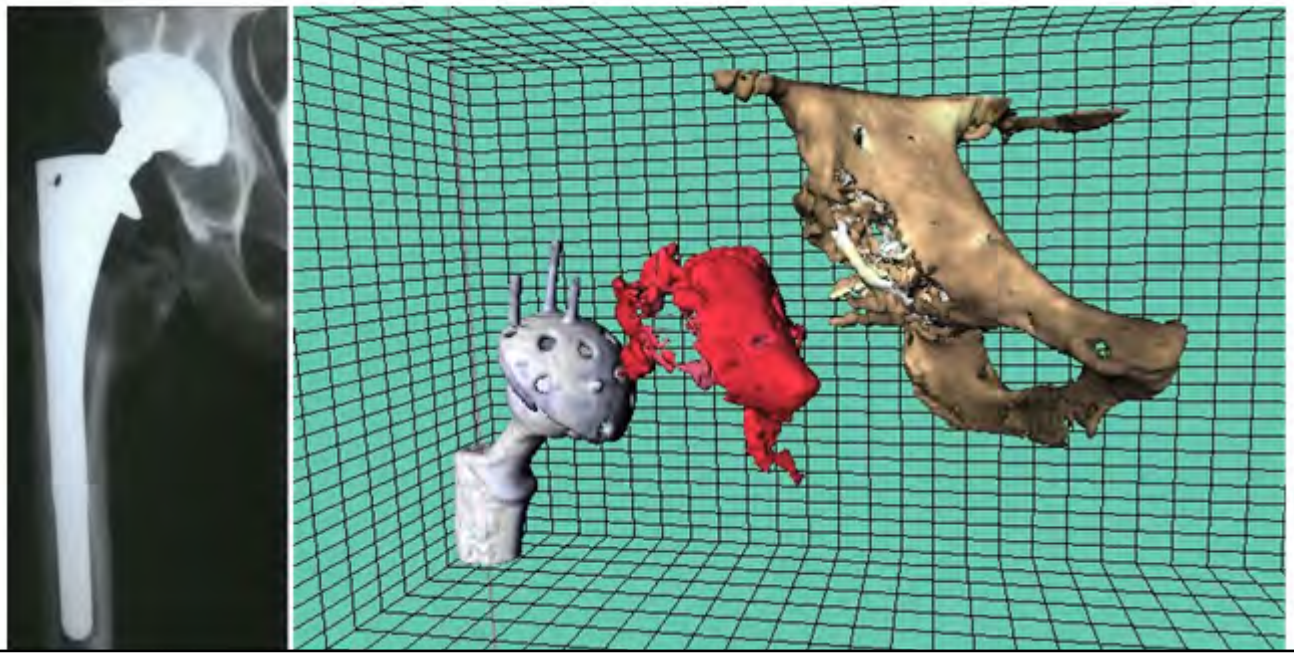


Figure: G2A2: Plain films of hip joint prosthesis and 3-D reconstruction based on CT scan. Area in red shows area of inflammatory mass that contributes eventually to joint loosening.

One of the main challenges for translational biomedical research is the need to develop **rational approaches to the identification of disease-specific drug targets** suitable for therapeutic application. This task is notoriously difficult and unpredictable because cell regulation is complex, and cell behavior is controlled by multiple signaling inputs. For example, cancer represents a group of multi-factorial and multi-genic diseases associated with the deregulation of cellular signaling networks. Identification of effective cancer treatments with decreased side effects therefore requires the discovery of cancer cell-specific drug targets and, as clinical experience indicates, drug target combinations that permit selective destabilization or destruction of such cancer cell-specific regulatory networks. Technologies suitable for efficient analysis of multiple disease-related variables are not available. Investigators in the Departments of Biomedical Genetics and 'Biostatistics and Computational Biology' (Land, Yakovlev) are integrating experimental and computational approaches for rational discovery of disease-relevant targets based on perturbation of multiple genes affecting the biological response of interest and mathematical modeling of gene networks.

Investigators at the **Center for Future Health** are developing prototypes of "ambient health monitoring" technologies that become an invisible part of the user's environment and aggregate information in a private personal health record. These technologies are being tested as health assessment tools applicable at all life stages from infancy to old age. An important feature of this approach is that it employs continuous longitudinal (over time) monitoring, which enables the individual and their health care providers to learn what is "normal" for the individual and to detect and monitor trends that may indicate developmental or incipient health issues. The goal is to move the detection of such conditions to the earliest possible stage to enable timely and minimal interventions for the maintenance of health and wellbeing. Sensing modalities under development include inertial measurements for body motion and gait analysis employing accelerometers and gyroscopes, computer mouse tracking to monitor fine motor motion, RFID sensing to monitor activity and interactions in the home and community and sound measurements to monitor breathing and speech patterns. Technical issues that are being addressed include how to make such sensing technologies accurate enough, small enough and low enough in power consumption to enable them to become truly ubiquitous and non-obtrusive. A central feature of our approach is that information is collected by the individual not by the environment to preserve the users personal privacy.

G2A4. Methods

The review of protocols for implementation on the GCRC is currently an established function of the existing GCRC Advisory Committee (to be called the GCRC Advisory Committee). While submitted proposals that include new methodologies and methods will often receive a favorable review, current GCRC proposals are typically focused on using a particular technique, in a specific application, in a hypothesis-driven clinical research study. As described above (section C), there are a large number of new methodologies that are an important component of individual protocols currently underway in the GCRC, and will be part of the GCRC function of the new CTSI. In addition, we propose to expand the support available through the CTSI to include projects specifically designed to advance potential novel approaches to translational research with broadly applicable utilization. If the development of a technology is successful, then this new technology could be routinely offered to CTSI investigators as part of the core laboratory function.

G2A4a. Develop New Methodologies For Translational Research With Interdisciplinary Application To A Variety Of Clinical Scenarios.

1) Solicit And Review Proposals For Development Of Novel Methodologies And Approaches. We propose to form a new research review process for novel methodologies. This panel will be modeled after the review panel for CTSI clinical projects, but with a different focus. The review panel will be chaired by the director of the novel methodologies core function, and its membership will include representatives of imaging sciences, the Human Immunology Center, core laboratories, active translational researchers, and other stakeholders in new methodologies. We anticipate that this committee will meet on a quarterly basis, although this can be modified if the volume and frequency of submitted projects warrants this.

Projects will be solicited from within the University community as well as from the broader community of scientists within Western New York, including industry. The specific proposals must satisfy three important criteria: (1) they must address a recognized roadblock to translational research, (2) they must be broadly applicable across disciplines, and (3) they must be at a sufficient state of development such that support by the CTSI core function can have a meaningful positive impact in advancing their application towards translational research.

Applications from young investigators and from underrepresented minorities will be actively solicited, and where possible, will be given high priority for implementation. This will also require appropriate attention to intellectual property (IP) issues and technology transfer. Our extensive previous experience in collaborations between industry and academia, such as the recent development of human papillomavirus (HPV) vaccine using virus-like particle (VLP) technology developed at the University of Rochester, should facilitate these arrangements. A unique feature of our center, as discussed in section G2i, is our recognition of the importance of understanding intellectual property in the development of new technologies.

A recognized roadblock in the pathway from the bench to clinical practice is intellectual property. Although counter-intuitive, failure to appropriately address and license intellectual property can often preclude the further development of a promising technology or methodology, because there are no economic incentives to do so, on the part of either industry or academia. The passage of the Baye-Dole act, allowing federally funded research to be patented and licensed, is widely viewed as a breakthrough in the translation of new discoveries to the bedside. Thus, researchers bear a responsibility to properly protect their intellectual property so that their discoveries can be appropriately developed into marketed products to improve health.

As also described in G2I, the University of Rochester Office of Technology Transfer provides training to investigators in intellectual property, including guidance, based on our prior experiences, on what IP is, how investigators can protect themselves and how to use their IP to obtain additional funding.

Intellectual property issues will also be considered in decisions regarding funding of pilot projects. If a novel methodology has licensing potential, we will facilitate interactions with the office of technology transfer. In addition, projects with high scientific merit will be given additional priority if they also have high potential for licensing, since these types of projects are most likely to develop into widely applicable methodologies.

Evaluation of success: The effectiveness of the Committee to solicit and evaluate projects to develop novel methodologies will be reviewed biannually for the number of proposals evaluated and the number of projects initiated by the core function. We will also monitor the diversity of input from various departments, with the goal that no more than 25% of novel methodologies should be developed by any single department, center, or institute within the University community. We will also track the impact of these methodological projects on

the submission and funding of clinical and translational research projects, and on the scientific impact of publications of such methodologic studies (e.g., through the use of citation indexes).

1) Provide Support For Especially Promising Proposals To Develop New Methodologies. We recognize that extensive funding from the CTSI to completely support new methodologies is unlikely to be available. However, the CTSI core function could be extremely helpful to investigators attempting to develop new methodologies in two ways. First, the CTSI investigators represent a cohort of supportive colleagues who may be able to make important intellectual contributions. Second, the CTSI can provide clinical resources and funding for pilot programs designed to validate new methodologies against other clinical endpoints. Thus, we propose that the CTSI will fund two pilot projects per year devoted to clinical development and validation of new methodologies. These methodologic pilot projects will be chosen using the criteria described previously in section G2A4a 1). It is important to note that these projects will be supplemental to the pilot and collaborative projects supported in the key function described in section G2B.

We provide three examples of current projects that could become more extensive pilot projects with the help of additional funding through the CTSI core function.

In vivo labeling of human lymphocytes is being developed by Eun-Hyung Lee and Tim Mosmann (GCRC protocol 1057). In this project, healthy subjects ingest non-radioactive deuterated water, and peripheral blood mononuclear cells (PBMC) are isolated by ficoll-hypaque gradient centrifugation. After purification of the CD3 positive (T cell) and CD19 positive (B cell) populations by positive selection using magnetic beads, enrichment of the DNA with deuterated hydrogen will be assessed by mass spectrometric analysis. Incorporation of $2H_20$ can then be used to assess the *in vivo* proliferation rate of immune cells. In later studies, selected T and B cell populations will be isolated from fewer time points and selected by fluorescent activated cell sorting which will allow analysis of proliferation rates of specific T subsets.

3D-CT of peri-prosthetic osteolysis is being developed by GCRC investigators (R. John Looney, Regis O'Keefe) as the primary outcome measure of clinical trials to produce the first therapeutic intervention for aseptic loosening of orthopedic implants. Currently, there is no validated outcome measure to predict the stability of an implant with x-ray evidence of peri-prosthetic osteolysis, nor a way to evaluate drug effects on implant failure. Based on results from the first clinical pilot using 3D-CT as the primary outcome measure, a power calculation has been derived for an efficacy trial of 172 patients. The trial design is relatively straightforward compared to larger crossover and other trial designs, and is cheaper, but requires biostatistical expertise as well as pharmacy support available through the GCRC.

Web and PDA-based tools used for smoking cessation. The Center for Tobacco Cessation (S. McIntosh, D Ossip-Klein, J. Klein) has carried out large studies using hand-held devices (PDA's) to both collect data and perform interventions. These tools use the "5 A" model (Ask, Advise, Assess, Assist, and Arrange) - an evidence-based brief intervention model designed to take as little as 1-3 minutes. This technology makes it possible to implement extensions of Internet-based training and support for physicians in office settings, such as the relatively straightforward model of behavioral change used in the proposed intervention. This model could be downloaded from a support website and used as a tool on their handheld device to remind physicians of their training and of their Intervention protocol, and facilitate specific evidence based decisions and interventions. In addition, a web-based tool, Web-Assisted Tobacco Intervention (WATI), is being evaluated. An available but understudied modality for intervention with adolescent smokers is the use of internet adjuncts which, along with telephone quitlines, serve as future frontiers for adolescent smoking cessation research. This group is examining teen website use, including telecounseling-type services delivered through instant messaging chat using the Monroe County (New York) GottaQuit program. Although outcome data are not yet available, early utilization data suggest that 0.6 to 2.0% of adolescents are using quitlines or web chats, which is similar to usage observed among adult smokers for community quit lines.

Compliance with applicable Federal Regulations: All pilot projects developed under this key function will comply fully with all applicable Federal policies, rules, and guidelines for research involving human subjects. This compliance will be assured by review of all projects by the regulatory key function (G2E)

Monitoring the progress of pilot projects: Regardless of the specific projects chosen for further development, we will institute a rigorous program of evaluation of progress. It is anticipated that most developmental programs will have an approximately two-year period between initiation and when a final decision can be made regarding the ultimate utility of the developed novel methodology. Projects will be evaluated for progress every six-months, assessing whether problems have occurred, whether there are

potential solutions to these problems, and whether the assessment of the overall feasibility and validity of the novel methodology has changed since the project was initiated.

1) Establish Travel Grants For Investigators To Travel To Other Institutions To Learn To Use New Methodologies. An important role for the CTSI will be to acquire methodologies developed elsewhere and bring them to the URCTSI where they can be employed in a variety of research projects. Therefore, we will include within this key function funds to sponsor travel for investigators at all levels of development to visit other institutions to learn new methodologies that could be applied usefully within the CTSI

G2A4b. Facilitate Interactions Between Available Or Potentially Available Methodologies And Clinical/Translational Researchers.

Since research methodologies are not useful until they are actually applied to important clinical research questions, a critical function of the CTSI is to put methodologies together with translational researchers in an efficient and productive way. This important objective will be accomplished both through the activities of the GCRC Advisory Committee as well as through a combination of educational initiatives designed to improve access throughout the research community.

1) Provide Information Regarding Novel Methodologies In Widely Available Sources (Intranet, Newsletters) In Non-Technical Accessible Formats Lack of information is frequently listed as a barrier to the implementation of new methodologies, and when methodologies are first reported, it is often in a highly technical manner that may not be easy to appreciate by individuals not directly involved in the relevant technical field. Therefore, communication can clearly be of benefit in applying novel methodologies. As is the case with all other types of communication, announcements and descriptions of potential new methodologies must compete for attention with many other high priority communications in the very hectic work day of most translational researchers. Thus, effective communication must have two characteristics: it must be very readily available, i.e., not requiring effort to find, and the core message must be communicated effectively in a relatively short period of time. Our communication strategy will mostly rely on electronic sources of information, including a standing website and an electronic newsletter that would highlight developments in research methodology in an easily accessible manner. Translational researchers who found these methodologies to be potentially useful would be directed to additional, more detailed sources of information as appropriate. The model for this system would be the current Dean's newsletter, offered by the principal investigator of the proposed CTSI and widely read by the University community.

Other approaches to making information available will be through the CTSI seminar series, which will include occasional lectures dedicated to introducing a new methodology or technology or publicizing an existing one. In addition, the CTSI will offer tours or "field trips" to show off technologies and conduct a periodic "nuts and bolts" forum allowing investigators to highlight how they used a new methodology or technology.

Assessment of success in disseminating information: We will use email-based surveys of researcher knowledge and satisfaction with the availability of information regarding new technologies to assess whether our educational efforts are successful. These surveys will be included as part of our overall effort to disseminate information via newsletters and ongoing needs assessment, described below.

2) Include Review Of Possible New Technological Approaches As Part Of The Standard Review Of Potential Protocols By The GCRC Advisory Committee. Review of new proposals for implementation by the participant and clinical interactions resource function (see section G2f) of the CTSI will be performed by the GCRC Advisory Committee. As outlined in section G2f, the GCRC Advisory Committee is composed of a diverse mix of translational researchers, as well as the nurse manager of the patient center, the head of the informatics core and other core members. Protocols submitted to the GCRC Advisory Committee will be reviewed for scientific validity and priority, as well as the need for core resources and for protection of subject safety by the Subject Advocate. In addition, we propose that as part of the novel methodology core function, all submitted protocols will also be reviewed with two objectives: (1) to identify protocols that use new methodologies, and (2) to identify protocols that would be enhanced by new methodologies that currently exist within or are being developed by the CTSI.

G2A4c. Assess Research Needs And Proactively Address Future Needs Of Institute Members

The establishment of the CTSI within the University of Rochester will have a large potential impact in removing barriers between development of methodologies and application to translational research. One important way this can be accomplished is through the judicious use of CTSI resources to acquire new

methodologies identified by translational researchers as of widespread and critical utility, but which do not currently exist within the CTSI. Essentially, this is a strategic planning function within the CTSI, and could greatly facilitate ongoing strategic planning carried out by the Dean of the Medical School and others within the Medical Center leadership group. There are two components to this process: (1) needs assessment, and (2) acquisition.

1) Conduct Routine Needs Assessments Among Members. We are currently conducting an extensive assessment of research needs for new methodologies among active GCRC investigators to gain an appreciation for what translational researchers view as potential technical enhancements. This is an ongoing process that will continue beyond the grant submission date. However, the following resources have been identified as of potential interest to GCRC translational investigators:

a. Development of better access to state-of-the-art electronic diaries for subject self-report and transmission of the data. These diaries are currently in use in some projects, and we propose that as part of the novel methodologies core, we will provide better access to this methodology for researchers engaged in studies using diaries and memory aids. This will be accompanied by efforts to develop wireless access throughout the center for web-based data entry.
b. Improved access to genetic tools, SNP analysis, and gene expression profiling. These technologies are being developed as part of the CTSI key function of translational technologies and resources (G2h), and the novel methodologies key function can assist investigators in the appropriate use of this technology and in adapting elements of the technology to translational research
c. Mechanisms for carrying out medium or high throughput screening to identify new therapeutic agents was also identified in our survey. Thus, development of some of the gene chip analysis discussed above could be very helpful in this regard.
d. Improved proteomic capabilities, such as MALDI-TOF, to investigate clinical research questions. As discussed in section G2h, the proteomics core facility currently provides full service protein identification for the translational researcher, including mass identification and protein sequence for proteins isolated from gels. The core facility also provides separation methodologies, including solid phase extractions, 1D and 2D gel electrophoresis, and high performance liquid chromatography, as well as support for the isolation, extraction and identification of proteinaceous materials originating from cell lysates and patient fluids.

   The level of service of this facility could also be improved with the incorporation of improved separation systems, including an ultra performance liquid chromatograph to reduce run time and sample size requirements; a capillary electrophoresis system to provide automated, high throughput analysis with separation techniques not available on LC systems; and an automated 2D gel electrophoresis system with robotic spot excision and integrated software for protein pattern detection.
e. GMP facilities to generate pilot lots of potential therapeutic or disease prophylaxis agents suitable for phase I or POC studies in humans has also been identified as a potential need.

2) Request Development Of Specific Methodologies If ongoing needs assessment suggests that there is a critical need for a new type of methodology that (1) is not currently available in the CTSI or is underdeveloped, (2) is not available at another institution, and (3) that would serve the needs of multiple members, the novel methodologies review committee can actively solicit specific proposals using an RFA mechanisms. These developmental projects would be performed in the same way that other projects within this key function are peformed.

G2A5. Key Function Interactions

The novel methodologies function will interact with the following institute functions:

G2A5a. Pilot And Collaborative Translational And Clinical Studies: The novel methodologies will be incorporated into pilot programs, which will validate these methodologies and make them available to the research community.

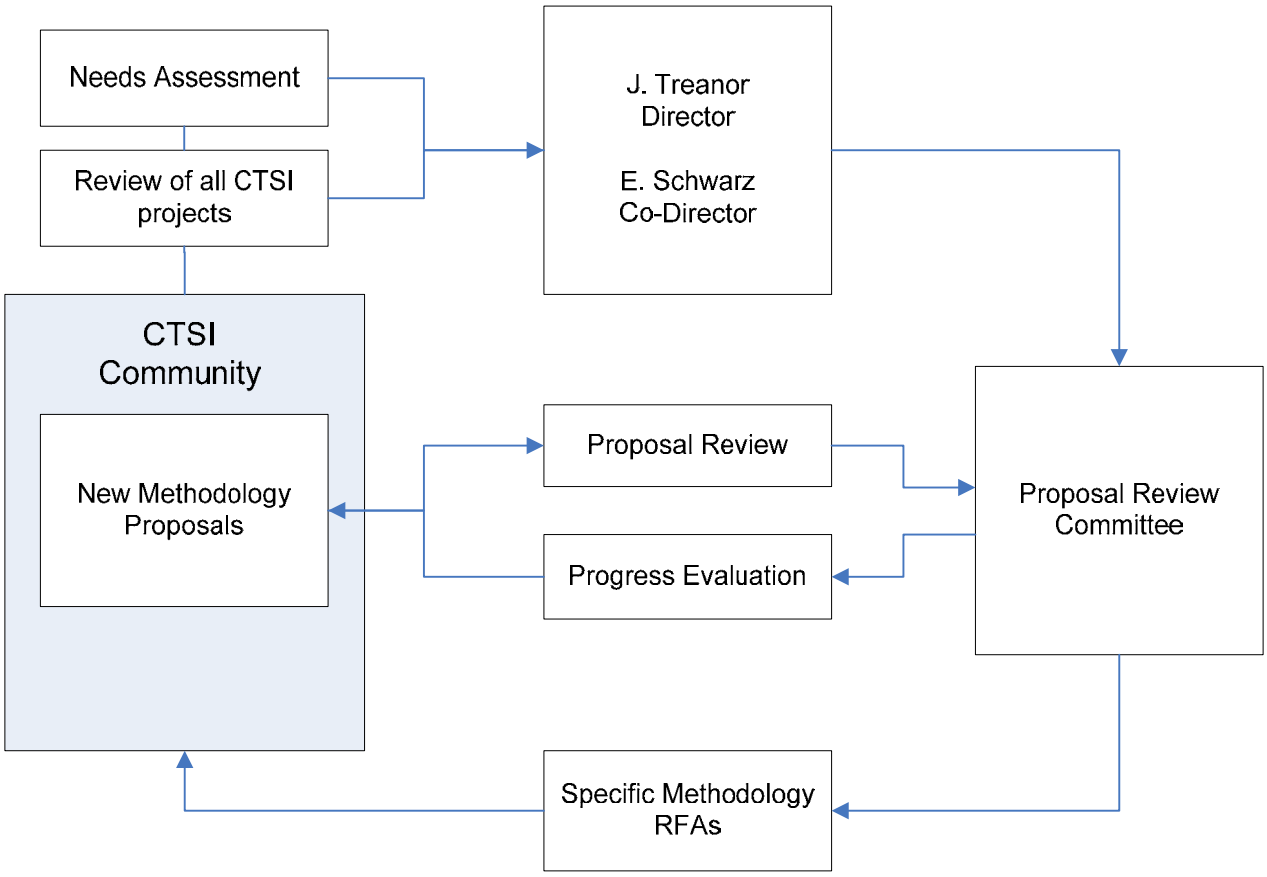
G2A5b. Translational Technologies And Resources: This functionality will essentially replace and enhance the existing GCRC core laboratory function. The novel methodology function will develop new methodologies, which if validated and found to be widely applicable, could become a core translational technology.

G2A5c. Participant And Clinical Interactions Resources: Studies to evaluate and validate novel methodologies will interact with the patient and clinical interactions function as they are applied to patient-oriented research conducted by the Institute.

G2A5d. Biomedical Informatics: Novel methodologies will involve data processing, potentially as in the case of novel proteomic and genomic approaches, with large datasets. The novel methodology function will interact with bioinformatics in the development of data analysis approaches to these novel methodologies.

Organizational Structure

The structure of the novel methodologies group will consist primarily of those individuals with responsibilities for developing and evaluating new methodologies. This will consist of stakeholders, including both core heads as well as end users as described in section G2A4a1).



G2B. PILOT AND COLLABORATIVE TRANSLATIONAL AND CLINICAL STUDIES

G2B1. Specific Aims

The overall goal of the Pilot and Collaborative Translational and Clinical Studies Program is to provide research support for preliminary and proof-of-concept studies critical to moving basic laboratory findings into clinical applications. High priorities of the Program are to facilitate development of enabling technologies, new therapeutic, diagnostic, or outcomes assessment approaches, and novel cross-disciplinary collaborative programs. The pilot funding will be targeted at research proposals that demonstrate ability to be catalytic in terms of generating new programs, directions, and funding for clinically applied research and methodologies. The Program will interact with the other key functions and components of the CTSA to enhance the recruitment and quality of applications for pilot and collaborative translational and clinical studies. A unique feature of the proposed Pilot Program is that it will utilize a number of funding mechanisms to ensure flexibility in supporting the goals of the CTSA and in its ability to take advantage of new opportunities to leverage resources both within the CTSA and with external funding sources. The Program will provide funding for trainees to obtain new skills, technological development, critical clinical trial preliminary data, new collaborative approaches, and new outcomes assessment and bioinformatics advances. In addition, there is support for traveling fellowships to allow establishment of external collaborations and acquisition of new techniques and models. There will be both investigator-initiated and RFA-type solicitations. To enhance the flexibility of funding new investigators, the Program will give priority to pilot studies that facilitate education of applicants concerning optimal study design, development and refinement of end point measures, and long-range considerations, such as, expectations by FDA and potential funding agencies, such as, NIH, private foundations, and industry.

Specific Aim 1. Facilitate production of critical preliminary data to support submission of new clinical and translational research proposals. This would include generation of data to support applications for novel pivotal clinical trials, and for trainees to develop new skills and methods.

Specific Aim 2. Provide support for proof-of-concept studies seeking clinical applications for basic science findings. This would include testing ideas that could create new enabling technologies to drive clinical applications of basic research, and technical advances. Since technical developments often are non-hypothesis-driven research projects, support would help to generate the compelling preliminary data needed to justify submission of proposals for these types of projects to federal and other funding sources.

Specific Aim 3. Stimulation of new cross-disciplinary collaborations, within the Institution and externally. This would help to create new approaches to research questions and applications of techniques and information derived from across a wide range of disciplines. Cross-disciplinary work could involve collaborations between clinical or basic science departments or centers within the Medical Center. Such interactions could also more broadly involve entities such as departments within the College of Arts and Sciences, including Biology, Mathematics, Computer Science, Engineering, Optics, the Center for Brain and Cognitive Function, and the Laser Laboratory. The School of Nursing and Simon School of Business Administration would be other components of the University from which new collaborative interactions could be created. Of particular importance will be the interactions between established investigators in various disciplines and young investigators or trainees in programs such as the K12 Clinical Science Training Program or the Experimental Therapeutics Training Program. In addition, external local collaborators could include organizations such as the Monroe County Health Department, the Ithaca College School of Physical Therapy, and the robust technological programs of the Rochester Institute of Technology, as well as the broader New York Upstate Consortium.

G2B2. Background and Significance

The University of Rochester Medical Center has a strong historical culture of interdisciplinary collaboration. It took root and flourished decades prior to the more recent advent of a compelling need for such collaboration to push science forward effectively, given current levels of complexity of biomedical science. This collaborative culture extends across our biomedical enterprise, from clinical care programs to basic and clinical research. Nearly a decade ago, as part of its strategic plan, the Medical Center embarked on a massive expansion of its biomedical research enterprise, with creation of over 250,000 square feet of state-of-the-art basic research facilities and recruitment of over 70 new scientists to the Institution. Central to this evolution was the creation of a group of new, interdisciplinary Centers to co-localize scientists of different backgrounds working together in specific research fields.

The Centers, as currently configured, include Aging and Developmental Biology, Vaccine Biology and Immunology, Oral Biology, Cardiovascular Medicine, Musculoskeletal Research, Pediatric Biomedical Research, and a Department of Biomedical Genetics (formerly Center for Cancer Biology). The Centers are structured such that the scientists have faculty appointments in basic science or clinical departments within the Medical Center, fostering a greater level of integration and collaboration across the Institution. Even the physical configuration of the new research space, with open architecture designed specifically to maximize interpersonal interactions within and between laboratories, was created to enhance collaborative and interdisciplinary interactions. A priority of the University of Rochester Clinical and Translational Science Institute (CTSI) will be to take advantage of this highly interactive environment to enable the nurturing of young investigators who have interesting ideas for new pilot studies or research directions, or who will bring necessary help to new collaborative studies.

Significance: The culture of collaboration has been the foundation of our expansion of translational research, facilitating scientific working relationships between clinicians and basic scientists. The Pilot Program described in this section of our application is essential in its ability to promote further collaborative science, and enhance dialog and interaction between clinicians, clinician-scientists, and basic scientists from a wide variety of disciplines. This Program has the potential to create the driving force to initiate new technical advances and applications of basic findings to translational studies or new clinical trials. Medical science will be unable to improve health of patients and delivery of care without evidence-based approaches to discovery and treatment, and the randomized clinical trial is central to this effort. The Pilot Program, by providing avenues to stimulate technological development, new translational and clinical grant proposals, and novel interdisciplinary collaborative approaches and interactions, will have a truly catalytic function within the CTSI, ultimately resulting in more novel clinical trials deriving from basic discoveries. In addition to the coordinated interaction with other key core functions of our CTSI designed to prioritize and optimize the use of all support funding, the Pilot Program will incorporate support mechanisms for mentorship, interdisciplinary interaction, and new skill acquisition by trainees. This frugal and flexible approach will broaden the scope of the Pilot Program and strengthen the scientific base and infrastructure for development of future investigators in the field of clinical and translational science.

G2B3. Prior Experience

The University of Rochester has had a number of successful internal pilot grant programs in the past, as well as a long-standing General Clinical Research Center. Some pilot project funding programs have been administered as components of specific Center grants or other programmatic funding, and some through University endowments and the Medical School. Examples of highly successful internally peer-reviewed and administered pilot programs include the Wilmot Fellowships of the Cancer Center (Institutional career development awards) and other pilot project research awards through the Cancer Center, pilot project programs through the Medical School, the Center for Biophysical Assessment and Risk Management Following Radiation, and pilot grants within our Environmental Health Science Center, among others. These programs have provided over a dozen pilot awards annually in the $25,000-$75,000/year range which have helped establish careers of young scientists and clinician-scientists, and have funded high risk/high impact pilot studies to provide preliminary data for other competitive federal funding sources. The Departments of Neurology and Psychiatry provide Paul D. Wellstone Muscular Dystrophy Cooperative Research Center and Saltzman fellowships, respectively, which are peer-reviewed granting processes providing career development mechanisms. Community Health Pilots have been a part of “Project Believe” of the Center for Future Health, providing pilot support for bedside to community translation (Translation 2) types of studies. Thus, the processes of solicitation, peer review, and prioritization of these types of awards are well established at the University.

In the University of Rochester Center for Musculoskeletal Research and the Environmental Health Science Center, annual solicitations are sent to Center faculty as well as collaborating clinicians and scientists, and a brief NIH-style application is submitted by the applicants. The applications are assigned to a peer-review committee with appropriate scientific and clinical expertise, formal proposal reviews are generated, and at a review meeting the applications are discussed, scored, and prioritized similar to using standard NIH methodologies. Emphasis in these examples is on fostering novel technologies, approaches, or collaborations, with a goal of producing preliminary data suitable for an investigator-initiated application sufficiently competitive for federal or other funding sources.

A similar format is used in the Center for Biophysical Assessment and Risk Management Following Radiation at the University of Rochester. Abstracts are solicited and reviewed by a panel of internal and external reviewers, followed by annual invitation of selected proposal abstracts as full applications. The applications are reviewed and scored in an NIH format by an external review panel, and 2-4 awards of up to $50,000/year are awarded. Thus, there is ample experience within the Medical Center of rigorously peer-reviewed pilot funding programs for both bench to bedside (Translation 1) and bedside to community (Translation 2) types of translational and clinical research. We will be able to build on our experience with these programs to ensure efficient operation of the Pilot and Collaborative Translational and Clinical Studies Program of the CTSI.

G2B4. Methods

Eligibility for pilot funding:

Pilot funding applications will be solicited from the broad clinical and basic scientific community of the University twice per year. Any faculty member of the Medical Center with a doctoral level degree will be eligible as a pilot principal investigator applicant, including clinicians, clinician-scientists, and basic scientists. The Program will also consider applications from trainees seeking to acquire critical skills or methodologies, or training in study design and outcomes measurement. This will be especially important where the project ultimately has potential to drive a larger new program. Trainees applying for collaborative pilot study funds will need to have multiple mentors (at least two or more co-mentors) that include at least two or more disciplines other than the discipline of their primary mentor. Traveling fellowships will be awarded to enable faculty or trainee investigators to visit other institutions to gain new skills, methods, models, or technologies. In addition, investigators from outside the Medical Center, including the departments of the College of Arts and Sciences, Simon School of Business Administration, and School of Nursing within the University, and outside institutions and organizations such as the Monroe County Health Department, Ithaca College School of Physical Therapy, and Rochester Institute of Technology can apply as co-investigators with Medical Center faculty for the Pilot Program support. Collaborative grants can be used to create interdisciplinary interactions between investigators in different fields or investigators and trainees bridging different fields.

Funds from the Pilot and Collaborative awards will not be used to support faculty salary, though support of research personnel, supplies, animal or clinical costs, and other research costs necessary for the pilots are permissible.

Types of Awards

In an effort to maximize its flexibility and impact the Pilot Program will fund several categories of awards. This is a major innovative feature of the proposed Pilot and Collaborative Translational and Clinical Studies Program. The types of awards are specific for trainees or faculty investigators and collaborators, and are summarized below.

Pilot Awards for Trainees:

1) Trainee pilot projects - Trainee awards will provide support for acquisition of new skills, methodologies or technologies, study design development, outcomes measures development, or experimental work to obtain essential new data for a project with promise of further funding. Trainees will be expected to identify a mentor or mentors as noted above with appropriate expertise to oversee the project. These awards would have a maximum of $25,000 for one year of support.

2) Minority support fellowships – Minority support fellowships would be provided to fund meritorious research projects or training for acquisition of specific new skills, methods, technologies, outcomes measures development or study design development to enhance productivity and future success of minority investigators. Funding would be for one year with a maximum award of $25,000, and a mentor with appropriate expertise to oversee the fellowship would be required.

Pilot Awards for Faculty Investigators:

3) Investigator-initiated pilot projects – Faculty investigators would be eligible for these awards that would be solicited semi-annually. Special priority will be given to senior fellows and junior faculty. Applications could be from new investigators requiring support for essential preliminary data needed for future funding or established investigators embarking on new translational or clinical applications of their research or new collaborative approaches, development of new technologies or proof-of-concept new clinical or translational pilots, generation of compelling preliminary data for non-hypothesis-driven applied research, or critical data to propel pivotal clinical trials. These awards would have an annual maximum of $50,000, and would generally

be funded for one year, though renewal for a second year would be possible if justified by the type of project and level of potential impact.

4) Requests for Application (RFAs) from the Pilot and Collaborative Translational and Clinical Studies Program to target research activity in specific areas - Of the ten semi-annual solicitations for proposals over the five years of the CTSA, it is anticipated that three of the solicitations would focus on a specific target research area identified by the Pilot and Collaborative Translational and Clinical Studies Coordination Committee, with input from the Pilot Project Oversight Subcommittee. Thus, during these solicitations submissions would need to respond to the topic area or goals of a specific Request for Proposals which would be conveyed by the Coordination Committee to the investigators of the CTSI. As for non-targeted investigator-initiated awards, the maximum would be for $50,000 for one year, with potential for exceptions allowing a second year of support.

5) Interdisciplinary conference awards - A function of the Pilot and Collaborative Clinical and Translational Studies Program will be to stimulate research and collaborative interactions through semi-annual interdisciplinary conferences focused on a specific research area, and involving investigators of the CTSI along with external collaborators (see below). The Coordination Committee will organize these conferences and select topics, with input from other Key Functions. However, investigator-initiated proposals for conferences, along with support for associated costs, can also be submitted at any of the semi-annual pilot proposal solicitation cycles. Funds could be used to cover travel expenses for a limited number of key participants from outside institutions, and these awards would carry a maximum of $5,000.

Pilot Awards for Trainees or Faculty:

6) Collaboratively funded projects between the Pilot Program, and the Community Engagement and Development of Novel Technologies and Methodologies Key Functions - Two other Key Functions, Community Engagement and Development of Novel Clinical and Translational Methodologies, provide pilot funding awards as part of their structured activities. Members from each of the pilot project committees of these two Key Functions will participate in the Pilot and Collaborative Clinical and Translational Studies Program Coordination Committee to provide input on projects that may be high priorities for funding by more than one of these Key Functions. This will allow leveraging of resources where support for meritorious projects could be split between Key Functions, and ensure interaction of these Key Functions with regard to the entire spectrum of pilot funding of the CTSI. Investigators would identify the project as responsive to the pilot solicitations of the two Key Functions so that collaborative review could be arranged by the Coordination Committee.

7) Traveling fellowship awards – These applications will be solicited along with the above types of applications, at each of the semi-annual award cycles, and could be submitted by either trainees or investigators. The awards would support travel and housing costs for scientists to visit one or more laboratories, research, or clinical sites at outside institutions, and could be from 1-2 weeks up to 2 months. This would allow investigators to acquire new skills, methods, technologies, or models to bring back to their research programs. Resources for these types of inter-institutional interactions are increasingly difficult to obtain in the course of usual funding mechanisms, and this poses a barrier to efficient adoption of novel scientific approaches developed at external institutions. Recent experience with a similar travel award in the University of Rochester Center for Musculoskeletal Research, which is funded by a foundation, resulted in acquisition of critical technologies and methods by a new investigator who subsequently obtained a 1.5%-tile score on first submission of an RO1 application to NIH. Thus, we feel this type of award can be extremely catalytic for young investigators, or established investigators moving into new translational directions. These travel awards would have a maximum funding of $10,000 and would not be renewable.

Application And Review Priorities

The translational matrix framework of the University of Rochester CTSI will markedly facilitate generation of new technologies, ideas, and directions. New ideas or directions will be reviewed semi-annually by the Administrative Subcommittee with the Program Co-directors, enabling RFA approaches to target the most potentially productive areas or ideas with broad or high levels of impact across research programs of the CTSI. Applications would be solicited twice per year, as detailed below. The solicitation and review process would include dissemination of the priorities of the Pilot Program.

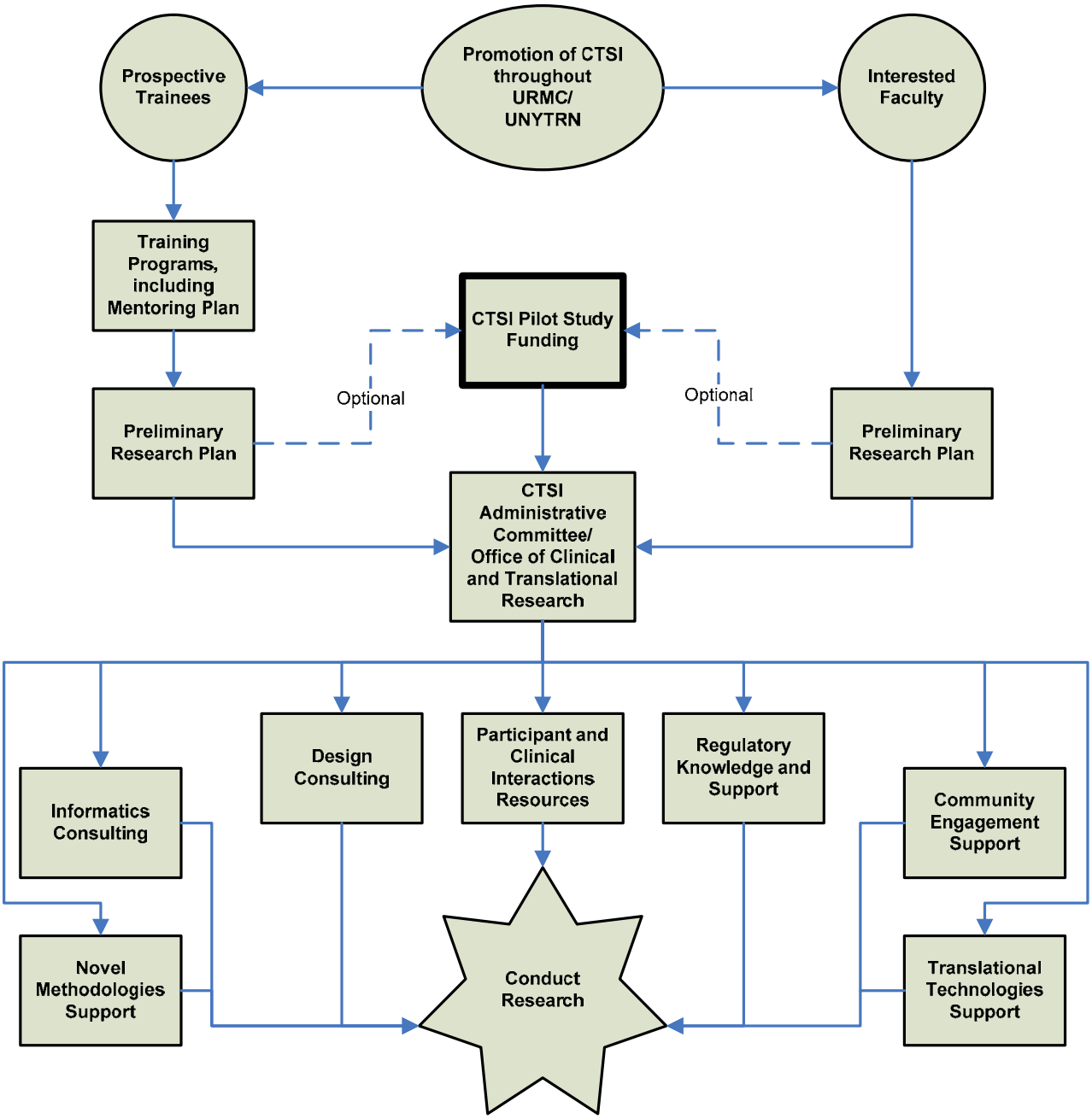
Priorities for awarding pilot funding as described under the Specific Aims and Methods above, with an overall goal of maximizing the impact of the pilot and collaborative awards on the progress of the CTSI as a whole, would include:

1. Generation of critical preliminary data for new submissions of translational and clinical applications for federal funding.
2. Stimulation of novel collaborative interdisciplinary interactions in the approach to a clinical problem or application of discovery to diagnosis or treatment, within the Medical Center, the University, and the local community or with other institutions or centers.
3. Proof-of-concept studies for novel techniques or enabling technologies, diagnostic or treatment methods.
4. Generation of compelling preliminary data for non-hypothesis-driven research proposal applications, which may create new technologies to propel translational or clinical research.
5. Generation of preliminary data essential for novel pivotal clinical trials.
6. New methodologies in clinical trial design, biostatistical approaches, and bioinformatics.
7. New approaches to ethics in clinical research, or innovations in approaches to compliance and interaction with regulatory pathways.
8. Projects that can take advantage of the Rochester community infrastructure, which is well evolved and organized, compared with most communities, to conduct population studies and interventions that make use of our “community laboratory.”
9. Proposals that may result in new intellectual property with significant clinical impact.
10. Improvement of research data and information sharing and dissemination within the local and broader research community to stimulate interdisciplinary collaboration, including information systems and web-based information dissemination and access.
11. New outcomes measurement methods and validation techniques to enhance information deriving from clinical studies.
12. Interdisciplinary collaboration between investigators and trainees in different disciplines, to foster cross-bridging training and interaction.

Overall Structure for Completion of the Specific Aims

Figure G2B1 shows the interaction of the Pilot Program with other resources for faculty and trainees within the CTSI.

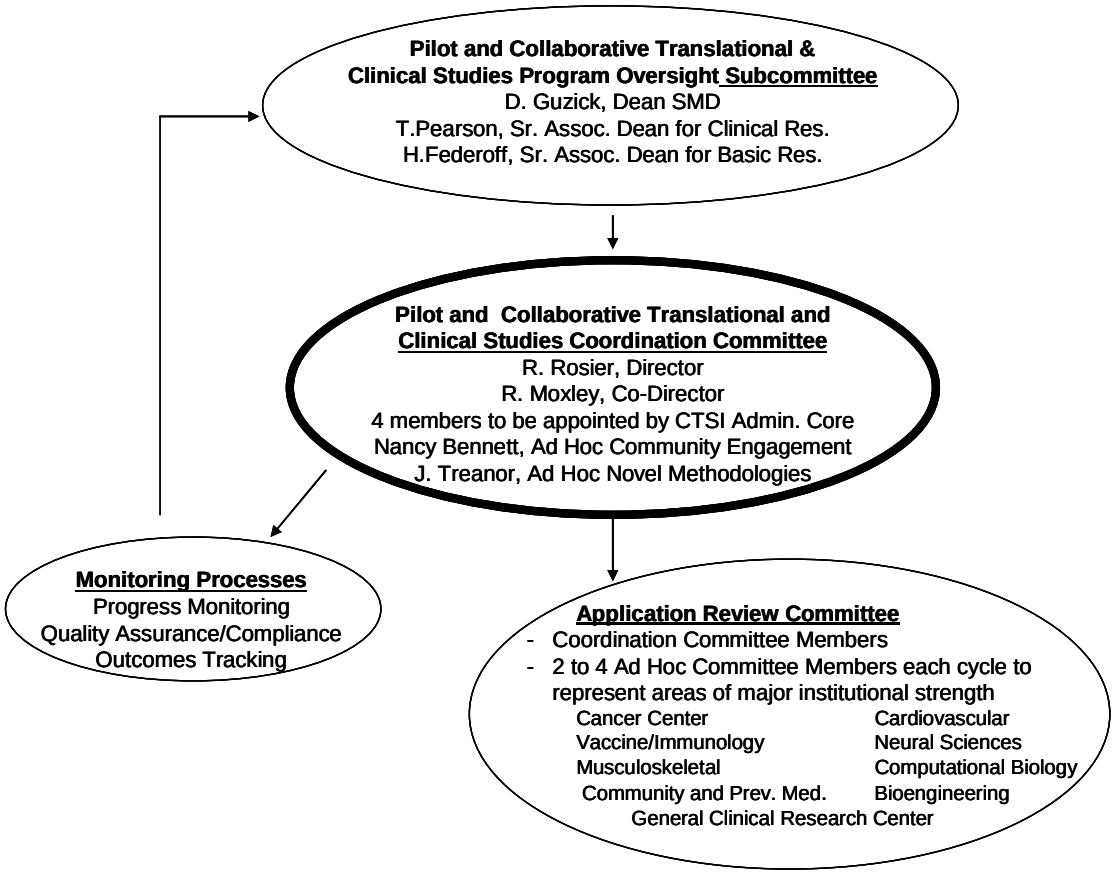
Figure G2B1. Meeting the Needs of CTSI Faculty, Trainees and Partners



The internal organization within the Pilot and Collaborative Translational and Clinical Studies Key Function in the highlighted block in Figure G2B1 above is depicted below in Figure G2B2:

Figure G2B2.

Organizational Structure of the Pilot and Collaborative Translational and Clinical Studies Program



The Pilot Project Oversight Subcommittee of the CTSI Administrative Committee (Consisting of the Dean of the School of Medicine and Dentistry, the Senior Associate Dean for Clinical Research, and the Senior Associate Dean for Basic Research) will provide oversight for the Pilot and Collaborative Program, with semi-annual reporting of the Program to the full CTSI Administrative Committee. A Pilot Project Coordination Committee will function as the implementation instrument of the Program, and will consist of the Pilot Program Co-Directors and four members appointed by the CTSI Administrative Committee for a term of two years. They will be selected from investigators within the primary components of our translational research areas shown in Figure G2B2. It will also include two additional ad hoc members from the Key Functions with pilot funding programs (Dr. Nancy Bennett from Community Engagement and Dr. John Treanor from Development of Novel Clinical and Translational Methodologies). The Coordination Committee will provide pre-review of submitted abstracts to select applicants for full application submission. Applications will be limited to a maximum of ten pages, and will be submitted in NIH format. The Coordination Committee members will also serve on the Review Committee for a term of two years and will solicit additional ad hoc reviewers to join the Review Committee for each round of review, to tailor the review expertise to the submissions received and supplement the standing Review Committee membership. Two to four ad hoc members will be appointed by the Coordination Committee for each cycle, depending on the number of applications to be reviewed. The ad hoc reviewers will be solicited from experts in the areas in which the major Institutional strengths lie in terms of translational research, as shown in the organizational diagram (Figure G2B2). External reviewers will be engaged in the review panels when needed for particular expertise, and the standing Review Committee members will execute appropriate conflict of interest documents and procedures to ensure fairness of the review process. We believe in this case that panels should not consist exclusively of external reviewers, since

the goal of the Pilot Program, the goal of maximizing its catalytic function within the CTSI, is dependent upon substantial understanding by the review panel of the strengths, priorities, and directions of the Institution internally.

The four standing members of the Coordination Committee/Review Committee will have two-year terms, and will be selected from investigators within the primary components of our translational research areas shown in Figure G2B2. Administrative support will be provided by the Senior Health Project Coordinator, who will organize the solicitations, notify reviewers and distribute applications, organize the semi-annual interdisciplinary conferences, collect and track progress reports and follow-up questionnaires, and make travel arrangements for outside consultants and external reviewers as needed.

Table G2B1. Annual Timeline for Functions of Pilot and Collaborative Translational and Clinical Studies:

	Month											
Function	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**
Solicitation				X						X		
Submission Pre-review					X						X	
Submission	X						X					
Review		X						X				
Awards			X						X			
Funding			X						X			
Progress Report		X						X				
Report to CTSI Administrative Committee				X						X		
Follow-up Questionnaires				X						X		
Interdisciplinary Research Conferences			X						X			

Two cycles of funding will occur per year. Table G2B1 above shows the timing cycle for the various elements of the process on an annual basis. Grants will be provided in the amount up to a maximum of $50,000 per year, generally for one year, but in special cases where the timeline for the work justifies a second year of funding, a renewal for a second year could be awarded. Pilot support for trainees would be of a maximal $25,000 amount. Traveling fellowship awards would be up to $10,000 to enable trainees or established investigators to spend time at other institutions to acquire new skills, technologies, models, or methods. Interdisciplinary conference applications would be funded at a maximum award of $5,000. This should enable funding of approximately 6-10 meritorious projects annually, depending on specific project budgets and award types. The funding can be used to support personnel, animal or clinical costs, supplies, minor equipment, and data analysis and other research costs. Limited travel, such as to visit another institution or attend a meeting or course critical to acquisition of knowledge, techniques, reagents, or skills essential to the project, could also be supported by the funding. The funding could not be used for faculty salary support.

The Pilot Program Co-Directors will be responsible for the solicitations twice per year by email to all Department Chairs and Center Directors. Announcements will also be made at the monthly Executive Committee meeting of all Chairs and Center Directors of the University of Rochester Medical Center. One month after the solicitation, a one-page abstract of the specific aims and significance of proposals will be due, and will be pre-reviewed by the Pilot Project Coordination Committee. Submissions of full proposals will be invited by the Committee after review, providing an initial level of conceptual review to ensure that the full submissions received are responsive to the goals of the CTSI and Pilot Program priorities. Suggestions

regarding utilization of appropriate Key Functions will be made by the Committee to applicants based on abstract content, to help applicants take advantage of the integrated infrastructure of the CTSI and optimize solicited full proposals. The timetable, as shown above, will allow 6-8 weeks following invitation of full proposals until they are due. During the month following receipt of the proposals, the Pilot Project Coordination Committee will solicit expertise-appropriate ad hoc reviewers for the Review Committee cycle, and applications will be reviewed by all committee members, followed by up to a half-day review meeting (depending on the number of proposals) to discuss and score all proposals. Each proposal will have a primary and secondary reviewer, and each reviewer will provide a brief, bullet-point style review containing the major strengths, weaknesses, and significance. The best scoring proposals falling within the budgetary limits will be notified of the award, and the funding initiated within a month, as shown in the timetable. The review process allows two levels of review, as well as guidance in taking advantage of Key Functions, strengthening the quality of the proposals ultimately selected, and ensuring optimal responsiveness to the Program goals and priorities. Although requiring more effort by the Pilot Project Coordination and Review Committees, having two cycles per year rather than a single annual cycle enables greater flexibility of timing for investigators to take advantage of requests for proposals and program announcements from NIH and other organizations that may occur at unpredictable times. This will enable a more nimble level of responsiveness to unique research opportunities that may arise, and facilitate generation of critical preliminary data in a timely manner.

Approximately every third application cycle there will be a Request For Applications (RFA) generated by the Coordination Committee with input from the Oversight Subcommittee of the CTSI Administrative Committee (See Figure G2B2). We anticipate announcing three such RFAs during the five-year term of the CTSI. These would be targeted to research areas, technologies, or diagnostic/therapeutic approaches to diseases of unique or developing strength within the Institution to stimulate research activity, translation, and collaboration which may emerge as new opportunities. This again creates a high degree of flexibility of the Pilot Program to maximize its impact on the CTSI overall.

Interdisciplinary conferences on specific research topics, diseases, or technologies, comprising a half-day symposium or colloquium format, will be implemented semi-annually, four months prior to each full application submission deadline. The Pilot Project Coordination Committee will select a conference topic in areas of strength or unique translational or clinical opportunity. The purpose of these conferences is three-fold: (1) periodic broad-based research interaction among the investigators in the various components of the CTSI; (2) dissemination of information regarding upcoming application solicitations from the Pilot and Collaborative Translational and Clinical Studies program; and (3) stimulation of new collaborative research in promising fields. One conference per year would take place on site and involve participants from the faculty and trainees of the School of Medicine and Dentistry, the School of Nursing, the Eastman Dental Center, and the College of Arts and Sciences of the University of Rochester. The second conference each year will be held off site in the region and will be focused on engagement of a high degree of external participation from other regional institutions and collaborators in the Upstate New York Consortium, local industrial partners, and community organizations. As an example, we would anticipate the first intra-institutional interdisciplinary conference to be on Stem Cells, an emerging area of translational strength and opportunity within the Institution. Examples of topics for the regional conference during the first year of the CTSI would be “New Genetic and Diagnostic Technologies,” or the “Role of Telemedicine in Clinical Research.” At each semi-annual application solicitation for the range of awards of the Pilot Program, investigators could submit proposals for intra-institutional or regional interdisciplinary conferences, which would be reviewed in a similar manner to the other application categories.

Qualifications: Suitability of Director, Co-Director, & Senior Project Coordinator for their Duties in the Pilot and Collaborative Translational and Clinical Studies Program

Director: Randy Rosier, M.D., Ph.D.: As Professor of Orthopaedics, of Oncology, and of Biophysics and Biochemistry since 1993, and as Chair of the Department of Orthopaedics and Rehabilitation since 2000, Dr. Rosier has established a broad spectrum of interactions within the University of Rochester, including formation of the Musculoskeletal Research Center, which now includes 16 scientists and clinician-scientist faculty from diverse Departments including Orthopaedics, Biomedical Engineering, Pathology, Rheumatology, and Endocrinology. The fundamental orientation and commitment of the Center is translational research. These interactions and network of contacts will facilitate Dr. Rosier’s ability to organize and direct the Pilot and Collaborative Translational and Clinical Studies Program. His experience as a leader of clinical care in our Medical Center, and his own research investigations, will enhance his ability to recruit trainees and faculty to

participate in the Pilot and Collaborative Studies Program. Dr. Rosier has been a funded clinician-scientist at the University of Rochester for the past 20 years. He currently has both basic science and clinical trials NIH funding. His major research focus is on the role of intracellular signaling processes in pathogenesis of osteoarthritis, and their potential therapeutic modulation. In addition, he is investigating the role of lead in bone as a possible cause of premature ossification in children and osteoporosis in perimenopausal women. Dr. Rosier and Dr. Moxley have both served terms on the University of Rochester Faculty Senate, which has provided them with contacts for partnering with colleagues in the School of Arts and Sciences as well as with colleagues representing other parts of the University. In the Medical Center, Dr. Rosier routinely meets each month with the Chairs of other clinical and basic science departments as a part of the Executive Committee function organized through the Office of the Dean, and serves on the Medical Center Board. These meetings will facilitate communication about the Pilot Program of the CTSI to other departments and their training programs. Dr. Rosier has served on numerous local and national committees which review grants and training programs, and he is well prepared to moderate the Pilot Project Coordination Committee, evaluate the requests for funding, critique projects, and prepare reviews of the applications. Over the past four years Dr. Rosier and Dr. Moxley have served together on the Advisory Council of the NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases, and as a part of their responsibilities have reviewed grant applications and training programs. They have worked together and have discussed the opportunities and challenges that need to be addressed in encouraging new investigators and in nurturing clinical and translational research.

Co-Director: Richard T. Moxley, III, M.D.: Dr. Moxley joined the faculty of the Department of Neurology in 1974. He has served as Professor of Neurology since 1984, Professor of Pediatrics since 1987, Director of the Neuromuscular Disease Center since 1986, as Associate Chair for Academic Affairs in Neurology since 1997, and as Associate Program Director of the University of Rochester General Clinical Research Center (GCRC) since 2004. Dr. Moxley has served as a member of the Dean's Review Committee for Research Projects and as a member of the Scientific Advisory Committee to review proposals to use the GCRC for many years. For the past five years he has served as principal investigator of the NIH National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members and has recruited patients and investigators to join and use the resources of the Registry, as well as coordinated the review of all applications to join and use the Registry. The Registry has received renewal of funding until 2010. Dr. Moxley is also principal investigator of the University of Rochester Paul D. Wellstone Muscular Dystrophy Cooperative Research Center (MDCRC), which is funded through 2008. He serves as overall PI – administrator for the Center and is also PI of one of the scientific projects, a trial of insulin-like-growth factor-1 complexed with IGF binding protein-3. As a part of his duties as overall PI, Dr. Moxley organizes meetings, reviews and prepares research reports, trains fellows, and networks with NIH staff, with principal investigators at the five other Wellstone MDCRCs, and with patient advocacy groups. These ongoing responsibilities and his past experience in evaluating and critiquing research prepare Dr. Moxley well to assist Dr. Rosier in carrying out the duties of Co-Director of the Pilot and Collaborative Studies Program of the CTSI.

Senior Health Project Coordinator: Christopher Chadwick, MPH: Mr. Chadwick has an MPH degree, and his training was focused in trial design and health research. He has three years' experience as a clinical data manager in all phases of clinical trial conduct and design. He has proficient computer and interpersonal skills, and also has past experience as an office business manager and two years' experience as a laboratory technician involved with gene therapy and molecular medicine therapeutics. He is extremely well qualified to coordinate the administrative functions of the Pilot and Collaborative Studies Program. His other duties involve functioning as a senior clinical coordinator and performing oversight of the quality assurance program of the Department of Orthopaedics and Rehabilitation, which occupy 75% of his time. There is excellent overlap of skill sets for his role in the Pilot and Collaborative Studies Program.

Completion of Specific Aims

Figures G2B1 and G2B2 outline the organizational structure and processes that are common to all of the Specific Aims and Methods, and summarize the steps that will enable completion of the three Specific Aims of the Pilot and Collaborative Translational and Clinical Studies program. The investigator-initiated and RFA-responsive pilot awards will directly support successful completion of Specific Aim 1, "Facilitation of production of critical preliminary data for new clinical and translational grant submissions." Funding of trainee awards, in concert with Key Function interactions with other programs within the University of Rochester CTSI, will address the acquisition of crucial new skills and methods by trainees, with enhanced support for minority trainees by that specific award category. Specific Aim 2, "Support for proof-of-concept studies seeking clinical

applications for basic science findings and non-hypothesis-driven technology or methodology research," will also be served by the same award categories, plus the specific mechanism of the collaboratively funded awards between Development of Novel Clinical and Translational Methodologies and the Pilot and Collaborative Studies key functions. Completion of Specific Aim 3 will be supported by all of the above awards plus the specific Traveling Fellowship and Interdisciplinary Conference categories of award.

Performance Monitoring

Annual progress reports will be required to be submitted by the end of the last month of the funding year cycle, and will be reviewed by the Coordination Committee. A report summary of the Pilot research activities and new awards funded will be prepared and submitted to the CTSI Administrative Committee twice annually, so that progress of all pilots and the context in which they affect the Institutional initiatives as a whole can be continuously monitored and evaluated.

During Year 3 of the CTSA, an external site visit panel will be convened to evaluate the structure and effectiveness of the Pilot and Collaborative Translational and Clinical Studies Key Function, and make formal recommendations to the CTSI Administrative Committee for changes or improvements. This panel will be constituted from three external investigators from other institutions receiving CTSAs, to optimize experience exchange in this evaluation process.

Project review priorities:

The selection of projects will be based on a number of criteria, with a goal of maximizing the impact of the pilot funding program on the CTSI. The review criteria for prioritization are listed above (See Application and Review Priorities), and will be expressly indicated in the application solicitations. The priority areas considered for funding during the review process have been previously presented above. High priorities in the review process will include critical components of enabling technology, novel therapeutic or diagnostic approaches, and creation of new interdisciplinary collaborative scientific approaches, consistent with achievement of the Specific Aims of the Program. Collaborations can be among scientists and clinicians within the Institution, or external as appropriate to the project. Advances that have potential to affect large numbers of patients or diseases that pose a large societal burden economically or in quality of life will be taken into consideration, since we wish to maximize the impact of the translational programs of the CTSI. Development of technologies, or diagnostic or therapeutic techniques which can advance clinical care across a wide range of disorders with specific organ system problems will also be given high priority.

Target research areas

The largest areas in which extensive clinical and translational research currently occurs within the Medical Center include Neural Sciences, Cardiovascular Disease, Cancer, Immunology, Vaccine Biology, Infectious Disease, and Musculoskeletal Diseases. It is anticipated that a substantial opportunity exists to further build on these strengths, and that novel translational and clinical pilot proposals will derive to a significant extent from these existing areas. In addition, these areas represent the strongest elements of the Medical Center's current strategic plan, given perceived strengths and opportunities, and the relatively large size of the scientific groups working in these fields at our Institution. We also have expertise in helping to develop new or better endpoint measures, including measures of patient reported outcomes that the FDA is now requiring for clinical trials, and this will constitute a target research area for development in pilot projects.

Metrics

The most straightforward metric of the Pilot and Collaborative Studies Program will be the ability to create new preliminary data critical to achieving new funding for research projects and programs. The semi-annual progress reports that will be provided from the Pilot Program to the full CTSI Administrative Committee will be assessed with annual follow-up questionnaires given to recipients who have received Program funding support. Analysis of the responses by the recipients over the subsequent years of the CTSA will help us determine if significant new research funding has resulted from each funded Pilot Project. This will enable quantitative longitudinal follow-up of the impact of the Pilot Program. Other important metrics will be the impact of any publications supported by the pilot funding, as well as successful application of techniques, methods, models, or products developed in the pilots by others. Obviously technologies, methods, or treatments leading to patent applications will also be included in the outcomes assessment for each project. New cross-disciplinary collaborations, especially those leading to further funding, would also be closely tracked to help assess program impact. The above measures should give the CTSI Administrative Committee a continuous readout of the productivity and efficacy of the Pilot Program. The questionnaire information summaries and

reports to the CTSI Administrative Committee on the Pilot Program will be the responsibility of the Pilot Program Co-Directors.

Quality assurance and compliance

Conflict of interest statements from all reviewers will be required at each review meeting to maximize fairness of the review process. Also, all investigators at the University of Rochester are required to submit updated conflict of interest statements annually as a requirement for conducting research at the Institution. We will use a "just-in-time" approach for IACUC and IRB approvals, which will be required to be submitted and approved before the funding of any meritorious pilot project can proceed. The University of Rochester has a robust infrastructure for the review and approval of all animal and human subjects research, and complies with all federal and NIH regulatory requirements. Our Office of Research Project Administration assists in assurance of compliance with regulatory requirements for all funded research. All mandatory training requirements, biosafety requirements, and HIPAA requirements are strictly enforced, both at the Medical Center and all remote patient care and research sites. The Coordination Committee of the Pilot Program will evaluate all proposals for regulatory compliance prior to approving funding, and any breaches in compliance will result in appropriate reporting and immediate discontinuation of the project and its funding.

G2B5. Novel aspects of the University of Rochester Pilot and Collaborative Translational and Clinical Studies Program

A number of features of the proposed CTSI at the University of Rochester are new, and the Pilot and Collaborative Studies Program will help to advance and build these new areas. The Novel Clinical and Translational Methodologies Program, Biomedical Informatics Program, Participant and Clinical Interactions Resources/GCRC Program, and Regional Clinical and Translational Research Consortium would all be programmatic components of the CTSI, which would be supported by the proposed Pilot and Collaborative Studies Program. This coordinated interaction between these key elements of the University of Rochester CTSI will enable funding for pilots deriving from investigators involved in these Program Functions to obtain the preliminary information needed to launch new translational initiatives and collaborations.

Several novel features are incorporated into this Key Function which utilizes a high degree of flexibility to maximize the impact of pilot funding on the CTSA overall. Novel features of the Pilot and Collaborative Studies Program include minority support fellowships for trainees, support for non-hypothesis and technological development projects; travel awards to stimulate inter-institutional collaboration and enhanced importation of crucial skills, models, methods, and technologies. In addition, the creation of interdisciplinary conferences or symposia to catalyze research group interaction around a specific topic, and internally and externally disseminate information to stimulate collaboration, is another innovative feature of the Program. Finally, the creation of interactions among the pilot funding key functions (See Key Function Interactions below) to leverage resources which can be used to co-sponsor specific awards, adds a further innovative approach.

Examples of Pilot and Collaborative Studies at the University of Rochester

The University of Rochester Medical Center investigators have created a number of unique and highly productive collaborative and translational programs, providing paradigms for further expansion of these or similar efforts. In addition, several areas have developed strong translational directions, including the Neuroscience components (Departments of Neurology, Neurosurgery, Neurobiology and Anatomy, and the Center for Aging and Development), Cardiovascular, the Cancer Center, and the Center for Musculoskeletal Research. There are a number of prominent examples of such programs which have started from relatively small-scale collaborative interactions.

In the Center for Musculoskeletal Research (CMSR), several recent examples of pilot projects leading to new translational programs and NIH submissions have occurred. A collaborative project between immunology and skeletal researchers has led to identification of a novel bacterial antigen associated with osteomyelitis, a new serum test for osteomyelitis, and the possibility for a novel immunotherapy technique for treatment of resistant bone infection. This has a very high level of potential impact on the clinical diagnosis and management of problematic bone infections, and derived from a small translational pilot project using a mouse osteomyelitis model. Collaboration between the CMSR, endocrinology, and the Cancer Center exploring parathyroid hormone (PTH) and parathyroid hormone-related peptide signaling in osteoblastic cells has led to the finding of crosstalk between these populations, with stimulation of hematopoietic stem cells by PTH. This has led to a Pugh scholarship, a new RO1 grant, and is being translated to potential treatment in bone marrow transplant patients. Interdisciplinary interactions between immunology and orthopaedics have resulted in a

new arthroscopic laser-activated gene therapy approach using adeno-associated viral vectors to enable focal gene transduction in skeletal tissues, as well as a method of revitalizing bone allograft transplants to restore bone remodeling and revascularization capability in cases of reconstructed segmental bone loss from trauma or tumors. Finally, a preliminary collaborative project between Orthopaedics and the Environmental Medicine Department has identified skeletal lead toxicity as an unrecognized risk factor for metabolic bone disease and impaired fracture healing, and has contributed materially to definition of a new field, osteotoxicology. This has resulted in a large NIH program project award on skeletal lead toxicity, and a Department of Defense grant to study nicotine toxicity to fracture healing.

The collaborations between the Center for Immunology and Vaccine Biology, Microbiology, Pediatrics, and Infectious Disease have led to major advances in treatment of infectious diseases with national impact. A number of years ago the *H. influenzae vaccine,* which has practically eradicated these infections in children, was developed in the Department of Pediatrics through collaborative interactions at the University of Rochester. More recently, such interactions have produced the Human Papilloma Vaccine currently being licensed by the University of Rochester for preventive treatment of cervical carcinoma. An immunotherapy spin-off company of the University, Vaccinex, has also been an outgrowth of cross-disciplinary collaborations at the Medical Center.

The Cancer Center and Department of Medical Genetics are involved in current collaborations to develop genetic diagnostic screening technologies for diseases, along with the involvement of the Department of Biostatistics and Computational Biology. In addition, the Cancer Center has developed a large and nationally-known clinical research effort in the treatment of lymphoma, with several novel treatments in pivotal trials which have arisen out of collaborative interactions. A recent collaborative project on cancer stem cells has helped pave the way for some novel drug treatments of bone marrow malignancies by targeting the NFkB signaling pathway. Interactions between Radiation Oncology, Pulmonology, and the Cancer Center have led to establishment of the Center for Biophysical Assessment and Risk Management Following Irradiation, funded by the NCI.

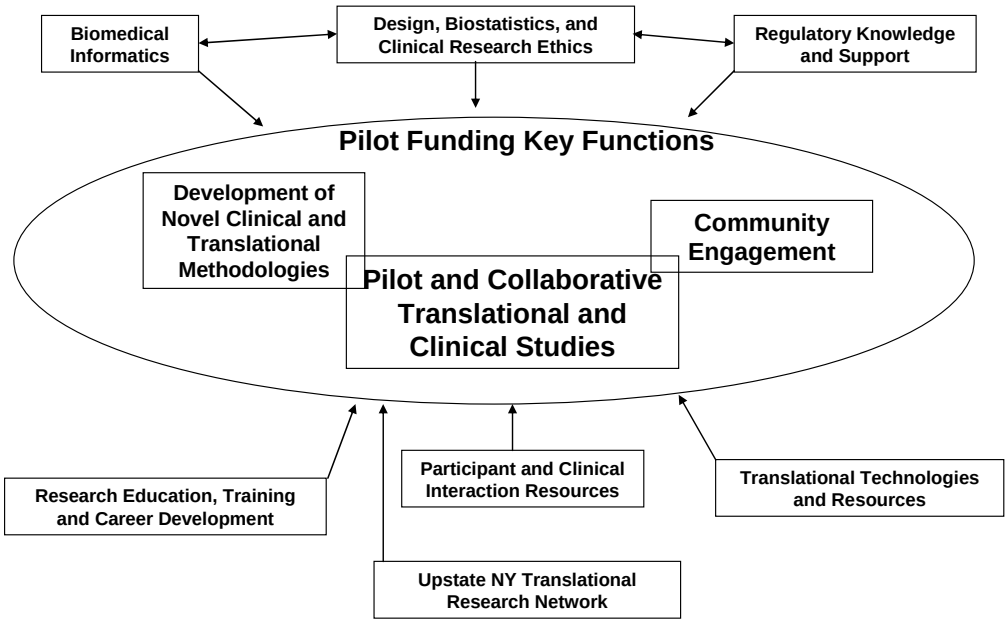
The large group of Neuroscience Centers and Departments at the Medical Center represents one of the major successes of the Institution, and is a major area of emphasis of the current Medical Center and University strategic plan, given the existing strengths and range of future opportunities. Some examples of collaborative and pilot studies leading to new programs of translational and clinical research include the creation in the Center for Aging and Development of genetic murine models of Parkinson's disease and Alzheimer's disease, which represent the early phase of Translation 1 types of research. The Department of Neurology carried out, as part of a long-term multi-institutional effort, the initial studies validating the use of prednisone as a treatment for muscular dystrophy, which has subsequently been adopted worldwide and is the only current effective treatment for the disease. This has also led to current epidemiologic long-term treatment outcomes studies in collaboration with the Centers for Disease Control of muscular dystrophy subtypes by these investigators across all of New York State, providing a strong example of two-level translational research, ultimately all the way from bench to community. Another important example in the neuromuscular field developed at Rochester is the use of IGF-1 for treatment of myotonic dystrophy, which has gone from bench to bedside, now in clinical trials with a new reagent (IGF-1 conjugated with IGFBP3) with promise of efficacy without side effects of free IGF-1.

In our Department of Emergency Medicine we have nurtured multidiscipline, collaborative studies to refine the diagnosis and develop new approaches to treatment of mild traumatic brain injury in adults and children, an injury that affects over 1.2 million Americans annually. This research began as a pilot study by two young emergency medicine physicians. Through collaboration with basic researchers in Center for Aging they are evaluating new potential biomarkers of axonal injury and through collaboration with colleagues in the Department of Radiology they are performing diffusion tensor imaging to detect axonal damage after concussion. Two intramural grants from the Center on Aging have supported these pilot studies. One of the young physicians, after completing his MPH, has pursued this research as a part of his Mentored Career Development Award (K23). He has developed preliminary data and submitted an RO1 application that has received a priority score of 151. Notification about funding is pending. This example provides further evidence of the commitment of the University of Rochester Medical Center to developing and supporting multidiscipline, collaborative research by young investigators and providing them with mentoring from all the pertinent disciplines that impact on the research being pursued.

G2B6. Key Function Interactions

The Key Functions of the Pilot and Collaborative Studies Program are grouped below in Fig. G2B3 indicating the manner in which interactions will be facilitated. The Development of Novel Clinical and Translational Methodologies and Community Engagement functions incorporate pilot funding programs, and therefore will interact directly with the Pilot and Collaborative Translational and Clinical Studies program. As described previously, this will entail representation on the Coordination Committee by ad hoc members of those two Key Functions, who will have two roles. The first will be to identify pilot proposals that achieve aims of Key Functions that overlap, enabling co-sponsorship of some projects by more than one of the Pilot Funding programs to leverage resources. The second role will be in the review of solicited abstracts to provide feedback to applicants from whom full proposals will be requested. In this capacity, the ad hoc Coordination Committee members will provide valuable feedback to applicants at this early stage to identify other Key Functions and CTSI resources which investigators or trainees can take advantage of to enhance their proposals in terms of study design and methods. This will help to provide integration across Key Functions and enhance the quality of submitted research proposals for pilot funding. The Biomedical Informatics; Design, Biostatistics, and Clinical Research Ethics; and Regulatory Knowledge and Support functions will be called on to cooperatively assist investigators in the study design (depicted at the top of Figure G2B3), while the other Key Functions will also be resources which can be utilized and incorporated in applications for the various categories of awards of the Pilot and Collaborative Translational and Clinical Studies. These relationships are depicted schematically below:

Fig. G2B3. Key Function Interactions with Pilot and Collaborative Translational and Clinical Studies



G2C. BIOMEDICAL INFORMATICS

G2C1. Specific Aims

Biomedical informatics is an important component of clinical and translational science (CTS) [1-2]. It provides informatics services to facilitate communication within the University of Rochester (UR) Clinical and Translational Science Institute (CTSI) and with the external collaborating organizations at the local, regional, and national levels, addressing issues such as sharing of data, knowledge, and other resources, and development and adoption of standards and protocols to ensure interoperability. More importantly, biomedical informatics can be applied as a novel methodology for CTS to improve the research translation process and to disseminate best practices in routine care. To address these aspects of its function, we propose the following specific aims for the biomedical informatics key function of the UR CTSI:

Specific Aim 1: Facilitate General Communication and Coordinate Use of the Existing Biomedical Informatics Resources.

1a. Provide general communication service for CTS activities, including delivery of online information, announcement of news/events, and dissemination of new methodologies, technologies, etc.

1b. Promote awareness of the existing informatics resources for data management, clinical trials, modeling and simulation, process management, behavioral intervention, and research administration and regulation, which are currently distributed in individual departments, centers, divisions, and labs.

1c. Provide routine consulting service to CTS investigators and trainees to select appropriate informatics resources to ensure their efficient and effective use.

Specific Aim 2: Incrementally Integrate the Existing Biomedical Informatics Services with Additional Developments to Eventually Formulate a Local Information Infrastructure that Provides Context-Specific and Integrated Support to CTS Activities at Different Stages of Their Lifecycle.

2a. Based on 1, identify requests to enhance current informatics support and to provide additional services for CTS activities at different stages of their lifecycle, with specific focus on: (1) collection, storage, processing, and integration of research data; (2) development of mathematical/statistical models to generate and to test new hypotheses through computer simulations; (3) identification of eligible research subjects; (4) monitoring and control of clinical trial processes; (5) generation of behavioral interventions to implement best practices in clinical care; and (6) administration and regulation of research.

2b. Based on 2a and 3a (described below), incrementally integrate the existing informatics resources and develop new functions in alignment with specific CTS activities to eventually create a local information infrastructure to facilitate one-stop information shopping for CTS research, operation, and administration.

Specific Aim 3: Facilitate Data Sharing and Process Knowledge Reuse Through Adoption and Development of Biomedical Informatics Standards and Protocols.

3a. Coordinate with standard development organizations (e.g., Health Level 7 (HL7) and Clinical Data Interchange Standards Consortium (CDISC)), other CTSA programs, and collaborating parties to adopt existing standards for data encoding and to develop new standards and protocols for data integration and process knowledge (e.g., clinical trial and practice guideline) representation, such that they can be used for 2b, 3b, and 4.

3b. Based on 3a, provide informatics services to support data sharing and process knowledge reuse within the UR CTSI and with the external collaborators in the local communities (e.g., Rochester regional health information organization (RHIO)), regional consortia (e.g., Upstate New York Translational Research Network (UNYTRN)), federal agencies (e.g., NIH and FDA), and other CTSA programs.

Specific Aim 4: Based on 1, 2, and 3, Assess and Optimize Individual Biomedical Informatics Services and their Integration, with Specific Focus on: (1) their Actual Use in CTS Activities, (2) User Feedback, and (3) the Impact on the Research Translation Process and the Dissemination of Knowledge in Clinical Practice.

We expect that the informatics services provided and the information infrastructure developed from this project will improve the efficiency and effectiveness of CTS activities. In addition, we expect that the standards and protocols adopted and developed from this project will facilitate data sharing and knowledge reuse within and across institutions. Finally, we expect that the framework developed from this project to integrate data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention in alignment with the CTS activities will provide a novel methodology to facilitate clinical and translational research, which can be set up as a model to be generalized to other institutions.

G2C2. Background and Significance

Addressing information needs is critical to all research activities, from conceptualization of studies, through execution of protocols, to dissemination of results. Since the 1960s, information technology has been applied to biomedical research [3] for general communication and specialized services such as data collection and storage [4-

5], data integration [6-8], model development [9-10], computer simulation [11], clinical trial facilitation [12], and behavioral intervention for health service improvement [13-14]. These services are usually developed for specific research projects, scattered throughout different sites of an institution, and not available to users other than the original developers. Meanwhile, many of these services can and should be shared to serve a larger pool of users for more efficient and effective use. Aim 1 directly addresses this issue through facilitation of general communication and coordination of the distributed informatics resources. These experiences will also contribute to the further work proposed for aim 2.

Information flow during the process of clinical and translational research requires integration of individual services to provide context-specific and integrated informatics support [15]. For example, development of a disease progress model usually requires integration of experimental data with clinical data, feeding of these data into a mathematical/statistical modeling tool, and validation of the model through computer simulations. Without the appropriate integration of multiple services in specific context, it would be impossible to conduct such studies. Yet little previous research investigated how individual pieces of informatics services could be integrated together to provide context-specific support for CTS. Consequently, there is little understanding on the overall process of CTS and the request for informatics support at each stage of its lifecycle. Aim 2 directly addresses this issue through investigation on how various informatics services can be integrated in alignment with specific CTS activities. The information infrastructure developed for this purpose will be the foundation for the further work proposed for aims 3 and 4.

Development and adoption of biomedical informatics standards, although considered to be critical to the success of information exchange and system interoperability [16], have not yet been sufficiently investigated. Most previous standardization work focused on controlled medical terminologies for clinical data encoding [17-18], which is only a first and essential step to facilitate information exchange. Additional work on standard and protocol (mechanism to use standards in specific informatics service) development is desperately needed for data integration and process knowledge representation, which are widely used in CTS [6-8,12]. Without such standards and protocols, it would be impossible to integrate data and disseminate knowledge on a larger scale, which in turn would significantly thwart key CTS activities. Aim 3 directly addresses this issue through adoption and development of standards and protocols to facilitate data sharing and process knowledge reuse. These standards and protocols will also be used for the work proposed for aim 2 and 4.

Research to define and to improve the integrated informatics services for CTS activities are expected to be crucial, yet they have not been adequately assessed [19]. It is not well understood how context-specific informatics services, which have been shown to be critical to success in other domains [20-21], can facilitate CTS. Additional studies are thus required to better understand how informatics services can improve the process and outcome of CTS. Aim 4 directly addresses these issues through assessment of the use of informatics services and their impact on the research translation process and the dissemination of best practices in routine care. The knowledge obtained from this assessment will direct our future work to provide better informatics services for CTS.

In summary, the proposed biomedical informatics component of the UR CTSI will take advantage of the existing informatics resources and develop new functions to provide support to various CTS activities at different stages of their lifecycle. In particular, it will directly address several critical issues, such as integration of various informatics services in alignment with the process of CTS activities, facilitation of intra- and inter-organizational communication based on standards and protocols, and assessment of an integrated approach to the improvement of the research translation process and the dissemination of knowledge in clinical practice. The proposed work will thus be able to significantly improve our understanding of these unexplored or inadequately investigated areas in biomedical informatics research and therefore to better serve CTS.

G2C3. Available Resources and Prior Experiences

Currently, there are several informatics resources at UR that are distributed in different departments, centers, divisions, and labs. We will begin with these resources to provide the informatics services for CTS activities. Eventually, we will develop an information infrastructure to incrementally integrate data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention. During this process, we will adopt and develop standards and protocols to facilitate data sharing and process knowledge reuse. In this section, we briefly summarize the existing informatics resources and our prior experience in the area of the proposed work.

G2C3a. Existing Biomedical Informatics Resources at UR.

The existing informatics resources at UR include faculties and staffs with expertise in data management, clinical trial support, mathematical/statistical modeling, computer simulation, process management, behavioral intervention, and research administration/regulation. These resources are currently scattered around in the Clinical Trials

Coordination Center (CTCC), the Department of Community and Preventive Medicine (DCPM), the Division of Biomedical Modeling and Informatics (DBMI), the Division of Medical Informatics (DMI), the General Clinical Research Center (GCRC), the Heart Research Follow-Up Program (HRFUP), the Miner Library, and the Research Subjects Review Board (RSRB).

The CTCC is a research unit operating since 1986 to foster multi-institutional academic research through development, management, and reporting of controlled clinical trials. The informatics services provided by CTCC focus on data management and clinical trial facilitation, with various specific tasks such as database development, data collection/storage/retrieval/sharing, case report form management, reporting, and user training. An Oracle database [22] and a suite of software tools from eResearch Technology [23] are used to support clinical trials on Parkinson's disease, Huntington's disease, HIV, Tourette's syndrome, attention deficit disorder, epilepsy, and cervical dystonia. These studies are funded by government, industry, and non-profit organizations, serving 350 academic investigators from the United States, Canada, Europe, and Australia.

The DCPM hosts health service research. The data lab within the department is funded by the Agency for Healthcare Research and Quality (AHRQ) to provide data management for various projects, focusing on data collection/storage/retrieval and reporting. Currently it manages 45 sets of survey, utilization, administrative, geographic, and population data.

The DBMI is recently established to conduct research and provide services on mathematical/statistical modeling, computer simulation, biomedical data and knowledge management, and development of clinical decision support systems. Software systems used at DBMI include mathematical/statistical modeling tools, such as MATLAB [24], SAS [25], and S-PLUS [26], Protégé-2000 knowledge acquisition tool [27], Guideline Execution Engine (GLEE) [28], and GESDOR ontology mapping tools [29]. Current research at DBMI are funded by NIH/NIAID, focusing on infectious diseases (HIV/AIDS, influenza virus) and immunology.

The DMI conducts applied medical informatics research addressing real-world problems that lead to institution-wide implementations at Strong Health. The division has ongoing collaboration with other faculties and staffs at surgery, community and preventive medicine, dermatology, pathology, DBMI, nursing, the Miner Library, the physician services of Strong Health, and the Information Systems Division of UR. Current and previous research and development include clinical data repository (CDR) and clinical data warehouse (CDW), provider portal, patient sign out system, surgical forms tracking, results notifier, medical imaging database, web-based patient profile system, and faculty database.

The GCRC is funded by NIH/NCRR to provide general support to clinical studies at UR. The informatics core of the GCRC provides data management service for these studies, focusing on database design and implementation, case report form management, protocol-specific software training, and reporting. The GCRC informatics core will be integrated into the CTSI biomedical informatics function (see Section G2C4f).

The HRFUP at UR, established since 1966, is dedicated to cardiovascular research through design, conduct, and analysis of worldwide multi-center clinical studies. Similar to CTCC, the informatics services provided by HRFUP focus on data management and clinical trial facilitation.

The Miner Library is the primary library serving the University of Rochester Medical Center (URMC) campus. It coordinates online information resources, including literature databases, e-journals, e-books, clinical evidences, drug databases, and other reference information. It also maintains most of the websites at URMC.

The RSRB is established to protect the rights and welfare of human research subjects at UR. It has recently instituted an online system for reviewing research projects, with the goal to streamline the process of submitting and tracking research applications. The system can be used to submit new applications, to make amendments, to file progress reports, and to report adverse events.

In addition to the resources described above, the UR has various bioinformatics resources, which are described in the Design, Biostatistics and Clinical Research Ethnics key function of the UR CTSI. Meanwhile, the UR has commissioned a university-wide effort to create a supercomputing initiative to support research activities across the campus. A multi-mode clustered computing center developed from this initiative will also be an important computing resource to support modeling and simulation, functional genomics computing, as well as other translational research requiring parallel processing.

To coordinate the existing informatics resources and to direct the future development, we recently created the UR Biomedical Informatics Program (BIP) [30]. Details of the BIP will be described in Section G2C4f. Table G2C1 summarizes the existing biomedical informatics resources at UR.

Table G2C1. Existing Biomedical Informatics Resources at UR

Location at UR	Expertise and Service
Clinical Trials Coordination Center	data management, clinical trials
Department of Community and Preventive Medicine	data management
Division of Biomedical Modeling and Informatics	modeling/simulation, data/knowledge management, decision support
Division of Medical Informatics	production systems, CDR/CDW
General Clinical Research Center	data management, clinical trials
Heart Research Follow-Up Program	data management, clinical trials
Miner Library	online information resources
Research Subjects Review Board	research administration and regulation

G2C3b. **Prior Experience: Development of CDR and CDW.**

The clinical data collected in electronic medical record (EMR) systems are important resources for CTS. The DMI is currently engaged in an enterprise-wide CDR/CDW development, led by Dr. David Krusch, Division Director and Chief Medical Information Officer of Strong Health. Key staffs on this project are a skilled Oracle database administrator and a system interface analyst with decade-long experience with HL7 and the local interface engine e*Gate (now Sun Microsystems) [31]. A live CDR is currently being created, with data populated from all of the clinical and demographic transactions generated by the production patient care systems. To further expand its utility for research, the data of the CDR is extracted nightly and reorganized for aggregate analyses into the CDW, which is optimized based on online analytical processing (OLAP) for cross-patient analyses. To date, the CDW includes: (a) inpatient medication data (URMC is one of the few academic medical centers in the United States with 100% inpatient CPOE), (b) all clinical laboratory data, and (c) the ambulatory data from the AllScripts TouchWorks EMR [32], which is currently used by 1000 users. The CDW is now serving many clinical investigators by generating data-marts or “snapshots” of data to help them answer questions posed by their studies in a more efficient manner, with examples such as: (a) concurrent analysis of radiology reports with pulmonary embolism and deep vein thrombosis indicators to improve patient care, (b) profiles of psychiatric medications to trigger guidelines of best practices, and (c) economic study of inpatient medication data to compare brand vs. generic prescriptions. The CDR and CDW place URMC in a unique position of being able to deliver real time, aggregated, and authoritative clinical data to our investigators.

G2C3c. **Prior Experience: Integration of Biomedical Data and Knowledge from Heterogeneous Sources.**

Integration of data and knowledge from heterogeneous sources is an important informatics service for CTS. In a previous project funded by NIH/NLM and the US Army, Dr. Dongwen Wang developed the GESDOR model of ontology mapping to facilitate biomedical data/knowledge integration [33]. This model consists of: (1) a set of local ontologies, each of which represents the data/knowledge structure from a specific domain/community; (2) a generalized reference ontology, which represents the data/knowledge structure that is extracted and integrated from individual domains/communities; and (3) a set of mapping relationships, each of which defines the mapping between an individual local ontology and the generalized reference ontology through a variety of mapping formalisms. With this model, data and knowledge from heterogeneous sources can be virtually integrated into a centralized view defined by the reference ontology without physical migration. During this process, the mapping relationships are used as rules to direct the translation and integration of the data/knowledge instances from each local site to generate the centralized view. To facilitate data/knowledge integration under this model, an editing tool and a set of guiding principles were developed to assist the specification of the mapping relationships. In addition, a parser of the mapping relationship was developed to automatically perform data/knowledge translation. This model has been applied to share clinical guidelines encoded in different formats and to create the links between medical errors and the underlying cognitive factors. It was proposed at HL7 as an initial framework for harmonization of guideline representation models. Additional technical details of this work can be found elsewhere [33].

G2C3d. **Prior Experience: Development of Mathematical/Statistical Models for Clinical Trial Simulations.**

Optimizing the design of complex clinical trials is a challenging issue for CTS. The combination of mathematical/statistical modeling and computer simulation can be used as a powerful tool for this purpose. Dr. Hulin Wu, the PI of several NIH/NIAID-funded projects, has extensive prior experience in use of this approach to improving the design of AIDS clinical trials [34]. Specifically, he and collaborators developed mathematical/statistical models for drug exposure [35] and HIV viral dynamics [36]. They incorporated these models into computer

simulation systems to facilitate the design of clinical trials of specific antiretroviral therapy for AIDS patients. Since computer simulation incorporated with domain-specific mathematical/statistical models can be used to project the process and outcome of specific clinical trials, it thus can help to optimize the setting of specific parameters at the design stage, which in turn can significantly improve the efficiency and effectiveness of clinical trials.

G2C3e. **Prior Experience: Development of Computer Systems for Healthcare Process Management.**

Computer systems can be used for healthcare process management to facilitate implementation of clinical trials and best practices. Dr. Dongwen Wang has previously participated in an NIH/NLM-funded project to develop the GuideLine Interchange Format (GLIF) [37-38], one of the most widely reported computer-based models to represent healthcare process. GLIF was originally developed as a template to implement clinical practice guidelines, but has also been used to facilitate critical pathways, clinical trials, and other healthcare processes in a variety of clinical domains. To interpret the process knowledge encoded in the GLIF format, Dr. Wang developed the GLEE engine [39]. This tool can be integrated with clinical databases to generate patient-specific recommendations in particular context of a healthcare process. When integrated with specific applications, these recommendations can be delivered as behavioral interventions in an appropriate format that best fits clinical workflow. GLIF and GLEE have been applied to address clinical problems such as improvement of immunization rate, facilitation of post-CABG critical pathway, screening of patients with major depression, documentation of foot care for diabetes patients, and HIV/AIDS patient management. GLIF was also proposed at HL7 as an initial framework for development of a standard guideline representation model. Additional technical details of GLIF and GLEE can be found elsewhere [37-39].

G2C3f. **Prior Experience: Delivery of Behavioral Interventions through Information Systems for Best Practices.**

Dissemination of best practices in routine care is a critical component of CTS. Using information systems to deliver behavioral interventions in appropriate formats to implement best practices is an important approach for this purpose. Dr. Dongwen Wang previously participated in a CDC-funded study that used an information system to generate behavioral interventions in different formats to improve childhood immunization rate [40]. In that study, he was the primary developer of the clinical decision support component of a web-based multi-institute childhood immunization registry, the EzVac system [41]. Various approaches were designed in EzVac to automatically generate interventions that were tailored to an individual patient [42]. A randomized clinical trial was performed to investigate the effectiveness of two such approaches, and the results showed that one of them contributed to the significant improvement of childhood immunization rate [40].

G2C4. Methods

As outlined in previous sections, the proposed biomedical informatics key function of the UR CTSI includes coordination of the existing informatics resources, incremental development of a local information infrastructure for CTS, adoption and development of standards and protocols for intra- and inter-organizational data sharing and knowledge reuse, and assessment of the informatics services and their impact on CTS. In this section, we describe the details of the methods in order to achieve the specific aims listed in Section G2C1.

G2C4a. **Facilitating General Communication and Coordinating the Existing Informatics Resources (Specific Aim 1).**

To provide informatics support to CTS activities, we will start from providing general communication service for the CTS community. During this process, we will focus on coordination of the existing informatics resources for more efficient and effective use. In addition, we will provide routine consulting service to investigators and trainees for their clinical and translational research.

1) Providing General Communication Service. The general communication service will focus on conventional approaches of information dissemination, such as delivery of online resources and announcement of news and events. For this purpose, we will work together with the Miner Library, the other UR CTSI functions, and external collaborators to develop a UR CTSI website to provide the following services: (1) general information about the UR CTSI, (2) regular announcement of all CTS-related news and events, (3) links to online CTS information resources, such as funding opportunities, administration and regulation of research, biomedical informatics, biostatistics, and other supporting services, and (4) publications and documentation about the latest CTS methodologies, technologies, and other resources. In association with the website, we will work with the other UR CTSI functions to provide the following services: (1) support to seek user feedback on their requirements for specific CTS services through emails or online comments, and (2) sending out email notifications of CTS news, events, funding opportunities, etc. Eventually, we will integrate the UR CTSI website and the associated informatics services with the CTS information infrastructure that will be developed for this project (see Section G2C4b).

2) Promoting Awareness of the Existing Informatics Resources. To promote awareness of the existing informatics resources, we will work together with the informatics faculties and staffs in different departments, centers, divisions, and labs to identify the details of the available existing resources at each place, including personnel, expertise, available services, running systems, and software tools. Based on this information, we will promote awareness of the existing resources through advertising in university directories and websites, in-person consultations, and educational efforts such as courses, seminars, and workshops. Currently, the BIP website has been developed to link to the specific informatics resources at UR. A new course, Introduction to Health Informatics, has been recently approved by the Committee on Graduate Studies and will be taught by Dr. Dongwen Wang starting from Fall 2006. This course will introduce our existing informatics resources and will be open to all graduate students, fellows, and faculties of the medical campus as well as graduate and senior undergraduate students from a related field (computer science, information science, cognitive science, statistics, etc.) of the river campus of the university.

3) Providing Routine Consulting Service to CTS Investigators and Trainees. To support CTS activities, we will provide routine consulting service to CTS investigators and trainees. The consultation will focus on selection of appropriate informatics services from the existing resources, with two specific goals: (1) to ensure that the resources selected will effectively serve their CTS activities, and (2) to ensure the shared use of the resources for better efficiency. We will hire an informatics service coordinator in BIP to do the initial triage and to direct the CTS investigators and trainees to specific resources for additional specialized services. With the incremental development of the local information infrastructure for CTS (see Section G2C4b), the consultation will gradually transit to focus more on taking advantage of the services provided by the infrastructure. Thus, it will continuously be a critical part of our informatics support. Although the consultation will be open to all CTS personnel, we will work together with the CTS training program to develop specific mechanisms to pay special attention to serving the needs of junior CTS investigators and trainees.

G2C4b. **Incremental Development of a Local Information Infrastructure for CTS (Specific Aim 2).**

Based upon the existing informatics resources, we will incrementally develop a local information infrastructure to provide context-specific and integrated informatics services for CTS. For this purpose, we will take a user-centered approach to the design and implementation of the informatics infrastructure [43]. Specifically, we will start from analyses of the CTS activities and identification of the requests for informatics support at each stage of their lifecycle. Based on these analyses, we will incrementally integrate the existing informatics resources and develop new functions in alignment with the CTS process. The overall development will be an iterative process with multiple rounds of analysis, design, implementation, and evaluation.

1) Analyses of CTS Activities and Identification of Requests for Informatics Support. To analyze the CTS activities, we will first pick up an initial set of key stakeholders involved in CTS, including, but not limited to, lab scientists, clinical investigators, data managers, statisticians, technicians/staffs, administrators/regulators, educators, external collaborators, funding/sponsoring organizations, and state/federal regulatory agencies. We will then establish focus groups to analyze typical use cases that involve these stakeholders. For each case, we will identify the role of specific stakeholders, as well as their collaborations in CTS. The selection of the use cases will address the CTS activities at particular stages of their lifecycle, from research planning (synthesis of hypothesis, design of research, plan for evaluation, etc.), through protocol execution (recruitment of subjects, monitoring of research process, administration and regulation of research, etc.), to dissemination of results (validation of mathematical/statistical models, delivery of behavioral interventions to implement best practices, etc.). During this process, we will pay special attention to identify the potential informatics services that might help specific stakeholders to perform particular tasks for their CTS activities. These stakeholders will be the potential users of the proposed local information infrastructure for CTS. For this purpose, we will conduct surveys, interviews, and

observations. We will use the Unified Modeling Language (UML) [44] as a tool to assist us to better understand user requirements, including individual tasks performed by users, collaborations among users, potential system functions, and interactions between users and systems.

Based on an initial survey of experts and literature, the existing informatics resources, and the expertise of our biomedical informatics team, we will focus on the following informatics services for the initial analyses:

a) *Management of Research Data*. This will include essential data management, such as collection, storage, and retrieval of data, as well as advanced data management, such as transformation and integration of research data. Analyses will focus on: (1) data elements, attributes, and values to define the variables of specific research experiments, such as patient characteristics, biological specimens, and other experimental materials; (2) data elements to define and to characterize the research projects themselves, such as administration/regulation data, lab experiment workflow, clinical trial protocols, patient visits, etc.; (3) use context of data elements in specific CTS activities and overall CTS process; (4) common data that are used in multiple scenarios of CTS activities; and (5) potential system functions that can be integrated with CTS workflow to assist data collection, retrieval, transformation, and integration. These analyses will drive the development of databases, virtual integration of research data, and implementation of applications to facilitate overall CTS workflow (see Section G2C4b 2).

b) *Development of Mathematical/Statistical Models for Syntheses and Validations of Hypotheses*. Analyses will focus on: (1) domain-specific mathematical/statistical models that might help to synthesize new research hypotheses, (2) domain-specific mathematical/statistical models that can be implemented in computer simulations to test specific hypotheses, (3) data elements related to the development of such models, (4) use context of such models in specific CTS activities and overall CTS process, and (5) potential system functions that can be integrated with CTS workflow to incorporate these mathematical/statistical models for hypothesis generation and testing. These analyses will drive the development of domain-specific mathematical/statistical models, performance of clinical trial simulations, and implementation of functions to facilitate overall CTS workflow (see Section G2C4b 2).

c) *Identification of Potentially Eligible Subjects for Specific Research.* Analyses will focus on: (1) criteria to define eligible subjects for specific research, (2) data elements related to such eligibility criteria, (3) use context of research subject identification in specific CTS activities and overall CTS process, and (4) potential system functions that can be integrated with CTS workflow to help recruit potentially eligible subjects for specific research. These analyses will drive the development of system functions to facilitate clinical trial subject recruitment and to improve overall CTS workflow (see Section G2C4b 2).

d) *Monitoring and Control of Clinical Trial Process to Improve Compliance with Research Protocols.* Analyses will focus on: (1) individual context in clinical trial process when monitoring and control are required, (2) data elements related to monitoring and control of clinical trial process, (3) use context of monitoring and control of clinical trials in specific CTS activities and overall CTS process, and (4) potential system functions that can be integrated with CTS workflow to monitor and control clinical trial process for better compliance with research protocols. These analyses will drive the development of system components to facilitate performance of clinical trials and to improve overall CTS workflow (see Section G2C4b 2).

e) *Generation of Behavioral Interventions to Implement Best Practices in Clinical Care Analyses will focus on*: (1) targets of behavioral interventions, (2) appropriate formats and use contexts of behavioral interventions to implement best practices, (3) data elements related to generation of behavioral interventions, (4) use context of behavioral interventions in specific CTS activities and overall CTS process, and (5) potential system functions that can be integrated within CTS workflow to generate behavioral interventions for best practices. These analyses will drive the development of system components to facilitate dissemination of best practices in routine care and to improve overall CTS workflow (see Section G2C4b 2).

f) *Administration and Regulation of Research.* Analyses will focus on: (1) requirements of research administration and regulation, (2) data elements related to research administration and regulation, (3) use context of research administration and regulation in the specific CTS activities and overall CTS process, and (4) potential system functions that can be integrated with CTS workflow to facilitate research administration and regulation. These analyses will drive the implementation of applications to facilitate overall CTS workflow (see Section G2C4b 2).

As shown in the previous description, these services constitute the backbone of the proposed information infrastructure. They interweave with each other to support CTS activities. We will describe the technical details of their integration in Section G2C4b 2.

2) Incremental Integration of Existing Informatics Resources and Development of New Functions. Based on the analyses described in the previous section, we will incrementally integrate the existing informatics resources and develop new functions in alignment with the overall CTS process, such that they will eventually constitute a

local information infrastructure to support CTS activities at particular stage of their lifecycle. Specifically, we will focus on the following aspects of integration and development:

a) *Development of a Process-Oriented Web Portal to Integrate Various Informatics Services for CTS*. The ultimate goal of our work is to provide one-stop information shopping for CTS. For this purpose, we will develop a process-oriented web portal to integrate various informatics services for CTS. We will use a three-tier architecture when developing this application, with a web-based user interface at the front-end, CTS business logic in the middle layer, and various databases, process knowledge base, and individual informatics service modules at the back-end.

At the front-end, the web portal will provide the user interface to serve individual users in conducting specific CTS activities for a particular research project, and thus the information presented and service available will be customized to address the needs in that context. In addition to supporting the current CTS tasks for an individual user, the front-end system will also provide a cross-sectional view of the CTS activities such that all relevant stakeholders will know each other's progress when performing collaborative tasks. Meanwhile, the front-end web application will support the browsing of activities that have already been finished and the projection of activities that have been planned for the future, thus providing a longitudinal view to the overall CTS process. Furthermore, the front-end system will facilitate communication among users (e.g., email exchanges between an institutional regulator and a principal investigator about specific regulation issues) and generation of behavioral interventions to better serve specific CTS activities (e.g., pop-up windows to remind a clinical trial coordinator to perform specific tasks according to a research protocol). Finally, the front-end web portal will provide flexibility in its customization such that a user can configure the information presented and service supported according to his/her individual preference.

In the middle layer, we will develop separate modules to deal with the business logic of CTS activities, which depends on individual research projects, stakeholders, overall CTS process, specific tasks, collaboration among users in that context, and interfaces with the front-end presentation and the back-end data. We will also define the context for integration of individual informatics services at this layer. To provide flexibility in definition of CTS business logic, we will encode them using a standard process knowledge model, the development of which will be described in Section G2C4c 1. The CTS business logic encoded in the standard format is then interpreted at runtime such that the services provided can be tailored to the context-specific needs.

At the back-end, the system will be integrated with various databases, process knowledge base, and individual informatics service modules. Here the databases are used to store research and administrative data. They include several existing databases distributed across individual departments/centers as well as a centralized UR CTSI database that we will develop. We will describe the details of these databases next. The knowledge base here is used to store clinical trial protocols, practice guidelines, and CTS processes. In addition to supporting specific informatics services at the UR CTSI, they will also be used for knowledge reuse across institutions. We will describe the details of process knowledge reuse in Section G2C4c 2. Individual informatics service modules here are self-contained software components to perform specific functions, such as virtual integration of data, development and validation of mathematical/statistical models, simulation of experimental process, facilitation of clinical trials, and delivery of behavioral interventions. We will describe the details of these modules next.

b) *Providing Integrative Views to Research Data Through Virtual Integration*. Providing integrative views to research data is an important aspect of data management for CTS. It can be used for various purposes, such as generation and testing of new hypotheses, development and validation of mathematical/statistical models, and facilitation of clinical trials. We will take two approaches to providing integrative views to research data: (1) integration of data from multiple contexts of a CTS process, and (2) integration/aggregation of data from multiple databases. During this process, we will develop mechanisms to ensure compliance with HIPAA and other regulatory requirements.

When integrating data from multiple contexts of a CTS process, we will focus on context-specific data attributes (e.g., the timestamp of a data entity). With a standard process knowledge model to encode CTS processes and a standard entity-attribute-value model [45] to encode data (see Section G2C4c 1), we will be able to identify the same data entity in different contexts of a CTS process. By grouping these data together, we will be able to investigate the relationship between data value and context-specific data attributes (e.g., the secular trend of the value of a specific variable).

When integrating/aggregating data from multiple databases, we will take an approach that is based on an enhancement of the GESDOR ontology mapping model [33]. Specifically, we will relax the requirement that the ontology representation has to follow specific syntax, such that the model can be generalized from Protégé ontology [27] to relational data model, which is used by most databases to organize their data. Meanwhile, we will enhance our ontology mapping tool such that it can be used to create schema mapping between relational databases. This

mapping can then be used to transform data formats such that common data stored in multiple databases can be pooled together to formulate data sets with a larger sample size.

In contrast to physically migrating data to a centralized database, we will only provide integrative views through virtual data integration at the initial stage. In addition to providing maximum flexibility such that a researcher can easily explore different ways to integrate data, this approach will avoid difficult organizational issues since several of our existing databases are developed and managed by different departments/centers. Furthermore, this approach can be easily applied to facilitate data integration across institutions, in which case a distributed rather than a centralized model is more appropriate. However, we will plan to develop a common UR CTSI data repository. This common UR CTSI data repository will serve new CTS research projects. As a long-term goal, we will gradually migrate data distributed in different places to this common UR CTSI data repository as our information infrastructure becomes more mature in the future.

c) *Providing Support for Development and Validation of Mathematical/Statistical Models*. Mathematical/statistical modeling is widely used in CTS. To support the development and validation of mathematical/statistical models, we will adopt commercial products, such as MATLAB, SAS, and S-PLUS, to integrate with the UR CTSI web portal. We will develop the interface between these mathematical/statistical modeling tools and the UR CTSI databases and data views. These functions can then be used by investigators for initial explorations or by professional statisticians/modelers for formal analyses.

d) *Providing Support for Experiment Process Simulation.* Simulation of experiment process is an important approach to facilitating the test of new hypotheses and design of clinical trials. We will enhance existing tools as well as adopt commercial products to support two types of process simulation: (1) an individual subject's pathway in a predefined experiment process, and (2) population characteristics at specific stages of an experiment process.

For simulation of an individual subject's pathway in a predefined experiment process, we will enhance the GLEE system [39] such that it can be applied to general experiment processes. For simulation of population characteristics at specific stages of an experiment process, we will enhance the batch execution mode of the GLEE system such that the simulation results of individual subjects can be aggregated together to derive population characteristics, which can then be processed by mathematical/statistical modeling tools. We will also explore the possibility to adopt commercial products such that they can be used for this purpose.

e) *Facilitation of Subject Recruitment and Process Monitoring/Control for Clinical Trials.* As a key CTS process, clinical trial deserves special consideration. The eRT software tools [23] are already in use at UR to facilitate clinical trial data collection and reporting. Based on these experiences, we will develop and enhance additional tools to facilitate clinical trials, with two specific focusing areas: (1) facilitation of subject recruitment and retention, and (2) monitoring and control of clinical trial process.

To facilitate identification of eligible subjects for clinical trials, we will develop a new function to link the subject recruitment criteria of clinical trial protocols with the integrative views of clinical databases. This function can be used to search multiple clinical databases through the integrative views such that a maximum number of potentially eligible subjects can be identified. Since the recruitment criteria of clinical trial protocols will be a standard component of the CTS process knowledge model (see Section G2C4c 1) and the integrative views of multiple databases will be another function that we will develop (see previous description), implementation of this linking function will be straightforward.

To facilitate monitoring and control of clinical trial process, we will enhance the GLEE system [39] such that it can be applied to monitor the execution of each step of a clinical trial process as defined by the protocol. Specifically, we will extend the interactive execution mode such that recommendations of specific tasks defined by the protocol can be generated and tailored to an individual subject. These recommendations are then delivered through an appropriate format of behavioral interventions to clinical trial staffs/coordinators/managers such that they can perform these tasks in accordance with protocol requirements. Meanwhile, we will implement another function to monitor the tasks that are actually performed by clinical trial staffs/coordinators/managers through regular query of relevant databases, such that reminders can be generated once these tasks deviate from those defined by the protocol. These reminders are then delivered through an appropriate format of behavioral interventions to specific persons such that they can take proper actions to address these deviations for better compliance with clinical trial protocols.

f) *Delivery of Behavioral Interventions for Best Practices.* Dissemination of best practices is a critical component of CTS. One approach to implementing best practices is to use information technology to deliver behavioral interventions in appropriate formats to specific targets. For example, in order to facilitate clinical trial execution, we can generate reminders of specific tasks that need to be performed in a particular context according to the definition of the clinical trial protocol. These reminders can be tailored to an individual subject and delivered to

an appropriate target person (e.g., a clinical trial coordinator who is in charge of that subject) through a proper format (e.g., a pop-up window with a list of tasks that need to be performed when the clinical trial coordinator opens the record for that subject).

To facilitate the dissemination of behavioral interventions for best practices, we will adopt and enhance the information routing model of the EzVac system [42] and develop a tool such that: (1) it can be combined with the CTS process model and the integrative data views to generate context-specific interventions, (2) it can be used to pick up individual stakeholders of CTS as the targets to deliver behavioral interventions, and (3) it can be integrated with the UR CTSI web portal, online information resources (e.g., literature database, clinical evidence, pharmacy information, etc.), telecommunication systems (e.g., email, pager, phone, fax, etc.), and other mechanisms to deliver the interventions in an appropriate format. We will use this tool to deliver behavioral interventions in clinical trial process to help improve compliance with clinical trial protocols, as described previously. We can also use this tool to deliver behavioral interventions in routine care, such as for community outreach, to help improve health services.

In summary, we will develop, enhance, and adopt a variety of informatics functions and integrate them under the UR CTSI web portal. This integration will be in alignment with CTS processes such that the local information infrastructure developed can provide effective support to various CTS activities at each stage of their lifecycle. Table G2C2 summarizes the new developments and their integration with the existing resources to build the local information infrastructure.

Table G2C2. New Developments and their Integration with the Existing Resources

New Development	Function/Goal	Existing Resources to be Integrated
process-oriented web portal for CTS	integration of existing resources	all
integrated data views	virtual integration of research data	data management
mathematical/statistical modeling tools	integration of modeling tools	data management, computer simulation, clinical trial, process management
process simulation tools	integration of simulation tools	data management, modeling, process management
clinical trial facilitation	subject recruitment, process monitoring and control	data management, process management, behavioral intervention
behavioral intervention	implementation of best practices	data management, clinical trial, process management

3) *Iterative Development, Continuous Evaluation, and Proactive Maintenance.* It is important to note that the development of the local information infrastructure is an incremental and iterative process. At the early stage, we will focus on routine administrative functions, such as essential management of research data and administration/regulation of individual CTS projects. Eventually, we will move to data integration, mathematical/statistical modeling, process simulation, clinical trial facilitation, and behavioral intervention. During this process, we will continuously evaluate the functions that have been developed (see Section G2C4d). These evaluations will then be used to direct new rounds of development and maintenance, such that system errors can be corrected, specific functions can be optimized, and additional features can be included. Finally, we will develop administrative policies for the UR CTSI information infrastructure, such that its development, evaluation, and maintenance can sustain continuous growth.

G2C4c. Facilitation of Intra- and Inter-Organizational Communication Based on Standards (Specific Aim 3).

As the 3rd aim of the proposed research, we will adopt and develop biomedical informatics standards and protocols for data encoding, data integration, and process knowledge representation when building the local information infrastructure for CTS. We will then use these standards and protocols to facilitate data sharing and process knowledge reuse within and across institutions.

1) Adoption and Development of Standards and Protocols for Data Encoding, Data Integration, and Process Knowledge Representation. At URMC, we have already begun to adopt a few biomedical informatics standards in building our systems and interfaces, including: (1) controlled medical terminologies for clinical data encoding, i.e., SNOMED-CT [17], ICD-9-CM [46], and CPT4 [47], (2) standard message syntax for clinical data interchange, i.e., HL7 2.5 [48], and (3) clinical data and document reference information models, such as HL7 Reference Information Model (RIM) [49] and HL7 Clinical Document Architecture (CDA) [48]. Since significant resources have been

invested in developing these standards and they are already considered as de facto references, we will focus on adoption of these existing standards instead of developing new ones when building the UR CTSI information infrastructure. On the other hand, the existing standards are not yet sufficient to support our proposed research to use a standardized approach to facilitating data sharing and process knowledge reuse for CTS. Specifically, SNOMED-CT, ICD9-CM, and CPT4 can be used for only clinical data, but not experimental data. In addition, HL7 RIM and HL7 CDA can be used as only a reference information model, which is still far from direct mapping to database schema and thus cannot yet be used in the real world for data sharing. Finally, there is no current standard model to represent biomedical process knowledge. To address these issues, we will work with standard development organizations, external collaborating parties, and other CTSA programs to adopt and develop the following standards and protocols:

a) *Data Encoding Standards for Biomedical Experimental Data.* To facilitate standard encoding of biomedical experimental data, we will explore the existing resources that could be leveraged, such as the genomic and proteomic databases, as well as other research efforts in this field, such as the data model developed by caBIG [50]. We will then investigate the feasibility to adopt these approaches in our work. Considering that there is no widely accepted and mature method at this moment, it is extremely important for us to collaborate with other CTSA programs during this standard adoption process.

b) *Protocols for Virtual Integration of Data.* As described in Section F2C4b 2, we will develop tools to provide integrative views to research data through virtual integration of multiple databases. Since we believe that this service will be widely used within and across institutions to pool data together for CTS, we will develop standard protocols to facilitate its wider adoption. Specifically, this set of standard protocols will be based on: (1) data encoding standards for individual datasets and cross-mapping of these standards, (2) a generic entity-attribute-value data model that can be used together with the data encoding standards to map to the schema of individual databases, and (3) the data schema mapping model developed in Section G2C4b 2. By wrapping this set of standard protocols into the framework described in Section G2C4b 2 and using them together with the data encoding standards, we will be able to share data within and across institutions.

c) *Standard Model for Representation of Biomedical Process Knowledge.* Several types of biomedical process knowledge, such as clinical trial protocols and practice guidelines, can be reused within and across institutions. For example, the process knowledge of clinical trial protocols can be used for both clinical trial simulation and clinical trial process monitoring and control; it can also be used across institutions for multi-site trials and dissemination of best practices. To facilitate process knowledge reuse, we will extend GLIF [37-38] such that it can be used as a standard model for representation of biomedical process knowledge. GLIF was previously proposed at HL7 as a standard to represent clinical practice guidelines. To extend it for representation of general-purpose biomedical process knowledge, we will focus on: (1) expansion of its task set such that various types of CTS tasks can be included, (2) support of multi-agent collaboration in specific biomedical process, (3) inclusion of a quantitative temporal model in task scheduling, and (4) interface with individual CTS informatics services, such as data integration, development and validation of mathematical/statistical models, and delivery of behavioral interventions. Meanwhile, we will work with standard development organizations, such as HL7 and CDISC, and other CTSA programs to include additional features into this process knowledge model. For this purpose, we will take the approach of the GESDOR framework [33] to develop a comprehensive representation format.

For all the standards and protocols adopted and developed, we will ensure their use in the development of the UR CTSI information infrastructure. When providing informatics services to support data sharing and process knowledge reuse across institutions for CTS, we will also ensure the use of these standards. We describe the details of these services in Section G2C4c 2.

2) Providing Informatics Support to Facilitate Data Sharing and Process Knowledge Reuse. Data sharing at the UR CTSI will be both investigator-specific and center-wide. All the data sharing will adhere to all provisions of HIPAA and other regulatory requirements. We will work together with the UR RSRB and Information Security Office to protect personal health information for all the data sharing initiatives. Two data sharing services will be implemented to provide flexible support to investigators' data sharing efforts. The first service pertains to the actual publications or documentations about research. For this purpose, we will use DSpace [51], which is a digital repository with UR as one of its major partners, to capture, store, index, distribute, and preserve the intellectual outputs of university faculties and staffs. The second service involves the direct sharing of the original research data, which will be based on data encoding standards and data integration protocols. Addition details about data sharing can be found in Section G2C4h.

We have already described in Section G2C4b 2 the use of these standards and protocols for sharing of research data within the UR CTSI. For data sharing with external collaborating organizations, we will develop a service that is based on agreements among the collaborating parties to use a specific set of data encoding

standards and data integration protocols to share data with each other. With these agreements, each participating party will provide services to assist others to identify the available data sets at the local site and to handle administrative and regulation issues. Once the negotiation is finished, the data at an individual site can be shared with its collaborators using the same mechanism that we will have implemented for data sharing within the UR CTSI. This data sharing effort will: (1) serve the local community to implement Rochester RHIO, with which URMC is a board member, to build an area-wide collaboration for continuity of care and other data sharing efforts, (2) serve UNYTRN and other regional consortia to pool research data together, (3) serve the federal agencies, such as NIH and FDA, to fulfill data sharing and reporting requirements, and (4) serve other CTSA programs for collaborative informatics efforts.

The informatics service for process knowledge reuse will be based on the standard model for process knowledge representation. For this purpose, we will develop: (1) a process knowledge repository to store the various CTS processes encoded in the standard format, and (2) a process knowledge execution engine to interpret them. For reuse of this knowledge within the UR CTSI (e.g., reuse of the process knowledge of a validated clinical trial protocol for clinical trial process monitoring and control), the business logic layer of the UR CTSI information infrastructure will handle the request for a specific piece of process knowledge by an informatics service, retrieve it from the repository, transmit it to the execution engine, and feed the results back to the original requesting service. Reuse of process knowledge across institutes will be based on agreements among the collaborating parties to use the standard model for process knowledge representation, similar to the approach used for data sharing.

G2C4d. Assessment and Optimization of Informatics Services (Specific Aim 4)

Assessment and optimization of the individual and the integrated biomedical informatics services will be based on their actual use in CTS activities, users' feedback, and their impacts on research translation and dissemination of knowledge in routine care. In addition to assessment of the specific services, evaluation of the overall performance of the key function will be based on regular tracking and analyses of the progress to implement the specific aims listed in Section A. Resources will be adjusted based on this analysis to ensure their successful implementation.

1) Monitoring of Actual Use of Specific Informatics Services. To monitor the actual use of the informatics services, we will keep records on all the services provided, including online resources, specific functions of the web portal, in-person consultations, and all the specialized services such as data management, mathematical/statistical modeling, computer simulation, clinical trial facilitation, process management, and behavioral intervention. To evaluate the use of the online resources and web portal functions, we will implement system logs to track all the visits to specific web pages, clicks of particular links, and the pathways of browsing. We will use these data, along with the user feedback described below, to optimize the individual and the integrated informatics services for their continuous development.

2) Seeking User Feedback. To seek user feedback on specific informatics services, we will conduct regular surveys, hold user meetings, organize workshops, implement online feedback forms, and provide help lines. In addition, we will select a few representative use scenarios to conduct field observations and interviews. This work will be an intrinsic part of the infrastructure development process. More importantly, it will be a continuous effort through the entire operation process of the UR CTSI. For frequently used services, we will focus on seeking feedback to improve them for more effectiveness and efficiency. For less-frequently used but desired services, we will focus on seeking feedback to identify the hindrance to their use and the potential ways to improve the usability. For services not really needed, we will focus on seeking feedback to estimate the potential negative effects if we terminate these services. During this process, we will seek advices from the BIP Advisory Committee and the NIH CTSA Informatics Steering Committee to supervise the evaluation (see Section F2C4f). Additional technical details on seeking user feedback to specific informatics services can be found in Section G2C4b 1.

3) Assessing Impacts on Research Translation Process and Knowledge Dissemination in Routine Care. As the ultimate goal to serve CTS, we will assess how data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention can be integrated together to improve the research translation process and to disseminate best practices in routine care. For this purpose, we will use specific example studies to assess and optimize our approaches.

Assessment of impacts on research translation will focus on: (1) integration of experimental and clinical data to facilitate development of mathematical/statistical models for clinical trial simulation, (2) facilitation of clinical trial subject recruitment and process monitoring/control, and (3) incorporation of research and administrative services within CTS workflow. Example studies at the initial stage include the HIV/AIDS clinical trial simulation study, the I-90 consortium for neurodegenerative disorders study, and the UR CTSI web portal usability study.

Assessment of impacts on knowledge dissemination in routine care will focus on: (1) integration of process knowledge with clinical information systems to generate patient-specific recommendations on best practices, and (2) integration of best practice recommendations with clinical workflow to improve effectiveness of behavioral

interventions. Example studies at the initial stage include the psychiatry medication guideline study and the HIV/AIDS patient management system study.

G2C4e. Novel Aspects of Biomedical Informatics.

The proposed biomedical informatics key function is unique in that it integrates a variety of informatics services, such as data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention, in alignment with CTS process to provide context-specific support for CTS activities at different stages of their lifecycle. Specifically, the incorporation of experimental and clinical data into mathematical/statistical models and computer simulation systems can be used to facilitate clinical trial design and synthesis/test of new hypothesis; the integration of data management, process modeling, and behavioral intervention can be used to assist subject recruitment/retention and protocol compliance for clinical trials; the embedment of research and administrative services within the workflow of CTS can be used to improve the efficiency of CTS activities; and the combination of process management and behavioral intervention can be used to individualize the dissemination of best practice in a more effective way.

In addition to the proposed context-specific and integrative services, we have unique informatics resources at UR CTSI. Of specific note is the value of the Allscripts TouchWorks EMR data. Touchworks captures discrete codified data on all of our ambulatory patients' medication, problem, allergy, and immunization history, as well as many coded and template driven documentation of patient visits. It also has an API to share continuity of care data between itself, other EMRs, and RHIOs. With Dr. David Krusch, Co-Director of the BIP (see Section G2C4f), sitting on the Rochester RHIO board and leading the implementation and management of CDR/CDW, the value of the coded data extracted from the AllScripts TouchWorks EMR and Rochester RHIO will provide an immensely valuable resource to both our clinical and translational scientists. As one of the few institutions to be able to provide such type of integrated data, the UR thus has unique advantage to provide informatics support for CTS.

G2C4f. Organization and Governance.

The biomedical informatics key function of the UR CTSI will be directed by the newly established BIP, which will report to the UR CTSI Director and Executive Committee. In addition to coordinating the existing biomedical informatics resources and to develop new functions, the BIP will participate in the NIH CTSA Informatics Steering Committee to ensure nation-wide collaboration. An advisory committee, which consists of the representatives from the current informatics faculties and staffs, the CTS informatics service users, and external collaborators, will be established to advise the work of BIP. An organizational chart of the biomedical informatics key function is shown in Figure G2C1. The leadership of the key function consists of:

(1) Co-Director: David A. Krusch, MD, Associate Professor of Medical Informatics, Associate Professor of Surgery, Director of Division of Medical Informatics, Chief Medical Information Officer of Strong Health. Dr. Krusch has extensive experience in development and management of clinical information systems (details in Section C). He will lead the coordination of the existing resources, the data management service, and collaboration with external partners. He will represent the UR CTSI to participate in the NIH CTSA Informatics Steering Committee.

(2) Co-Director: Dongwen Wang, PhD, Assistant Professor of Biostatistics and Computational Biology, Assistant Professor of Medical Informatics. As a formally trained informatician, Dr. Wang has extensive experience in biomedical informatics research and technical standard development (details in Section G2C3). He will lead the development of new functions and adoption/development of standards and protocols.

(3) Co-Director: Hulin Wu, PhD, Professor of Biostatistics and Computational Biology, Professor of Medicine, Professor of Community and Preventive Medicine, Chief of Division of Biomedical Modeling and Informatics, Director of Center for Biodefense Immune Modeling. Dr. Wu has extensive experience in biomedical modeling, simulation, and clinical trial research (details in Section G2C3). He will lead the development and service of mathematical/statistical modeling and computer simulations.

Currently, the BIP is intimately integrating and repurposing existing GCRC informatics resources for clinical trial support and data management into its infrastructure, including human resources (2.2 FTE staff), budget (about $750,000 in direct costs), software, and hardware. The effort will be an important first step for the further coordination and integration of other informatics resources to build the UR CTSI.

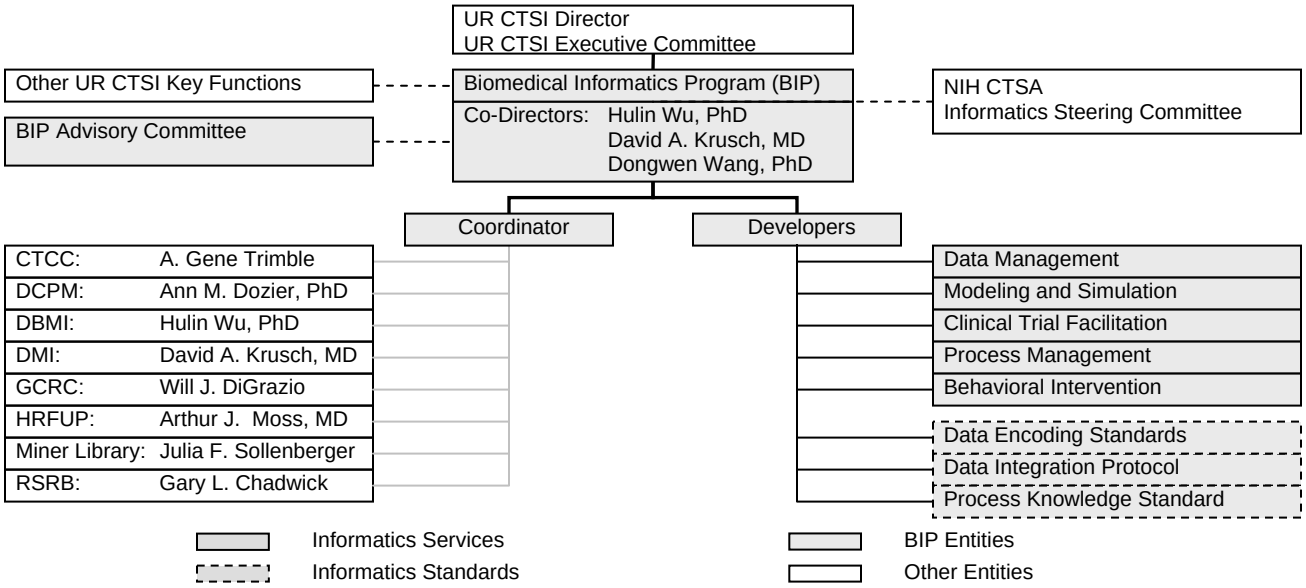


Figure G2C1. Organizational chart of the Biomedical Informatics Program (BIP) key function.

G2C4g. Interactions with Other UR CTSI Key Functions.

As the backbone of communication, the biomedical informatics function will interact with all other UR CTSI key functions through specific informatics services, as we have described in the previous sections. More importantly, the biomedical informatics key function will play a major role in the development of a novel methodology to improve the research translation process and to facilitate knowledge dissemination in routine care through integration of a variety of biomedical informatics services, such as data management, mathematical/statistical modeling, computer simulation, process control, and behavioral intervention. To validate such a framework, we will perform a series of pilot studies for proof of concept. The systems, tools, and technical standards developed from this work will be an important part of the translational technologies and resources. These resources will be shared with external collaborators in the local communities (e.g., RHIO), regional consortia (e.g., UNYTRN), federal agencies (e.g., NIH and FDA), and other CTSA programs. Finally, the biomedical informatics key function will contribute to the training and career development program through teaching of informatics courses and providing consulting services.

G2C4h. Plan for Sharing of Research Data and Technology.

This application is submitted in accordance with the final NIH statement on sharing research data issued on February 26, 2003 [52]. The UR CTSI affirms its support for the concept of data sharing, which greatly facilitates the translation of research results into knowledge, products, and procedures to improve human health. The UR CTSI also supports the timely release and sharing of final research data from all studies, regardless of sponsorship, which are carried out through the UR CTSI infrastructure. The definition of “timely release and sharing,” as taken from the NIH guidelines, is no later than the acceptance for publication of the main findings from the final data set.

Data sharing at the UR CTSI is investigator-specific. Several methods of data sharing may be used, including publication in peer-reviewed journals, documentation of research in public archives, and dissemination of the actual datasets of the research through web services. The nature of the data and the restrictions that may apply to it will guide investigators in their choice of data sharing methods. The UR CTSI encourages investigators to share data and will ensure that appropriate methods are developed and utilized to achieve data sharing in all appropriate situations. Data sharing must adhere to all provisions of HIPAA. The rights and privacy of people who participate in research must be protected at all times. Data for sharing should be free from any identifiers that would link the results to any individual research participants.

The BIP will implement specific strategies for two data sharing services that would provide investigators with the ease and flexibility required to meet the sharing provision. At the initial stage (first 2 years), we will focus on the archiving service pertaining to the publication and documentation of the research. We will use DSpace [51] for this

purpose. Since the UR is one of the six major research universities of the DSpace federation and an early adaptor of the system, we will take this advantage to provide the archiving support for data sharing efforts. Data shared through this mechanism will be primarily based on a text format, such as MS Word or PDF. Other researchers' use of such documentation data is straightforward, and thus no additional documentation and agreement are required.

The second phase of data sharing (from year 3) will be implemented along with the development of standards for data encoding, data integration, and process knowledge representation. At this stage, data sharing will entail the availability of the actual datasets generated from research. Since the dataset by itself is of little value without the knowledge of the study details and the context under which the research operated, we will thus still need to associate the actual datasets with the publication/documentation of the original research. DSpace will continue to be an option for this purpose to store both the publications and the associated datasets. For investigators that desire a more controlled method for sharing their data, the BIP will implement web service applications as a solution to support automatic data sharing, integration, and analyses. For this purpose, the datasets need to be in specific formats that can be automatically interpreted by computer systems for further processing and analyses. Therefore, data sharing through this mechanism requires agreements among the parties involved in the data sharing activities. An example of such a format for automatic data sharing is Extensible Markup Language (XML) [53], which can be used to wrap up both the metadata about the research (including the publication and documentation) and the actual datasets. The structure of the data represented in the XML format is defined by its schema, which must be agreed among all participating parties in order to correctly interpret the data. These common schemas for data sharing need to be standardized to serve a large research community. Additional technical details to develop standards for data sharing and process knowledge reuse can be found in Section G2C4c 2.

In addition to the actual datasets and the technical standards, we will also share the software tools (for example, the system for data integration and the execution engine of process knowledge interpretation, see Section G2C4c 2) developed from this project with collaborators, such that they can be used in together with the data. Additional details on software sharing plan can be found in the Governance Section.

It is important to note that sharing of data and technology will also need to address other non-technical issues, such as regulation requirements and intellectual property rights, which will also be included in the data sharing agreements. We will work with the NIH CTSA Informatics Steering Committee to develop mechanisms to address these issues to ensure the effective dissemination of data and technology.

G2D. DESIGN, BIOSTATISTICS, AND CLINICAL RESEARCH ETHICS

General Objectives

It is well recognized that professional multidisciplinary support is critical to the proper design, execution, analysis, interpretation and application of clinical and translational investigations. The provision of scientific leadership and expertise related to methodological, biostatistical, and ethical considerations in the conduct of research will be a critical component of the UR CTSI. While currently provided under the General Clinical Research Center (GCRC), such support will be significantly broadened in scope under the CTSI. Faculty having extensive and complementary training/experience in the fields of epidemiology, biostatistics, data management, and research ethics will collaborate in the provision of this key function. These faculty are committed to: assuming a direct role in addressing substantive issues related to each CTSI investigation; participating as an active and integrated member of each research team; and contributing innovative concepts and methodologies to assure the conduct of rigorous and successful translational and clinical investigations. Collaborative support for research design, implementation, and analysis will be available for all trainees and faculty investigators. By actively contributing to multiple research endeavors within the CTSI, faculty will be well poised to promote interdisciplinary interactions and cross-fertilization of scientific endeavors. The initiative also offers many new opportunities for further methodological studies in the fields of biostatistics, epidemiology, computational biology, and research ethics.

The over-arching goal related to Design, Biostatistics and Clinical Research Ethics within the UR CTSI is *to provide scientific leadership and expertise in the areas of epidemiological, biostatistical, and ethical methodology as they relate to the design, conduct and analysis of both observational and experimental studies developed within the CTSI infrastructure for translational and clinical research.*

G2D1. Specific Aims

1. Provide detailed consultation for the development of all study protocols. This includes guidance on both observational and experimental study design, identification of study populations and appropriate comparison groups, defining outcome variables and important covariates, developing appropriate measures and methods to obtain the relevant data necessary to properly answer the study questions, identifying appropriate statistical methods for analysis, and performing power and sample size calculations, identifying and proactively addressing ethical issues that might arise during the implementation of the protocol.
2. Provide necessary biostatistical, epidemiologic and ethics support during the conduct of the studies. This is facilitated by a synergistic relationship with CTSI core facilities to provide quality control and routine report generation, as well as to assist in making any decisions related to protocol revisions.
3. Collaborate in the interim and final statistical analyses of the study data. This includes identifying appropriate statistical methodology, statistical programming, data analysis, assisting with the interpretation of the results of analyses, producing final reports and graphical displays and collaboration in the preparation of presentations and manuscripts for publication.
4. Develop novel research methods to handle unique problems in the areas of statistical analysis, bioinformatics and computational biology, bias and confounding, risk profile modeling, and ethical considerations in translational research.
5. Focus on new areas of research regarding ethical perceptions of research stakeholders, impact and cost-effectiveness analysis of CTSI discoveries, and utility of current conflict of interest policy in managing emerging conflicts of CTSI-related investigations.

The ever-present challenges of scientific and administrative collaboration, interaction and communication will be greatly facilitated by CTSI resources. The currently available resources, expertise, and methodological achievements are described in the sections that follow. Some mechanisms for support of UR CTSI research endeavors are already in place. A new program in design, biostatistics, epidemiology, and research ethics will be formed by the CTSI from previously non-integrated units, thereby enhancing the infrastructure to support clinical and translation research at the University of Rochester Medical Center. The provision of funds to actually support faculty committed to the goals of the CTSI will alleviate competing responsibilities and enable talented individuals to address the complex challenges of translational and clinical research as a priority. For the purpose of clarity, the current environment and established systems for the collaboration of faculty

specializing in biostatistics, epidemiology and research ethics with clinical and translational research investigators will be described separately for each of these disciplines. Plans for enhancing the infrastructure to support UR CTSI research endeavors will be outlined in the last three sections.

G2D2. Biostatistics, Bioinformatics, and Computational Biology

G2D2a. Background and Significance.

The Department of Biostatistics, established as a Medical School division in 1970, underwent major expansion in 2002-2003. An "action plan" for the Department was developed in conjunction with Medical School administration, which called for doubling of biostatistics faculty and initiation of a Division of Computational Biology. After a national search, Andrei Yakovlev, Ph.D., was appointed Chair in Fall 2002. The name of the Department was changed to "Department of Biostatistics and Computational Biology" to reflect the new emphasis on bioinformatics/computational biology. Dr. X. Tu was appointed Director of the Statistical Consulting Center. This Center is a working mechanism for provision of biostatistical support for clinical and translational research. It will be enhanced and extended through the CTSI, allowing many more investigators to receive this support. The Department's Divisions of Computational Biology (led by A. Yakovlev, Ph.D.) and of Biocomputing and Modeling for Clinical Studies (led by H. Wu, Ph.D.) have been formed to extend the Department's research effort to new areas of biomathematics and biocomputing. The Department now has 18 tenured (or tenure-track) faculty, 7 research (i.e., non-tenure-track) faculty, 1 visiting professor, 7 adjunct professors, and 8 post-doctoral fellows. Further expansion (2 tenure-track faculty, 4 research faculty, and 2 post-doctoral fellows) is underway to support the NIH-designated *Center for Biodefense Immune Modeling* established within the DBCB in 2005. The Department also includes 6 programmers and 3 Master's level biostatisticians. The Department has a doctoral program in Statistics and participates in the Medical Scientist Training Program (MSTP) that allows qualified URMC entrants to obtain a Ph.D. in Statistics and an M.D. in a single course of study. Ph.D. students participate in many ongoing methodological and collaborative research projects. Although the existing infrastructure has proven quite efficient, it needs to be enhanced to extend services and collaborations to all promising projects in clinical and translational research. Many faculty have joint appointments in clinical departments; for example, M. McDermott (Neurology), X. Tu (Psychiatry), J. Roy (Pediatrics), and H. Wu (Community and Preventive Medicine and Immunology). Three DBCB biostatisticians, led by M. McDermott, are members of the University's NIH-funded General Clinical Research Center (GCRC). Consultations to cancer investigators are provided through the Cancer Center Biostatistics Shared Resource under the direction of D. Peterson, Associate Professor at the Department of Biostatistics and Computational Biology. This environment is ideally suited for collaborative research and consulting.

G2D2b. Prior Experience.

Department faculty have wide-ranging methodological research interests, including survival analysis, sequential analysis, clinical trial design, longitudinal data analysis, missing data methods, analysis of categorical data, measurement error models, multiple testing, analysis of gene expression data, network inference, statistical genetics, nonparametric smoothing and curve estimation, model selection techniques, robust inference, mathematical and stochastic modeling of complex biological systems, order-restricted inference, ROC curve analysis, nonparametric inference, Bayesian inference, functional response models, and small-sample asymptotics. The Department has expertise in virtually all fields of modern theoretical and applied statistics. Department faculty have served as Editors and Associate Editors of journals such as *Journal of the American Statistical Association*, *Biometrika*, *Annals of Statistics*, *Lifetime Data Analysis*, *Journal of Modern Applied Statistical Methods*, and *Neurology*. Many faculty also serve on NIH study sections or SEPs, or review for organizations such as the Muscular Dystrophy Association. Eleven faculty have practical experience in design and analysis of clinical trials. Some of these (D. Oakes, W. J. Hall, H. Zhao, M. McDermott, X. Tu, H. Liang, H. Wu) have also contributed to methodological research on analysis and modeling of clinical trials. Faculty members have published a total of 82 peer-reviewed methodological papers having a direct bearing on clinical trials.

Considerable emphasis is placed on statistical methods for computational biology, bioinformatics, and systems biology. A group of faculty, post-doctoral trainees, and support staff is engaged in exploring methodological avenues that have clinical and/or translational implications including: novel statistical methods for genomics and proteomics, pathway recognition and gene regulatory network reconstruction, construction of diagnostic and prognostic molecular signatures of diseases, theory of multiple testing with an emphasis on high throughput genomics data, and stochastic modeling of complex cell systems. The group collaborates with

the Department of Computer Science on computational issues in this research. The group members are heavily involved in both epidemiologic and statistical consulting to meet the needs for study design and analysis of genomic and proteomic data. Owing to a high demand for this consulting activity, the investigators have gained extensive experience in collaborative efforts, but considerably more can be done with the enabling resources of the CTSI.

G2D2c. Methods.

1) Biostatistical Support for Clinical Research. DBCB faculty and staff have a long history of involvement in clinical research at the University of Rochester and have helped to shape the direction of the research endeavor in many areas. The following examples of past and ongoing collaborative activities illustrate the Department's commitment to supporting clinical research at the University.

2) General Clinical Research Center (GCRC). The GCRC at the University of Rochester has had continuous NIH funding since 1960. Dr. M. McDermott, who is assisted by Dr. C. Feng and S. Messing, heads the Biostatistical Core. Dr. McDermott has been involved with the GCRC since 1990. All three biostatisticians are members of the GCRC Advisory Committee and all protocols submitted to the GCRC are reviewed by one of the biostatisticians. Investigators are encouraged to consult the biostatisticians prior to protocol submission. The biostatisticians also assist GCRC investigators with grant preparation, data form design, data management/quality control, randomization, sample size refinements, developing a statistical analysis plan, execution of statistical software, interpretation of results, and reporting (manuscripts, oral/poster presentations). They are frequently co-authors of publications arising from this research. They also participate in the planning and instruction of courses in biostatistical methods and clinical trials that are co-sponsored by the GCRC.

3) Clinical Trials in Neurological Diseases. The Department has collaborated with faculty in the Department of Neurology for nearly 20 years in the conduct of clinical trials and epidemiological studies. A major impetus for this collaboration was the founding of the Parkinson Study Group (PSG) in 1986 (led by Dr. I. Shoulson) to conduct the NINDS-sponsored multicenter trial of deprenyl and tocopherol anti-oxidative therapy of Parkinsonism (1;2). Out of this 800-patient trial grew a large infrastructure for conducting clinical trials, including the Clinical Trials Coordination Center (CTCC) in the Department of Neurology and the Biostatistics Center in the DBCB. This infrastructure has grown in the past two decades and now supports clinical trials and other clinical research studies conducted by several national and international research groups, including the Huntington Study Group (HSG), led by Dr. I. Shoulson), Muscle Study Group (led by Dr. R. C. Griggs), Tourette Syndrome Study Group (led by Dr. R. Kurlan), and many others. Over a dozen NIH-sponsored clinical research projects, several trials sponsored by the FDA Orphan Drug Division, and more than two dozen industry-sponsored trials have been conducted through this infrastructure in Rochester (63 clinical trials in all).

The DBCB is integrally involved with the planning, implementation, analysis, and reporting of virtually all studies coordinated by the CTCC, including department faculty, computer programmers, and graduate students. Recently, Dr. D. Oakes was awarded a grant from NINDS (NS 50573) to direct the coordination, data management, and biostatistical activities for a Phase III trial of high dosages of the dietary supplement coenzyme Q_{10} in 600 patients with early Parkinson's disease. This study will use a design suggested by Dr. Oakes that was successfully applied in a Phase II study of the same compound (3). Dr. M. McDermott was awarded a similar grant from NINDS (NS 52619) to direct the coordination, data management, and biostatistical activities for a Phase III trial of a high dosage of coenzyme Q_{10} in 608 patients with Huntington's disease followed for five years. This trial builds on promising results from an earlier, briefer trial of a lower dosage coenzyme Q_{10} in 347 patients (4). This collaboration has also led to methodologic development in clinical trial design (5).

4) Clinical Trials in Cardiology. The relationship between the Department of Biostatistics and the Heart Research Follow-up Program (HRFP) dates from the formation of The Multicenter Research Group (MRG) in 1976 with its leadership in the HRFP at Rochester (Dr. A. Moss) to study the long-term clinical course of patients following acute myocardial infarction. The MRG includes clinicians, biostatisticians and other scientists from throughout North America, and investigators in Israel and Italy. The primary biostatistician for the MRG through 1987 was Dr. C. Odoroff (the founding Director of the Division of Biostatistics) and since then, Dr. D. Oakes. The MRG has conducted several major multicenter clinical trials and published over 100 papers. The first major study of risk stratification following myocardial infarction (MI) demonstrated the importance of low ejection fraction as a major determinant of postinfarction mortality (6).

The Multicenter Diltiazem Postinfarction Trial (MDPIT) was instituted in 1983 to test whether diltiazem, a calcium channel blocker, would reduce the risk of mortality or of a recurrent cardiac event in patients recovering from an MI. The study enrolled 2466 patients. The prespecified primary analysis (7) showed no overall difference in cardiac event rates among subjects assigned to diltiazem and to placebo; however, there was a strong statistical interaction between diltiazem therapy and baseline pulmonary congestion on X-ray. Among the 20% of subjects enrolled with pulmonary congestion the event rate was greater among those assigned to diltiazem than those assigned to placebo, with the opposite pattern among the 80% enrolled without pulmonary congestion. This surprising finding was confirmed by further post-hoc analyses and spurred new methodological developments, including a novel time-dependent analysis based on “actual use” (8).

The Multicenter Automatic Defibrillator Implantation Trial–II (MADIT-II) (9), assessed the value of an automatic defibrillator in cardiac patients at risk for sudden death. The considerable health-care cost implications were also examined, leading to a separate methodological publication (10) and a doctoral dissertation by a Biostatistics student. Several other publications have arisen from secondary analyses. This trial, like its predecessor (11), had a fully sequential design and stimulated considerable methodological research in this area, resulting in over a dozen publications in statistical journals by department faculty and students. A new trial (MADIT-CRT) is now underway with involvement of DBCB faculty led by Dr. W. J. Hall and students. Department faculty collaborate in several other HRFP studies including a large investigation of hemostatic and lipid-related risk factors for cardiac events in postinfarction patients (12;13), and an epidemiologic study of long-QT syndrome (14). Participating faculty in HRFP studies include Drs. D. Oakes, M. McDermott, W. J. Hall, D. Peterson, and Ms. S. Eberly.

5) Clinical Research in Environmental Health Sciences. An excellent example of collaborative clinical research involving DBCB faculty and students is the “Seychelles Study,” a large observational study of the developmental effects of pre- and post-natal exposure to methylmercury from fish consumption. The Seychelles Islands population is ideally suited for this investigation because of their fish diet and the lack of emigration. The study aims to establish a dose-response relationship between fetal exposure, as measured by maternal hair mercury levels during pregnancy, and measures of development in offspring during childhood. More than 700 mother/child pairs are enrolled and developmental testing has been completed through 8 years of age. The study is a cooperative effort between teams in the Seychelles Islands and UR faculty from the departments of Environmental Medicine, Biostatistics and Computational Biology, Neurology, and Pediatrics. The results so far have aroused considerable interest among regulatory authorities. Over 50 publications have arisen from this study, nearly all co-authored by Biostatistics faculty. The study has also spawned substantial methodologic work by DBCB faculty in data smoothing, nonparametric function estimation, and measurement error models, see e.g. (15).

Since 1992, the Department has held a training grant in Environmental Health Sciences Biostatistics funded by NIEHS. This grant funds two predoctoral and one postdoctoral student. Graduate students are trained to conduct statistical research and to collaborate on the design and analysis of laboratory, animal and human studies in environmental health. The broad training environment is achieved by an integrated collaboration between biostatisticians and EHS researchers. The Seychelles Study has provided an excellent vehicle for involving these students in collaborative research, and most have graduated from the program with several publications to their credit. In addition, Dr. Thurston works actively with the Center for Reproductive Epidemiology on two large EPA funded studies.

6) Clinical Research in Psychiatry. The Department has collaborated closely with the Department of Psychiatry for over 20 years, providing instrumental support for study design and data analysis for a variety of studies. The collaboration started in 1986 when suicide research became a focus area in the study of Psychopathology in the Elderly (E.D. Caine, PI). Subsequently Dr. C. Cox in the Department of Biostatistics led a group of faculty and staff biostatisticians to provide study design and data analysis support for Psychiatry investigators. In 2003 Dr. X. Tu succeeded Dr. Cox in this role. In recent years, the Biostatistical Core Group (BCG) has also collaborated with investigators at the School of Nursing.

The BCG is actively involved with three large NIH-sponsored clinical trials. One is a randomized study on the effectiveness of an intervention program to treat children with behavioral and social-emotional problems (Dr. Wyman, PI). This trial has a target sample size of 400 children in grades 1-3 in five urban schools. The second is a trial to study comorbid medical conditions in elderly patients with depression in a primary care setting (Dr. Lyness, PI). This naturalistic study has recruited 756 patients, the largest cohort of older primary care patients characterized using well-operationalized, labor-intensive methodologies to assess a combination

of psychopathologic, medical, psychosocial, and functional domains. The third study is a large randomized trial to test the efficacy of an HIV-prevention intervention with 640 sexually active adolescent girls (Dr. Morrison-Beedy, PI). As well as collaborating in these large-scale trials, the BCG has also been mentoring junior investigators in the Department of Psychiatry and School of Nursing, assisting them in developing study designs and data analyses for smaller trials supported by K awards from NIH or UR internal awards such as the Salzman Awards.

7) Center for Biodefense Immune Modeling. To specifically foster multidisciplinary research in mathematics, statistics, computer science, engineering, and immunological processes, in September 2005, NIAID awarded Dr. H. Wu nearly 10 million dollars over 5 years to establish the University of Rochester Center for Biodefense Immune Modeling (CBIM) (AI 50020). The objectives of this Center are to: (1) develop mathematical and computational models to simulate immune responses to influenza A virus, both native and modified bioterror strains; (2) design and conduct *in vitro*, *ex vivo*, and *in vivo* experiments to identify, measure, and validate the immune response models; (3) develop statistical methods and user-friendly computer packages for immunology data analysis and immunity model identifications and predictions; (4) develop a deliverable web server-based software system for modeling and simulating immune responses to influenza A virus and other biopathogens; and (5) investigate the feasibility to extend and modify influenza mathematical/computational models to vaccine virus for immune response simulations in the context of vaccination to induce protective immunity to smallpox.

The CBIM multidisciplinary team is developing quantitative models of immune response to biopathogens and creating computational tools to explore such scenarios *in silico*. As part of the Center's primary objectives, an educational program is being developed to train graduate students and other interested parties in the techniques of mathematical modeling of immune responses.

Biostatistical Support for Translational Research. Virtually every disease has a genetic component, either as the primary cause or as a determinant of susceptibility to environmental causes. Moreover, responses to therapy can vary significantly because of genetic variation. However, in most cases we do not fully understand which genes are involved. Technological advances in the field of genomics allow us to evaluate routinely variations in genes and gene expression patterns at the level of the whole genome. Proteomics has not yet reached the comprehensiveness of genomics, but an increasing number of proteins will be quantifiable as the technology continues to improve. Proteomics is an essential partner to genomics because the abundance and functions of proteins encoded by the genes are determined not only by gene transcription, but also by regulation of translation and post-translational modifications. Studies based on genomics and proteomics methods will accelerate our understanding of disease etiology, since we no longer have to evaluate genes and proteins one at a time. This information will reveal new targets for pharmaceutical or behavioral interventions, and will allow us to predict which individuals will be the most or least likely to benefit from particular interventions. Provision of biostatistical support for translational research requires the use of appropriate methodology for data analysis. This is still an emerging field, and many methods in current use are clearly suboptimal. Our proposal therefore involves development and testing of new methodology as well as provision of consulting and collaborative services.

Novel Methods for Microarray Data Analysis. The microarray technology yields abundant multidimensional information on the functioning of the whole genome machinery at the level of transcription. From these data, much can be learned about interrelationships between genes, and about mechanisms by which the cell assigns tasks to different genes to maintain a specific function. However, this advanced technology continues to be used as a simplistic screening tool with a focus on large differences between mean values of expression measurements. At URMC, a research team led by Dr. A. Yakovlev is conducting systematic studies of various pitfalls in modern methods for microarray data analysis, with the goal of correcting these pitfalls in a manner that will lead to more reliable statistical inference. These studies demonstrate that ignoring the correlation structure of microarray data may produce misleading results. This conclusion has the most direct bearing on methods that resort to pooling expression measures across genes. In particular, we have studied the potential impact of the correlation between gene expression levels and associated test statistics on statistical inference based on nonparametric empirical Bayes methodology. Qiu et al. (16) reported evidence that this impact may be quite strong, leading to a high variance of the number of selected genes. Another disquieting effect is a high variance of the estimators proposed for the false discovery rate (16). We have also shown that some

commonly accepted normalization methods interfere in the true biological signal, thereby causing undesirable effects, the magnitude of which has yet to be assessed. The effects of normalization on correlations between *t*-statistics computed for different genes were studied by Qiu et al. (17). The effect of quantile normalization on the distribution of gene expression levels was explored by Chen et al. (18). We proposed resampling techniques to assess stability of gene selection procedures (19) and developed software for several distribution-free tests in conjunction with multiple testing procedures controlling the family-wise error rate (20;21). The knowledge these studies provide is very valuable in statistical consulting as it suggests improved strategies for design and analysis of microarray experiments.

In summary, our studies indicate that the strength of dependence between genes has been gravely underestimated in the development of statistical methods for microarray data analysis. In this connection, it is noteworthy that there has been a growing interest in correlations between gene expression levels in statistical methodologies for microarray analysis (16;17;19;22-27). As larger sets of microarray gene expression data become readily available, quantitative insights into dependencies between gene expression levels are gaining in importance. Modern methods of microarray data analysis typically employ two-sample (or multi-sample) statistical tests for testing differential expression of genes combined with multiple testing procedures to guard against Type 1 errors. Such methods are biased towards selecting those genes that display the most pronounced differential expression. Once the list of genes showing statistically significant differential expression has been generated, these genes are often ranked using purely statistical criteria, and this ranking is thought to reflect their relative importance. Quite typically, a certain number of genes with the smallest p-values are finally selected from the list of all “significant” genes. While most biologists recognize that the magnitude of differential expression does not necessarily indicate biological significance, in the absence of better methods, this remains the dominant means to initially prioritize candidate genes. From a biological perspective, however, the above-described paradigm falls far short of being a perfectly valid approach. Even a very small change in expression of a particular gene may have dramatic physiological consequences if the protein encoded by this gene plays a catalytic role in a specific cell function. Many other downstream genes may amplify the signal produced by this truly interesting gene, thereby increasing their chance to be selected by formal statistical methods. For a regulatory gene, however, the chance of being selected by such methods may diminish as one keeps hunting for downstream genes that tend to show much bigger changes in their expression. As a result, the initial list of candidates may be enriched with many effector genes that do little to elucidate more fundamental mechanisms of biological processes.

There are two ways to remedy the situation. One is to use bioinformatics tools that utilize prior biological knowledge, such as partially known pathways, for prioritization of candidate genes. This approach is now routinely used in biological studies and there are ongoing efforts to enrich it with specially designed algorithms (28). Another way is to extract additional information on relationships between different genes from microarray data by pertinent statistical methods. The latter research avenue has been our main focus in recent years. Recent studies from our research team (17;29) strongly suggest that the correlation structure of microarray data can serve as an important indicator of changes in transcription profiles between phenotypes. A fruitful idea is to select candidate genes that change their relationships (correlations) with other genes across the conditions (phenotypes) under study. This can be accomplished by designing a multivariate statistical test that detects changes in the whole correlation vector associated with each gene. We recently filed a provisional invention disclosure that implements this idea. The method is applicable to single-color oligonucleotide arrays, such as Affymetrix GeneChips and CodeLink Bioarrays, which are currently the most popular platforms in microarray studies. The proposed methodology is designed to work in the presence of a multiplicative random noise inherent in microarray technology and represents a radical conceptual change in the established paradigm focused solely on differentially expressed genes; it enriches currently practiced methods with quantitative inference on dependencies between gene expression intensities. An efficient multiple testing rule has been designed to combine the two approaches in a single procedure providing strong control of the family-wise error rate. This procedure will be extended to provide strong control of the false discovery rate as well. We envision many future research avenues emerging from the new paradigm suggested by our recent studies. One of the most topical questions is how to strike an optimal compromise between the multivariate analysis based on correlations and currently practiced methods for selecting differentially expressed genes. Yet another important question is how to make the best use of statistical inference on correlation vectors in the discovery of pathways. This may be an interesting problem for future research.

Diagnostic and Prognostic Molecular Signatures of Diseases. This research is very important to many clinical and translational investigators in general and those engaged in molecular profiling for clinical risk assessment in particular. The development of effective biochemical markers typically begins with the construction and validation of diagnostic and prognostic molecular signatures. When constructing such signatures from the high dimensional genomic or proteomic data, it is of critical importance to substantially reduce the initial dimension of the vector of feature variables. It is common practice to use univariate methods for this purpose. The group led by Dr. A. Yakovlev has developed a method of multivariate data reduction based on a new distance between multivariate probability distributions (23;30;31). In applications to microarray gene expression data analysis, an empirical counterpart of this distance, termed the *N*-statistic, can be used to select significant transcript *combinations*, rather than individual transcripts. The *N*-statistic has proven efficient in univariate analyses as well (32). Our preliminary studies have demonstrated distinct advantages of multivariate methodology over univariate approaches in situations where the number of differentially expressed individual genes is small. We will continue exploring this methodological avenue in the context of the transcriptomic and proteomic data generated by multiple research projects.

Translational studies aimed at finding biochemical markers require not only the selection of important transcripts/proteins (or transcript/protein combinations), but also adequate and constrained estimation of the adjusted associations of each with the disease outcome, given the others as well as any available clinical covariates. While we believe that variable selection is an important component, by itself it is insufficient, for the information from the multiple predictors must be intelligently combined and calibrated to form the final composite predictor. Many commonly used procedures over-fit the training data, miss many important predictors, or both. We believe that any method that selects transcripts or proteins based solely on unadjusted univariate associations is doomed to failure, except in very special cases such as the linear model context with nearly orthogonal predictors.

With the support from a DOD concept grant, Dr. D. Peterson conducted a simulation study that illustrates this point in the context of Cox proportional hazards regression models for censored survival data. His preliminary results strongly suggest that only about half of the relevant genes are typically identified via univariate searches, including such popular approaches as SAM (33), even when only a handful of genes are truly predictive. Moreover, such univariate methods tend to select about as many irrelevant genes as predictive ones, further degrading the prognostic performance of any model based on all such selected genes. In contrast, Dr. Peterson's prototype multivariate techniques can identify over 50% more of the true genes, typically without increasing the number of false discoveries, resulting in significantly superior prognostic performance. One of these novel prototype multivariate methods is similar to Tibshirani's LASSO approach (1996), in its forward stage-wise nature with constrained parameter estimation. Importantly, his methodology also remedies some of the apparent deficiencies of the LASSO, which tends to either over-shrink parameter estimates or include too many irrelevant predictors. In the near future, these methodologies will undergo further refinements, including judicious and novel uses of cross-validation and bootstrap techniques, as well as extensions to other generalized linear model frameworks.

Pathway Recognition and Gene Regulatory Network Reconstruction. Drs. A. Almudevar and P. Salzman have been developing methodology for a fully Bayesian approach to graphical models with applications in the inference of biological networks. This approach permits a principled assessment of model uncertainty and the assignment of confidence levels to any particular model feature. This is a crucial, and overlooked, issue since currently available genomic data will rarely contain sufficient information to resolve a set of putative models into one single plausible estimate (34). Our group has shown that careful estimates of model complexity can lead to more accurate Bayesian model averaging procedures in simulated and actual gene regulatory networks (35), yielding reductions in the inference of spurious connectivity while having only a minimal impact on the detection of true connectivity. We are also developing methods of scoring graphical models based on the Minimum Description Length principle (36). We have seen some initial success in this approach in relationship networks (37), both in terms of model estimation accuracy and the feasibility of Bayesian model averaging, and we plan to extend this methodology to Boolean network models of gene regulatory networks.
Combining such methods with multivariate analysis of microarray data can be very powerful and is well illustrated by a joint project with the Department of Biomedical Genetics. This research is concerned with the phenomenon of gene cooperation in response to two oncogenic mutations and is supported in part by an NIH grant awarded to Dr. Yakovlev. The first component of this project deals with multivariate methods for finding

the set of cooperative response genes from microarray gene expression data. The second component aims at finding a therapeutic target through reconstructing the underlying gene signaling network from gene perturbation experiments. This project represents a complete cycle of the necessary steps towards a useful medical application: from exploratory analysis of microarray data to validation of biological relevance of candidate genes and then to a final network reconstruction. We have conducted a simulation study suggesting that Bayesian averaging methods can be used to select those perturbation experiments yielding the highest model resolution (38). This may result in a more flexible approach to perturbation design than the parsimony approach proposed in Ideker et al (39).

Bioinformatics Support. With the explosion of genetic information there is a need to utilize specific analytical tools to ascertain genetic, molecular and biochemical information on biological systems. Moreover, with development of microarray systems has come the need to link, manage and explore large amounts of data generated by individual studies as well as combined from multiple studies. Similarly, integrated management of clinical and research information is becoming necessary. Many advanced programs are currently available for sequence comparison, multiple sequence alignment, motif extraction, post-translational modification identification, and structure superposition. In particular, we intend to use PSI-BLAST, PHI-BLAST, HMMer, MEME, CLUSTAL, T-COFFEE, EXPASY, and COMPASS. We will also access meta-servers for fold recognition. In addition to our original methods, we intend to use packages that are tailored to high-dimensional data such as Spotfire, Partek and BioConductor. For gene lists annotations, we will use Annotate and AnnBuilder packages (Bioconductor) that include interface functions for extracting information from specific meta-data libraries. These packages allow associating particular genes with locations on chromosomes, GO terms (Gene Ontology Consortium), KEGG metabolic pathways and other useful information. We have also developed our own database search engine for gene annotations which filter out the problematic redundancy or homologous genes from closely related species. Pathway Studio/Pathway Assist and Ingenuity Pathway Analysis NCBI are available for pathway analysis in basic research. When required, use will be made of phylogenetic inference packages, such as Phylip, PAUP*, MEGA3, Mesquite, MrBayes, Molphy, PAML.

Biomathematical/Biostatistical Support for Cell Biology. Recent decades have seen impressive advances in experimental approaches to *in vivo* cell kinetics. These advances have made it possible to distinguish many cell types by antibody labeling so that cells of different types can be counted in the dissociated tissue by using flow cytometry. In other words, it is now possible to make snapshots of multi-type cell populations as they develop in time. However, the potential of these technological advances remains to be unveiled. There is a wide spectrum of biological and translational applications of stochastic modeling of complex renewing cell populations, including the generation of oligodendrocytes in cell culture, embryonic development of spinal cord, and proliferative responses of the population of leukemic cells to drug treatments; the latter having far-reaching translational implications. Since the typical pathogenesis of leukemia, for example, results in a competitive advantage for malignant cells, one must conclude that the balance between various kinetic processes favors the leukemia population. In order to effectively suppress or destroy the leukemia, it is therefore necessary to develop therapeutic regimens that sufficiently alter the kinetics of leukemic stem cells (LSC) to favor the competing normal counterparts. The efficacy of various drugs for targeting LSCs can indirectly be measured using biological assays. However, this process is expensive, time-consuming and cumbersome. Certainly, any kind of high-throughput screening at the cellular level is not feasible for LSC. Thus, we propose that mathematical modeling of leukemia kinetics will provide a viable alternative approach. By creating a mathematical description of leukemia development, it should be possible to rapidly predict how various drugs affect the LSC population. This in turn will enhance our ability to identify those drugs with the potential to reduce LSC competition and therefore mediate therapeutically meaningful consequences. A collaborative research project on stochastic modeling of proliferation and differentiation of cells *in vitro* and *in vivo* is currently underway at the DBCB. This research effort is supported in part by an NIH grant (Dr. A. Yakovlev) and involves the Department of Medical Genetics, Department of Medicine, and James P. Wilmot Cancer Center. The research team has published 13 peer-reviewed papers in this field, with 3 more submitted. Owing to analytic findings from our preliminary studies we are now able to consider the utility of a new class of multi-type branching stochastic processes with non-homogeneous immigration in modeling and analysis of the processes of proliferation and differentiation of leukemic cells and their responses to chemotherapeutic agents. Such stochastic processes can be used as building blocks for designing stochastic models of cell systems of

increasing complexity. Along related lines, the research team is also involved in stochastic modeling of immune responses under the auspices of the CBIM.

G2D3. Epidemiology

Epidemiology is a core requirement in many translational research initiatives. Classic epidemiologic designs are often the best initial way to move new "bench" discoveries to the "bedside" and take novel clinical observations back to the laboratory for further investigation and/or confirmation. Such observational studies are often the most efficient, cost-effective and ethical means of moving the new discovery along the research continuum. Findings from such studies are likely to require definitive confirmation through controlled clinical trials. In the final phase of translational research, i.e. bedside to community, community trials and extended cohort studies are critical for establishing the long-term effectiveness of therapies emanating from the initial laboratory "discovery." The Division of Epidemiology, Department of Community & Preventive Medicine will collaborate with the DBCB to address the design, analysis and interpretation of all epidemiologic research conducted under the CTSI initiative. Epidemiology faculty will provide support to trainees and senior investigators as needed to assure that CTSI-supported studies are planned and implemented so as to reflect a stringent scientific approach and optimize the potential for a successful investigation and appropriate dissemination of research findings. Epidemiology faculty will assist in identifying study populations, determining appropriate comparison groups, establishing exposure and outcome definitions, developing operational approaches for implementation, estimation and description of subject risk profiles, managing issues of bias and confounding, and applying analytic methods for estimating and interpreting individual and population risk.

G2D3a. Background and Experience.

The Division of Epidemiology, led by Dr. S. Fisher, now has 6 full-time faculty, 3 full-time administrative, coordination and programming staff and numerous adjunct faculty in diverse clinical areas. A new doctoral program in Epidemiology currently includes 15 full-time students. The faculty also actively supports the Masters of Public Health program, including teaching graduate courses and mentoring students as they meet the thesis research requirements of the program. Six current fellows in the Preventive Cardiology Training Program (T32) (T. Pearson, PI) also participate in many of the activities and projects within the Division of Epidemiology. Division faculty have broad interests and expertise related to disease prevention and health promotion. They are committed to excellence in educational endeavors and in health-related, epidemiologic investigations. They have solid methodological foundations and strong analytic skills. A team approach to scientific inquiry and life-long learning enhances interactive participation of faculty, trainees and staff. These priorities will be nurtured to enhance the progress and accomplishments of investigators conducting research under the auspices of the CSTI. Division faculty have extensive experience in the conduct of research. They currently conduct numerous independent epidemiologic studies and have garnered local, state and federal funding support for this research. Division faculty are also co-investigators on many research studies led by PIs throughout the University.

G2D4. Clinical Research Ethics

Under the CTSI, Clinical Research Ethics Program will support and bridge research and educational functions to foster new disciplines concentrated in the following three areas: 1) Improving Research Decision-Making, 2) Impact Analysis and Cost-Effectiveness, and 3) Managing Conflicts of Interest.

G2D4a. Background and Significance.

Many challenges face future clinical and translational research efforts. Key areas of CTSI innovation will be improved disease prevention, better detection of subclinical or early clinical disease, and treatments for established disease. Many of the innovations have the potential to greatly affect the costs and outcomes of health care, but most agree that the new discoveries will not be cost-savings, but cost-enhancing (40). In addition, many of the CTSI innovations will require the testing of novel "high-risk" interventions in human subjects for the first time using study designs associated with ethical controversy (e.g., sham procedures) (41). Indeed, it would be ethically troubling if patients agreed to participate in high-risk translational research that used suboptimal study designs or if patients misestimated the risks and the benefits. Finally, as these translational research opportunities evolve, so too will the potential for conflicts of interest and the continued erosion of public trust in the research enterprise (42). The CTSI Clinical Research Ethics Program will be positioned proactively to address methods to improve research decision-making, the cost-effectiveness of future translational diagnostics or therapeutics, and methods to minimize bias (perceived or real) in the conduct

of such studies. In addition, the program will have the flexibility to adapt and address other ethical, social, and community consequences not currently part of its core functions. Contributing to these efforts will be over 15 faculty and investigators from a variety of departments (Community and Preventive Medicine, Medical Humanities, Medicine, Neurology, Pediatrics, Pathology, Orthopaedics) and support areas (Research Subjects Review Board, Office of Research Project Administration, Office of Technology Transfer). In the past six months, assistance has been given to the departments of: Anesthesiology, Biology, Chemical Engineering, Emergency Medicine, General Surgery, Medicine, Microbiology and Immunology, Neurology, Ophthalmology, Pathology, Plastic Surgery, Radiology, Vascular Surgery and many others. As this list grows, consultations may involve a laboratory setting or a multi-center clinical trial.

G2D4b. Improving Research Decision-Making.

Members of the Clinical Research Ethics Team have been exploring various aspects of clinical research ethics as part of pipeline project VIII for the Parkinson's Disease Gene Therapy Study: Measuring and Explaining Parkinson's disease (PD) Patients' Participation Preferences Regarding Phase I Studies in Gene Transfer Therapy (H. Federoff, PI U54-NS45309). We have explored various stakeholders' perspectives on the science and ethics of sham-surgery controls when used to test novel interventions such as gene-transfer for PD (43). We asked various stakeholders (PD researchers, PD patients, and primary care patients) to imagine they are a member of an ethics review committee whose job it is to decide whether or not to allow certain studies (approximately 60% response rate). Table G2D1 shows the percent of respondents who would definitely or probably allow an unblinded (open) versus a blinded (sham) control study design to test a hypothetical novel gene-transfer technique with promising phase I results. The results showed that the PD clinical research community strongly endorses sham-surgery designs and, in fact, would be unlikely to accept a future treatment as highly efficacious unless sham conditions were used to test it. On the other hand, patients (both PD and primary care clinic patients) predominantly preferred an unblinded design, deciding against sham surgery primarily due to procedure risks rather than ethical considerations.

Table G2D1: Percent Who Would Definitely or Probably Allow Open and Sham Controls

Study Design	PD researchers (n=103)	PD patients (n=56)	Primary Care patients (n=119)
Would you allow the **unblinded** study of the gene transfer intervention?, %	50	81	81
Would you allow the **blinded** study (sham surgery**)** of the gene transfer intervention?, %	94	54	55

In addition, we also wanted to understand why patients may participate in high-risk translational research even when they are unlikely to benefit from the therapy. Therefore, we explored why patients with PD might volunteer for an early phase I gene-transfer study and compared the results to patients who would not participate (44). Of the 92 subjects interviewed, 46 were willing to participate and 46 were not willing to participate. The two groups (willing versus unwilling) were similar in terms of their demographics and clinical characteristics. They did, however, differ in terms of their reasons against and for participation. (Table G2D2) PD patients willing to participate in a phase 1 gene-transfer study perceived a lower probability of risk, were more tolerant of risk and were more optimistic about the study's benefit to society. In addition, they were more decisive and action-oriented.

Table G2D2. Ratings of Reasons Against and For Participation

Reasons	Willing n=46	Unwilling n=46	p-value
Reasons against participation			
It seems too dangerous	3.0 (1.0)	3.6 (0.6)	.001
I don't like the idea of brain surgery	2.6 (1.1)	3.0 (1.0)	.04
I don't want to be a guinea pig	1.8 (1.0)	2.4 (1.2)	.009
Reasons in favor of participation			
It's better to do something rather than just waiting	3.4 (0.9)	2.7 (1.0)	.001
I want to contribute to science	2.9 (0.9)	2.5 (1.1)	.04

Values are expressed as mean (SD); range of scores, 1=not a reason, 2=minor reason, 3=moderate reason, 4=strong reason

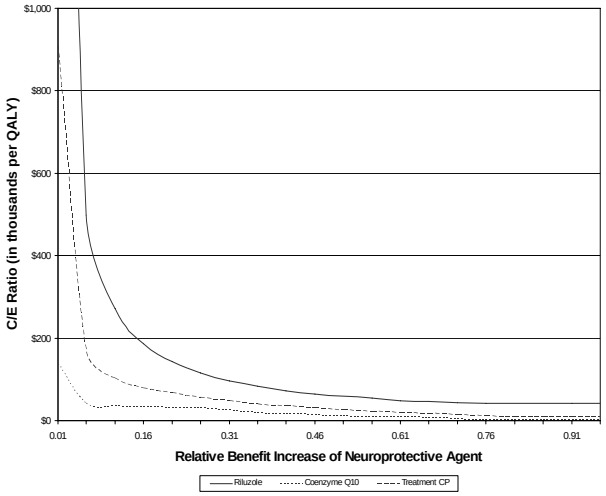
These studies emphasize the importance of risk information in deciding whether or not to participate in early phase gene-transfer studies, at least for PD patients. Questions remain about patients with other diagnoses, about the type of high risk intervention (e.g., non-neurological, surgical vs. medical, preventive vs.

disease modifying), and how risk information should be conveyed to facilitate patient decision-making in the informed consent process.

G2D4c. Methods.

We will collaborate with CTSI investigators to apply and extend our work on measuring and explaining participation preferences to high-risk CTSI initiatives. This work will be highly collaborative and multidisciplinary, and the Clinical Research Ethics Team will be integrated closely throughout all phases of the translational and clinical studies. We will adapt our already created survey methodologies to obtain patient perceptions and preferences of risks and benefits to identify areas of patient concern or misestimations. We anticipate that participation preferences will be obtained from at-risk populations, those with manifest disease, and those actually considering study participation, depending on whether the studied technology will be diagnostic (e.g., bionomic signatures for Alzheimer's disease [AD]) or therapeutic (e.g., stem cell therapy for multiple sclerosis). Lessons learned will be incorporated into the informed consent process and studied further if needed (e.g., evaluating graphical versus numerical display of risk information to potential subjects). In addition, other stakeholder perspectives will be sought and obtained. For example, we will obtain community views on pre-symptomatic diagnosis of PD and AD in order to develop consensus policies for maintaining appropriate ethical standards in the conduct of research and eventually in clinical practice.

Figure G2D1. How effective does a neuroprotective agent in Parkinson's Disease need to be to be cost effective?



G2D5. <u>Impact Analysis and Cost-Effectiveness</u>

G2D5a. Prior Experience.

The Clinical Research Ethics Team has considerable experience in the conduct of impact and cost-effectiveness analysis. They have overseen the conduct of at least four clinical-economic trials, and have published extensively on decision-modeling, quality of life assessments, and methods to analyze uncertainty in cost-effectiveness estimates (45-47). Their work has included the cost-effectiveness of both diagnostic as well as therapeutic technologies, and preventive as well as targeted-symptom therapies. For example, we studied the cost-effectiveness of Deep Brain Stimulation (DBS) for PD compared to best medical management (48). The results of this analysis suggested that DBS may be cost-effective in treating PD if quality of life improves 18% or more compared with those receiving best medical management. The results were used in planning a large randomized, clinico-economic trial comparing DBS to best medical management currently underway and were used as part of the evidence base to justify insurance coverage. Finally, we have performed a worldwide burden of disease analysis for PD using published and estimated age-specific prevalence rates of PD and census projections from the U.S. Census Bureau's International Database (49). The results show that by 2030, the number of individuals over 50 years old with PD in the ten most populous nations and five most populous European nations will more than double to 8.7 to 9.3 million.

We also have performed several cost-effectiveness analyses of potential neuroprotective therapies for neurodegenerative conditions. From these studies, we have developed a cost-effectiveness framework with policy implications for developing future neuroprotective therapies (50). For example, as the efficacy of a putative treatment to delay the progression of Huntington's disease increases, the cost-effectiveness of treatment decreases (Figure G2D1). A threshold analysis from this study indicates that an inexpensive, well-tolerated therapy (less than $1,000 annually for therapy and the management of side effects), even if only marginally effective, is likely to be cost-effective (i.e., less than $100,000 per quality-adjusted life year). Conversely, even moderately expensive therapies ($10,000 annually) are unlikely to be considered cost-effective unless highly efficacious. In this way, one may identify innovations that may be more effective, but at a price tag greater than society is willing to pay. Although these results should not deter the pursuit of costly

treatments, it highlights their considerable economic impact if put into practice and may help to focus energies on less expensive and better tolerated approaches.

G2D5b. Methods.

We will adapt our projection modeling paradigm to CTSI-enabled technological innovations. Performing such analyses will be a multidisciplinary effort drawing on the expertise of the translational researchers, epidemiologists, health economists, clinical trialists, quality of life experts, and, when necessary, health policy analysts. These analyses will be used to responsibly plan for future clinical trials and to assist in sample size calculations. In addition, these actuarial decision models will be tailored to different potential decision makers in determining future resource needs by conducting analyses from different perspectives (e.g., society, Medicare, patients). Although we recognize the limits of modeling future events, we believe that incorporating this approach is better than simple extrapolations of data from past experience or a small number of experts.

G2D6. Managing Conflicts of Interest

G2D6a. Prior Experience.

Most conflict of interest (COI) discussions in research have dealt with financial conflicts of interest as they relate to clinical trials (e.g., receiving personal remuneration for consulting activities from the same company for which one is planning, conducting or reporting the results of a clinical trial) (51). Little, however, has been written about the potential COI that may arise when conducting translational research. The early experience of the URMC COI committee suggests that potential conflicts in translational research more often involve intellectual property holdings and ownerships of commercial spin-off companies. Our current COI policy allows such faculty relationships (with a management plan) in human subjects research as long as the study is only generating pilot data to inform a larger pivotal clinical trial (52). If, however, the clinical trial will lead to data in support of FDA approval or is a post-marketing study to refine or support expanding indications, then the faculty must recuse from the study or divest their interest.

G2D6b. Methods.

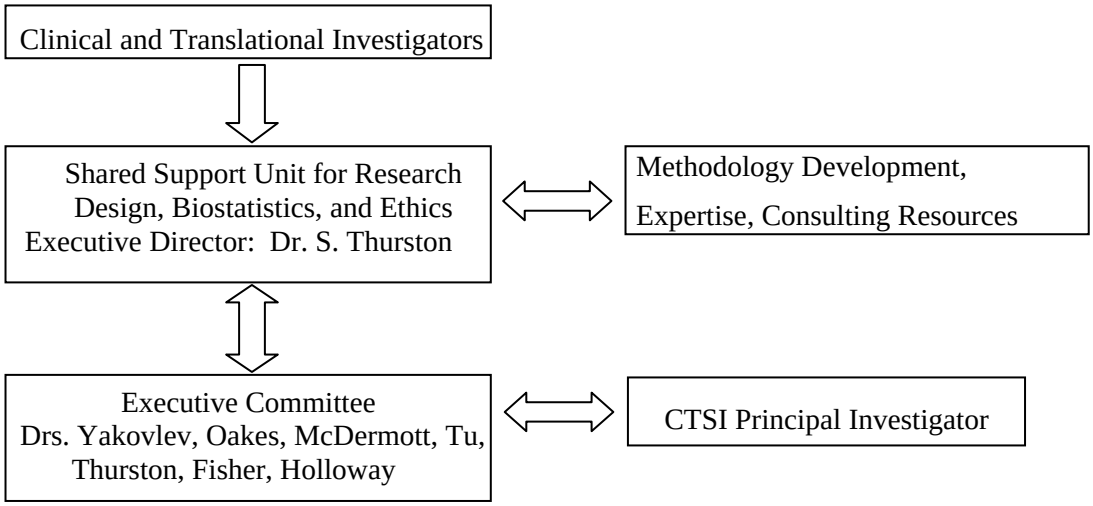
We plan to conduct innovative research on evolving COI arrangements of translational research at the interface between academics and industry. We plan to test the feasibility of our current COI policy for CTSI-related research. This programmatic analysis will include descriptions and categorizations of potentially conflicting relationships, as well as the frequency and content of conflict of management plans, divestitures, and contingency plans for recusals. We will also compare how COI relationships differ by different research categories (basic research, clinical trials, health services research, and epidemiology) and the acceptability of such arrangements to various stakeholders including patients.

G2D7. Shared Support Unit for Research Design, Biostatistics, Epidemiology and Ethics Program

Faculty with expertise in epidemiology, biostatistics, bioinformatics, and research ethics are integrally involved in collaborative research activities in many areas, including (but not limited to) Biomedical Genetics, Environmental Medicine, Cardiology, Psychiatry, Pediatrics, Dental Research, Infectious Diseases, Community and Preventive Medicine, Neurology, the Center for Aging and Developmental Biology, and the Cancer Center. The Department of Biostatistics and Computational Biology currently offers a statistical consulting service to Medical Center faculty. The Biostatistical Consulting Service is headed by Dr. X. Tu and coordinated by S. Messing, M.S. Services range from purely advisory assistance to complete mathematical/statistical analysis and data management support for projects. Department faculty are available as research collaborators and statistical consultants, with support from research associates and graduate research assistants. The Department's programming group, including programmers and information analysts, also works with the faculty statisticians to provide programming and data management support. In order to appropriately support CTSI projects, this consulting service will be expanded to address epidemiologic considerations and special ethical concerns. Faculty from the Division of Epidemiology under the direction of Dr. Susan Fisher, and from the Ethics in Clinical Research Program under the direction of Dr. Robert Holloway, will assess the specific respective needs of each project and provide the indicated consultative services. Although the existing infrastructure has proven quite efficient it needs to be enhanced to extend services and collaborations to all promising projects in clinical and translational research. The CTSI Biostatistics, Epidemiological and Clinical Research Ethics Program will oversee and coordinate a consulting service available to all CTSI projects and trainees. While many members of the Biostatistics Department, Division of Epidemiology and Clinical Research Ethics Program will have close collaborative relationships with selected departments, the Consulting

Center will serve all Medical Center departments. All resources, statistical and computational are available to assist the investigators and students requesting our services.

Figure G2D2 : Organizational Chart of the Design, Biostatistics and Clinical Research Ethics Program



Within the CTSI the ability of URMC to provide design, biostatistics and clinical ethics expertise to CTS investigators will be substantially upgraded. With related experimental design and conceptual components, some of the quality control and analytic issues will be shared among the projects. By using the shared resources related to design, biostatistics and clinical ethics of the UR CTSI, all projects will benefit from the experience gained in each project, while simultaneously saving costs since any potential duplication of expensive services and efforts will be eliminated. Without a centralized support system, the costs of the proposed clinical and translational research would likely be prohibitive, or else the quality would be compromised due to insufficient collaboration. The organizational chart of the Design, Biostatistics and Clinical Research Ethics Program is presented in Figure G2D2.

Prioritization of Research Projects. An executive committee including Drs. Yakovlev, McDermott, Oakes, Tu, Thurston, Fisher and Holloway will review all requests for biostatistical, epidemiological, and ethical support for clinical and translational research. An applicant requesting support will be invited to discuss relevant technical issues. Criteria that will be considered include: a) alignment with the overall goals of the CTSI, as spelled out by the CTSI Steering Committee; b) scientific novelty and importance; c) impact on patient care; and d) potential for future methodological development. Pilot projects funded from the CTSA mechanism will be given the highest priority at all stages of research from study design to final analyses. This executive committee will be responsible for assigning CTSI resources (biostatistical, epidemiologic and ethical) to different projects. The system currently used by the Consulting Service to track the status of ongoing projects and effort expended will be expanded to cover all CTSI activities. The executive committee will conduct semi-annual reviews of all ongoing projects to ensure that they are on track and that resource usage is in accord with that budgeted.

Educational Activities to Support Trainees. The following courses are available to support the training of students and faculty within the various CTSI training initiatives.
Introduction to Biostatistics – This is an introductory course in biostatistical methods that covers topics from data description up through analysis of variance and simple regression and correlation.
Statistical Methods for Biomedical Applications – This is a continuation of the introductory course above that covers analysis of variance, analysis of covariance, multiple regression, analysis of contingency tables, introduction to generalized linear models, and introduction to survival analysis. Model checking is strongly emphasized. Numerous examples are used to illustrate the practical application of the methods.

Design of Clinical Trials – This focuses on important aspects of the design, analysis, and reporting of clinical trials, including protocol development, hypotheses and objectives, specification of response variables, defining the study population, randomization, blinding, ethical issues, factorial designs, cross-over designs, equivalence studies, clinical trial monitoring/interim analyses, sample size determination, issues in data analysis, reporting of results, and evaluating clinical trial reports.
Current Topics in Bioinformatics – This is a course taken by graduate students in Statistics as well as investigators and students in translational research programs.
In addition to these existing courses, we plan to design a special short course in study design and data analysis specifically geared toward investigators in clinical and translational research. We had positive experiences with such courses in the past. For example, in 2004 Dr. O. Hyrien provided a series of ten lectures on introductory biostatistics to residents and fellows in Radiation Oncology.
Doctoral students in Statistics, in addition to their required core coursework, will have the opportunity to become involved in translational research projects. Depending on the interest of the student and the nature of the research project, the student may be advised to take courses outside the Department in order to enhance the interdisciplinary effort. Clearly involvement in collaborative translational research provides a wealth of educational opportunities, including the potential that this collaboration may yield problems in statistical methodology suitable for dissertation research.
Introduction to Epidemiology: This three-credit course provides an introduction to the concepts of risk estimation, disease surveillance, study design, and bias and confounding.
Field Epidemiology: This course emphasizes the tools and applications required to conduct clinical research, providing hands-on experience in the planning and implementation of a study.
Advanced Epidemiology: Methodologic and analytic approaches in epidemiologic research are emphasized in this curriculum.
Multivariate Analysis in Epidemiology: This advanced course focuses on higher level analytic techniques, including conditional logistic regression, Cox proportional hazards modeling with time-dependent covariates, matched multivariate methods, and hierarchical modeling.

A targeted short course in epidemiology analogous to the one biostatistics will also be offered. There are considerable resources available to support the clinical research ethics education of students, fellows and faculty enrolled in the K30 curriculum, the K12 career development program and the various T32 training opportunities. Specific courses to support clinical research ethics education include Ethics and Professional Integrity in Research Biomedical Sciences, Recruitment and Retention of Human Subjects, and Cost-Effectiveness Research. These are described in detail in section G2I of this application.

G2D8. Evaluation of the Design, Biostatistics and Ethics Function

This key function will be evaluated through the following mechanisms: (1) Methodological developments and their dissemination will be reported by Director of the Shared Support Unit (SSU) to the Executive Committee on the annual basis. These reports will be reviewed by the Committee and summarized in its biannual and final reports to the CTSI PI. (2) Every investigator receiving support from the SSU will be requested to fill out an evaluation questionnaire. The results of such surveys will be reviewed by the executive Committee and included in its biannual report to the PI. (3) An electronic system will be implemented to track the ultimate outcomes such as grant applications, peer reviewed publications, inventions, and presentations. (4) The Executive Committee will prepare 2 biannual and 1 final reports for the CTSI PI.

G2D9. Novel Aspects of Design, Biostatistics, and Clinical Research Ethics

The proposed framework is innovative in the following respects: (1) it brings together three functions (Biostatistics, Epidemiology, Ethical Consultation), which have traditionally been seen as separate, under a common umbrella, thus facilitating “one-stop” shopping by clinical and translational investigators, (2) it provides a mechanism for developing innovative methodology in these areas as it is needed for specific projects so that investigators do not have to rely on “off the shelf” solutions and (3) it provides procedures for prioritizing, monitoring and evaluation in terms of contributions to the overall research endeavor, (4) The clinical research ethic projects propose to better understand the patient’s perspective in designing and participating in clinical trials, particularly of high-risk innovations, highlighting the need for “patient-centered” research participation. In addition, the impact analysis and cost-effectiveness projects will begin to address as rigorously and scientifically possible whether society will see a return on its translational research investment. Finally,

keeping pace of the conflicts of interests that may arise as the Roadmap unfolds will be critically important, and we propose to use innovative research methods to inform how best to set future conflict of interest policies.

G2D10. Design, Biostatistics and Ethics Program Leadership

Andrei Yakovlev, Director, is Professor and Chair, Department of Biostatistics and Computational Biology. He will bring his expertise in computational biology and statistical methods for basic and translational research to the program. He will be responsible for overall direction and coordination of the program.

David Oakes, Co-director, is a Professor at the Department of Biostatistics and Computational Biology. He will be responsible for the clinical component of the program.

Susan Fisher, Co-director, is an Associate Professor and Chief of the Division of Epidemiology, Department of Community & Preventive Medicine. She will be responsible for the epidemiological aspects of the program.

Robert Holloway, Co-director, is an Associate Professor of Neurology and Community and Preventive Medicine. He will be responsible for the clinical research ethics component of the program. He has expertise in quantitative and qualitative methods in conducting research on decision-making under conditions of uncertainty (e.g., patients deciding to participate in clinical trials). He also has more than 10 years of experience in performing cost-effectiveness research.

Sally Thurston, Executive Director of the Shared Support Unit for Research Design, Biostatistics, Epidemiology and Ethics Program, is an Assistant Professor at the Department of Biostatistics and Computational Biology. She will provide day-to-day scientific and administrative management of the Unit in accordance with the organizational chart presented in Figure G2D2.

The credentials of the above-listed individuals are presented in their biographical sketches.

G2E. CTSI REGULATORY KNOWLEDGE AND SUPPORT PROGRAM

G2E1. Specific Aims:

The Specific Aims of the CTSI Regulatory Knowledge and Support Program are:

1. To ensure that CTSI researchers are trained in the science and ethics of CTSI-related human subjects research in order to optimize study design, regulatory review and the informed consent process.
2. To conduct quality improvement / good clinical practice guideline audits to provide onsite guidance to CTSI researchers and to assist decision-makers to determine state of compliance with regulations, institutional policies and IRB requirements.
3. To develop an educational and assistance program (computer-assisted as well as in-person help) to assist CTSI researchers in developing regulatory review submission documents and informed consent forms for CTSI-related projects.
4. To ensure that conflicts of interest are eliminated or managed appropriately for all CTSI research.
5. To provide integrated training, support and information not only within the CTSI, but to share these services and CTSI "best practices" in support of regulatory knowledge and compliance with the entire University, the Upstate New York Translational Research Network, and the National CTSI Consortium Steering Committee.

The goal of the CTSI Regulatory Knowledge and Support Program is to enhance the model support services already in place at the University by providing "researcher-focused" and "translational research specific" support for regulatory compliance and management. We will accomplish these aims by 1) developing a team of specialized regulatory support personnel for the CTSI that are well versed in regulatory requirements, easily accessible to investigators and that routinely participate in University, Medical Center and Upstate New York Translational Research Network compliance activities; 2) supporting and interacting with the CTSI ethics and research educational and training functions to foster regulatory compliance through an understanding of ethical underpinnings and oversight structure; 3) an ongoing evaluation of the effectiveness of regulatory support via advisory groups and ongoing audit. This program is innovative because specialists in translational research and associated regulations will be assigned to support investigators in areas that are unique to this type of research.

G2E2. Background and Significance

There are many regulatory challenges facing the clinical and translational research efforts. To be clinically proven, CTSI treatment innovations will require "phase 1" testing of novel "high-risk" interventions in human subjects. Some study designs will be associated with ethical controversy (e.g., sham procedures, gene transfer, and xenotransplantation) (1-3). It is critical that patients who participate in high-risk translational research are fully informed, understand, and voluntarily agree to participate through the informed consent process and that investigators comply with both the letter and the spirit of the human subject protection regulations. Regulatory compliance will help foster public support and trust in the clinical and translational research enterprise (4).

In addition, settlements and findings of recent years have demonstrated that the HHS Office of Inspector General and the Department of Justice are concerned with universities' adherence to costing and administrative requirements of the Office of Management and Budget and of the NIH. Compliance in all areas of award administration is critical to ensure that the CTSI and the University are being proper stewards of scarce federal resources. The Council on Governmental Relations publication entitled "Managing Externally Funded Research Programs: A Guide to Effective Management Practices" suggests the numerous compliance areas where universities should review overall management and internal controls and serves as a guide for the University of Rochester and will be for the CTSI as well (5).

The CTSI Regulatory Knowledge and Support Program, through its Office of Regulatory Compliance and Support (ORCS), will pro-actively monitor and address compliance issues in the conduct of all studies. In addition to dedicated staff described below, collaborative and coordinated efforts will be undertaken with other current University support activities (Research Subjects Review Board (RSRB), Office for Human Subjects Protection (OHSP), Office of Research and Project Administration (ORPA), Clinical Research Review Process Improvement Team (CRRPIT) and University Audit) and will leverage the other activities of other CTSI key functions in pursuit of these goals.

Conflict of interest (COI) has been a concern within the scientific community for many years. In part, the potential for COI has increased due to the Bayh-Dole Act of 1980, which provided opportunities and incentives for translational research, but which also increased the likelihood of COI situations to develop. The international research community and the public became acutely aware of the problem after the death of a volunteer subject in 1999 in research that was conducted and supported by a university and a spin-off company, which was partially owned by the principal investigator and the university (6-8).

The CTSI Regulatory Knowledge and Support Program will build upon the outstanding programs that currently support clinical and other research at the University. Rather than replacing these functions, the CTSI Regulatory Knowledge and Support Program will leverage the current structure and support to create a new and vital level of specialized support specifically aimed at translational research.

G2E3. Specific Aim 1: Training and Support in Research Regulation Compliance

G2E3a. Prior Experience. The University of Rochester has been a national model in the areas of human subject protection and research administration. Gary Chadwick, Associate Provost and Director of the Office for Human Subjects Protection (OHSP), is the co-author of the major investigator training manual used in many academic medical centers (9). Both he and Gunta Liders, Associate Vice President for Research Administration and Director of the Office of Research and Project Administration (ORPA), are very active on national advisory panels and hold leadership positions in their professional organizations. These two people will be important advisors and collaborators in the development and operation of the CTSI Regulatory Knowledge and Support Program and its Office of Regulatory Compliance and Support, as well as in other CTSI key functions (see sections G2J and G2I). Both will devote dedicated time (non-salaried) to serve as lead consultants to the CTSI Regulatory Knowledge and Support Program.

Improving the review process and strengthening the oversight of research without undue burden has been an emphasis area of the University for some years. The Senior Associate Dean for Clinical Research chairs an active committee – the Clinical Research Review Process Improvement Team (CRRPIT) – that regularly reviews policies, process, outcomes and resources associated with clinical and translational research. The University operates two conflict of interest (COI) committees – one at the University level and one at the Medical Center. These operate under the auspices of the Provost and the Dean of the School of Medicine and Dentistry, respectively. The University maintains a patient advocate position (Research Subject Advocate) with its General Clinical Research Center and the lessons learned from the operation of this program will inform the development of the CTSI patient/subject advocate role in the Regulatory Knowledge and Support Program.

Education in research ethics and regulatory compliance is a major strength of the University. The most significant educational innovations follow:

1. The University developed and instituted a training requirement and program for investigators before the NIH required it. When announcing the requirement, the Secretary of Health and Human Services referred to the University's training program as an example of the type of training that investigators should receive (10;11). The University provides two levels of training for investigators, depending on whether they are conducting research that is minimal risk or greater than minimal risk (Ethical Principles in Research Programs and Human Subjects Protection Program, respectively).

2. For the past three years, the University has operated a classroom-based educational program consisting of basic and comprehensive instruction for sponsored programs compliance entitled Continuous Learning for Administrators of Sponsored Programs (CLASP). The CLASP program is a "continuous learning" program for research administrators and related personnel, and is nationally recognized as a model for a certification program aimed at research compliance. The preliminary mandatory modules of CLASP include a four-hour overview, pre-award functions (including proposal development and costing issues), post-award administration of sponsored awards, cost-sharing and effort reporting and close-out of sponsored programs accounts. Ongoing annual educational requirements include at least periodic attendance at monthly research administrator meeting and several electives. The elective offering is extensive, and includes the administration of training grants, administration of subawards, clinical trial agreements, etc. The University requires that each department that is involved in sponsored research identify a CLASP-certified individual who will oversee sponsored programs in the department. The CLASP program will be applied to CTSI activities to ensure proper adherence to standards and compliance with regulatory requirements.

3. In addition, to enhance services and provide principal investigators the information they need to comply with federal regulations, the University has developed an interactive Web resource, which provides faculty and staff an interactive portal for understanding the obligations imposed by funding sponsors, especially federal agencies. This Regulatory Compliance Web Portal is currently being utilized by the Rochester Clinical Research Curriculum (RCRC) to provide basic instruction on regulatory and administrative compliance to new faculty as a potential pilot for a university-wide educational requirement or a University Research Compliance Education Program.

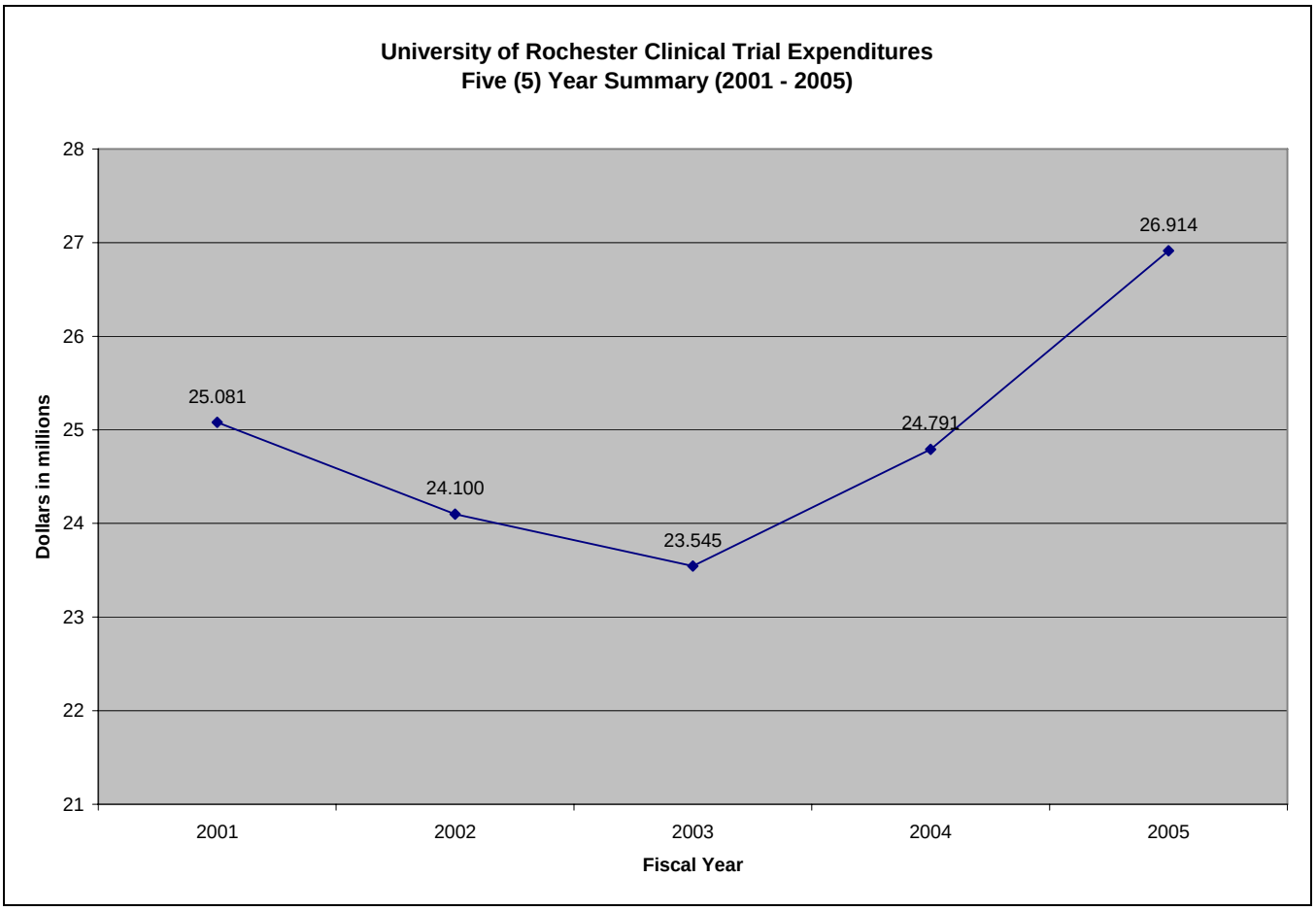
4. As noted elsewhere in this proposal (see Section G2I), the RCRC also requires completion of an Ethical Conduct of Research training program, as well as offers lectures, seminars and experiential learning labs in human subject protection and regulations. In addition to the innovative training and education already provided to investigators conducting human subject research, administrators, and new clinical faculty, the University provides comprehensive training and an ongoing lecture series for clinical study coordinators. Akin to research administrators, study coordinators are a key resource and provide front-line management for regulatory compliance. Within the University, there is an active study coordinator support group that has proven to be effective in working with and supporting new coordinators and new programs.

Innovation when dealing with industry and sponsored clinical trials has been a cornerstone of University policy for a decade. The Research Subjects Review Board (RSRB) is the University's institutional review board (IRB) for human subject research. A novel step was the use of an independent IRB (Western Institutional Review Board, WIRB) to review industry-sponsored industry-initiated research. The University of Rochester was the first academic medical center to gain approval of the addition of WIRB to its federal assurance. Many academic medical centers now follow this same model, which allows a more focused approach when reviewing studies, better allocation of IRB resources and rapid turn-around times while maintaining high levels of protection for human subjects. Another mechanism is the provision of assistance to investigators who are filing INDs and IDEs with the FDA. The Office for Human Subjects Protection has three staff with extensive industry experience and one with FDA experience and, although not a focus, the Office does provide advice and help to investigator-sponsors for FDA filings. The CTSI will expand and formalize that capacity as noted below.

As noted in Section G2D, the institution has extensive experience in working with multi-site trials and with the FDA with respect to studies involving investigational new drug application procedures. The Huntington's Disease Study Group (HSG) and the Parkinson's Disease Study Group (PSG) are both headquartered in the Department of Neurology. Both HSG and PSG operate multi-site and multi-national studies with funding from NIH, industry and foundations. That Department also operates a Clinical Trials Coordination Center (CTCC) that has coordinated multi-site clinical trials and provided protocol authoring, site selection, investigator training, site monitoring, data collection and analysis. The Department of Cardiology operates many multi-site studies; for example, both MADIT I and II trials were coordinated from the University. The PSG/HSG has also been successful in establishing a unique forum that facilitates discussion on compliance and research ethics. What began as a standing meeting to discuss ways to expedite the PSG/HSG multi-site clinical trials, the Contract Administration Working Group (CAWG) has morphed into a meeting that involves faculty, research administrators, RSRB staff, legal counsel, industry relations, public relations, federal relations and the Dean of the School of Medicine and Dentistry. While simple in principle, the CAWG is a truly cross-disciplinary and innovative group that routinely discusses, among other topics, improvements and exciting innovations in clinical and translational research administration and compliance. It is a model that can easily serve the CTSI and its User Advisory Board as noted below.

The University's expenditures in clinical trials are noted below, predominantly represented by multi-site clinical studies led and coordinated by the PSG/HSG and Cardiology. As noted elsewhere in this proposal, the University's experience in multi-site clinical trials matches its robust portfolio of clinical research, in general.

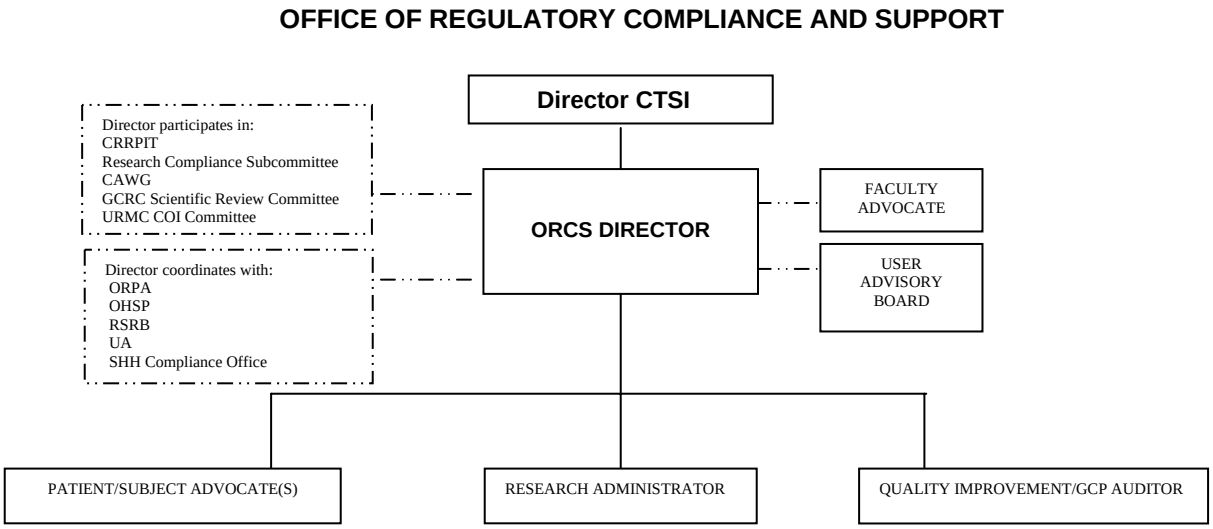
Figure G2E1: University of Rochester Clinical Trials Expenditures, Five-Year Summary



In summary, the University of Rochester has already established a variety of effective educational programs, committees, and a wealth of experience that the CTSI can leverage to establish a successful program of regulatory knowledge and support.

G2E3b. Methods. In order to achieve Specific Aim 1 as well as the other aims noted in this Section, the CTSI will add an Office for Regulatory Compliance and Support (ORCS) as an integral part of the Regulatory Knowledge and Support Program. This office (ORCS) is intended to be a new and specialized program of support that builds upon the resources already in place at the University, i.e., it will function in cooperation with ORPA, the RSRB and OHSP to enhance human subject protection and regulatory compliance. The ORCS will report to the Director of the CTSI (see CTSI organizational chart of key functions in section 1) and will be headed by a Director of Regulatory Compliance and Support. ORCS will be staffed with patient/subject advocates, a research administrator, and a quality improvement / good clinical practice auditor. In addition, the ORCS will retain a "faculty advocate" as a consultant who will provide guidance and advice to its staff with respect to the methods and level of assistance that ORCS is providing to faculty investigators. The ORCS will establish a User Advisory Board that will include, at a minimum, its faculty advocate, the Directors of ORPA, OHSP and CTSI Research Education, as well as three additional CTSI principal investigators, at least one of whom will be a new investigator. This advisory board will meet regularly and help to ensure that ORCS remains user-friendly and customer-oriented. Any issues that cannot be resolved within ORCS and its User Advisory Board will be brought to CRRPIT as noted below. To help ensure that CTSI is responsive to the needs of patients, subjects, and researchers, the ORCS Director will co-chair CRRPIT, and this committee will be organizationally supported by ORCS.

Figure G2E2: Office of Regulatory Compliance and Support



ORCS will participate in the activities outlined in the Clinical Research Ethics Program described in Section G2D, namely to assist the clinical research ethics team in its effort to foster new disciplines in improving research decision making, impact analysis and cost effectiveness and managing conflicts of interest. In addition, ORCS will provide oversight and assistance in the following key areas: protocol development (regulatory, administrative and budgetary sections); consent process monitoring and consent form development; and regulatory reporting including reports of unanticipated problems and adverse events.

ORCS will serve as a resource for investigators and provide assistance in filing investigational new device (IDE) exemptions and investigational new drug (IND) applications. The regulation governing the submission of an IND (21 CFR 312.23), for example, is the longest regulation in all of Part 312. It is easy for an individual investigator to become discouraged and confused while attempting to put an application together. Having readily available and knowledgeable staff to advise and assist will help ensure that promising new treatments are properly investigated and that all regulatory prerequisites are completed correctly. In addition to OHSP staff who have experience in working with the FDA to file INDs and IDEs and the necessary regulatory reports, ORCS will provide a formal consultative service (through its Director) for investigators who need to interface with the FDA when conducting CTSI-related research.

Under general direction from the Director of the CTSI, the ORCS Director will be responsible for oversight and development of CTSI policies and procedures for compliance with human subject and research administration regulations. The ORCS Director will manage the compliance, quality improvement, subject advocate and educational aspects of the Regulatory Knowledge and Support Program. The ORCS Director will provide administrative oversight in order to ensure maintenance of high ethical standards and regulatory compliance for clinical and translational research. The ORCS Director will provide oversight for the ongoing work and growth of the ORCS including responsibility for the administrative operations and implementation of policies and procedures. The ORCS Director will be responsible for developing, implementing, maintaining, and providing leadership, strategic direction and oversight of compliance and training activities for the Regulatory Knowledge and Support Program. He/she will provide guidance and advice on incorporating compliance-related activities into the day-to-day operations of the CTSI. The ORCS Director will ensure regulatory and policy updates are disseminated to investigators and research staff in a timely manner, ensure ongoing monitoring of all areas of research compliance, and will act decisively and effectively on issues of potential non-compliance.

The Regulatory Knowledge and Support Program will include patient/subject advocates who will be independent from the RSRB and the University compliance office, who will act as a sounding board for potential research participants, serve as advocates for research participants, and work with investigators, trainees, and research teams to ensure that research involving human subjects gives the highest priority to human subject protections. One of these advocates will be a senior faculty member that will facilitate interaction with CTSI investigators. One of the duties of these advocacy positions will be to routinely monitor the consent process for CTSI studies and prepare reports for the ORCS Director (and the RSRB as appropriate) on the status of compliance and any unanticipated problems in the consent process. A advocate positions currently exist in the GCRC, and these people will function as team-members of ORCS. The scope of activities will naturally increase and involve activities across the CTSI and the University.

The ORCS research administrator will be CLASP-certified and will have a primary responsibility to assist in grants management oversight, as well as providing leadership for CTSI administrative support. The ORCS research administrator will provide overall support in proposal development, ensuring allowable allocation of costs, proper allocation of payroll distribution, monitoring of subrecipients, post-award administration, interface with the University's Office of Research Accounting and Costing Standards, liaison with ORPA and OHSP, space management and other compliance requirements. CLASP certification will enable the research administrator to attend monthly update meeting that include ORPA, OHSP, Purchasing and Human Resources, as well as attend CLASP electives on subrecipient administration and clinical trials administration. While a structure as large as the CTSI would mandate such a position, the placement of a research administrator in an office specializing in regulatory compliance is novel and will aid in supporting compliance activities on a global scale.

In addition to dedicated and experienced staff that will provide support on a day-to-day basis, the CTSI and ORCS will benefit from and support the workshops described in the Research Education, Training and Career Development section (G2I). The RCRC already utilizes a novel mix of academic leaders, faculty, administrators and regulatory experts in delivering its curriculum that will further enhance the regulatory "responsiveness" of the CTSI. The Director of ORCS is expected to utilize in its own programs and participate in the various skill building workshops required for key competencies in education and training in Clinical/Translational research, such as in the Ethical Conduct of Research Workshop and the Clinical Research Skills Workshop on Research Project Management.

In order to remain engaged in University compliance priorities, and to ensure that the CTSI is fulfilling its compliance mission, the Director of the ORCS will also participate in the following activities: 1) co-Chair and support the CRRPIT, the University's Research Compliance Subcommittee (the latter is a subcommittee of the University Compliance Committee) and the CAWG (the latter in gaining experience in leading the ORCS User Advisory Committee); 2) become a member of the General Clinical Research Center Advisory Committee; and 3) participate on the URMC COI committee and lead an effort to refine current COI policy and management strategies for CTSI-related research as described in Section G2d of this proposal.

The participation and interaction of ORCS staff of noted University activities will initiate a cross-fertilization of ideas, innovations and processes that will benefit CTSI regulatory knowledge and support, as well as facilitate procedures and processes for its investigators.

G2E4. <u>Specific Aim 2 Regulatory Compliance Monitoring and Improvement</u>

G2E4a. Prior Experience. The Office for Human Subjects Protection (OHSP) has considerable experience in the conduct of quality improvement / good clinical practice guideline audits. They have overseen the conduct of at least 40 audits yearly for the past few years. In addition to reviewing performance and reporting on compliance, the OHSP program emphasizes education during the review process. Immediate feedback on regulatory compliance and the application of good clinical practices is provided by the OHSP auditor. This "on-the-job" training has been well received by investigators and study coordinators and extends the University's mentoring program for investigators. Additionally, the results of these reviews are used to develop educational efforts by OHSP and seminar topics. Special short course offerings and the like have been developed and presented to meet needs identified through this monitoring activity.

Sponsored research is an integral component of the Office of University Audit (OUA), which is the University's internal audit department and operates a risk-based audit program. OUA representatives participate in the ongoing development of the CLASP curriculum and its instruction; audit the controls regarding sponsored awards compliance and of the actual level of compliance (using a combination of

analytic procedures and a sample of historic transactions) for departments on the annual audit plan that have significant levels of sponsored program activity; and provide ongoing advice regarding best practices for compliance through participation in monthly meetings of sponsored program administrators and on a one-to-one basis via phone and email.

G2E4b. Methods. We will add a staff person to conduct quality improvement / good clinical practice guideline audits for CTSI-related research. Although we recognize the limits of audits in ensuring compliance, we believe that this approach is a critical part of the overall oversight process and provides the CTSI program with information that can be used to bolster compliance and develop corrective actions as necessary. The CTSI audit function will be an important source of information for ORCS, OHSP and the Ethics Training Program as each of these will work together to develop coordinated and focused training whenever unmet needs become evident. In addition, the Quality Improvement/Good Clinical Practice Auditor will interact with the Office of University Audit to leverage excellent existing audit programs, as well as with ORCS staff tasked with Specific Aim 1: Training and Support in Research Regulation Compliance.

G2E5. Specific Aim 3: Computer-assisted Regulatory Document Assistance

G2E5a. Prior Experience. The RSRB office provides excellent guidance to investigators as a routine part of their activities, but investigators must seek these resources out for themselves. The Office for Human Subject Protection and the RSRB conduct ongoing training and educational materials are available on their websites (12;13), but again these tend to be passive resources. Similarly, the ORPA faculty Regulatory Compliance Web Portal (14) is a useful tool and good introduction to regulatory and administrative compliance, but more interactive education and training would be preferred by investigators. The current Regulatory Compliance Web Portal offers an introduction to the following topics:

Table G2E1: Contents of the ORPA Regulatory Compliance Web Portal

Responsible Conduct of Research	Cost Principles
Environmental Health and Safety	Award Terms and Conditions
Protection of Research Subjects	Salaries and Effort Accounting
Export Control Regulations	Administration of Subawards
Conflict of Interest	Documenting Allocability
Publication, Data and Intellectual Property	Monitoring Project Spending
Scientific Integrity	Equipment
University Sign-off Procedures	Project Closeout
Financial Management/Audit	

This introduction is very valuable but would be even more effective if augmented in the manner noted in the methods section described below.

G2E5b. Methods. We plan to develop online interactive tools and outreach, for example with assistance in developing informed consent forms for different research categories (e.g., clinical trials, health services research and epidemiology) and preparing documentation for University review and oversight functions (e.g., RSRB and ORPA). To supplement the breadth of information that University provides on its websites, we plan on seeking advice from adult learning experts to help inform the University on optimal educational resources for busy clinical and translational investigators. Tools will then be developed that will allow investigators to maximize resource utilization and assist in some common tasks. As an example, the Regulatory Compliance Web Portal will be modified to provide such tools in accordance with specific regulatory requirements. In addition, topics relevant to clinical and translational research will be added such as the mechanisms of an IND/IDE submission, as well as other FDA requirements. ORCS will utilize not only experts in adult education, but will also leverage the work of the Biomedical Informatics Key Function in support of analysis of (a) requirements of research administration and regulation, (b) data elements relevant to research administration, (c) use context of research administration and regulation in the specific CTSI activities and overall CTSI processes, and (d) potential system functions that can be integrated with CTS workflow to facilitate research administration and regulation (see Section G2C). As the University develops these tools, they will be shared with the CTSA National Steering Committee and the Upstate New York Translational Research Network.

In addition, we propose to expand upon the use of the improved Compliance Web Portal currently used in the RCRC to investigators participating in the research education, training, and career development programs noted in Section G2i, as a pilot of initiating mandatory compliance education to all CTSI investigators and

University research faculty. The Director of ORCS will work with the Director of Research Education, Training and Career Development in developing the optimal process for certification, and maintenance of certification in this important initiative.

G2E6. Specific Aim 4: Conflict-of-Interest Management

G2E6a. Prior Experience. The University of Rochester has been sensitive to conflict-of-interest (COI) issues and the potential for negative impact on research conduct and reporting for many years. The University operates two COI committees: a University-wide committee and a School of Medicine and Dentistry (SMD)/Medical Center (URMC) committee. The University-wide committee is involved in reporting and management of institutional COI and sets policy for the University. The URMC committee is involved in reviewing medical center investigator disclosures, recommending COI management actions/plans and setting policy for the School and Medical Center. Currently, the University committee is operated out of the Office of the Provost. The URMC committee reports to the SMD Dean, and is chaired and supported by the Senior Associate Dean for Academic Affairs.

G2E6b. Methods. ORCS staff will be responsible for operating the COI program for CTSI and participation in the URMC COI committee. ORCS staff will ensure timely submission and review of disclosure reports, and assist investigators in compliance with federal guidance. This will ensure that not only are CTSI projects in compliance with federal and University COI policies, but will provide an example for the University in this vital effort. In addition, the ORCS Director will assist the CTSI clinical research ethics team in the analysis and management of potential COI that may result in translational research, such as with descriptions and categorization of potentially conflicting relationships, and the content of COI management plans as described in Section G2D of this proposal.

G2E7. Specific Aim 5: Development and Sharing Best Practices

Working with the University CRRPIT group, ORCS will develop best practices that reduce or remove institutional impediments to clinical and translational research. The CRRPIT group has been able to develop indemnification policies related to PI-initiated studies, Phase 4 studies and studies involving very seriously-ill subjects to facilitate these clinical trials while still adequately protecting subjects and the University. CRRPIT also provides ongoing surveys of clinical investigators to gauge both satisfaction of administrative processes and faculty understanding of regulatory requirements. Facilitating regulatory review and approval, as well as streamlining of administrative approvals required for clinical and translational research is the main emphasis area for CRRPIT and the CTSI ORCS will support and add to this ongoing effort.

The CTSI Regulatory Knowledge and Support Program will support and participate in the Upstate New York Translational Research Network. Specifically, activities will include the ORCS Director's participation in several working groups, such as the Regional Assistance with Regulatory Compliance, Human Subjects Issues and Education and Training.

The University of Rochester will support a National CTSA Regulatory Support Steering Committee to facilitate interaction with the Regulatory support personnel at other CTSA institutions. Such interaction will facilitate collaborative clinical and translational research activities by sharing policies, procedures, and best practices. The University of Rochester is willing to support the establishment of such a Steering Committee within the ORCS structure. Whether a single site, such as the University of Rochester, is the home of the Steering Committee or whether a rotating home between the participating CTSA sites is the best model will be discussed with the other sites. Whichever model is selected, the University will actively participate and fully support this important dissemination and collaborative tool. The University of Rochester has much to contribute to such a group, and can bring its regulatory experience and "success stories" to provide models for other CTSA-supported institutions.

G2E8. Evaluation and Measurement

The program will include ongoing review of the effectiveness of all aspects of the program (including service development and faculty needs and satisfaction). The Program Director will obtain feedback from trainee and faculty investigators to help identify areas for improvement in the program. The Program will include information on educational program attendance; grant proposals and awards submitted/developed, and quality improvement data from audits. The Program Director will ensure proper monitoring, response and modification based on appropriate recommendations from the faculty advisor and the Advisory Committee.

The ORCS Director will review of the effectiveness of all aspects of the program on a routine basis with the CTSI Director.

G2E9. Novel Aspects of Key Functions

The CTSI Regulatory Knowledge and Support Program will build upon the outstanding programs that currently support clinical and other research at the University and will leverage these to create a new and vital level of specialized regulatory support specifically aimed at translational research. This will result in a program that is innovative in that a dedicated unit of specialists in translational research will be assigned to support investigators in areas that are unique to this type of research. For example, to conduct clinical research that will support a change in labeling for new indications/uses requires investigators to file INDs and/or IDEs with the FDA. This is an area that few investigators are familiar with and rarely do university support departments have working knowledge that can support investigators making such applications. The University of Rochester has a long history of good relationships with industry and with federal regulatory agencies such as the FDA. Within the Rochester community are people who have expertise in FDA filings. From this pool, the University will hire staff for the CTSI Regulatory Knowledge and Support Program who have the experience to guide translational investigators in FDA filings and other interactions with federal agencies. This will carry us well beyond what is able to be provided through traditional support programs.

The CTSI Regulatory Knowledge and Support Program will develop online interactive tools for assistance in developing informed consent forms and preparing documentation for University oversight functions. Developing tools that will improve review submissions, regulatory compliance and human subject safety will have a major impact on this and, through sharing, other CTSA-supported programs.

We will build upon the current existing Faculty Compliance Web Portal used by the RCRC to incorporate regulatory areas critical to translational research, as well as improve upon the delivery of information. In addition, we propose to expand upon the use of the improved Portal currently used in the to all investigators participating in the CTSI research education, training, and career development programs noted in Section G2I, as a pilot of initiating mandatory compliance education to all CTSI investigators and University research faculty.

G2E10. Key Function Interactions

The educational models and skill building workshops noted in Table I3, Section G2I will be incorporated into the CTSI Regulatory Knowledge and Support Program educational offerings and training in regulatory compliance. ORCS will promote these developed workshops for CTSI faculty, and possibly for other CTSI staff and study coordinators. ORCS will work with the Director of Research Education, Training and Career Development and other University officials in piloting a mandatory Research Compliance Education Program for CTSI faculty.

ORCS will assist in supplementing and formulating translational research resources that will effectively support all the member institutions of the Upstate New York Translational Research Network (Section G2J). The Director of ORCS will serve on working groups to assess the needs of regulatory issues on a regional basis, as well as to develop programs. Specifically, the Director of ORCS will serve on the Regulator Compliance and Humans Subjects Issues working groups.

Biomedical Informatics (Section G2C) will interact with ORCS and its education consultant to build and provide state-of-the-art educational tools and process oriented web portals. These tools will aid CTSI faculty in learning and adhering to the requirements of research administration and regulations specific to CTSI activities and overall CTSI processes.

The ORCS Director will interface with the Clinical Research Ethics team in promoting new disciplines as noted in Section G2D. Specifically, the ORCS Director will assist in the analysis and management of potential COI that may result in translational research and the formulation of conflict of interest management plans.

G2F. PARTICIPANT AND CLINICAL INTERACTIONS RESOURCES

G2F1. Specific Aims

The overall goal of the Participant and Clinical Interactions Resources Key Function is to provide an environment that encourages and supports participation in patient-oriented clinical and translational research. This Key Function represents an upgrading of the functionality of the UR General Clinical Research Center (GCRC). The research done at the GCRC involves direct investigator-subject interaction (i.e. patient-oriented research) as opposed to other types of research within the scope of the CTSA such as epidemiology, outcomes research, or gene array analysis which may not necessarily involve direct investigator-subject interactions. The patient-oriented research to be conducted on the GCRC for the most part would be considered translational research, i.e. studies primarily involving 1) the delineation of normal human physiologic processes, 2) the pathophysiology and natural history of disease states, and 3) development and evaluation of new therapeutic modalities.

Achievement of the overall goal of this Key Function requires efforts to: educate, recruit, and train translational investigators; assist in recruitment of appropriate subjects and facilitate their participation; reduce barriers for investigators to engage in patient-oriented research; and encourage basic scientists to become involved in translating their bench discoveries into bedside applications. Currently, the GCRC is effective in each of these areas, but its impact on clinical and translational science throughout the University of Rochester and nationally would be greatly enhanced by upgrades in several areas that would be supported by the CTSA. These include biostatistics (see section G2D), biomedical informatics (see section G2C), and core laboratories (see section G2H) which will become key functions in the University of Rochester Clinical and Translational Science Institute (CTSI). However, enabling resources provided by the CTSA will additionally contribute to achieving our overall goal of providing an optimal environment that encourages and supports participation in clinical and translational research.

Therefore the **specific aims** of the Participant and Clinical Interactions Resources Key Function are to:

1. expand support for clinical and translational investigators and research participants, including space, personnel and ancillary services;
2. foster collaborations between clinical, translational and basic science;
3. expedite initiation of protocols by investigators;
4. encourage and facilitate participation of subjects in studies;
5. assist investigators in protocol initiation activities; and
6. promote introduction of novel research techniques into use for clinical studies

G2F2. Background and Significance

A patient-oriented research unit has been in operation at the University since the 1940s. Early on it participated in studies of the effects of radiation in humans as part of the Manhattan Project. In November of 1960, the University of Rochester was one of the first eight GCRCs funded by the NIH, and has been continuously funded since its inception. In March of 2005, it underwent a competitive renewal site visit and, as a result, has been refunded for an additional five years with a recommended annual direct budget of approximately $2,000,000.

Except for clinical trials in specific research areas, e.g. oncology and neurology which are primarily conducted in specialized centers (Cancer Center and Neurology's Experimental Therapeutics Program), the GCRC has been the focal point where almost all patient-oriented clinical and translational research is conducted at the University of Rochester. It has provided 1) nurses skilled in various specialized research procedures (e.g. glucose clamps) to assist investigators with their protocols; 2) bionutritional services (metabolic kitchen and a research dietitian); 3) a bioinformatics core to assist investigators in their data management; 4) a biostatistics core to assist investigators in the design of their studies and analysis of their data; 5) a core laboratory which provides for sample processing, body composition measurements (e.g. DEXA), and analysis of blood specimens for specific activities, enrichments (mass spectroscopy) and concentrations of metabolites and hormones, as well as technical assistance to investigators; and 6) ancillary support. The unit also contains specialized equipment for testing of muscle strength and cardiovascular function.

The GCRC, through its Clinical Research Feasibility Funds (CReFF) Program, provides funds to support pilot projects by young investigators as a means to obtain data with which to compete for more substantial

extramural support and promote their careers as clinical investigators. The program provides funding for research projects of up to $20,000 per year for one year with the potential to apply for a second year of funding of up to $20,000. This funding is in addition to traditional GCRC resources (i.e. inpatient days, outpatient visits, bionutrition services, core laboratory services, bioinformatics services, biostatistical consulting, and support for ancillary services) that the project may utilize. Preference is given to projects which use traditional GCRC resources. Junior faculty at the rank of Assistant Professor or below at the University of Rochester are eligible to apply. Senior faculty are also eligible to apply if the research proposed represents a substantial change in career path. Applicants must have an MD, PhD, PharmD, or DDS degree. Applicants may not have NIH or comparable external funding for the project proposed, although recipients of K23 or other career development awards may supplement those funds with a CReFF award.

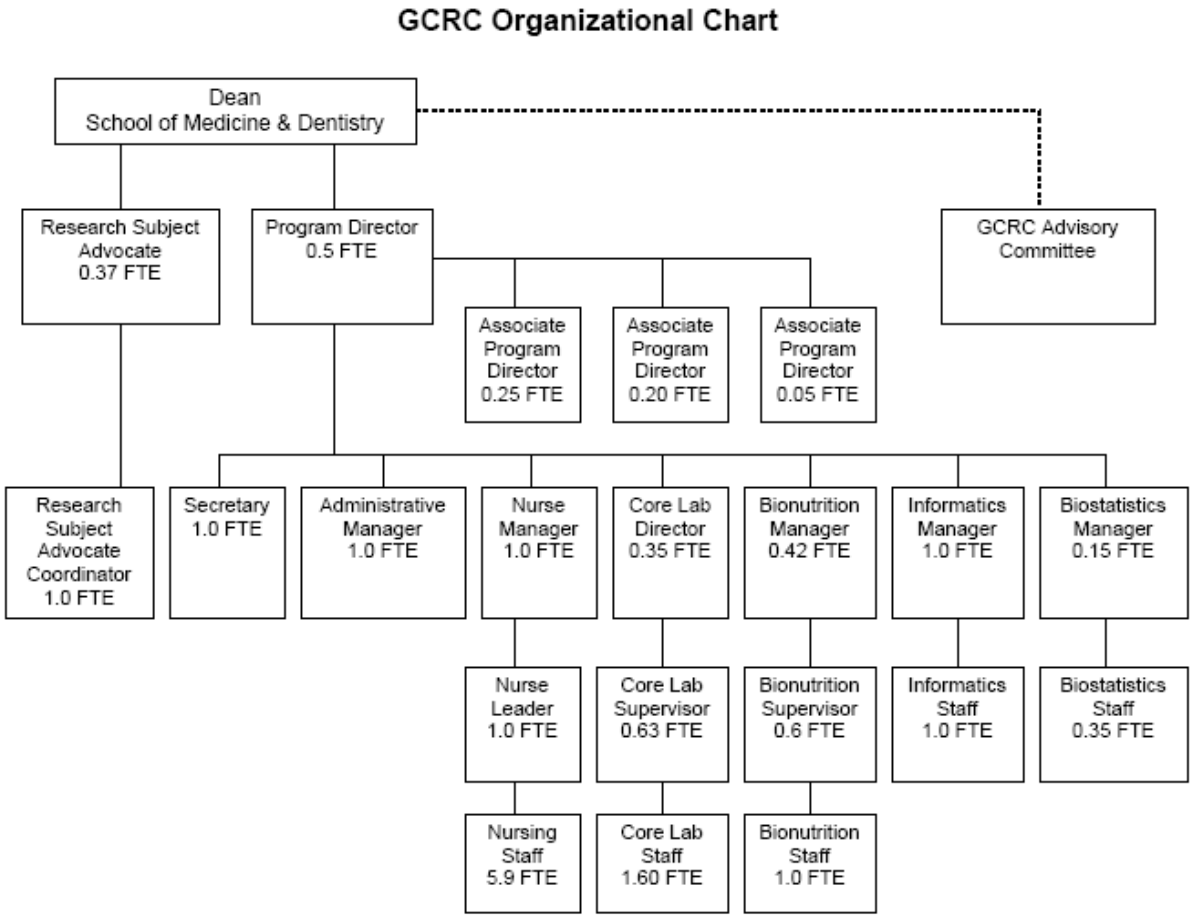
In addition to the above modalities to assist investigators in the initiation and performance of their studies, the GCRC has been heavily involved in educational activities involving undergraduates. The Summer Undergraduate Research Fellowship (SURF) Program is a nine-week program designed to enhance the competitiveness of undergraduate students interested in medicine, research and science who belong to groups historically underrepresented within these areas. The program is designed to strengthen participants' science and research skills and expose them to biomedical research and clinical medicine. The GCRC Program Director has mentored a number of students in this program. The hope is to increase the number of minority physicians involved in translational research so that there will be improvement of recruitment of minorities into clinical protocols. Medical students also have been educated in research on the GCRC via a summer program. The GCRC has stipends for medical students who work with a GCRC investigator on a GCRC project during the summer. The 12-week experience in clinical research encourages career path decisions in this area. The student must prepare a written report of his/her accomplishments, detailing how this experience influenced his/her career desires, acquisition of new knowledge or skills relevant to his/her future, and an overall evaluation of the program. Medical students have also been more extensively involved in research on the GCRC as part of the School of Medicine and Dentistry's Academic Research Track, wherein a student spends an entire year working on research projects with a GCRC investigator as a mentor.

The GCRC nursing staff has also been involved with a number of students from high schools who are interested in healthcare and/or research, with the Cornell University dietetic interns, with medical students from the University of Rochester, and with enrollees in the Rochester Clinical Research Curriculum program (K30 award). Dietetic interns, nutrition fellows, undergraduate students and high school students gain exposure to nutrition research through the bionutrition department on the GCRC. During their one-week rotation, Cornell dietetic interns gain exposure to research design and nutrition research methodologies. Nutrition fellows from the Leadership Education in Adolescent Health and Leadership Education in Neurodevelopmental Disabilities Programs (UR School of Nursing) also gain exposure and, when available, get involved in relevant research projects. Undergraduate and high school students who shadow the bionutritionist develop an understanding of the role of dietitians in research.

Finally, many of the GCRC protocols have involved fellows in our subspecialty clinical and research training programs. A clear example of the role of GCRC experience in promoting fellows to seek careers in academic research is provided by the fellows in endocrinology who have trained under the GCRC Program Director, Dr. John Gerich. Since he came to the University of Rochester in 1994, nine fellows have completed fellowships that included working with him on GCRC protocols. Of these, eight presently have full-time faculty positions at medical schools. Most have been successful in obtaining extramural research funding, and one is a Chief of a Department of Medicine.

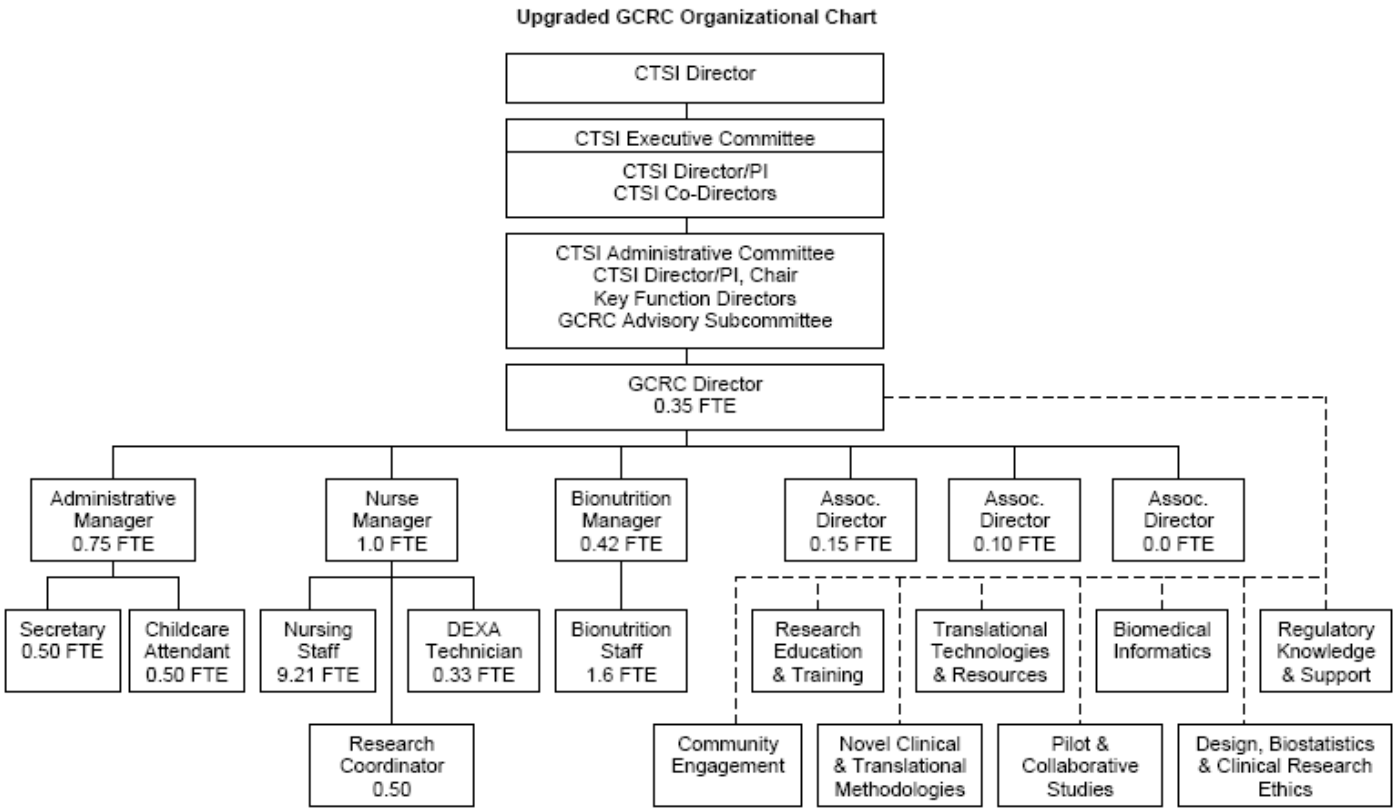
The major formal education program of the GCRC has been the responsibility of one of our GCRC Associate Program Directors, Dr. Thomas Pearson, who is Senior Associate Dean for Clinical Research and the Principal Investigator of the University's K30 grant. A description of this curriculum and its outstanding accomplishments are described in detail in section G2I and will not be reiterated here.

Figure G2F1: Organizational Chart for Current GCRC



The organizational chart of the current GCRC is shown in Figure G2F1. The Dean, Dr. David Guzick, who is to be the principal investigator of the CTSA, is the principal investigator of the GCRC and, in addition, an active user of the GCRC. The current GCRC Program Director, Dr. John Gerich, is Director of the Participant and Clinical Interactions Resources Key Function. He has been responsible for the overall day-to-day operation of the GCRC for the past 12 years. The GCRC Advisory Committee is responsible for oversight of the unit, and for protocol review and policy decisions. This will remain under the CTSI. The GCRC Research Subject Advocate, who is responsible for assuring subject safety and protocol adherence and reports on a regular basis to the Dean, will become the Subject Advocate of the CTSI and be administratively located within the Regulatory Knowledge and Support Core (see G2E). The organizational chart of the upgraded GCRC under this Key Function is shown in Figure G2F2. The major changes are that core laboratory, bioinformatics, biostatistics, and research subject advocate personnel are now subsumed in other Key Functions of the University of Rochester Clinical and Translational Science Institute and the GCRC Advisory Committee will be a subcommittee of the UR CTSI Administrative Committee. However, their functions and intimate interaction with the operations of the GCRC will continue.

Figure G2F2: Organizational Chart for Upgraded GCRC



In the past, investigators wishing to use the GCRC submitted their protocol on paper separately to the GCRC and the IRB. In 2005 we established an online application for simultaneous submission to the GCRC and the IRB. Only faculty members who have passed an IRB test in human subjects protection are qualified to use the GCRC. The submitted protocol undergoes evaluation by a primary and secondary reviewer, and others as described in G2F2a. The Advisory Committee gives the protocol a scientific and need score, evaluates the appropriateness of the budget and requested services, and gives final approval for the study to be initiated after IRB approval and satisfactory responses to Advisory Committee suggestions/inquiries/concerns have been received. This general procedure will continue in the proposed UR CTSI.

It has been the responsibility of the GCRC Advisory Committee to evaluate the quality of science of submitted protocols, their ethical status, biostatistical and design rigor, safety, and justification for use of GCRC resources, as well as the evaluation of progress of protocols to justify their continued use of the GCRC. This will continue with the GCRC Advisory Committee under the UR CTSI.

G2F2a. GCRC Advisory Committee (GCRC-AC).

The GCRC-AC will be a subcommittee of the CTSI Administrative Committee. It will meet monthly, or more frequently as needed, to evaluate new protocols, discuss policy issues, and review operations of the GCRC. Members will be appointed by the CTSI Principal Investigator in consultation with the Program Director and the Chair of the GCRC-AC. Appointed members will be reviewed for reappointment or rotation off the Advisory Committee every three years. Dr. Richard Reichman will continue his role as Chair. He has provided exceptional support and looks for ways to streamline the operations of the GCRC, as well as assist individual investigators. Dr. Reichman, a major user of the GCRC, understands the importance of thoughtful and timely protocol review. Under his direction the application process continues to be “customer friendly.” Dr. Reichman has also assisted in recruitment of additional members to the GCRC-AC who represent a broader segment of the medical school’s faculty and who bring needed expertise for protocol review. In the past, the GCRC-AC

has requested periodic comprehensive updates from the Administrative Manager regarding the financial status of grant funds. This will be continued under the UR CTSI.

All protocols submitted to the GCRC will be reviewed initially by primary and secondary reviewers who prepare written critiques which they present to the Committee at formal monthly meetings. In addition, each protocol will be reviewed by a Subject Advocate, a representative of the IRB, and by a biostatistician who will perform an assessment of statistical methodology and power calculations. Specific needs for nursing, bionutrition, bioinformatics, and core laboratory use will also be evaluated. Subsequently, a general discussion will be held and priority scores based on scientific merit and need for the GCRC given. In its deliberation, the Committee will also examine protocols for human subjects issues (including issues related to gender and minority status of potential study subjects, inclusion of children, and patient safety) and the appropriateness of support requested from the GCRC (justification for patient days, ancillary services, and core laboratory assays). The GCRC-AC will also designate each protocol as Category A, B, or D. Category A protocols are investigator-initiated studies funded by the NIH, a foundation, or a department. Industry-supported protocols may also be categorized as Category A if they are investigator-initiated or study a rare disease. Category B protocols are those in which the patient's insurance pays for the stay. Category D protocols are those which are both initiated and supported by industry. The GCRC will be totally devoted to research, and therefore there will not be any Category C patients on the unit, i.e. individuals who represent overflow from general hospital patients. As will be described subsequently, cost-sharing initiatives will be initiated for A-, B-, and D-type protocols.

Following review and discussion by the GCRC-AC, protocols will be either approved, approved contingent upon satisfactory resolution of issues raised by the Committee, deferred pending major revision, or disapproved. The outcome of each protocol review will be communicated in writing to the investigator. An approved protocol will result in the investigator receiving a newly-assigned GCRC protocol number which will permit the study to proceed. A protocol approved contingent upon a satisfactory resolution of issues raised by the Committee will result in a letter to the investigator detailing the issues of concern. The investigator's response to the Committee will then be forwarded to the primary and secondary reviewers and appropriate GCRC staff for their comments. At this point the Committee members reviewing the investigator's response could approve the protocol, request additional information, or bring the protocol back to the GCRC-AC for further review. When protocols are deferred pending major revision, or disapproved, a detailed letter will be sent to the investigator and assistance or mentoring will be made available. No protocol can be initiated without final approval by the GCRC-AC and written documentation of approval by the IRB.

The GCRC-AC will also review and give final approval to the selection of students and mentors for summer research projects, and the selection of pilot project awards. Notices for these will be posted and mailed out, soliciting applications and inviting telephone inquiries to the Center office. Preliminary review of applications will be done by the Director, who then will bring recommendations to the GCRC-AC. The Committee will have final say in these decisions.

In addition, the GCRC-AC will conduct annual reviews of all protocols which will coincide with the annual progress report required by the IRB. It will be the purpose of this annual review to track the progress of protocols to ensure that protocols using GCRC resources are being conducted according to the highest scientific standards, including evaluation of progress (utilization), protocol adherence, and adverse events (patient safety). These evaluations will be used to determine whether continued use of GCRC resources is justified and whether problems executing protocols can be identified and alleviated. Support for protocols deemed unworthy of continuation will be withdrawn. In addition, publications from GCRC protocols will be evaluated to determine whether data analysis and reporting meet the highest standards and, if not, what remedial action by one of the CTSI key functions might be helpful.

Table G2F1: The GCRC Advisory Committee

Name	Professorial Rank	Department
Richard Reichman, MD	Chair, Professor	Medicine – Infectious Diseases
Robert DiCenzo, PharmD	Adjunct Assistant Professor	Medicine – Infectious Diseases
James Eichelberger, MD	Associate Professor	Medicine – Cardiology
Mark Frampton, MD	Professor	Medicine – Pulmonary & Critical Care
Jennifer Griggs, MD	Assistant Professor	Medicine – Hematology/Oncology
Russell Hilf, PhD	Professor	Biochemistry
Kathleen Hoeger, MD	Associate Professor	Obstetrics and Gynecology
Nicholas Jospe, MD	Associate Professor	Pediatrics – Endocrinology
Jane Liesveld, MD	Associate Professor	Medicine – Hematology/Oncology
Dale Phelps, MD	Professor	Pediatrics –- Neonatology
Giovanni Schifitto, MD	Associate Professor	Neurology
Charles A. Thornton,MD	Assistant Professor	Neurology
Wojciech Zareba, MD	Associate Professor	Medicine – Cardiology
Ex Officio		
Mary Adams	Administrator	Office of Human Subjects Protection
Robert Betts, MD	Professor	Medicine – Infectious Diseases
Will DiGrazio, MS	Bioinformatics Manager	Medicine – GCRC
Changyong Feng, PhD	Research Assistant	Biostatistics
John Gerich, MD	Professor, Program Director	Medicine – Endocrinology
Kathleen Jensen, RN, MHSA	Administrative Manager	Medicine – GCRC
Michael McDermott, PhD	Associate Professor	Biostatistics
Susan Messing, MA, MS	Associate	Biostatistics
Richard Moxley, MD	Professor Associate Program Director	Neurology
Nancy Needler, BS	Subject Advocate	Medicine – GCRC
Thomas Pearson, MD, PhD	Professor	Community & Preventive Medicine
Patricia Pincus, RN,MPH,CIC	Nurse Manager	Medicine – GCRC
Noya Rackovsky, MS	Core Lab, Tech. Assoc.	Medicine – GCRC
Patricia Stewart, PhD, RD	Sr. Instructor	Pediatrics
John Treanor, MD	Associate Professor Associate Program Director	Medicine – Infectious Diseases
Stephen Welle, PhD	Professor Associate Program Director	Medicine – Endocrinology

Table G2F1 gives the present make up of the GCRC Advisory Committee. In addition to present members of the GCRC-AC, representatives from other Key Functions will be added. These will include, but not necessarily be limited to, Research Education Training and Career Development (see section G2I), Translational Technologies and Resources (see section G2H), Community Engagement (see section G2G), Regulatory Knowledge and Support (see section G2E), Design, Biostatistics and Clinical Research Ethics (see section G2D), Biomedical Informatics (see section G2C), Pilot and Collaborative Translational and Clinical Studies (see section G2B), and Development of Novel Clinical and Translational Methodologies (see section G2A). At the present time, it is not possible to list who these individuals will be since it will be the responsibility of the specific Key Functions to nominate appointees. However, as a part of the organizational structure and function of the GCRC, there will be close coordination between this committee and the committees that are part of the other key functions noted above. This broader representation of disciplines within the Advisory Committee will help integrate various functions of the Clinical and Translational Science Institute into the operation of the GCRC. For example, having a representative of the Community Engagement Key Function will permit assessment of whether community needs are being met and having a representative from the

Regulatory Knowledge and Support Key Function (i.e. Subject Advocate, IRB member) will ensure that appropriate numbers of minority groups are being included in studies.

The GCRC-AC will also be responsible for instituting cost-sharing procedures. In the past, the GCRC did not routinely require cost sharing from A protocols. Although D protocols (pharmaceutical/device company-initiated studies) did have to "pay their way," our prior method of accounting probably did not recover as much as it could, i.e. we charged an hourly fee based on 1/24 of the cost of a hospital bed. In the future, better cost sharing is planned. Thus, in the future all investigators receiving new grants will be required to cost share on a basis similar to that described for core laboratory services (see section G2H). All potential investigators who might use the GCRC will be informed and required to include in their budgets reimbursement for GCRC services. This will be accomplished in conjunction with the Regulatory Knowledge and Support Key Function which includes the Office of Research Project Administration, so that investigators planning new grants will be notified of this requirement well ahead of submission dates so that their budgets can include cost sharing. Prior to submission for external funding, investigators will submit a list of services requested from the GCRC. This itemized list will be costed out by the GCRC administrator and, as a general rule, investigators of non-Category D studies will be required to seek at least 50% of the cost in their grant. The actual amount (percentage) covered by the GCRC will depend on the amount awarded in the grant so that additional subsidization may be given by the GCRC if the investigator can demonstrate that the external funding is inadequate. Moreover, we plan to charge D protocols (~$1000) for review of their protocols by the GCRC-AC (as is now done by many GCRCs) and to itemize charges for services rendered by the GCRC as well as continue the present room charge. This cost-sharing policy should enable the GCRC to do more with less funding anticipated from the NIH for GCRCs in the future.

G2F2b. Limitations.

Although our GCRC has been successful in obtaining continuous funding and in being productive as evidenced by progressively increased usage and increases in resultant peer-reviewed publications (see past experience section below), it is not functioning optimally because of space, personnel, and logistical limitations. All of these will be improved by establishment of the CTSI.

1) Space limitations. We do not have a conference room; we have inadequate space for storage of equipment and supplies, and certain critical support personnel are located at inconvenient off-site locations, e.g. biostatistics, IRB, regulatory personnel. With the CTSI, the GCRC will move into newly-renovated larger space. This new facility will provide space to accommodate a conference room, adequate storage of equipment and supplies, and office space for key personnel. Prior to initiating a protocol, an investigator often must consult a biostatistician, a subject advocate, an IRB representative, a Research Administrator from the Office of Research and Project Administration, etc. Setting up appointments and traveling to different locations makes initiating a protocol troublesome to say the least. Having representatives of all these necessary support individuals in one place located where the research will be done and where nursing, bionutrition, and core lab support are also located will greatly simplify the steps investigators have to take to initiate a protocol submission. The new Clinical and Translational Science Building will house most of the essential core support functions. It is planned that this new building will be located across the street from the new GCRC. Until the building is completed and perhaps even afterward, the GCRC will have satellite representatives of these core functions on site where the research will be done and where other components (e.g. nursing, core lab, bionutrition and GCRC administrative personnel) are located. This will be a great advantage.

2) Personnel Limitations. Our nursing, biostatistical, and bioinformatics personnel are limited and will be inadequate for future needs. Our support for investigators in recruiting subjects and coordinating studies is presently nonexistent.

a) Nursing. At our recent GCRC site visit, it was recommended that our nursing staff be increased by 2 FTEs. With our present complement of nurses, we have to close on weekends. Implementation of protocols is frequently delayed, and often studies are cancelled if a nurse gets sick. The latter inconveniences the volunteer and investigator and often results in substantial expense when costly reagents, e.g. isotopes, have been prepared and must be discarded. Due to flat funding for GCRCs, the recommended addition of two nursing FTEs will not be funded. However, with the CTSA, funding for these positions can be provided.

b) Biostatistics. The GCRC currently funds a 0.50 FTE for biostatistics. Although extremely helpful for design, power calculations, and statistical evaluation, more sophisticated biostatistical analyses are often needed and desirable (e.g. mathematical modeling). Presently the GCRC cannot offer this support. Under the CTSI, biostatistics will be expanded into a separate key function (see section G2D) which will be able to provide enhanced services not currently available, although this will involve cost sharing.

c) Bioinformatics. Currently the GCRC has 2.0 FTE bioinformatics support. It is inadequate for the needs of our investigators since many requests for assistance cannot be handled in a timely fashion and the core cannot offer the more sophisticated support of which it is capable. As in the case of biostatistics, with the CTSI, bioinformatics will be expanded into a separate key function (see section G2C) which will be able to provide enhanced services not currently available. This also will involve cost sharing.

d) Recruitment/Study Coordination. Currently the GCRC provides no support in this area. This represents a significant barrier to new investigators and many established investigators who have intermittent recruiting and coordinating needs. One of the shortcomings in recruitment is the lack of coordinated volunteer lists. The GCRC will take the lead in developing a volunteer database in conjunction with the Biomedical Informatics Key Function and the Community Engagement Key Function. Assistance will also be provided in the form of coordinating/recruiting personnel who will be present on site in the GCRC as part of our "one-stop shopping" concept. This is further described below in Specific Aim #5.

3) Logistical Limitations. These are partly the result of space and personnel limitations. For example, currently our biostatistical support is off site, our bioinformatics space is severely cramped, and we have no area for investigators and their coordinators to meet with clinical trial monitors. The latter is an important drawback because patient charts are located on the GCRC. Moreover, our GCRC Advisory Committee functions well in overseeing operation of the GCRC (e.g. budgets, core usage), establishing and monitoring policy issues and reviewing protocols, but it lacks the breadth to take advantage of basic science developments and translate them into human studies. All of the above limitations will be ameliorated by the CTSI. A representative of the Design, Biostatistics, and Clinical Research Ethics Key Function (see section G2D) will be onsite in the upgraded GCRC as mentioned above as part of our "one-stop shopping" concept. Space available for Biomedical Informatics will be provided as part of the new enlarged in- and outpatient unit (described below in the Methods section). On this unit space will be provided for investigators and their coordinators to meet with clinical trial monitors. Finally, the GCRC Advisory Committee will be revamped as a subcommittee of the CTSI Administrative Committee and its members will include representatives of the Development of Novel Clinical and Translational Methodologies Key Function (see section G2A), Pilot and Collaborative Translational and Clinical Studies Key Function (see section G2B), Translational Technologies and Resources Key Function (see section G2H), Design, Biostatistics and Clinical Research Ethics Key Function (see section G2D), and other relevant Key Functions so that in addition to the present functions of the GCRC Advisory Committee, this new committee will integrate a broad array of expertise made possible by the CTSI to exploit basic discoveries in the laboratory and encourage their translation into human studies.

Currently GCRC nurses are employees of Strong Memorial Hospital in whose space the GCRC is located and are administratively under Nursing Services. The new GCRC will be located in University medical school space, not hospital space. It would therefore seem logical that GCRC nurses be employees of the medical school. At present, at some GCRCs (e.g. Washington University), nurses are employees of the medical school; thus, this approach would not be without precedent. Although such an approach at the University of Rochester would not entail any savings in salaries and benefits, there would be several advantages of this reorganization. These include, but would not be limited to:

a) Alleviation of the possibility that GCRC nurses would be "pulled" for clinical duties.
b) Alleviation of restrictions on recruiting nursing personnel. At present, if the GCRC needs to fill a nursing vacancy, it cannot advertise the position in the local newspaper, but must rely on the Nursing Service to fill the vacancy. Since there is a nursing shortage in Rochester and since filling hospital vacancies has financial implications for the hospital, there is a conflict of interest in this situation.
c) Greater efficiency can be achieved by eliminating participation of GCRC nurses on various hospital committees. Currently the GCRC nurses participate in many hospital committees. Since the GCRC will not be involved in patient care as in the past when the GCRC had

Category C hospital patients, lack of involvement of GCRC nurses in hospital committees will free up their time for more direct involvement in research activities.

d) Improved loyalty and esprit de corps among GCRC nurses should result from this organization. The nurses will perceive that their job security will relate more to the productivity of the GCRC than that of Strong Memorial Hospital.

e) Alleviation of restrictions placed on hospital nursing will enhance cost-effective usage of GCRC personnel. At present, hospital regulations restrict procedures done, for example, by clinical technicians such as serial blood draws from intravenous lines. Not being bound by this regulation would permit the GCRC to employ clinical technicians to perform these procedures rather than requiring nurses. Clinical technicians have substantially lower salaries than nurses. Therefore considerable cost savings would be anticipated.

As this grant application is being prepared, the Dean and PI of the CTSA is promoting this organizational change, which would be facilitated by the CTSA.

4) Core Lab. Currently the core lab offers a limited repertoire (e.g. radioimmunoassays, microfluorometric assays, GC-mass spectrometry, specimen preparation and storage) focused on metabolic research. Proteomics, genomics and other cutting-edge technologies are not offered. With the CTSI, the organizational structure for laboratory support will change so that these other technologies become as accessible to clinical and translational researchers as the current services for metabolic research. The GCRC core lab Director, Dr. Stephen Welle, will work closely with the CTSI Director of the Laboratory Support Center (see section G2H) and the Novel Clinical and Translational Methodology group (see section G2A) to expand the capabilities of our investigators and attract basic scientists to collaborate with clinical investigators. Cost sharing will be an integral part of support for laboratory services.

G2F3. Prior Experience

G2F3a. Recent History.

Notwithstanding the ~60 year-history of our patient-oriented center, only our experience during the last five years will be covered here. During this period, a total of 295 protocols were performed on the GCRC. This included 34,471 outpatient visits and 1309 inpatient days. As a result of these studies, there were 152 publications. There has been a progressive increase in use of the GCRC and, as indicated earlier, the above usage and accomplishments were considered outstanding at the competitive renewal site visit; we have been refunded for five years.

G2F3b. Recent Translational Research – An Example.

The University of Rochester GCRC recently played a critical role in the conduct of an exciting translational research study that brought bench work to the bedside. Dr. Thomas Guttuso, a young neurologist who recently completed residency and fellowship training, made the observation that in one of his post-menopausal patients the prescription of gabapentin for her migraine resulted in an apparent decline in her frequency of hot flashes. Based on basic investigations in the literature, there was a plausible mechanistic explanation of how gabapentin might alleviate postmenopausal symptoms. He therefore formulated a hypothesis and proceeded to test it in a study conducted on the GCRC. Through the Experimental Therapeutics fellowship program (T32) he received guidance from his mentors in regulatory issues (for example, filing an investigator IND which was eventually approved by the FDA) and negotiating the internal IRB review process, two things he was completely unfamiliar with and initially did not realize he had to comply with. He was able to file an eventually successful patent application, based on limited initial information, through support of the Office of Technology Transfer. The resources of the GCRC were crucial in supporting his study as he did not have financial resources to support a place to see the patients nor to pay for data management (covered by the GCRC) or for biostatistical services (also covered by the GCRC). He had access to senior Neurology faculty (Dr. Karl Kieburtz) who were willing to provide mentorship (under the auspices of a K24 grant) and also financial resources to purchase the gabapentin and placebo for the study. He had access to an investigational pharmacy that was able to prepare the gabapentin and matching placebo for the study. A high level of interdepartmental collaboration was possible and facilitated. For example, Dr. Guttuso had to work closely with colleagues in OB/GYN and the Cancer Center to recruit women with hot flashes, something most neurologists

would not be able to do on their own. In addition, Dr. David Guzick (then Chair of OB/GYN) individually was strongly supportive of the project and an eventual co-author on the publication. This level of interdepartmental collaboration on a novel project by a junior investigator is particularly unusual.

We anticipate there will be numerous studies, such as those of Dr. Guttuso, in the future, especially Phase I clinical trials, as we bring to fruition our goal of establishing more collaborations between basic scientists and clinical investigators.

G2F3c. Upgrade and Relocation of the GCRC.

The GCRC currently has 8474 sq. ft. of space. To aid in accomplishment of the goals of the CTSA which will require an expansion of our activity, the GCRC will be relocated to new space which will be larger (10,495 sq. ft.) and more strategically located to facilitate usage by volunteers and investigators. This new space will be closer to many of the hospital resources used by our investigators (e.g. radiology) and will be more readily accessible to subjects. It will be located on the ground floor near an entrance to the Medical Center and close to parking, in contrast to its present location on the fourth floor of the hospital, some 150 feet away from the nearest elevators. The new space will have additional features to assist investigators and facilitate patient participation.

G2F3d. An Opportunity and Need to Establish "One-Stop Shopping."

As indicated earlier, a major barrier to initiating research protocols is the need for investigators, especially new investigators, to seek assistance from support key functions which are geographically scattered throughout the Institution. The IRB, Biostatistics, Biomedical Informatics, Regulatory Personnel, Subjects Advocate are all scattered about, requiring the investigator to travel about the campus. We propose—to facilitate and expedite initiation of studies—that the new GCRC provide "one-stop shopping"; namely that the GCRC will have on site all of the support personnel needed by an investigator to expedite approval of his/her protocol by the GCRC Advisory Committee. We propose that within the geographic space of the GCRC there will be on site satellite, shared offices for 1) Subject Advocates to assist in protocol writing which conforms to NIH and IRB guidelines, 2) a biostatistician to assist in design, analysis and power calculations, 3) an IRB representative who will develop with the investigator an acceptable consent form, 4) a pool of research coordinators from which investigators with short-term or pilot studies can obtain assistance, and 5) a biomedical informatics office to help investigators set up databases with which to conveniently evaluate their data.

With this "one-stop shopping" approach, an investigator could, by visiting the GCRC in a matter of a few hours, meet with all the people he/she needs to interact with so that, when his/her protocol is presented to the GCRC Advisory Committee, it is essentially a fait accompli.

G2F4. Methods

G2F4a. Achieving the Specific Aims of the Participant and Clinical Interactions Resources Key Function.

1) To achieve Specific Aim #1, e.g. expand support for investigators and participants in clinical and translational science, the GCRC will move to a location previously described, providing it with additional space and, to accomplish other specific aims, will increase its personnel. The new space will provide for anticipated expansion of patient-oriented research and its support. Thus the new unit will have satellite, shared space for (1) Subject Advocate activities described below, (2) Bioinformatics, (3) Biostatistics, (4) IRB personnel, (5) Regulatory Personnel, and (6) the current GCRC cores (e.g. nursing, bionutrition, core laboratory, etc.).

In addition, we will continue our efforts to expand the user base for the GCRC. This will include usage of the GCRC by investigators not primarily geographically located in Rochester who could use our facilities or have satellites established at their institutions (see section G2J, Upstate New York Translational Research Network). An example of the former is the case of Dr. Kimberly O'Brien. Dr. O'Brien was recruited to Cornell University in Ithaca. Her NIH-funded research required the use of a GCRC. She was therefore given an appointment at the University of Rochester so that she could use the GCRC. Furthermore, we have established a liaison with Cornell University in Ithaca to promote collaborative research in the areas of nutrition (for which Cornell University is well funded and well reported) and aging since the Cornell community has a stable subject base of healthy well-educated retirees who are predisposed to participate in aging studies.

2) To achieve Specific Aim #2, foster collaboration between clinical, translational and basic science investigators, a new GCRC Associate Program Director position will be created. This individual will liaison with the Novel Clinical and Translational Methodologies Key Function (see section G2A), the Translational Technologies and Resources Key Function (see section G2H), and the Pilot and Collaborative Translational and Clinical Studies Key Function (see section G2B), as well as the Senior Associate Deans for Clinical and Basic Research. These interactions will promote awareness of basic science developments which may have clinical applications. In addition, the Associate Program Director will be responsible for updating our current web-based basic research inventory, so that translational/clinical investigators may search for basic research studies being done in Rochester or other members of the Upstate New York Translational Research Network whose outcomes may have clinical applications. This position will also be responsible for arranging connections between basic scientists and appropriate translational/clinical investigators to discuss the potential for clinical development.

It is proposed that Dr. Stephen Welle become the new Associate Program Director. He has been at the University of Rochester since 1978 and is currently the GCRC Core Laboratory Director and the Director of the Functional Genomics Center. Dr. Welle is an investigator who traverses basic, translational, and clinical science. He has been a user of the GCRC for clinical studies and has been a member of the GCRC Advisory Committee. Thus Dr. Welle has extensive contacts with both clinical and basic scientists and is extremely well suited for the proposed duties.

To encourage collaborations between basic and clinical scientists, support for initial pilot studies will be provided by several key functions of the CTSI. We will work with other pilot programs throughout the CTSI as needed. The GCRC also has its own pilot program in the form of Clinical Research Feasibility Funds (CReFF). This support will be specifically targeted toward bringing basic research discoveries into patient-oriented research to be done on the GCRC. This support will be advertised throughout the Institution by e-mail and flyers explaining the program and calling for submissions on an annual basis. Submissions will be competitively reviewed by the GCRC Advisory Committee using the following criteria: originality, potential to become practical, feasibility, soundness of design, and need for GCRC resources. In addition to monetary support, the GCRC will assist investigators in preparing the protocol and consent form to be suitable for approval by the GCRC Advisory Committee and IRB, provide biostatistical and bioinformatics help, as well as any nursing, dietary, and core lab assistance that may be needed. Progress reports will be reviewed semiannually by the GCRC Advisory Committee.

3) To achieve Specific Aim #3, to expedite initiation of protocols by investigators, we shall initiate a new monthly lunchtime seminar explaining to potentially new investigators the prerequisites needed for initiating a patient-oriented protocol and support that can be provided by the GCRC. In addition, we shall add a second part-time Subject Advocate who, with our present Subject Advocate, will be available to work one-on-one with investigators to prepare their protocols and arrange consultation with bioinformatics and biostatistical advisors and other CTSI key function representatives as needed to satisfy IRB and GCRC requirements so that submitted protocols may require only minor modifications for administrative and other oversights. This is part of our “one-stop shopping” concept wherein an investigator can find the help he needs in one geographic location, thus avoiding the need for multiple appointments and visits to multiple sites.

4) To achieve Specific Aim #4, to encourage and facilitate participation of subjects, several new measures will be taken: as discussed above, the GCRC will move to a new convenient location which will make it easier for patients to find and obtain close parking. Secondly, given the geography of Rochester (most subjects would be expected to live within 15-30 minutes of travel), funds will be made available on a cost-sharing basis with investigators as needed for taxi fare. We shall also look into the feasibility and cost-effectiveness of initiating a van service to provide transportation for volunteers. This may help in recruiting subjects from densely populated inner city areas where taxi and bus service may not be readily available and thus increase participation by minority groups. Thirdly, to facilitate participation of subjects with young children, the GCRC will provide a drop-in Childcare Program where children can be supervised and receive meals. This program will basically expand the one already in operation in the Pediatric area of our Ambulatory Care Facility. This service is intended to provide children of GCRC research participants a safe environment to wait and play in while parents (or siblings) are at the GCRC. The program accepts all children on a nondiscriminatory basis without regard to race, color, creed or sex. The program accepts children from ages 18 months to ten years of age on a first come, first served basis under the supervision of a child life staff member and a volunteer.

5) To achieve Specific Aim #5, assist investigators in recruitment of subjects, the GCRC will provide research coordinators on a cost-sharing basis. Just as it is important to maintain a cadre of nurses specialized in research techniques, it is important to maintain a cadre of research coordinators. Young investigators do not have sufficient time to recruit and train a coordinator each time they start a new protocol. Some coordinators presently working on protocols do not have their full salary covered; others lose their jobs when the protocol is completed. Therefore we plan to establish a clinical research coordinator office (CRCO) to assist investigators in obtaining the temporary help they may need for short-term studies. This would be particularly important for pilot translational study grants described above. To jumpstart the program, we request .50 FTE coordinator funded by the GCRC. The coordinator will assist investigators in advising their studies and will liaison with other CTSI components, e.g. epidemiology, bioinformatics, practice-based networks, hospital records to develop a HIPAA-compliant database of potential volunteers (e.g. patients attending clinics or admitted to the hospital will be given a questionnaire asking whether they would like to receive information regarding research projects for which they may qualify. Those individuals positively responding will be sent information on relevant protocols with a follow-up telephone call). This CRCO will be an important component of our "one-stop shopping" concept for the new GCRC. The subject advocates normally interact with most research coordinators as part of their duties and therefore know most on a personal basis. They will also assist in train

6) To accomplish Specific Aim #6, to promote the introduction of novel techniques into use for clinical trials and other patient-oriented studies, will be another responsibility of the newly-established Associate GCRC Program Director discussed under Specific Aim #2 above. In addition to his previously mentioned duties to bring basic and clinical scientists together, he will establish a monthly lunchtime seminar in which basic scientists and others (e.g. genomics/proteomics), will explain various basic techniques and their potential clinical applications. One specific example would be research imaging. We currently have an NMR research facility which is largely used for brain research but has numerous applications (e.g. quantification of visceral fat, studies of glycogen metabolism) of which investigators may not be aware. In addition, specialized techniques currently available on the GCRC about which investigators might not be aware, will be presented. Examples include body composition measurements, isotope dilution techniques, mass spectroscopy measurements, glucose clamping, etc.

G2F4b. Industry Relations.

Under the CTSA, the GCRC will encourage and support investigators collaborating with industry, not only for investigator-initiated projects, but also for Phase I, Phase II, Phase III, and Phase IV clinical trials. Identification of potential clinical trials in which GCRC investigators may participate will be provided by a web database of clinical trials accessed via the Biomedical Informatics Key Function (see section G2C). As in the past, industry-initiated studies will be required to completely reimburse the GCRC for services rendered. Phase I, II, and III clinical trials are necessary to bring basic discoveries into the clinic. Early proof-of-concept and mechanism of action studies are also important, not only for promoting scientific knowledge and translation of bench discoveries to the bedside, but to provide an opportunity for career advancement. An example of this is the studies performed by Drs. Woerle and Meyer while fellows working with GCRC Program Director, Dr. Gerich. A protocol was submitted to GlaxoSmithKline to determine the effects of the thiazolidinedione rosiglitazone on pathways of postprandial glucose metabolism. This, of course, necessitated determination of what the normal pathways were first in nondiabetic individuals. Applying for the first time a novel triple isotope technique, Drs. Woerle and Meyer determined normal changes in glycogenolysis, gluconeogenesis, glycolysis (oxidative and nonoxidative) after meal ingestion. These results were published in the *American Journal of Physiology* (Woerle H, Meyer C, Dostou J, Gosmanov N, Islam N, Popa E, Wittlin S, Welle S, Gerich J: Pathways for glucose disposal after meal ingestion in humans. *Am J Physiol Endocrinol Metab* 284:E716-E725, 2003). Subsequently, results in the largest number of patients yet studied (725)—baseline data prior to randomization to placebo or rosiglitazone—were compared to those of previously published and additional nondiabetic volunteers. These results were published in the *American Journal of Physiology* (Woerle HJ, Szoke E, Meyer C, Dostou JM, Wittlin SD, Gosmanov NR, Welle SL, Gerich JE. Mechanisms for abnormal postprandial glucose metabolism in type 2 diabetes. *Am J Physiol Endocrinol Metab* 290:E67-77, 2006. Epub 2005 Aug 16). Participation in these pharmaceutical company-funded studies by these young investigators contributed to their training (acquisition of new techniques), advancement of their academic careers (publications in respected journals), and enhancement of opportunities for future funding. Both Drs. Woerle and Meyer have full-time academic appointments as medical school faculty and both have been successful in

obtaining extramural funding.

G2F4c. Governance and Oversight.

Governance and oversight to ensure quality of science, resource utilization, statistical rigor, ethical evaluation, adequacy of design, analysis, implementation and reporting, as well as participant safety, is the responsibility of the GCRC Advisory Committee, which is a subcommittee of the UR CTSI Administrative Committee. This has been described in detail (see G2F2).

G2F4d. Mentoring.

In collaboration with the Chair of the Department of Medicine, Dr. Bradford Berk, and training program directors of subspecialties in Medicine and Pediatrics, a mentoring program involving the GCRC has been established for all fellows. In brief, the program will begin each year early in August as two half-day sessions at which all new fellows and potential mentors from throughout the CTSI meet. Topics to be discussed the first day are: the academic career—what are the options; the physician scientist—what are the steps and prerequisites; picking a project—the Ten Commandments; picking a mentor—discussion of being a mentor and a mentee. The second day will focus on individual fellowship programs, research and grant preparation, and support for career development provided by the CTSI in general, the GCRC, and coursework available through the K30 award. These introductory sessions will each be concluded by a lunch for social interaction. Throughout the coming year there will be monthly scientific-social get-togethers during which successful faculty who would be potential mentors explain how they got to be where they are in their careers to provide examples to the fellows and encourage them to pursue academic careers. Some specifics of their current research will be included to provide fellows with information on possible areas of research available. Interspersed amongst these presentations would be those of more advanced fellows explaining their current or planned research projects. Each of these sessions would be followed by a social hour or buffet dinner during which fellows and diverse faculty would interact. Over time we anticipate that this program would evolve into a fellows' organization with fellows taking a major role in planning and running the sessions. We anticipate that the mentoring functions will also be coordinated with the educational and pilot study planning functions of the Development of Novel Clinical and Translational Methodologies Key Function and the Pilot and Collaborative Translational and Clinical Studies Key Function.

G2F4e. Evaluation.

The GCRC has in place a system for collecting information relevant to its operations; this system will continue to be used for evaluation purposes after funding of the CTSA award. Data collected include process measures such as numbers of protocols supported, and services provided in support of those protocols, and also outcome measures such as numbers of publications resulting from projects conducted with GCRC support. With the assistance of the CTSI Evaluation Core, additional measures will be developed and tracked. A number of proposed new measures are listed in the table below.

Table G2F2: Process and Outcome Measures Relevant to the Performance of the GCRC

Process Measures	**Outcome Measures**
# of investigators receiving a tour of GCRC	# of investigators using the GCRC for the first time
# of one-on-one informational interviews with investigators	# of protocols proposed by investigators experienced with the GCRC
# of feedback surveys returned	Satisfaction with GCRC services as reported by investigators
Cycle time from submittal to approval of proposed protocols	

On an annual basis, the GCRC Program Director will submit an Evaluation Report to the CTSI Executive Committee. This report will summarize all performance measures and propose a plan to improve performance in targeted areas.

G2F5. Novel Aspects of Participant and Clinical Interactions Resources

Innovative initiatives proposed for this Key Function are summarized here. These innovations represent not only an example of institutional support (e.g. renovations and new enlarged space for GCRC), but also the integration and cooperation of the various core functions within the CTSI.

1. Innovations to improve human subject participation
   - Relocation of upgraded GCRC to a more convenient location nearer parking, bus stops, and an entrance to the Medical Center
   - Establishment of a drop-in childcare center
   - Courtesy van to pick up volunteers in inner city
   - Provision of taxi cab fare
   - Collaboration with Community Engagement Core (see section G2G) to increase awareness of participant opportunities in communities, especially those where minority populations reside
2. Innovations to improve and encourage young translational investigators
   - Establishment of a Clinical Research Coordinator's Office (CRCO)
   - Expansion of role of Subject Advocate to assist in protocol content from a regulatory and safety point of view.
   - Expansion of a mentoring program within the Department of Medicine to include all fellows and young faculty throughout the CTSI
   - Provision of support for pilot projects
3. Innovations to improve efficiency, cost effectiveness, scientific oversight and integration of various CTSI key functions
   - Expansion of membership of GCRC Advisory Committee to include key members of CTSI key functions and, in the process, enhance coordination of review procedures, priority for funding, monitoring of projects, and coordination to eliminate any budgetary overlap of key functions.
   - Performance of annual reviews of protocols to assess progress and problems
   - Establishment of cost-sharing procedures and more realistic reimbursement from pharmaceutical/device companies
   - Reorganizing of nursing staff as CTSI employees
4. Innovations to enhance recruitment of and collaborations between basic scientists and clinical translational investigators
   - Establishment of a GCRC Associate Director whose function will be to promote collaborations
   - Pilot project support for translational studies
   - Initiation of a monthly lunchtime seminar series under the direction of the new Associate GCRC Program Director to be attended by both basic scientists and clinical investigators. Its mission will be to explore possible clinical applications of laboratory techniques and discoveries, and to present areas of technical-methodologic needs for areas of clinical research. An additional goal will be the exposition of techniques-methodologies currently available for clinical research and their uses.
5. Innovations to enhance the overall function of the GCRC.
   - Enhancement of current bioinformatics, biostatistics, and the core laboratory by establishment of these functions as independent and enlarged key functions within the CTSI
   - Increase nursing, subject advocate personnel
   - Provision of "one-stop shopping" to expedite protocol formulation and approval with involvement of representatives from various key functions
   - Institution of cost-sharing programs to permit more to be done with anticipated less direct NIH support for the GCRC.
   - Expansion of use of GCRC and CTSI resources by outside investigators through establishment of satellites under the auspices of the Upstate New York Translational Research Network (see section G2J) and growth of collaborations such as we presently have with Cornell University in Ithaca.

G2F6. Key Function Interactions

Because a substantial portion of the research that takes place with the support of the UR CTSI will make use of GCRC resources, the GCRC will constantly interact with each of the other CTSI key functions. It is for this reason that we propose appointing Dr. Welle as a new GCRC associate program director. In this role, Dr. Welle will be specifically responsible for ensuring that communications between the GCRC and the other key functions are effective and efficient, and that barriers to interaction are quickly identified and overcome. Dr. Welle's role and his qualifications are described in Section G2F4 above.

At another level, most key functions will appoint representatives to the GCRC Advisory Committee (see Section G2F2a above). Specific representative identified include, but are not limited to, the Director of the Office of Regulatory Compliance and Support and the Director of the Laboratory Support Center (see Sections G2E and G2H respectively). This will allow other key functions to monitor GCRC protocols continuously, and direct the resources of their functions to GCRC investigators, especially where gaps are identified in proposed protocols. This process will play a major role in increasing the productivity of GCRC investigators.

Specific interactions with other key functions include those listed below.

- Novel Clinical and Translational Methodologies. The representative of this key function on the GCRC Advisory Committee will ensure that protocols are reviewed specifically for their use of novel methodologies, or the potential applicability of novel methodologies to the proposed research.
- Pilot and Collaborative Clinical and Translation Studies. Pilot studies proposed for funding through this key function will be reviewed for the applicability of GCRC resources to their studies. Where appropriate, funded pilot studies will be encouraged to use the GCRC, and GCRC leadership and staff will devote extra care to ensuring that these investigators are assisted in making use of GCRC resources.
- Biomedical Informatics. Investigators making use of GCRC resources will be encouraged to utilize the services offered by the Biomedical Informatics key function for data collection and data management.
- Design, Biostatistics and Clinical Research Ethics. As with Biomedical Informatics, investigators interested in making use of GCRC resources will be directed to the Research Design Shared Support Unit prior to presenting their protocol to the GCRC Advisory Committee. This will streamline the review process by improving the quality of initially-submitted protocols.
- Regulatory Knowledge and Support. The staff of the Office of Regulatory Compliance Support will provide GCRC investigators with assistance in many "nuts and bolts" compliance issues, such as designing informed consent forms and managing conflicts of interest.
- Community Engagement. GCRC investigators will be a key focus of the training and consultation services offered by the Community Engagement key function.
- Translational Technologies and Resources. The Director of the Laboratory Support Center will work closely with GCRC leadership and staff to see that laboratory services are well-coordinated with all other aspects of research protocols.
- Research Education, Training and Career Development. CTR Scholars in CTSI training programs will learn about the GCRC through an already existing skill-building workshop, and will be encouraged to make use of the GCRC for their Masters or PhD research projects.
- Upstate Consortium. One of the working groups proposed for the Upstate New York Translational Research Network is devoted to GCRC issues, and the GCRC Program Director will serve as its chair. Investigators from throughout the region will be encouraged through this mechanism to use the GCRC.

G2G. COMMUNITY ENGAGEMENT

The transformation of biomedical research in the United States requires the development of a true continuum from bench to community (1;2). For too long, the three segments of the American health system have been separated with little communication. These three segments can be described as: 1) the academic community composed of investigators and educators; 2) the practice community composed of health professionals and health care agencies; and 3) the public health community composed of governmental/non-governmental organizations and associations and the community individuals that they represent. To assure that these three sectors come together to improve the nation's health, we must develop new organizational structures and communication channels to support sustainable collaboration. The community engagement component of the University of Rochester Medical Center (URMC) Clinical and Translational Science Institute (CTSI) will implement best practices to achieve this transformation.

The URMC is uniquely positioned to develop true community engagement in clinical and translational research. Long in the vanguard of community health, the Medical Center currently has more than 250 programs, representing over $32 million in investment, which contribute to the health of the community. Many programs have been recognized as national models for community-based education, research, and service. The URMC has also made substantial efforts to link the three sectors of health, as evidenced by the longstanding partnerships with the Monroe County Department of Public Health and many other organizations in the community such as the Rochester City School District and the Deaf Health Task Force.

However, these efforts have had limitations that will be addressed by this proposal: 1) lack of strong, consistent community and health care provider participation in the planning, design and execution of research; 2) lack of linkage between community programs and clinical research; and 3) lack of a centralized structure to support community engagement. Recently, the URMC has established a new foundation for community engagement by adding community health to the mission of the URMC and by establishing the Center for Community Health (CCH). The CCH provides the infrastructure for implementation of the CTSI community engagement mission and strengthens collaboration with public and private community agencies. The establishment of the CTSI will provide the additional resources necessary to support participatory clinical and translational research, and to facilitate communication and genuine partnerships among investigators, health care providers, and community members to assure a continuum from bench to community.

G2G1. Specific Aims

G2G1a. Promote Community Participation In clinical And Translational Research.

1) Establish core CTSI community engagement activities in the Center for Community Health (CCH).
2) Establish and promulgate community criteria for CTSI research.
3) Expand expertise in community-based participatory research.
4) Establish long-term research partnerships with community organizations.
5) Engage organizations/individuals in developing priorities, design, and implementation strategies.

G2G1b. Promote Participation Of Community Health Care Providers In Research.

1) Create the Rochester Office for Practice-Based Research Networks (ROCH-PBRN), in the CCH.
2) Coordinate existing adult and pediatric primary care PBRNs and facilitate new PBRN research.
3) Implement training and consultation for investigators and practitioners on practice-based research.
4) Develop innovative communication strategies between health care providers and investigators.
5) Improve recruitment for research studies from health care settings.

G2G1c. Improve the ability of investigators to understand and incorporate community perspectives.

1) Develop training program for investigators and trainees.
2) Develop curriculum for training program.
3) Continuously evaluate and revise training.

G2G1d. Increase the level and diversity of subject participation in research.

1) Increase awareness of and interest in clinical research among the lay public.
2) Design and test innovative community-driven recruitment and retention strategies.
3) Maintain an annotated bibliography of evidence-based recruitment/retention strategies.
4) Establish a working group on recruitment/retention to review literature and provide consultation.
5) Maintain a database of past and current research being conducted in the Finger Lakes region.

G2G2. Background and Significance

While Americans hold medical research in high esteem, they are increasingly discouraged by controversies regarding safety, clinical relevance, and ethical improprieties (3). The media dominates communication about research with no consistent, direct dialogue between investigators and communities, sometimes causing misinformation, confusion and distrust. To transform clinical and translational research, academic health centers (AHCs) must conduct it in a context that acknowledges and seeks the guidance of the community. As AHCs establish their critical and distinct roles in their communities, it is imperative that they communicate the value of their mission, beyond patient care, to the public and to the community organizations that influence the public. The research mission is especially important to communities, not only for its potential to improve the health of the population, but also for its frequently unrecognized potential to support economic development. Despite extensive efforts to inform the public about the importance of research and to conduct research that benefits the health of the community, communities are sometimes mistrustful of university-sponsored research, and reluctant to participate. In the face of increasing demands on the public health system and economic decline in Western New York, our community has increasingly looked to academic institutions to help ensure "the health of the people" as well as to spur economic development. Even in Rochester, with its long history of community-based research and successful collaborative programs that have demonstrated improvements in health and reductions in health disparities, attempts to engage the community in planning and designing research are sometimes met with skepticism and the concern that the University "takes" but does not "give back." This environment is not unique to Rochester and was recently addressed at a workshop sponsored by the NIH Director's Council of Public Representatives, "Inviting Public Participation in Clinical Research: Building Trust through Partnerships" (4).

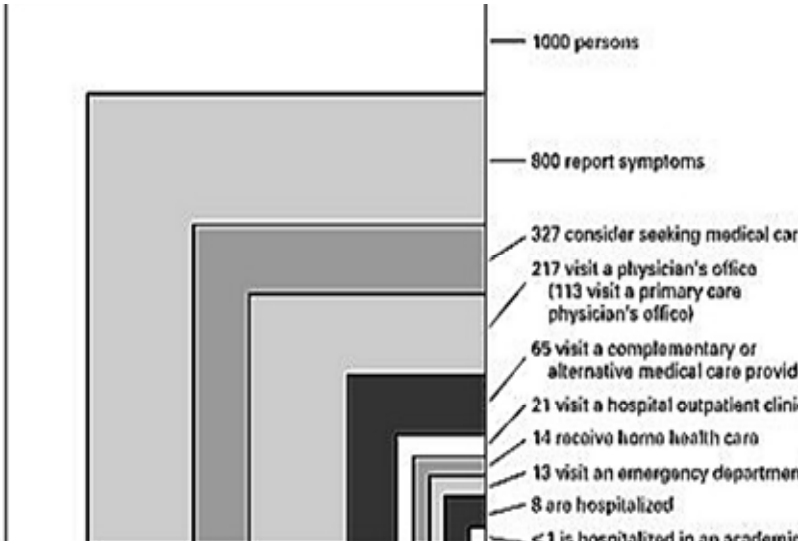
Lack of community involvement in research is due to many factors. In addition to the historic distrust of research, communities are sometimes cynical about the community commitment of AHCs. Institutions are increasingly recognizing the importance of strong partnerships with community organizations at all levels from government to schools to churches to community-based organizations. The recommendations of the NIH Workshop (4) combined with the concepts of community-based participatory research (5) form a useful road map to increase community involvement and participation in clinical research. While many AHCs have developed a variety of volunteer services and strong partnerships for particular projects or grants, it is rare that an AHC explicitly commits significant resources to develop an infrastructure to support community involvement in the work of the health center. However, AHCs are likely to be more successful in implementing these recommendations if they are embedded in the context of the institution's multi-level commitment to community engagement and service. This commitment must include resources and infrastructure to support a variety of activities responsive to the needs of the community. As institutions seek to transform their research paradigm, to assure the relevance of their work, to improve health and to reflect the needs of the population, they must assure that strong and sustained partnerships reflect the willingness of the AHC to encourage information sharing, mutual exploration of priorities, and shared decision-making with groups and individuals in their local community.

Community-Based Participatory Research (CBPR) theory provides a framework for full community participation in research, based on key principles describing a collaborative model that equitably involves community members, organizational representatives and investigators in all aspects of the research process (6;7). CBPR requires a commitment to sustained involvement with the community with continuous exchange of knowledge, skills and resources (8). CBPR is a paradigm for scientific inquiry that stresses community partnerships, action for social change, and reductions in health inequalities, as integral concepts in the research process (9). CBPR has proven useful for developing trust and mutual respect between researchers and communities (10). Community involvement in decision-making and planning is more likely to produce meaningful and sustainable health improvement (11;12). Although CBPR is now commonly acknowledged in AHCs, institutional barriers have prevented CBPR from becoming an accepted research model (13). To address these barriers, AHCs must support the engagement of faculty and researchers in community programs and partnerships. This is a foreign paradigm for many AHCs, but is critical to developing effective interventions and improving the health of communities (14).

Translational research requires the establishment of effective partnerships with all health care delivery sectors. In their seminal work in 1961 describing the ecology of health care, White, Williams, and Greenberg (15) suggested a conceptual framework based on use of health care services by a defined population. Updated reports (16;17) have confirmed their findings. Out of a population of 1,000 persons, in an average month, 800

had symptoms, 217 consulted a health care provider, 8 were hospitalized, but only 1 was seen in an AHC. These findings demonstrate that the vast majority of people have no interaction with AHCs, but many interact with health care providers including primary care/specialty offices, Emergency Departments, home nursing, and alternative providers. Research aimed at understanding disease and health among populations, disparities in health, and programs to improve health care, must involve settings other than AHCs.

Figure G2G1: A Typical Month of Health care in the US (16;17)



The need for local research networks is clear. In addition to small numbers of patients visiting academic medical centers, types and severity of disease vary according to health care venue. For esearch findings to be generalizable, representative populations are needed, and often these can best be obtained through networks of providers that serve large populations. Subject enrollment is often facilitated through engagement at health care sites such as the physician or dentist's office, long-term care facility or even the home itself, in the case of home care patients. Descriptive studies of the burden of disease, disparities in care, and the "process of care" (18), including technical and interpersonal dimensions, all require both representative subjects and real-world variations in provider characteristics. Studies of interventions such as randomized clinical trials of new technology, medications, or delivery methods are most applicable if performed in representative settings without the selection biases of academic-based settings. Well-functioning local research networks actively engage community clinicians (physicians, dentists, nurses, and others) in research. Levels of engagement can include: 1) community clinician-initiated research, 2) collaboration as co-investigator, 3) referral source for subjects, and 4) participation as clinician-subject. Each of these levels offers the potential for reinforcing the others. Strong infrastructure is needed to maintain clinician engagement at all these levels.

Investigators and health professionals are rarely trained in the field of community engagement or participatory research. However, community-based participatory research (10) methods have proven useful in developing trust and mutual respect between researchers and community members, and include a skill set for researchers to acquire "community competence" – the knowledge and understanding of the community, and the skills and attitudes necessary for effective communication and interaction. Health professionals, including investigators, must learn the principles and practices of applied population medicine and at every stage of training, must understand all the parameters of community engagement to effectively integrate community needs with health service delivery plans (19). Essentially, researchers look at their research subjects with an "etic" perspective, that of an outsider to a community or group. Training seeks to broaden their view to include an "emic" perspective, or that of an insider (20). Investigators must understand the community context of their work to be effective in recruitment and retention of research participants. Only then will they successfully communicate their findings and create open communication, building support for continued research.

Recruitment and retention of community members into clinical research presupposes their positive attitudes toward clinical research. As is well-documented, achieving this requires more than news reports or articles about research projects or findings (21). Additionally, traditional methods of recruitment and newer internet-based approaches still leave out key segments of the community. Social marketing strategies (22;23), coupled with less-traditional, culturally-grounded methods, can serve to raise awareness and interest among potential research subjects, their friends, families and the general public.

Also well documented, albeit not well understood, is that interest and eligibility do not translate into study enrollment. While recruitment and retention frustrations abound in clinical research settings, guidance from the literature is sparse with mixed evidence relative to effective approaches. A growing body of evidence provides some direction in improving research recruitment efforts for minorities (24-27). Interestingly in these studies,

recruitment yield among minorities was lower than with passive or traditional methods; however retention rates were higher.

The need for concerted attention to recruitment and retention is clear but often under-appreciated by investigators. As noted in a chapter by Chin and Dozier, working with community members places additional obligations on the researcher (28). In addition, recruitment and retention often suffer from inadequate planning time and resources, and poor understanding of barriers to participation, recruitment strategies and material development.

G2G3. Prior Experience

The URMC has a long-standing commitment to improve the health of the Rochester community dating back to George Eastman's founding gift to the Medical School, with which he instructed the University to use its skills and talents to create the world's healthiest community. Today, community health is formally recognized as the URMC's fourth mission, along with the three traditional academic missions of research, education and patient care. In recognition of the depth and breadth of the Institution's commitment to community service, the American Association of Medical Colleges awarded its 2004 Outstanding Community Service Award to the URMC. A recently completed five-year strategic plan to advance the community health mission of the URMC includes the commitment of substantial resources to establish an effective organizational structure to support the mission of community health. The new Center for Community Health (CCH) facilitates community-based partnerships and collaboration across disciplines, and supports schools, centers, hospitals, and provider networks in establishing community health initiatives. A national advisory board assures guidance from the experiences and expertise of other medical centers, health professionals and scientists from throughout the country. In addition to a faculty advisory group, the Community Advisory Board (CAB) provides community oversight to the CCH in research, program implementation, and the design of clinical services. The CAB is chaired by the Director of the Monroe County Department of Public Health (MCDPH) and is composed of representatives from local government and community groups such as the Hispanic Health Coalition and the African American Health Status Task Force, the provider community, and business leaders. With this structure, opportunities are provided for information sharing, discussion of priorities and shared decision-making. The CAB provides a vital conduit to existing community organizations and the individuals they represent.

G2G3a. Infrastructure - Community Resources and Partnerships The Rochester community provides an unusual level of organizational structure to support the development of community engagement in research. Several key community partnerships provide access to large numbers of organizations and have been designated by the community as leadership coalitions. While the URMC has participated in each of these, it has not previously formed explicit partnerships with them to address research. These coalitions afford the opportunity for bi-directional communication with large segments of the community.

Health Action: The MCDPH, the agency charged with the responsibility for public health in Rochester and Monroe County, leads Health Action (www.healthaction.org), an initiative to establish a framework for community health improvement. Through a community engagement process, local health data are collected and presented in "report cards," priorities for action are selected, and community partnerships develop interventions to address the priorities. The evaluation of interventions informs the next cycle of improvement. Health Action priorities for action for children, adolescents and adults are congruent with the Healthy People 2010 goals, but informed by local data. This process is guided by a Steering Committee with representatives from all the area health systems, insurers, community health centers, community-based organizations (CBOs), the Medical Society, business, and health planning agencies. The URMC was one of the founders of Health Action and bases its strategic planning for community-based programs on Health Action priorities.

African American-Hispanic Health Leadership Conference Committee (AAHHLCC): The leadership of the Hispanic Health Coalition and the African American Health Status Task Force convened the AAHHLCC in January 2004 to address issues common to the African American and Hispanic populations related to the elimination of health disparities. Members of the AAHHLCC serve on the Community Advisory Board of the Center for Community Health. In addition, the Director of the Center for Community Health and the CCH's Director of Community-Academic Partnerships have been meeting regularly with the AAHHLCC to explore ways that the University and the AAHHLCC can form a deeper partnership.

Health Associations Collaborative: In September 2005, representatives from a variety of health organizations convened a collaborative to develop a more comprehensive, efficient approach to the implementation of activities in African American churches. A variety of organizations are represented, for

example, local chapters of national organizations such as American Heart Association, American Cancer Society, National Kidney Foundation; local organizations such as the Perinatal Network of Monroe County, and AIDS Rochester; and finally, community-based organizations. In an effort to coordinate and organize programming in African American churches, the group sponsored a forum in March 2006 with ministry leaders to explore ways that the Health Associations Collaborative can assist ministers in promoting health in their congregations. The members of the collaborative have since committed to continuing to work together to develop joint health promotion projects and to serve as a research advisory group to the CTSI. This collaborative represents a unique approach to organizing the many diverse resources and constituencies concerned with health promotion in the community.

Regional Healthcare Information Organization (RHIO): Another indication of unusual collaboration is the Rochester RHIO. Based on the federal strategy to improve health information technology, the Rochester Business Alliance has entered into a partnership with health care payers and providers to establish a RHIO. The first project was to develop a community wide, HIPAA compliant, secure e-mail application. The next phase of the implementation plan includes support for the implementation of electronic medical records, community e-pharmacy solutions, and a health data repository for lab, radiology reports and digital images. In the future, the RHIO could provide a critical informatics infrastructure for clinical and translational research. The Rochester RHIO will be unique in that it will cover a very high proportion of the area's population.

G2G3b. Community engagement and community-based participatory research As previously noted, the URMC has over 250 local community-based projects and research programs. A number of current research projects are designed to address priorities that specific populations or communities have self-identified, and employ the principles of community-based participatory research. Examples include:

The Healthy Living Program (HLP): The Healthy Living Partnership, a 24-member community coalition led by MCDPH and URMC members, was developed to address a community priority goal: *to promote healthy behaviors to prevent chronic disease*. Lack of physical activity and poor nutrition were identified as priority areas and community data suggested that these risks were more prevalent among African Americans and Hispanics. The Healthy Living Partnership worked with faith-based partners to develop the HLP. The HLP, administered by the URMC Center for Lifetime Wellness, is a church/community-based program delivered in the City of Rochester with over 1200 enrollees to date. At the start of the program, only 17% of participants met the Healthy People 2010 moderate physical activity goal. Most (90%) were overweight or obese (BMI$\geq$25), approximately 45% of the group had hypertension, and 19% had diabetes. Participants have shown significant improvements in physical activity, nutrition habits, and overall well being at 6 and 12 month intervals. For its unique and novel approach and its positive outcomes, this community-based intervention was awarded the 2005 DHHS Secretary's Award for Innovation in Prevention.

Racial and Ethnic Adult Disparities in Immunization Initiative (READII): While Monroe County had achieved relatively high baseline rates of influenza and pneumococcal vaccination for white seniors, African Americans and Hispanics had markedly lower rates, and this was identified as a top concern by these segments of our community. The URMC and the MCDPH, along with a diverse community advisory board, developed Rochester READII, one of five demonstration sites funded by the Centers for Disease Control to study effective interventions to reduce disparity in immunization rates. The Community Advisory Board designed and implemented a community-wide action plan and a primary care practice intervention, in partnership with the provider community, which included an embedded randomized clinical trial. Despite barriers such as vaccine shortages and distribution disruptions, influenza immunization rates for African American Seniors improved from 39% in 2001 to 69% in 2005, and pneumococcal immunization rates improved from 42% in 2001 to 64% in 2005. In addition, practice-based research was successfully carried out in a network of community health centers, creating a model for future efforts. READII was awarded the National Partnership for Immunization 2005 Excellence Award in Addressing Disparities and is a flagship program highlighted by CDC.

Rochester Prevention Research Center (RPRC): Deaf and hard of hearing (D/HOH) individuals represent more than 9% of the US population, making hearing loss the sixth most common chronic condition in the US. Rochester is believed to have the highest per capita deaf population in the world with an estimated 10,000 to 15,000 primary American Sign Language users. The prevalence of hearing loss is increasing faster than the population is aging, yet little is known about health knowledge, attitudes, risk behaviors or disease prevalence among the D/HOH. In August 2004, the Rochester Deaf Health Task Force released a report describing barriers to care experienced by this population and recommendations for health improvement.

Under a cooperative agreement with the CDC, the URMC created the Rochester Prevention Research Center (RPRC), one of 33 CDC-funded Prevention Centers nationwide, whose goal is to involve members of the D/HOH community and partnering organizations to better understand how to prevent disease and improve health in the deaf community. The research plan of the RPRC emphasizes community participatory research as a means to improve the health of the D/HOH population.

G2G3c. Health Care Provider Community Rochester has a long history of research performed in practice-based settings. For example, the Department of Pediatrics has been studying child health care from the community perspective since the days of Robert J. Haggerty (29) and Burtis Breese (30) in the 1960s. Descriptive and intervention studies of childhood immunization delivery have involved virtually every pediatric and family physician practice in Monroe County. This work has demonstrated that translating immunization interventions from selected practices to a network of urban practices can virtually eliminate preexisting disparities in immunization rates between urban and suburban children, and among white, Hispanic, and African American children (31). Recent expansion of this concept to adult immunization delivery with the creation of a network of urban adult primary care practices to improve influenza and pneumococcal immunizations (READII, described above) resulted in equally dramatic improvements in immunization delivery and reduced disparities. Studies linking childhood asthma care between urban practitioners and all City of Rochester elementary schools have demonstrated improved asthma outcomes among urban children (32).

The Department of Family Medicine has developed a practice based research network (PBRN) that has supported study of physician-patient communication. Almost 100 internists and family physicians participated in a study of the effect of patient-centered communication on costs (33). Following physician consent, two unannounced “standardized patients” (actors trained to portray specific patient roles) were seen by participating physicians and visits audiotaped. The PBRN participated in a second study using this methodology to examine the impact of patient-directed pharmaceutical promotion on physician prescribing (34). Many members of the PBRN are currently participating in an NCI-sponsored trial of patient navigation to reduce disparities in cancer-related care. In each instance, the PBRN participation has been driven by University of Rochester investigator initiatives. These practice-based research models and linkages between PBRNs with other community-based sites will be expanded, and include more bidirectional activities.

G2G3d. Community and Population Health Training The URMC has both the experience and capacity to undertake the proposed development of “community competence” among the URMC investigator and health care provider community. The Community Health Graduate Programs at the UR, which offer both master- and doctorate-level degrees in public health, are highly ranked by US News and World Report. The Department of Community and Preventive Medicine currently has 138 graduate students, of whom approximately 70% are physicians. The Medical School curriculum also includes both prevention and diversity themes, includes a required Community Health Improvement Clerkship in the fourth year, and was recently awarded the Outstanding Preventive Medicine Curriculum Award by the Association of Teachers of Preventive Medicine. Most K30 fellows take Preventive Medicine 450 which includes placement in community agencies. Through the partnership with the MCDPH, the CCH Director of Education developed a community-based education program in 1998, to increase the knowledge of prevention and population health among health professions students. Called the “Action for Health Education Program,” its unifying theme is the linkage of student teams to community health improvement initiatives responsive to community goals (19). The web-based and interactive curriculum for this course has been modified for use in several courses in the medical and nursing schools. Although universities have often involved students in community projects, the projects have rarely been defined through a community process. The University of Rochester School of Medicine and Dentistry is one of the few medical schools in the nation with an office of Student Enrichment Services to coordinate and support volunteer service in response to community-identified needs, and also one of the few with a required community health clerkship.

In 2004, the Department of Community and Preventive Medicine (DCPM) introduced a course on Recruitment and Retention of Human Subjects into Clinical Research. Using online resources, didactic presentations, in class and online discussions, and small group work and case studies, students explore the common and unique issues associated with recruitment of ethnic groups, children, elderly, women and the disenfranchised. While intended for MPH and PhD students, half of the students completing the course have been fellows, clinicians, and research staff who incorporate coursework into grant applications or ideas for new grant proposals. The DCPM has extensive experience training individuals and teams of professionals and paraprofessionals from community-based organizations (e.g., state and local health departments).

G2G4. Methods

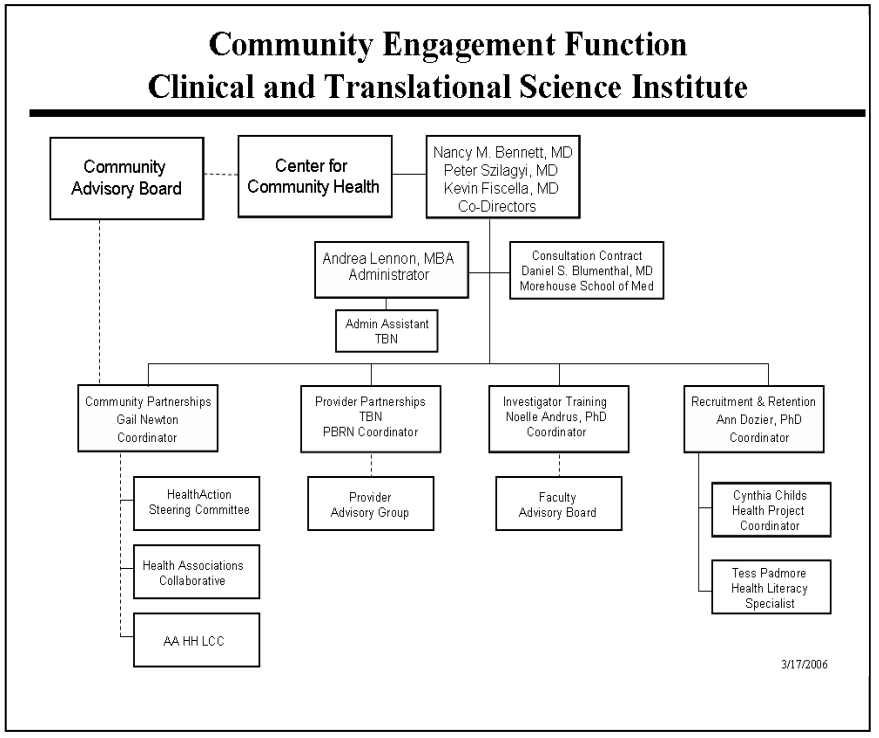
The URMC serves a region that includes Rochester (population 250,000), surrounded by Monroe County (740,000) and the additional eight counties of the Finger Lakes, NY region (1.2 million). The CTSI will serve this region with additional linkages to the Upstate New York Translational Research Network (UNYTRN). The region has vast socioeconomic diversity, including an impoverished City of Rochester with high concentrations of African American and Hispanic populations and the ninth highest rate of child poverty in the US, affluent suburbs, and relatively impoverished rural areas. It is critical that through community engagement, the CTSI reflect the concerns and interests of this diverse population.

Specific Aim A: Promote Community Participation in Clinical and Translational Research

A1. Establish core CTSI community engagement activities in the Center for Community Health (CCH).

The CCH will provide infrastructure and be responsible for overseeing and implementing all activities of the CTSI community engagement function. The overall mission, strategic plan, organizational structure, and activities of the CCH provide the perfect context for enhancing community engagement in research. The infrastructure of the CCH, including the Community Advisory Board, will lend itself to supporting the goals of the CTSI. The CCH provides a conduit to community organizations and individuals for URMC faculty, as well as a single, identifiable point of entry to the University and the CTSI for the community. The Director of the CCH, a Professor in the Department of Medicine, Nancy M. Bennett, MD, MS, and two senior colleagues, one in the Department of Pediatrics, Peter Szilagyi, MD, MPH, and one in Family Medicine, Kevin Fiscella, MD, MPH, will lead the community engagement core of the CTSI. In addition, the Executive Director of the CCH, Andrea Lennon, MBA, will provide administrative oversight for the CTSI community activities. Members of the CCH will coordinate each Specific Aim. The CCH Director of Community-Academic Partnerships, Gail Newton, will oversee linkage to community organizations. Drs. Szilagyi and Fiscella and a TBN Coordinator will be responsible for the engagement of the provider community. The CCH Director of Education, Noelle Andrus, PhD, will oversee the training of researchers in population health. Ann Dozier, PhD, a senior member of the Department of Community and Preventive Medicine, will oversee the recruitment and retention segment.

Figure G2G2: Organizational Chart



In addition, the CCH Community Advisory Board (CAB), with broad community representation, will provide oversight of the activities of the community engagement core of the CTSI, and community input into research priorities, design and implementation strategies for research performed in the CTSI. The CAB and the staff of CCH will provide linkage to three key community partnerships: Health Action, the Health Associations Collaborative, and the African American Hispanic Health Leadership Conference Committee. The CCH CAB is composed of representatives of key community constituencies such as the MCDPH, Mayor's Office, the African American Health Status Task Force, the Hispanic Health Coalition, the Rochester City School District, community-based organizations, and the business community.

A2. Establish and promulgate community criteria for CTSI research. The CCH/CTSI faculty will develop and establish review criteria for CTSI research, based on the principles outlined by the NIH Public Trust Initiative (4) to assure: community support and acceptance, cultural competency, assurance of long-term follow-up, appropriate communication strategies, and logistic feasibility. The faculty and staff will solicit and incorporate the views of the CCH Community Advisory Board through structured sessions, preferably in retreat

format. Once the criteria have been established, the CCH/CTSI will share the review criteria with the CTSI Administrative Committee and other key function groups as well as provide training to interested investigators in their use to assess the fidelity of studies to them. The CAB will be expected to provide feedback on research plans when requested, and to direct investigators to appropriate community partners. When appropriate, investigators will be invited to present research designs to the CAB for more in-depth feedback and to promote understanding between investigators and community members.

A3. Expand expertise in community-based participatory research. As demonstrated by successful community–based projects outlined above that were created out of community-based participatory processes such as Health Action and the Deaf Health Task Force, the Rochester community is a national model for public health-oriented community engagement, and the leaders of the CCH are frequent consultants to other communities seeking to emulate our participatory-based public health-academic partnership projects. The next step is to expand this participatory process to our clinical and translational research enterprise. The community-based participatory research (CBPR) model provides a vital link between the transformed clinical and translational research endeavor and community interests. An early step will involve the development of enhanced expertise in CBPR. To this end, we will consult with Daniel S. Blumenthal, MD, MPH, the Principal Investigator of the Prevention Research Center and Chairman of the Department of Community Health and Preventive Medicine at Morehouse School of Medicine, in year 1 to develop enhanced CBPR competencies within the Department of Community and Preventive Medicine and the Center for Community Health. The CCH has already included building CBPR capacity in its five-year strategic plan. However, the proposed CTSI will expedite the development of this capacity and provide resources for its implementation through training and consultation with Dr. Blumenthal.

A4. Establish long-term research partnerships with community organizations. As previously noted, the University has had success in developing project-specific partnerships with community organizations, which serve as a foundation for expanding our work into community involvement in research. The Community Advisory Board, with representatives from the key sectors of the community: education, business, human services, media, and representative organizations, provide an ongoing conduit for community involvement and collaboration, and will be complemented by strengthening three key partnerships. (See Section **G2G3a.** for description of each organization.)

1) **Health Action Steering Committee**. The CCH/CTSI will partner with Health Action to assure that research performed in the CTSI has relevance to the priorities for community health improvement defined through the Health Action process.

2) **African American and Hispanic Health Leadership Conference Committee**. The CCH/CTSI will work with the AAHHLCC to incorporate their input regarding research in the minority community, and to explore participant recruitment and retention through community-based organizations and the faith community.

3) **Health Associations Collaborative**. The CCH/CTSI will establish a strong working relationship with this collaborative of voluntary health associations to assure input of their members and volunteers into research priorities and design, and to explore recruitment through these associations.

These partnerships will provide more comprehensive integrated community input, reflecting the views of multiple community organizations and individuals, to the Community Advisory Board (CAB). The input of the organizations will be communicated and incorporated into the CAB's oversight of the CTSI. CCH/CTSI staff will be responsible for assuring this communication. In addition, members of the three groups are also members of the CAB. The establishment of long-term partnerships with these groups will assure sustained communication with the individuals and smaller organizations represented in these groups. The partnerships will establish communication channels with all segments of the broader community and assure an organized approach to community participation. These communication channels will be augmented by general public relations communication, but our experience has shown that while broad, one-way media approaches serve to stimulate interest and awareness, direct, face-to-face, bi-directional and sustained communication with a targeted group is more effective in establishing engagement and involvement. While these three partnerships will be central to our efforts, additional input will also be sought through existing partnerships (e.g., the Deaf Health Task Force).

A5. Engage organizations/individuals in developing priorities, design, and implementation strategies.

To truly engage the members of the partner organizations described above, the CCH/CTSI faculty and staff, with the assistance of the Morehouse School of Medicine Prevention Research Center, will develop and present a brief orientation to clinical and translational research. This curriculum will include, for example: the

role of research in improving health and supporting economic development, exploration of population health data as the context for community input regarding research priorities, a brief introduction to research design, and the importance of participation by diverse populations. This introduction will attempt to demystify research, provide a background for discussions, and help to empower members of diverse constituencies to provide meaningful input. This approach has recently been used to garner public input into pandemic influenza planning with great success (35).

CCH/CTSI staff will be responsible for developing yearly focus groups, or other interactive sessions, with each of the organizations to elicit input into the research activities of the CTSI. The Director of Community-Academic Partnerships will lead this activity and be responsible for assuring that the recommendations proposed in these sessions be fully communicated to the CAB and the Directors of the CTSI. When requested, CTSI staff will arrange for investigators to speak at meetings of these organizations or their member organizations and agencies. CTSI staff will work with investigators to develop talks reviewing design and results of studies, assuring that they are community competent and relevant to health improvement.

Specific Aim B: Promote Participation of Community Health Care Providers in Research

B1. Create the Rochester Office for Practice-Based Research Networks (ROCH-PBRN) in the CCH. The establishment of the Rochester Office for Practice-Based Research Networks (ROCH-PBRN) is central to achieving collaborative research involving clinical practices. This office will work closely with the URMC's established Center for Primary Care (CPC), which is an integrated virtual organization comprised of URMC-sponsored practices, community-based private practices, primary care residency training programs, executive health program and clinical support linkage services such as palliative and hospitalist care. The ROCH-PBRN will coordinate PBRNs for the purpose of increasing provider involvement in research. Core staff will include a practice liaison/office administrator, primary care faculty (Drs. Szilagyi and Fiscella, with consultants), and administrative support staff. Adjunct staff will include IRB consultants/liaisons, health project coordinators, research assistants, programmers, and data analysts available through other core services in the Clinical and Translational Science Institute. Since practice-based research involves special challenges distinct from other components of the CCH, we will establish a ROCH-PBRN Advisory Group consisting of several local practitioners who participate, several community leaders, local academic researchers, and an external PBRN specialist from the National Pediatric Research in Offices Settings (PROS) PBRN (36), for which Dr. Szilagyi serves as an advisor. The practice-level members will meet quarterly, and the entire advisory group (including local and external advisors) will meet annually to review current ROCH-PBRN activities and future directions.

B2. Coordinate existing adult and pediatric primary care PBRNs and facilitate new PBRN research. The ROCH-PBRN will coordinate studies across the two major PBRNs (pediatric and adult primary care practices) and serve as a liaison to other CTSI activities. Most studies previously conducted by these PBRNs involved health services research. The ROCH-PBRN will provide the infrastructure to facilitate translation from the bed to the community and link researchers with practitioners to facilitate community-based research in a wide spectrum of research, including experimental therapeutics and translational research (e.g. using the outpatient GCRC). Projects will include descriptive studies, e.g., measures of the burden of disease across the population, secular trends in disease, disparities in health, and longitudinal cohort studies such as the National Children's Study which has targeted Monroe County as one of 105 counties; and process of health care studies, using the conceptual framework of the Medical Outcomes Study (18) to include both technical and interpersonal care. Examples are doctor-patient communication strategies, variations in disease management, integration of electronic medical records to improve quality, examination of health care costs, and disparities in health care. Experimental therapeutics and interventional studies, such as randomized clinical trials or other experimental designs, using the patient, physician or practice as the unit of analysis, will be facilitated. Examples of patient-level studies are pharmaceutical or behavioral interventions. Examples of physician-level interventions include academic detailing to promote quality of care through implementation of care guidelines at point of care and/or use of electronic medical record algorithms. Practice-level interventions include quality improvement initiatives focused on redesign of systems of care. Major studies will be funded externally, and the Core Office will provide infrastructure support to carry out the fieldwork and analyses, and coordinate activities with the Biomedical Informatics; Design, Biostatistics, and Clinical Research Ethics; and Translational Technologies and Resources functions.

The ROCH-PBRN will provide the resources to directly engage community physicians in establishing priorities for research, and facilitate recruitment of subjects from community practices. The ROCH-PBRN will facilitate the evolution of existing PBRNs from project-specific research networks to continuous, permanent

upstate PBRNs that facilitate practitioner involvement in all phases of translational research from conception to dissemination. This will include linkages with the GCRC and academic-based laboratories. It will also foster trust between clinicians and the University, and provide multiple opportunities for clinician participation in research.

B3. Implement training and consultation for investigators / practitioners on practice based research.

The ROCH-PBRN will implement a training program for investigators, field staff, and practitioners, to teach the principles, strategies, barriers, facilitating factors, and analytic issues related to practice-based research. These sessions will be integrated into the training program described under Aim 1C. Sessions will be taught by faculty or the ROCH-PBRN liaison. Since most of the practice-based research will involve externally-funded projects, the ROCH-PBRN faculty will provide consultation to investigators in various phases of project development from the conceptualization phase to fieldwork and analytic phases.

B4. Develop innovative communication strategies between health care providers and investigators.

The ROCH-PBRN will develop a list-serve of practitioners to inform them of new or ongoing studies, provide information on fieldwork challenges, and provide feedback on findings applicable to practice. The liaison will also work with community practices to devise convenient ways to post and update information about studies within practices using some of the culturally appropriate materials developed in other sections of the CCH. Additional activities that coordinate with the Biomedical Informatics Core are described below.

B5. Improve recruitment for research studies from health care settings. The ROCH-PBRN liaison will be an integral person within the activities described under the section on increasing subject participation (Specific Aim D). The liaison will focus on recruitment within primary care and other clinical practices, while other components will involve recruitment directly from the community.

The table below describes specific activities of the ROCH-PBRN. University-based or community-based investigators will have access to a database and core personnel to help plan research projects. For example, an investigator studying diabetes can work with core faculty and staff to outline optimal strategies for subject recruitment using bioinformatics, fieldwork methods, and analyses from epidemiology and design. Core staff will regularly solicit ideas from PBRN members and use quarterly meetings of the Advisory Group to address challenges and barriers, improve communications, and facilitate linkages with investigators from other cores. A state-of-the-art communication strategy will be developed using online electronic communications in conjunction with the Biomedical Informatics Core. In addition to consultations, Core Faculty will advise investigators in how to access small grants specifically designed to assist investigators in gathering pilot data prior to major grant submission.

Table G2G1. ROCH-PBRN Activities.

Need	Type of Activity	Description of Activity of the ROCH-PBRN
Description of community practices	Establish and maintain database	Establish a database for each PBRN that includes patient, provider and practice characteristics.
Engagement of physician community in research	Liaison	Conduct interviews and surveys of community physicians regarding: 1. Practice-based research ideas and research priorities 2. Desired level of engagement in research 3. Methods to inform patients in practices about clinical trials.
Knowledge of benefits of community research	Communication	Provide education through medical societies and community hospital clinical departments regarding benefits of PBRN research and clinical trials participation.
Support for PBRN-initiated research	Infrastructure for community physician research	Facilitate linkages with faculty mentors and research support staff. Provide training of investigators, field staff, and practitioners. Provide consultation to developing and ongoing projects.
Linkages between upstate practices	UNYTRN infrastructure	Provide consultation regarding PBRN issues including IRB and HIPAA. Provide consultation for developing PBRNs in the upstate New York region.
Participation of patients in the community in clinical trials	Practice-based patient recruitment into trials	Establish centralized expertise in practice-based clinical trials recruitment including optimal communication with physicians and recruitment of patients for clinical trials. Post information in practices about clinical trials. Provide consultation regarding linkages with GCRC and laboratory-based studies.
Funding research	Funding specialist	Assist practices in identifying small grants for pilot studies.

<u>Specific Aim C:</u> Improve The Ability Of Investigators To Understand/Incorporate Community Perspectives

C1. Develop training program for investigators and trainees. A course for investigators and trainees will be developed to introduce them to general concepts of community and population health, specific community structures and health priorities, and best practice recruitment and retention strategies. The course will build on several existing courses and incorporate online learning and experiential modalities. It will be fully integrated with the Education and Training Key Function.

Focus groups and key informant interviews with senior and junior researchers and research staff will be undertaken to identify the barriers to and perceptions about community collaboration and perceived benefits and opportunities. The results will form the basis for a coordinated strategy of communication that includes URMC publications, presentations at grand rounds, department business/research meetings, and informational sessions. A key theme will be how community engagement/competence prevents "missed opportunities" and supports success in research.

Training will be required of fellows and other students participating in the K30 and K12 grants and offered to all investigators and trainees associated with the CTSI. The approach will be structured. Participants will complete six required modules and choose two additional modules based on their particular interest area, all designed for self-paced learning. Each module will include didactic, experiential, and group work. Individuals will work as members of a team to complete online didactic components, to complete group assignments, and to develop projects applicable to their research interests. Skills building will be provided through online instruction using adult learning methods. A team-based approach will enable a PI and his/her research team to complete the training concurrently. Modules will be instructor-supported through e-mail feedback, meetings, or team conference calls. A mentoring model will be used to give investigators and trainees the opportunity to work in small groups to partner with experienced mentors. As trainees gain experience, they will be asked to mentor new trainees.

Each module may take up to four weeks to complete; enrollment cycles would occur three times each year, with rolling start-ups considered after the first year of deployment. Each module will include a community component. Trainees will attend community meetings, spend time in targeted communities, interview key stakeholders, and meet with community agency directors and staff in both urban and rural communities to identify local resources, and to gain a better understanding of conditions within a particular community. Community leaders, both formal and informal, will be included in the design of the training and their voices and perspectives will be central components in each module. In addition to instructor feedback, final products will be presented to a group of community members for their feedback.

C2. Develop curriculum for training program. Training content will include an introduction to the concepts of community and population health and focus on general principles and practice of CBPR and on the critical elements in community-based participatory research, outlined in the AHRQ Evidence Report (37).

Table G2G2. Curriculum elements for CTSI Community Engagement Training
• CBPR background and process
• forming the research team and potential for forming a research partnership
• principles of community collaboration (e.g., empowering communities, types of collaboration)
• cultural competency
• principles of communication (including literacy issues)
• framework for change (organizational theory, behavior change theories, etc.)
• the use of CBPR to define the research question
• methods for intervention design and implementation (design/revise/tailor data collection/instruments)
• data analysis and interpretation
• research translation

Curriculum development and pre-testing will require 12 months. A committee for training and evaluation will be formed, and faculty with relevant specialty areas and community experience will serve on committee. Experiences and lessons learned from trained teams will be incorporated into subsequent years' modules.

C3. Evaluate and revise training. The goals for evaluating the training program will be to assess the training needs of the participants, to assess the effectiveness of the program, and to identify ways to improve training. Participatory evaluation will be used. Process evaluation will assess the implementation of the program activities and quality of training. Outcomes evaluation will focus on the immediate effects of the training program, how well the objectives of the training program were met, and the extent to which the goals of the program have been achieved through assessment of changes in practice/research approaches (38;39).

Methods for process evaluation will include the use of interviews and surveys for tracking training inquiries, enrollment and completion of training by department and academic position, and feedback from individuals regarding the overall satisfaction with the course process and content, including the online component, software, quality of community presentations, the applied community experience, and the timeline. This evaluation will be implemented immediately upon course completion and six months later.

Methods for outcomes evaluation to determine the extent to which the goals and objectives of the program are met include: 1) participant feedback through periodic journal entries regarding their lessons learned during the course of training; 2) content module evaluation summaries; 3) team meeting effectiveness surveys to assess team progress; 4) pre-test and post-test knowledge assessment surveys to assess the level of knowledge in key areas; 5) exit surveys to determine whether or not the training objectives were met; and 6) surveys and interviews to determine changes in practice/research approaches. Experiences (lessons learned) from trained teams will be incorporated into subsequent years' modules. In addition, as feasible, manuscripts and brief reports regarding recruitment and retention experiences either from individual studies or collectively across several studies will be submitted for publication.

Specific Aim D: Increase The Level And Diversity Of Subject Participation In Research

D1. Increase awareness of and interest in clinical research among the lay public. Creating increased awareness and interest through a social marketing strategy requires involvement of formal and informal community leaders (e.g. Health Action, Health Associations Collaborative, AAHHLCC) and community members including existing community-based organizations that partner with the University of Rochester (e.g. school districts, Children's Institute, community coalitions). Key informant interviews and focus groups assure participation across age, gender and other key sociodemographic factors. Issues to be discussed will include general perceptions about clinical research findings and participation, perceived benefits/liabilities, and sources of attitudes. The public will be engaged in learning how to create greater visibility of research activities/findings (e.g. community successes that were the result of research, national research successes). Embedded in this approach will be: 1) questions to generate a broader message regarding the positive impact of research on local job creation and economic growth, 2) assessment of the current public image and perception of NIH among the general public and potential ways to improve it, and 3) marketing strategies for research recruitment.

Use of social marketing experts in the design and interpretation of findings will result in design and testing of core research messages for the public (e.g., value of clinical research and motivational messages to promote participation including a tag line). A broad-based communication/dissemination strategy expanded beyond traditional media outlets will include:

- Routine presence at events across the target communities (e.g., health fairs, festivals, sports events)
- Messages/stories for inclusion in local and neighborhood newspapers, health insurance/other mailers,
- Posters with tag line/message for use at pharmacies, medical supply stores, grocery stores,
- Web-presence to promote research participation, success stories and messages.

Personal outreach will supplement the marketing strategy, to present clinical research to key lay groups, business groups, community advisory boards and community-based organizations. Target organizations will include existing individual membership organizations (faith-based groups, fraternal organizations, unions and health/illness/disability-based associations) and health/human service agencies (e.g. neighborhood centers, nutrition centers). As feasible, presentations open to the general public will be conducted through the extensive town-based continuing education activities. In addition to logistical support (e.g. mailings, scheduling), the CTSI staff will provide resources and a speaker's bureau of teams of investigators and community members.

Building on the above, the CTSI will develop and deploy a Health/Media Literacy Program to improve the understanding of research reports in the media. This program could be offered through the above groups, would be deployed through distance learning, and made available to high school and college students.

D2. Design and test innovative, community-driven recruitment and retention strategies. Recruitment and retention principles will be tailored to area populations (e.g. African Americans, Puerto Ricans, rural, disenfranchised, disabled), and to developing credibility with the community (visibility, relationships, norms, communication and listening), using community knowledge to design and adapt effective methods and evaluating results. Through existing partner groups and community coalitions associated with the CCH, we will work with members of target groups to: 1) pilot evidence-based methods (24-26); 2) tailor materials (see below) to specific sub-groups; and 3) evaluate results after pilot testing, and again following deployment in clinical research recruitment.

As recommended by Yancey et al (27), and consistent with federal guidelines, we will establish recommended standards, templates and toolkits for development, pre and pilot testing of recruitment materials. This work will be based on Kreuter et al.'s (40) typology of cultural adaptation/tailoring (peripheral, linguistic, evidential, constituent involving, sociocultural), and incorporate findings from the social marketing efforts. Through the users group (see below) we will provide an internal review mechanism for researchers to use prior to deployment of materials. Key to this effort will be collaboration with the CTSI Regulatory Knowledge and Support Function.

An existing University of Rochester resource, CLIC-on-Health, will serve as a tool to promote clinical research and to connect users to studies. This web portal is a project of libraries, health organizations and associations, health care systems, and educational institutions, to provide high-quality health care information and resources. The project features: 1) a web portal with information specific to Rochester health care and directions to credible web resources related to health – a "one-stop-shopping" site for health information; and 2) training in the use of health information on the Internet.

For research conducted under the auspices of the CTSI, we will work with the investigators/research team to track results of recruitment strategies by referral/method (number approached/contacted, percentage of those who volunteer, are eligible, who enroll and remain with the study). To complement quantitative data, we will conduct focus groups and key informant interviews among individuals who choose to participate and not participate. Additionally, the staff will assess the experiences of individuals involved with recruitment (community member, local agency) through use of survey and focus groups or interviews. In addition to study-specific analyses, we will aggregate findings across studies to provide additional information for future researchers. Findings will be presented to user groups and other interested parties, and submitted for publication as appropriate.

D3. Maintain annotated bibliography of evidence-based recruitment and retention strategies. Using existing databases of published articles in addition to databases from national meeting presentations, we will establish a database of recruitment and retention strategies. The database will be updated quarterly by students in aforementioned courses. A working group on clinical research recruitment and retention will be established to review literature and provide consultation for researchers. Additionally, this group will serve as consultants to individuals preparing proposals to conduct translational research in the community, to assure that the most up-to-date, evidence-based, current strategies are included.

D4. Establish a working group on recruitment/retention to review literature and provide consultation.

A working group, composed of investigators, recruitment staff, and CTSI staff, led by Dr. Dozier, will provide a forum for discussion of best practices. Regular meetings will support the above activities, including assisting in template/toolkit development and providing feedback to new and funded researchers regarding proposed recruitment/retention methodologies. Presentations will include speakers from the community who will discuss current recruitment/retention strategies.

D5. Maintain a database of past and current research being conducted in the Finger Lakes region.

In collaboration with the University's IRB, a database of local research will be established that includes recruitment and retention methods used, timeframe for data collection, target audience, recruitment/retention results and contact information. Through this and the above working group, a listing will be created of internal experts with community recruitment experience who will be available for consultation with newer/less experienced community researchers**.**

G2G5. <u>Novel Aspects of Key Functions</u>

All of the activities related to community engagement of the CTSI are embedded in a broader strategy to engage the community in education and patient care as well as research. This context is likely to contribute significantly to building trust and gaining support for research. In addition, this proposal is organized by a simple concept – the silos of academic medicine, medical practice and broadly defined public health/community must be replaced by partnerships established to further the goals of research and the improvement of health. The Aims directly reflect this concept and the proposed activities address multiple constituencies, relying on their existing, natural organizational structures. The CTSI staff will assure that the University reaches out to broadly representative groups that include the disenfranchised and the disabled.

The URMC has an excellent record of community programs and is poised to develop a model of community engagement in research. The significant institutional commitment and URMC Center for

Community Health's infrastructure, with the addition of enhanced expertise in participatory research, will assure that our model for community engagement is applicable to all institutions committed to transforming the relationship between community and research.

The approach to building partnership with the practice community is novel in two respects. First, it uses PBRNs as means for facilitating the participation at differing levels by community clinicians. By tailoring engagement to the needs of the clinician, the ROCH-PBRN will advance the goals of enhanced research of different types. Second, it will facilitate the coordination of primary care PBRNs with clinical research and develop novel communication strategies. This ambitious project can only be contemplated in a community, such as Rochester, that enjoys a high degree of collaboration among practitioners.

The CTSI will provide a coordinated resource for researchers. The centralized approach to training investigators in community engagement and participatory research concepts employs a novel team-based, distance learning approach. In addition, investigators will be invited to participate in community forums and retreats with community organizations to discuss their proposed research and to communicate research outcomes as they become available. The applied approach to investigator training is realistic in its use of an interactive online curriculum, but is strengthened by the team approach and experiential learning opportunities.

Social marketing approaches will be used to address the community's understanding of research and to support participation in clinical trials. The proposed health literacy program will be a direct outgrowth of this understanding. In addition, the URMC CTSI will implement and evaluate a variety of strategies for recruitment and retention of research participants, again using "natural" community organizations and a proactive approach. The results of this exploration will be disseminated to all institutions seeking to increase recruitment and retention of diverse populations. Through work with the various CTSI-affiliated research projects, we will be in a key position to evaluate strategies across studies being conducted in the community. This will enhance our local capacity and knowledge and add to the literature on recruitment and retention effectiveness.

G2G6. Key Function Interactions Table G2G3.

Specific Aim/Activity	Relationship to other CTSI Functions
A. Community Partnerships	Provides input to: 1) CTSI Administrative Committee regarding research priorities 2) Design Consulting regarding community acceptance 3) Pilot Studies regarding priority areas for research 4) Novel Methods regarding community acceptance 5) Regulatory regarding recruitment/retention procedures and ethical concerns Provides linkage to community for all investigators Disseminates methods to UNYTRN institutions for implementation in their communities
B. Provider Partnerships	Provides input to: 1) CTSI Administrative Committee regarding research priorities 2) Design Consulting regarding use of PBRNs 3) Pilot Studies regarding use of PBRNs 4) Novel Methods regarding provider needs Receives support from Informatics Provides linkage to provider community for all investigators Provides consultation to UNYTRN institutions
C. Investigator Training	Embedded in Training Programs Works closely with Design Consulting to assure training reflects interests Provides community training to all investigators Shares curriculum and structure with UNYTRN institutions
D. Recruitment and Retention	Provides input to: 1) Design Consulting regarding best practices 2) Pilot Studies regarding new methods 3) Regulatory re impediments/facilitators of recruitment/retention Design Consulting and Pilot Studies provide direction regarding methods Supports evaluation of recruitment and retention strategies for studies Provides consultation to other institutions in UNYTRN to implement successful strategies

G2G7. Evaluation and Dissemination of Findings

Participatory evaluation will be used to the extent possible, with outcomes and measures defined through a process that includes community participants, especially the Community Advisory Board, and investigators. The table below outlines a series of preliminary outcomes and measures that will be refined through the participatory process. Both qualitative and quantitative approaches will be employed, including tracking logs; participant and community surveys; pre-post assessments of participant knowledge, intention and attitude; and focus groups/key informant interviews. Results will be presented to the CTSI Administrative Committee.

Feedback and CQI methods will be used throughout the project to assure implementation of needed modifications.

Table G2G4. Evaluation Goals and Measures

Evaluation Indicator	Assessment Method
Specific Aim A: Promote community participation in the development of clinical and translational research	
Participation and diversity of members/key groups	Member participation log
Participant satisfaction with engagement	Feedback Survey; qualitative methods
Advisory Groups effectiveness	PSAT*; qualitative methods
Effect on research activities (e.g. prioritization, feedback, design)	Meeting Minutes, participant and investigator surveys
Knowledge and awareness of clinical research among groups	Pre/post assessments
Effectiveness of participatory research partnerships	PSAT*; qualitative methods
Specific Aim B: Promote participation of community health care providers in research	
Number of participating practices / practitioners	Baseline, then annual survey of practices in PBRNs
Number of researchers/practitioners trained on PBRNs	Database of trainees.
Identification of barriers/facilitators to participating in research	Annual survey of MDs in and out of PBRNs
Satisfaction with participation/involvement	Feedback about consultation service by users (survey)
Number of patients recruited in PBRN-related studies	Database maintained by the ROCH-PBRN
Number and types of PBRN-related studies/grants/ research dollars generated and number of manuscripts	Database maintained by the ROCH-PBRN
External evaluation: overall effectiveness, improvements	Provider Advisory Board- annual meeting/feedback
Specific Aim C: Improve the ability of researchers to understand and incorporate community perspectives	
Number of courses offered/participants attending/completing	Track course offerings and participants
Course modifications made	Track changes made; focus group
Satisfaction among course participants	Participant feedback survey; journal entries
Number of departments with “community” trained research staff	Track participants
Number of “community competent” researchers and research staff	Pre/post assessments; qualitative methods
Changes made to trained researchers’ protocols	Track changes and survey
Specific Aim D: Increase the level and diversity of subject participation in clinical and translational research	
Deployment of marketing messages	Track distribution of materials (number, location), and numbers of presentations (diversity of audiences)
Determine extent of exposure among general public to clinical research messages	Community surveys (telephone, mailed, in-person) in future years
Assess change in attitude and interest among general public	Community surveys (as above); qualitative methods
Assess investigator access to and use of resources	Track utilization of bibliography, templates, toolkits, expert/user groups
Participation in user and expert groups	Track participation
Satisfaction among user group and expert group members	Feedback Survey; qualitative methods
Number of research projects collaborating with CTSI	Track research project participation
Number of individuals enrolled and retained in clinical research among CTSI participating researchers	Track research participants screened, enrolled and retained (first timers; repeat subject participants; ethnic/other cultural subgroups; gender; other specifically-targeted groups based on research conducted (deaf, homosexual, disease specific))
Scholarly productivity relative to recruitment and retention	Track proposal, manuscript, and abstract submissions

*The Partnership Self-Assessment Tool (PSAT) developed by the Center for the Advancement of Collaborative Strategies in Health, New York Academy of Medicine, is a tool used to assess the effectiveness of community partnerships (41-44).

A variety of methods will be used for dissemination of information related to the proposed work. Findings will be shared most immediately with other members of the UNYTRN and with community engagement cores of other centers across the country. Successful methods and strategies will be reported to the NIH and other interested parties. Publications will be prepared when appropriate.

G2H. TRANSLATIONAL TECHNOLOGIES AND RESOURCES

G2H1. Specific Aims

The future of medicine demands increasingly more specific knowledge of pathophysiologic mechanisms to drive improvements in health care. Clinical and translational investigators frequently require access to specialized and expensive technologies and equipment that exceed their expert qualifications and their research budgets. This is especially true for new investigators. Thus, it is essential that the CTSI facilitate access to key resources for clinical and translational research. The University already has made substantial investments in such resources, which are used for both basic and clinical/translational research, but the environment can be enhanced by further investment in state-of-the-art facilities. To move toward accomplishing these general goals, the specific aims for the first five years of the CTSI are as follows:

Specific Aim 1: To establish a Laboratory Support Center, which will promote collaborations between investigators and University core resources, assist investigators with details of accessing these labs, be responsible for determining the level of financial support required for new projects, and be responsible for monitoring the progress of supported projects. *Rationale: Facilitated interactions between experts in technology applications and translational researchers and their teams will enhance project progress and successful completion.*

Specific Aim 2: To establish a translational technology access subsidy for new projects that are deemed highly meritorious. *Rationale: Translational projects that can successfully traverse from the laboratory to a clinical application will be significantly enhanced by additional subsidy over and above that already provided through the University of Rochester Medical Center (URMC) core facilities budget.*

Specific Aim 3: To upgrade the physical infrastructure and to support personnel for selected technologies that are expected to have broad applicability for enhancing clinical and translational research at the University of Rochester, including animal and human imaging, genomics, and proteomics. *Rationale: A Medical Center-wide strategic planning effort led to the identification of these technologies as key elements for enhancing our translational research output and enriching training opportunities for new investigators and perhaps established investigators just entering translational research.*

G2H2. Background and Significance

The spectrum of translational research at the URMC is diverse. Our translational research faculty span a broad scientific set of disciplines, and often the success of an effort hinges on access to critical expertise and sophisticated technologies. An overarching issue for most investigators is finding an expedient and scientifically and clinically rigorous path towards a defined goal. Here, we provide two vignettes of how technologies to be supported by the CTSI played an important role in translational research projects. We believe that many similar stories will emerge after the University of Rochester CTSI is established.

Pharmacogenomics Vignette. A holy grail of clinical practice has long been the development of truly "personalized" medicine, the ability to tailor treatments to the individual and his or her unique disease process. While the reality of personalized medicine remains a number of years in the future, the advent of new high-dimension, high-throughput technologies has provided both basic and clinical scientists the tools necessary to interrogate larger and larger complements of biological molecules involved in normal and pathologic processes. From individual genes to complex metabolic profiles, state-of-the-art in bionomic technologies and biostatistical methodologies are beginning to elucidate the pathways important to the pathogenesis, diagnosis, progression, and treatment of a number of human diseases. The coupling of these technologies with clinically well-characterized patient cohorts, along with the partnering of both clinical and basic scientists, will prove vital as we evolve toward the practice of personalized medicine.

Over the past few years Howard Federoff, MD, PhD, Tim Mhyre, PhD, and collaborators have begun to utilize a number of these bionomic technologies to better understand neurodegenerative diseases and their treatments. Building upon the work of Dr. Paul Coleman and others, their group has focused upon examining biological profiles in peripheral leukocytes to report central nervous system dysfunction and therapy in disorders such as Alzheimer's disease (AD) and Parkinson's disease (PD). In one study they examined the transcriptomic and proteomic profiles of AD patients following treatment with the histone deacetylase inhibitor, valproic acid (VPA), a therapy for neuropsychiatric symptoms that may also have neuroprotective potential. Using a number of these technologies, their team was able to discover and validate a subset of peripheral leukocyte proteins and transcripts that were differentially expressed following VPA pharmacotherapy. Equally

important was the discovery that certain individuals had different proteomic response profiles, which may be an important predecessor in determining “responder” or “non-responder” status for VPA treatment. Adjunct studies in tissue culture and animal models of neurodegenerative diseases are ongoing, which will provide more definitive links between biological profiles in peripheral and central cellular populations and will also help further the translation between the bench and the bedside.

While much work remains on understanding the true utility of peripheral biomarkers in central nervous system (CNS) disease, the work of Drs. Federoff, Mhyre, and colleagues is laying the groundwork. Building upon their transcriptomic and proteomic studies in leukocytes, future studies will be able to examine genetic determinants (e.g. single nucleotide polymorphisms, SNPs) of CNS disorders and therapy. Using high-throughput technologies and biostatistical methodologies, their group intends to identify a host of biological signatures that will ultimately: 1) Allow for earlier, presymptomatic diagnosis of neurodegenerative diseases; 2) Allow for segregation of each of these diseases into molecularly defined and mechanistically dissimilar entities; 3) Establish the biochemical basis for shared peripheral and central neuronal molecular signatures within these diseases; 4) Identify biochemical pathways important to the pathogenesis, progression, and therapy of these diseases; 5) Relate signature biomarkers with their encoded genes and polymorphisms associated with their regulation, and; 6) Use these methodologies and technologies to identify peripheral biomarkers in similar experiments for other neurodegenerative disorders. These and future studies will provide important foundations in our further understanding of neurodegenerative disease pathogenesis, diagnosis, and therapy.

Biomarker Vignette. As an Emergency Physician, Jeff Bazarian, MD, MPH, is frequently required to diagnose and treat injuries, one of the most common of which is concussion (mild traumatic brain injury [TBI]). This injury affects over 1.2 million Americans annually. Disabling post-concussive symptoms and cognitive deficits last up to 3 months in 50% of patients and up to 1 year in 25%. There are currently no treatments. In 2001, Dr. Bazarian was awarded a Mentored Career Development Award (K23) from the NIH to study the epidemiology of mild TBI as part of an effort to reduce disability through primary prevention. However, in the course of enrolling 1924 subjects over 24 months, a fundamental problem with mild TBI diagnosis emerged.

The current diagnosis of mild TBI relies on witnessed or self-reported symptoms such as loss of consciousness or amnesia. There are no objective diagnostic aids. Many Emergency Department patients were either unable to report these symptoms (e.g. pre-verbal infants, demented elders) or unsure about them (syncope patients, patients who had seized, or those intoxicated). Dr. Bazarian quickly realized that this problem resulted in both under and over diagnosis of brain injury in this patient group. Not only did this lack of diagnosis present a problem for describing the epidemiology of mild TBI, it clearly was an obstacle to developing and testing potential therapies.

In order to address the issue of mild TBI diagnosis, Dr. Bazarian enlisted the help of Brian Blyth, MD, a fellow emergency physician here at the University of Rochester and researcher in the Center for Aging and Developmental Biology. With Dr. Blyth’s help, Dr. Bazarian studied the accuracy of two brain-derived serum proteins purported to correlate with brain damage after mild TBI. These proteins, cleaved tau and S-100B, were found to be neither sensitive nor specific for abnormal head CT or adverse outcomes after mild TBI in two cohorts of emergency patients at the University of Rochester. While the idea of a serum test to diagnose mild TBI seemed like a good one, the existing protein assays were not clinically useful. This led Dr. Bazarian and Dr. Blyth on the path to developing new, more accurate biomarkers of mild TBI.

A review of the pathophysiology of brain injury after a concussion suggested that the most appropriate target for an objective diagnostic test was axonal injury. However, it rapidly became clear that before a new putative serum marker could be discovered and validated, a gold standard for the identification of axonal injury in living humans after mild TBI needed to be developed. Realizing that obtaining brain tissue or even CSF after a concussion was impractical, the pair looked to neuroimaging for a reference standard. With the help of Jianhui Zhong, PhD in the Department of Radiology, Drs. Bazarian and Blyth proposed two pilot studies designed to examine the ability of diffusion tensor imaging (DTI) to detect axonal damage after concussion. DTI is a relatively new form of dynamic MRI imaging that is ideal for detecting the subtle changes in water motion thought to accompany axonal damage. Two generous intramural grants allowed these DTI pilot studies to proceed. Preliminary results suggested that abnormalities detected by DTI were clinically relevant and likely represented axonal damage. These pilot data were analyzed with the help of Voyko Kavcic, PhD from the Department of Neurology, and Derick Peterson, PhD, in the Department of Biostatistics and Computational Biology.

Finally, in order to identify putative serum proteins unique to the process of axonal injury, blood from patients in these pilot studies was sent to Gerard Hoehn, PhD, a former graduate student at the University of Rochester and current Director for Clinical Proteomic Applications at the NIH, for a preliminary proteomic analysis of the serum. These results were encouraging and were included in a R01 application to NIH to explore these concepts in a larger cohort. This application received a Priority Score of 151. Notification of funding is pending.

Facilitating the use and affordability of translational technologies. A central tenet of the CTSI is that shared laboratory resources are essential to promote clinical and translational research. The Research Resources program at NIH has supported this concept with shared instrument grants and General Clinical Research Center (GCRC) core laboratories. For example, our GCRC core laboratory, which has supported clinical research for over 40 years, provides several services (at no charge) to support human metabolic research, including hormone and metabolic substrate assays, mass spectrometry for isotopic tracer assessment, indirect calorimetry for assessment of substrate metabolism, and body composition measurement by dual-energy X-ray absorptiometry (DEXA). Moreover, the costs of several assays done by the hospital clinical chemistry and hematology laboratories are paid by the GCRC. When our GCRC was reviewed by NIH in 2005 (the competitive renewal was successful), one question raised was why the GCRC core laboratory did not provide services in other cutting-edge technologies such as genomics and proteomics. The answer was that the University already had established core laboratories for such services, and that it would be inefficient to duplicate them specifically for the GCRC. While this answer is accurate, it raises the question of why metabolic research is supported in full while only partial subsidies support clinical investigators for projects involving genomics, proteomics, cell sorting, imaging, and other key technologies (these resources are available to clinical researchers and are dependent on user fees). A goal of the University of Rochester CTSI is to enhance access and to reduce costs to clinical and translational investigators for various laboratory resources, not just those provided by the GCRC core laboratory. In essence, there will be a shift in emphasis from deciding *a priori* which specific laboratory resources will be most heavily subsidized to having the immediate needs of clinical and translational investigators drive resource allocation. In this application, we are requesting funds to enhance the resources in certain specific areas (imaging, genomics, and proteomics), and also to help investigators utilize the services of any shared laboratory resource. To enhance access, and to support the broadest range of research, our proposed Laboratory Support Center requires flexible funding to maximize investigator productivity. These requested resources will amplify on the University of Rochester extant commitment that in aggregate exceeds $1 million per annum.

Imaging. Optics and imaging have played a vital role in the development of modern medical science. Through high-resolution imaging, researchers and clinicians developed our current understanding of the origin, progression and classification of disease. Even today, imaging of the cellular and tissue morphology of pathology sections remains the gold standard for tissue categorization and disease diagnosis. Modern clinical research thrives on non-invasive imaging using MRI, PET, CT, and a variety of optical and ultrasound modalities. *In vivo* animal imaging using MRI/MRS, micro-PET, micro-CT, and fluorescence optical imaging is essential for cutting-edge basic and preclinical research.

Led by the Department of Imaging Science (formerly Radiology) and the Rochester Center for Brain Imaging (RCBI), the URMC has made substantial strides in the past three years to upgrade the clinical and basic research facilities for MRI, PET, and CT imaging. The use of these resources for translational research would be enhanced by a program to promote interactions between basic and clinical researchers with complementary expertise in preclinical science and clinical treatment of human disease. This is an overall goal of the CTSI, and specific positions within the GCRC (Section G2F) and the Translational Technologies and Resources Key Function (current section) will be responsible for fostering these interactions. Given the outstanding faculty in optics and imaging and the strength in clinical research and treatment, all the pieces are present to push the URMC to the first level in the use of imaging for translational research.

Genomics. Given that most, if not all, diseases have a genetic component, and that genes also influence responses to treatments, genomics will have a strong presence in the CTSI. Revolutionary progress has been made in the fields of genomics and proteomics in the past decade. Complete sequences of the genomes of humans and model organisms are publicly available, and data on genetic variations among humans has grown rapidly. The technology to assess these variations has improved to the extent that it is feasible to relate diseases to genetic variations at the whole-genome level. Methods for assessing how diseases and treatments affect the patterns of gene expression (both mRNAs and proteins) and post-translational modifications to

proteins in humans and animal models have markedly improved over the past several years. Taking advantage of these technologies to improve disease diagnosis and treatment is one of the goals of the CTSI.

Although the University has subsidized genomics and proteomics research with space, equipment, and support for personnel, it cannot fully cover the costs of supplies, reagents, and technical staff for all meritorious research projects. Thus, investigators must pay fees for these services. The overall cost for such research, for example studies involving gene expression or SNP arrays, can be quite expensive per subject. Often, researchers are forced to include fewer subjects than are justified based on statistical considerations because the total cost would be too high for their research budgets. Thus, the CTSI will further subsidize the genomics and proteomics core laboratories for clinical or translational research projects.

The most common variations in the genome are single-nucleotide polymorphisms (SNPs). Most of the SNPs are functionally irrelevant, but serve as markers for neighboring polymorphisms, SNP or otherwise, that do have functional significance. Neighboring SNPs have high linkage disequilibrium (often $r^2 = 1$) within discrete haplotype blocks, which are regions in which recombination is rare. The average haplotype block size is ~ 5-15 kb, each containing ~ 4-5 common SNPs (minor allele frequency > 5%) (1). In theory, a well-selected panel of ~ 300,000-500,000 SNPs should be able to capture all of the information needed for genome-wide assessment of genetic associations with phenotypic traits. With recent technical advancements, it now is feasible to do this in a large number of subjects. Thus SNP analysis will be the leading method for research on the genetic basis of polygenic diseases, or discovery of candidate genes in heritable conditions for which previous research has not identified any leading candidates. A recent example of the utility of this approach is a study in which an array that assessed 116,000 SNPs identified a strong association between age-related macular degeneration and the Complement Factor H gene, with only 96 cases and 50 unrelated controls (2). One can readily envision a future in which SNP assays will be used as a routine part of health assessment, to assess disease risk and to tailor treatments to fit the individual genotype. Thus, upgrading our facilities for SNP analysis is a priority.

Proteomics. While expression of a majority of genes is regulated transcriptionally, expression of a significant minority is regulated by post-transcriptional mechanisms. Moreover, post-translational modifications can be as important as levels of gene expression in determining function. Protein biomarkers potentially can be found in easily sampled fluids such as serum, saliva, or urine. Moreover, CSF proteins potentially can serve as biomarkers for CNS disorders. Thus, the technology to characterize and quantify proteins in tissues and body fluids is needed in any major clinical/translational research center.

Other resources. While the specific technologies described above are expected to have broad use by clinical and translational investigators, there are many other core biomedical research resources that are available at the University of Rochester (a few are listed in Section G2H3 below). Some of the most innovative and important clinical and translational projects might require these other resources rather than (or in addition to) the core resources already mentioned. These are not discussed in detail here because of space limitations and because we are not requesting funds to upgrade these resources at this time. However, it must be emphasized that a goal of the CTSI is to enhance the ease of use and to reduce the cost to the investigator for any University laboratory resources needed by the most meritorious clinical and translational research projects.

In some cases, an investigator might require laboratory resources that are not available at the University of Rochester. Although we strive to provide our faculty with state-of-the-art facilities, sometimes the demand for certain services does not reach a level that makes it economically feasible to provide on-site services. In these cases, the Laboratory Support Center may assist the investigator by helping to establish a collaboration with a lab at another academic institution. The translational technologies access subsidy (Aim 2) might be used to pay a commercial lab to provide services if that is the best solution.

G2H3. Prior Experience

The University of Rochester has recognized the importance of shared laboratory resources for many years, so that most of the facilities that will be required by most clinical and translational projects already are in place. Moreover, there is a spirit of collegiality here such that most investigators and departments are willing to collaborate and share their resources even if they are not officially designated as core laboratories. Our plan to subsidize and upgrade these existing resources rather than to use this grant to build entirely new core laboratories should not be viewed as a lack of innovation, but rather as a reflection of the existing strength of the URMC. Below, we describe existing resources that will be used extensively by clinical and translational

investigators. Those for which we are not requesting specific funds for equipment or personnel are described more briefly. They will be supported by the CTSI only if specific projects request such support (Aim 2).

Imaging. The Department of Imaging Sciences houses three 1.5T GE magnets for MRI/MRS at Strong Memorial Hospital, and a PET scanner located off-site. The RCBI houses a research-dedicated 3T MRI facility in a building adjacent to the URMC. The current RCBI space consists of approximately 6,000 square feet and a staff of seven to provide MRI/fMRI/MRS of both human and non-human subjects. Table G2H1 provides a partial list of some of the clinical and translational projects utilizing some of these resources, out of ~30 ongoing clinical/translational research projects, and a few of the planned projects.

Table G2H1. Partial list of projects utilizing imaging resources at the URMC

Investigator	Project	Status
Kwok	New MRI sequences/RF coils for hand psoriatic arthritis	Ongoing, started 2003
Laurin	Neonatal intensive care image harvesting and image processing parameter optimization	Ongoing, started 2005
Ning	3D tomographic angiography	Ongoing, started 1993
Ning	High resolution breast imaging	Ongoing, started 2004
Reubens	3D sonoelastography imaging for prostate cancer	Ongoing, started 2003
Saad	IVC filter retrieval out to 12 weeks without interim filter retrieval utilizing the Gunther tulip vena cava filter	Ongoing, started 2005
Waldman	Imaging human subjects with a prototype digital radiography system	Ongoing, started 2004
Waldman	Cardiovascular outcomes in renal atherosclerotic lesions	Ongoing, started 2002
Waldman	Carotid stenting trial for high-risk surgical patients	Ongoing, started 2004
Wandtke	Chest radiographic image database and CR new grid evaluation	Ongoing, started 2005
Zhong	Biophysical basis of brain iDQC MR imaging	Ongoing, started 2002
Foster	Photophysics of photodynamic therapy	Ongoing, started 2003
Wang	HUD treatment of wide necked cerebral aneurysms	Ongoing
Davis	Early detection and treatment of breast metastases to the lung	Planned
Cook	MRI to quantify visceral obesity in adolescents	Planned
Chen	Cone-beam CT studies: non-linear inter-spectral image procession for cancer diagnosis; volumetric depiction of breast tissue elasticity	Planned
Zhong	Alteration of WM DTI indices in several neurological diseases	Planned

Genomics and Proteomics. The University has built an infrastructure to support genomics and proteomics research, both basic and clinical, through the establishment of core laboratories and expansion of the Department of Biostatistics and Computational Biology to include faculty with expertise in this area.

The physical infrastructure for laboratory aspects of genomics research already is very solid. The Functional Genomics Center (FGC) recently moved into renovated laboratories at the Cardiovascular Research Institute, with over 3,000 sq. ft. of space for microarray technology (expression and SNP arrays), DNA sequencing, genotyping, multiple PCR applications including high-throughput quantitative RT-PCR, mutation screening, DNA and RNA extraction and quantitation, and liquid-handling robots for high-throughput applications. Electronic sample registration and transfer of results to investigators has been automated with custom LIMS applications. The FGC supports a data analyst to assist investigators with basic computations and data interpretation, although higher level statistical issues are handled by Biostatistics and Computational Biology. The FGC is supported by user fees, the University, and a grant from AMDeC, a consortium of New York institutions performing biomedical research. The FGC is the coordinating institution for the AMDeC Microarray Resource Center. Stephen Welle, PhD (Professor of Medicine) was named the Director of the FGC in 2005. He also has been involved with the GCRC for more than 20 years as an investigator, and is the Director of its core laboratory and member of its advisory committee. Thus, he is in a very good position to strengthen interactions between clinical/translational researchers and the FGC. The FGC has many ongoing and recent collaborations with investigators doing clinical and translational research, more than 20 over the past two years. Table G2H2 briefly describes some of these projects. This table does not cover the numerous other investigators using the FGC for DNA sequencing services. Moreover, many animal studies could be considered translational, but are too numerous to list here.

Table G2H2: Partial list of projects utilizing the FGC.

Investigator	Description	Status
Khorana	Expression profiling to predict recurrence of outside-criteria transplanted hepatocellular carcinoma	Started 2006
Fazili/Crispe	Modulation of gene expression in human liver Kupffer cells treated with ribavirin and interferon	Started 2006
Bottaro	Genome-wide screening of SNPs in population samples currently under study for a variety of immunological phenotypes, to identify genetic factors contributing to population variability in immune system function and responsiveness to vaccines	Planned
Sanz	Comparison of gene expression profiles of autoreactive (9G4+) and non-autoreactive human B-cells, indicating that autoreactive B-cells have anergic and pro-apoptotic profile explaining the censoring of these potentially dangerous cells in healthy subjects. Data led to funding of an R21 grant and contract with Biogen/IDEC to perform systematic microarray analysis of human B-cells in healthy vs. SLE patients.	Initial study completed. New studies to be started 2006
Jin/Smith	Predictive value of APOBEC3G gene expression for HIV disease progression	Ongoing, started 2004
Crispe/Pierce	Genes induced during stellate cell activation in mouse model of chronic viral hepatitis and liver fibrosis	Started 2006
Reeder	Use of SNP arrays to genotype recurrent human bladder tumors resected at different times, to determine if they carry the same or different allelic imbalances or loss of heteozygosity. Currently generating preliminary data and optimizing techniques for large clinical study to determine if a specific therapy decreases clonal recurrence of human bladder tumors.	Ongoing, started 2005
Buchsbaum	Identification of genetic basis for familial concordance of urinary continence status in postmenopausal women, using gene expression arrays and whole-genome SNP arrays. Gene expression study has started, SNP study planned.	Ongoing, started 2004
Hassane/Jordan	Use of gene expression profiles to identify mechanisms responsible for pharmacologic ablation of leukemic stem cells	Ongoing, started 2005
Muyan	Gene expression in cellular model of breast cancer under different conditions to modulate estrogen-driven gene expression, to understand how genomic responses correlate with cell phenotypes, potentially leading to identification of therapeutic targets or prognostic markers	Started 2006
Land/McMurray	Identified a number of genes whose expression is changed in transformed cells when compared to normal cells (this was done by arrays). Treating these cells with certain compounds which are in clinical trials for chemotherapeutic use against cancer reverts the gene expression profile of the transformed cells to something much more like a normal cell (using ABI microfuidics cards), which correlates with inhibition of tumor formation in mice. Studies in progress on the mechanism at work in the transformed cells and the role of various genes (in the set of 384 genes being analyzed) in the responsiveness to the drugs.	Ongoing, started 2004
Schifitto	Effects of valproic acid and minocycline on gene expression profiles of CD14+ monocytes from HIV-infected subjects	Ongoing, started 2005
Thornton/Tawil	Use of expression profiling to elucidate molecular basis of myopathy in myotonic dystrophies and facioscapulohumeral dystrophy	Manuscripts in preparation

The proteomics core laboratory is relatively new. Directed by Alan Friedman, PhD, it provides full service protein identification, providing mass identification and protein sequence for proteins isolated from gels by the investigators. The proteomics core facility also provides separation technologies, done in the lab or in consultation with the researcher's lab. Separation technologies currently offered include solid phase extractions, 1D and 2D gel electrophoresis, and high performance liquid chromatography. In addition, the facility provides support for the isolation, extraction and identification of proteinaceous materials from cell lysates and patient fluids. The facility currently houses four mass spectrometers, a matrix-assisted laser desorption/ionization (MALDI) mass spectrometer (Applied Biosystems Voyager DE), a Surface Enhanced

Laser Desorption Ionization (SELDI) mass spectrometer (Ciphergen Biosystems PSII) and two ion-trap LC-MS/MS systems, an LCQ (in collaboration with the Center for Oral Biology) and an LTQ (both Thermo Electron Corporation). Table G2H3 lists some of the clinical/translational projects supported by the proteomics core.

Table G2H3. Partial list of projects utilizing the Proteomics Core.

Investigator	Description	Status
Phipps	Identification of human blood proteins including pPAR-gamma in relation to diabetes	Started in 2005 (ongoing)
Fay	Identifications of cross-linked Factor VIII	Started in 2005 (ongoing)
Maines	Identification heme metabolic pathway proteins as a component of the cell signal transduction pathways	Started in 2005 (ongoing)
Stodgell	Isolation and identification of early marker proteins for developmental syndromes	Started 2006
Federoff/Mhyre	Identification and statistics for biomarkers of neurological disorders	Started 2006
Reeder	Isolation and identification of bio-markers proteins for bladder cancer and Interstitial Cystitis	Started in 2005 (ongoing)
Hyman	Isolation and identification of bio-markers proteins for pediatric disease (Autism Spectrum Disorders)	Started in 2005 (ongoing)
Ricke	Isolation and identification of bio-markers proteins for Prostate Cancer	Started 2006

Human Metabolism Laboratory. Currently, this is the GCRC core laboratory. It supports studies of body composition (DEXA and bioimpedance) and energy metabolism (indirect calorimetry), performs assays of metabolic substrates and hormones, and has a GC-mass spectrometry lab for stable isotope tracing of metabolic pathways. The GCRC budget currently supports a Laboratory Director (35% effort), 2.2 FTE technical staff, and all reagents and supplies for these activities. The budget requested for personnel and equipment for the core laboratory in our successful competitive renewal application last year was approved in full by the study section. In a typical year, this lab assists 10-15 principal investigators.

With the reorganization after the CTSI is established, the activities of this laboratory will be divided into two parts. The DEXA, bioimpedance, and indirect calorimetry instruments, which are operated on the GCRC, will remain as integral services of the GCRC, which will be responsible for their operation and maintenance at no charge to GCRC investigators. The laboratory services will be transitioned to the same fee-for-service system that is employed by the other core laboratories described here. Because several current GCRC investigators have ongoing projects in which these services are not charged (and were not budgeted in their grants), there will be a transition period during which ongoing projects are fully supported through completion. New projects will be charged, but will be eligible to apply for subsidy from the Laboratory Support Center as they would for any other core lab service.

Cell sorting resources. The cell sorting core assists users to adapt and modify existing flow cytometric methods or to develop new procedures for their specific requirements. This core is directed by Peter Keng, PhD. The three flow cytometer/cell sorters in the facility are equipped with dual lasers, forward angle light scattering detectors, 90¡ light scattering detector and four PMT tubes for multi-parameter analysis and cell sorting. The routine services include: Immunofluorescent measurements (surface and intracellular markers, single and multi-parameters) for antigen and antibody distributions; DNA, RNA, and nuclear antigens for cell cycle, apoptosis, and cell proliferation (BrdU) analysis; sterile cell sorting and auto-cloning based on light scatter and fluorescent intensities (antibodies, DNA, RNA, GSH, GFP, etc.); measurement of green fluorescent proteins (GFPs) for analysis and cell sorting; bulk cell separation by centrifugal elutriation for large quantities of host and malignant cells, and cells at different phases of the cell cycle. The core also assists users to adapt and modify existing flow cytometric methods or to develop new procedures for their specific requirements. The core offers both formal and informal training to users who are interested in the theoretical and practical aspects of flow cytometry and cell separation technology. In addition to this URMC-wide core facility, several departments and centers have cell sorting equipment with additional capabilities.

Histology and microscopy resources. The Department of Pathology and Laboratory Medicine offers a full range of histology services for investigators, including tissue sectioning, special stains, and immunocytochemistry. The Electron Microscope research Core can perform either transmission or scanning

electron microscopy, including specimen sectioning and staining. Investigators can view their specimens in real-time along with the technical director as the digital images are displayed on a monitor, or can analyze them later after they are saved as “TIFF” files. AnalySIS software is available for morphometric data analysis. The Pathology/Morphology Imaging Core serves as the information hub for URMC resources centered around histological processing, imaging, and quantitation from high-quality images. It provides constant or intermittent assistance as needed for all procedures. Instruments include a Leica laser confocal microscope (can be used with upright or inverted microscope) as well as upright light and fluorescent microscopes (Olympus AH-2), SPOT camera, computers with ImagePro Plus v.3 and Adobe Photoshop software, PixCell laser capture microscope with full computer support, and color printers (laser and dye sublimation). The Real-Time Confocal Core provides access to a Noran OZ laser-scanning confocal microscope and associated SGI computers for operating the instrument and off-line data analysis. These instruments can dynamically image rapid cellular events associated with signal transduction and movement within living cells on a time frame of a few milliseconds. Training (2-day course) is provided to users by the core staff.

G2H4. Methods

G2H4a. Resources to be Offered and Plans for Prioritization, Availability, Management and Tracking.

Methods to accomplish Aim 1. The first specific aim is to establish a Laboratory Support Center, which will promote collaborations between investigators and University core resources, assist investigators with details of accessing these labs, be responsible for determining the level of financial support required for new projects, and be responsible for monitoring the progress of supported projects.

The Laboratory Support Center will have a faculty-level Director, who is familiar with each URMC core facility, charged with its day-to-day functioning. The Director will be proactive in spreading information about resources for facilitating clinical and translational research, and will be have an office in the Clinical and Translational Research Building. The Director of the Laboratory Support Center will be selected by the Director of the CTSI, Dr. Guzick, in consultation with Dr. Howard Federoff, Senior Associate Dean for Basic Research, and Stephen Welle, PhD, Director of the FGC and the GCRC core laboratory. The person chosen for this position will have a PhD or MD degree, will have experience both in basic science and in clinical/translational research, must have excellent communication and organizational skills, and must have a commitment to collaborative and service-oriented activities. Both internal and external candidates for this position will be considered.

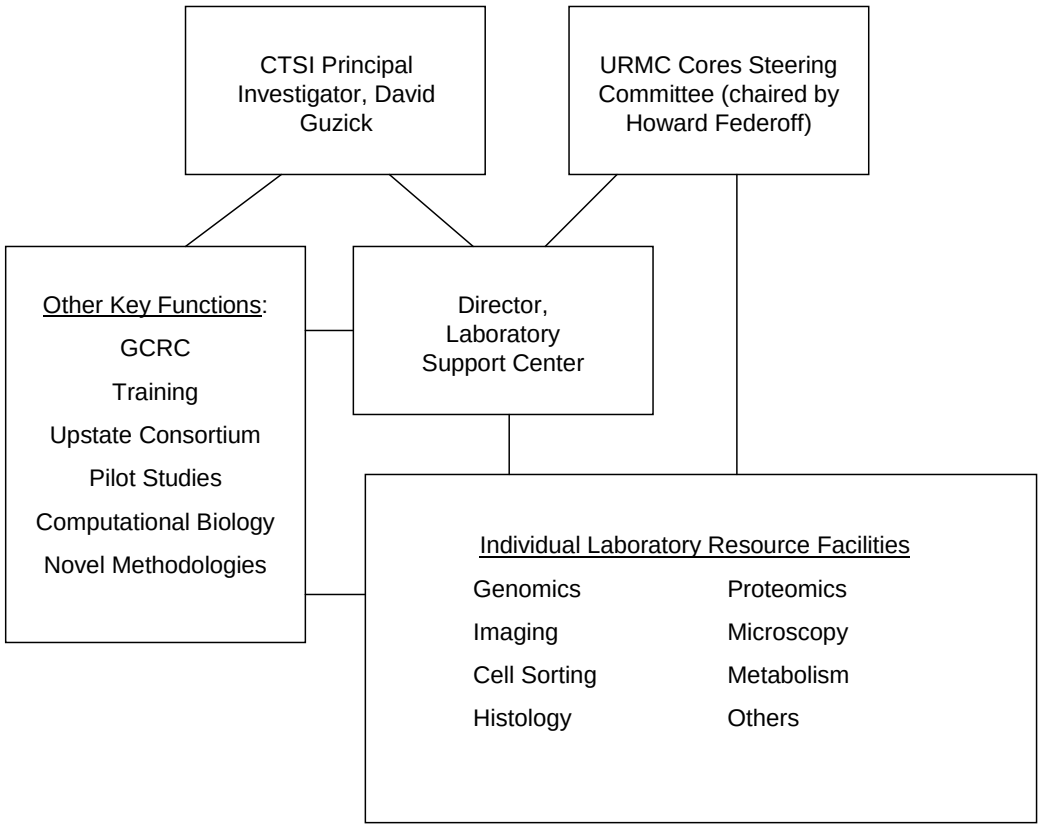
The Laboratory Support Center will partially support scientists from selected core facilities (those expected to have the most extensive use by clinical and translational investigators) to serve as the contact person and facilitator for clinical and translational projects. A web-based interface will be constructed to guide translational investigators to the appropriate person for a consultation. The Support Center will facilitate the entry of projects into core facilities, assist in securing resources if needed (Aims 2 and 3), and monitor the progression of each project with respect to data generation.

This Center will facilitate interactions between clinical/translational investigators and University shared resources. It will have a discretionary budget to provide financial assistance to investigators for using these resources (Aim 2) and/or to support core laboratories with equipment or personnel (Aim 3). Key aspects of the Support Center will be:

- Director with a general familiarity with all key resource facilities
- committee to review requests for support
- website to provide information on available resources
- assistance for investigators with details of working with laboratories (standard protocols, etc.)
- seminars/workshops on available resources, especially for new investigators
- a course on translational technologies to be organized by the Director

Evaluating the value of the Laboratory Support Center. The principal investigator of the CTSI will convene a panel of internal and external scientists every 2 years to review not only the adequacy of core resources (Section G2H4c), but also whether the Laboratory Support Center is having a beneficial impact on the conduct of clinical and translational research. This panel will interview investigators who have interacted with the Center and will look at objective measures of progress such as growth in the number of clinical and translational projects supported or requesting support, success rates of grant applications with preliminary data facilitated

by the Center, and publications of projects supported by the Center. The Cores Steering Committee (an extant University committee) will interview directors of each core lab annually to obtain feedback about whether the Center is effective in facilitating use of the cores for clinical and translational projects.



Methods to accomplish Aim 2. The second specific aim is to establish a translational technology access subsidy to increase the number of translational projects that can successfully traverse from the laboratory to a clinical application.

The Director of the Laboratory Support Center will regularly notify by email all Department Chairs and Center Directors of this ongoing program. Announcements also will also be made at the Executive Committee meeting of all Chairs and Center Directors of the University of Rochester Medical Center. A web-based application will be created that a translational investigator will complete and submit. The proposal will be brief so as not to discourage applications. A proposal can be submitted at any time rather than at fixed deadlines, so as not to delay progress. An expedited review will be undertaken by several *ad hoc* faculty-level reviewers, who are members of a small translational reviewer reserve pool, and who have familiarity with the proposed technology and the intended use. Review criteria will be similar to the NIH criteria for R01 proposals, especially significance and innovation. There will be less emphasis on track record for new investigators, and less emphasis on preliminary data except as necessary for patient safety. The recommendations of the faculty reviewers will be forwarded to the Director of the Laboratory Support Center and resources allocated as needed based on priority score and availability of other support for the project. Only the most innovative and significant projects will receive full funding for their laboratory costs. If funds are available, partial support may be given for excellent proposals that do not achieve the highest scores.

Monitoring of resource expenditures and impact on project success will be conducted by the Director of the Laboratory Support Center. The subsidy will be in the form of direct reimbursement for services to the relevant laboratory, rather than a cash grant to the investigator. This approach will ensure that the funds are expended for the intended purpose, and will also make it easier for the Center Director to track progress in real time. Because of this flexible approach, it is not possible to project exactly how many projects will be supported each year, but we anticipate that the CTSI will award the subsidy to about six projects and that the average subsidy will be approximately $25,000. Investigators will provide annual progress reports if continued support is needed. It is expected that extramural sources of support will be identified by the investigator as a project matures, and attempts to secure such funding will be one of the review criteria for renewal of support. Our major goal is to get new projects off the ground efficiently, not to fund large projects over the long term.

Methods to accomplish Aim 3. The third specific aim is to upgrade the physical infrastructure and to support personnel for selected technologies that are expected to have broad applicability for enhancing clinical and translational research at the University of Rochester.

a. Imaging. Instrumentation for imaging is very expensive and not within the scope of the current application. The URMC will continue to upgrade the infrastructure and instrumentation for imaging technologies through other mechanisms. A pressing need caused by the high demand for research use of imaging resources is the availability of additional technical staff members to facilitate the use of these resources. Currently, there are not enough personnel to spend a significant amount of time with investigators in planning, conducting, and analyzing data. Thus, we propose to create two new positions (Clinical/Translational research Coordinators) in the Department of Imaging Sciences. These will be filled by experienced technical staff with practical knowledge of MRI, CT, and PET, and other imaging methods. The coordinator's roles would involve explaining the resources available and requirements for using them, aiding in IRB approval, and ensuring scientific integrity. These coordinators would also be responsible for data acquisition and storage and will serve as liaisons between investigators and scientists in the Imaging Sciences department for both the study design and data interpretation phases of projects. This collaborative effort would greatly enhance protocol writing and evaluation along with data assessment and management.

b. Genomics. The CTSI will support 10% of the time for the Director of the FGC and 0.5 FTE technician for clinical and translational genomics projects. This level of support is justified because the FGC already has a key role in numerous clinical/translational projects (Table G2H2 above), and probably would be used by even more clinical investigators if FGC services became more accessible and affordable. Even projects that do not receive direct funding from the Laboratory Support Center (see Aim 2) would benefit from this subsidy. The support for the Director of the FGC will allow him to spend additional time with investigators in planning studies, interpreting their data, and helping them write manuscripts and grant proposals.

The main competing platforms for whole-genome SNP genotyping are the Affymetrix Mapping 500K Array Set and the Sentrix HumanHap300 BeadChip (Illumina). The latter system has better SNP selection based on the HapMap project and has better SNP call rates than the Affymetrix system. Illumina also has many other high-quality genotyping arrays. We are therefore requesting funds in year 1 to obtain the Illumina BeadStation so that we can employ this platform.

The real-time PCR resource at the FGC is being used heavily by clinical and translational researchers. One problem in keeping this high-throughput resource affordable is that it is being leased with a substantial monthly fee (lease expires in 2007). The cost per sample to investigators could be lowered substantially if the equipment were owned outright. Therefore, we are requesting funds in year 2 to purchase an ABI Prism 7900 when the lease expires. Also in year 2 will be the acquisition of an additional liquid handling robot to improve efficiency and precision of RT-PCR and other procedures.

c. Proteomics. The CTSI will support 10% of the time for the Director of the Proteomics Core and 0.5 FTE proteomics technician salary. The support for the Director of the Proteomics Core will allow him to spend additional time with investigators in planning studies, interpreting their data, and helping them write manuscripts and grant proposals. The level of subsidization of the technician's salary is based on current workload for clinical and translational projects. This subsidy will help to keep costs reasonable for investigators. A critical need for upgrading the laboratory is a capillary electrophoresis system to provide automated, high throughput analysis with separation techniques not available on LC systems, which is requested for year 2. In years 3 and 4 the proteomics lab will be further upgraded with an additional mass spectrometer with improved resolution to enable de novo peptide sequencing.

G2H4b. Integration of Resources with Similar Resources at the Institution and Affiliates.

The resources described here do not duplicate other resources of the University of Rochester or its affiliates. Instead, the goal is to make it easier and more affordable for clinical and translational investigators to use existing resources, and to improve some of these resources.

G2H4c. Responsiveness to Changing Needs.

Progress in biomedical research technology is rapid, faculties turn over, and unpredictable factors influence the nature of the research being done, so it is important that we continually evaluate how funds should be allocated. The principal investigator of the CTSI will form an independent panel of approximately five scientists from relevant disciplines (internal and external), at two-year intervals, to review the adequacy of existing resources and make suggestions for changes in direction. This is part of the process for evaluating the value of the Laboratory Support Center, as described above.

G2H4d. Evaluating Studies for Continued Support.

The Laboratory Support Center will review all supported cores and projects annually. The decision to continue support for a project will be determined primarily by whether it has achieved its initial specific aims or benchmarks, as well as peer-reviewed publications, patents, or other objective evidence for significant progress. In most cases, continued support will require that the investigators continue to seek external sources of support for their projects. Feedback from external reviews will be taken into consideration. We will regularly evaluate not only support for specific projects, but also the more general support for specific laboratories (e.g. the FGC technician) to determine whether funds should be shifted to support other laboratories instead.

G2H4e. Cost Recovery from Funded Investigators.

Applications for support will include the investigators' itemized budgets submitted to external funding agencies (more detailed budgets will be required if external support was obtained with the NIH modular budget format). Those with support from external sources generally will pay the ordinary University research rate for services (which typically is lower than actual costs because of University subsidization), although additional subsidization could be granted if the investigator can demonstrate that external funding is inadequate for significant progress.

G2H4f. Quality Control, Standardization of Laboratory Services.

Each laboratory is responsible for maintaining its own standard operating procedures and appropriate quality control steps. The University of Rochester selects experienced faculty and staff to direct its laboratories to ensure that good laboratory practices are used. If certain tests must be performed in a CLIA-certified (or some other certification) laboratory, for example if FDA approval of a device or biologic is at stake, then the Director of the Laboratory Support Center (who will have information on the certification status of each University laboratory) can assist the investigator in finding the appropriate lab if not available within the University. For cutting-edge technologies, national standards and certifications might not be established. For example, the FDA and NIST currently are working on standards for microarray laboratories, but this is still a work in progress. Laboratory directors will be encouraged to stay up to date on such issues, and the Director of the Laboratory Support Center will explore these issues in the course of regular interactions with the lab directors and staff members.

G2H5. <u>Novel Aspects</u>

The Laboratory Support Center with a faculty-level Director devoted to fostering the efficient use of multiple core resources, assisting investigators with their laboratory needs, and teaching students, fellows, and faculty about translational technologies bridging basic and clinical sciences is a new resource that goes far beyond the traditional "GCRC core laboratory." Instead of saying to investigators "this is what we offer for laboratory services," we will be asking them "what can we do to help you succeed in finding and paying for the laboratory resources needed to ensure successful completion of your project?" This represents a new attitude toward supporting clinical and translational research. The opportunity to apply for financial assistance to cover all or part of the laboratory expenses of new projects is a new resource that will be especially critical to junior faculty or fellows whose departments or extramural training grants can accommodate salary support but often not the expensive laboratory resources required for clinical and translational research. A novel aspect of our approach is directing these funds to the laboratories providing the services rather than giving the investigator a fixed grant for a project. This will ensure that funds are not used for other purposes, and will ensure that projects do not stop with insufficient data because the money has been depleted from a fixed grant.

G2H6. Interactions with Other Key Functions

G2H6a. Upstate Academic Consortium (Section G2J).

Many collaborations among upstate NY academic institutions are ongoing. For example, there are several collaborations in which investigators in Buffalo or Ithaca (Cornell) are using the facilities of the Human Metabolism Laboratory or the FGC, or investigators in Rochester are sending samples to laboratories in Buffalo or Ithaca. Such collaborations greatly increase cost efficiency if expensive laboratories that are operating below full capacity are not duplicated at each institution. An important task of the Director of the Laboratory Support Center will be to become familiar with core laboratory facilities across the upstate region and to make these other institutions aware of the facilities available at the University of Rochester.

G2H6b. Development of Novel Clinical and Translational Methodologies (Section G2A).

It is anticipated that development of new methods often will require comparisons with more established methods, and such work could be subsidized by the Laboratory Support Center. The Director of the Laboratory Support Center will be involved in the review of all proposals requesting support to develop new laboratory methods. If a new method has wide applicability, eventually there might be support from the Laboratory Support Center for equipment or personnel to offer it as a core resource to all clinical and translational investigators.

G2H6c. Pilot and Collaborative Translational and Clinical Studies (Section G2B).

Many of the pilot projects supported by this key function will require access to core laboratory facilities. If the available funds for the pilot project cannot cover the full costs of the laboratory component, the investigator can seek additional support through the program described under Aim 2. Even if financial assistance is not provided, the Laboratory Support Center will be a valuable resource for pilot projects by facilitating the interactions between investigators and core laboratories.

G2H6d. Participant and Clinical Interactions Resources (Section G2F).

The most obvious interaction here is that the CTSI will continue to support the historical GCRC core laboratory functions because there is a broad user base, although after the CTSI is established the GCRC core laboratory will be known as the Human Metabolism Laboratory. Moreover, many of the projects that will utilize the various core laboratories supported by the CTSI will be done within the GCRC. Thus, the Director of the Laboratory Support Center (and staff of individual core labs) will work closely with GCRC staff to see that samples are correctly obtained, labeled, and stored prior to laboratory analysis. The Director of the Laboratory Support Center will be a member of the GCRC Advisory Committee. The new GCRC Associate Program Director position for promoting basic scientist-clinician interactions will communicate regularly with the Director of the Laboratory Support Center and core laboratory directors to keep abreast of technological capabilities and advances, and will be a reviewer for the proposals submitted to request laboratory support.

G2H6e. Research Education, Training and Career Development (Section G2I).

The Director of the Laboratory Support Center will work closely with Dr. Pearson in curriculum development to incorporate teaching about cutting edge technologies to the trainees. A course on translational technologies will be organized by the Director in conjunction with Dr. Pearson. Seminars about research projects utilizing various technologies will be a regular part of the Clinical Research Seminar Series, with core laboratory directors present to discuss the laboratory aspects of the projects. Core laboratories are expected to be an important part of research projects being done by some of the trainees. The Laboratory Support Center will facilitate such projects, in some cases by subsidization of the costs of the laboratory analyses, but also by facilitating interactions of the trainees with the cores and helping the trainees to identify faculty and staff with the appropriate technical expertise to ensure successful completion of their research projects.

G2H6f. Design, Biostatistics, and Clinical Research Ethics (Section G2D).

Genomics and proteomics technologies generate extremely large, multivariate data sets. A significant issue in such projects is achieving the correct level of statistical conservatism to keep the false discovery rate sufficiently low without requiring such stringent statistical criteria that most of the real effects are overlooked. Dr. Yakovlev and his colleagues in Biostatistics and Computational Biology are experts in dealing with this issue, so collaborations between these key functions will be extensive. Moreover, interactions with this key function are necessary to train laboratory personnel in the proper handling of samples and data from studies involving human subjects, to ensure compliance with HIPAA regulations, and to maintain strict confidentiality and data security.

G2i. RESEARCH EDUCATION, TRAINING, AND CAREER DEVELOPMENT

G2i1. Specific Aims

The overall goal of this key function is to develop and integrate a program of research education, training, and career development that has the breadth and flexibility to meet the needs of new investigators who are committed to careers in clinical and translational science and who require additional knowledge and skills to contribute to multidisciplinary teams of investigators. The Research Education and Training Program of the University of Rochester Clinical and Translational Science Institute (UR-CTSI) will build on existing graduate training programs in Clinical Research and Basic Biomedical Sciences, but add considerably to the URMC Program by initiation of Master's and Doctoral training programs specifically focused on the key functions of Translational Research. These new educational modules will be integrated with existing clinical research training modules, related doctoral programs, skill-building workshops, and seminars to provide the flexibility to meet the needs of investigators across the spectrum of disciplines needed for successful translational research. Flexibility will be enhanced by organizing predoctoral, post-doctoral, and career development programs to meet the needs of trainees at a range of career stages.

To achieve this goal, the UR-CTSI Research Education, Training, and Career Development Program has the following specific aims:

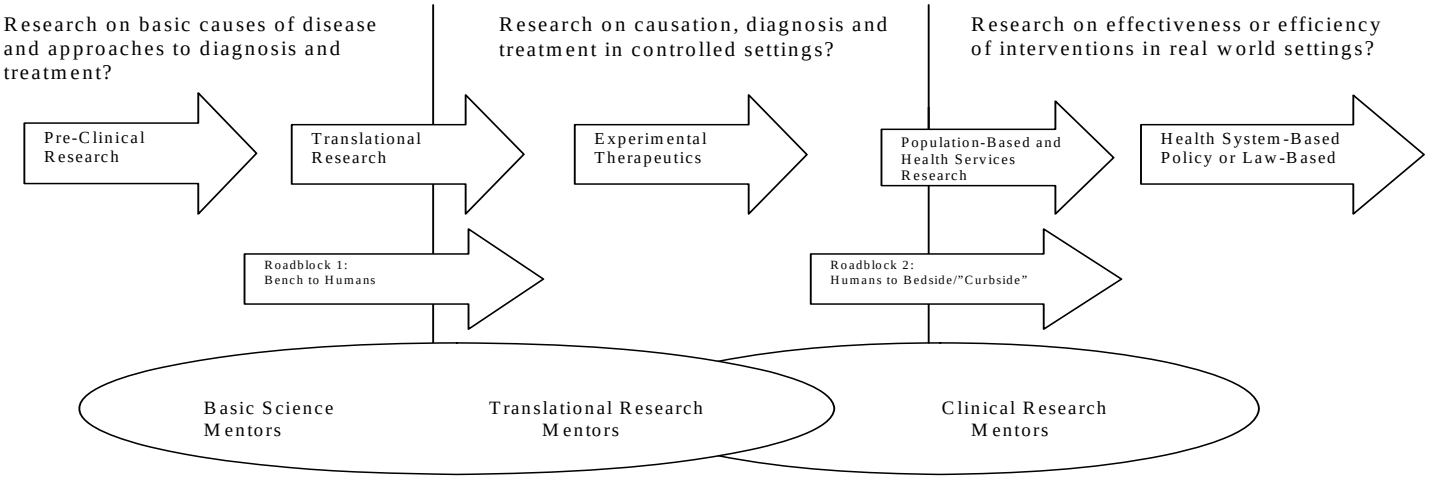
1. To organize URMC research and training programs in clinical and translational research within the UR-CTSI to promote interaction and integration between existing programs and key function groups, and to provide shared administrative support.
2. To create new curricula leading to a Master's Degree in Clinical Investigation, a Master's Degree in Translational Research, or a PhD Degree in Translational Biomedical Sciences.
3. To expand a mentor development program to enhance the quality and quantity of mentors in translational and clinical research who can meet trainees' needs for research mentorship in short term, graduate (Master's or PhD), or career development programs.
4. To develop a predoctoral (T32) training program using the new curricula, skill-building workshops, seminars, and mentored research experiences leading to an advanced research track for medical students (MD-MS degree), a graduate program leading to a PhD in Translational Biomedical Science, or an MD-PhD Program with the PhD in Translational Biomedical Science.
5. To initiate a Clinical/Translational Research Career Development (K12) Program tailored to fellows and junior faculty members' needs through didactic curricula leading to Master's or PhD degrees, skill-building workshops, and mentored experiences in clinical/translational research.
6. To evaluate the performance of the overall Research and Training Program and its Predoctoral (T32) and Career Development (K12) components through development and application of objective criteria measuring success in creating clinical and translational investigators.

At the end of the period of support, the UR-CTSI will have established a broader and deeper offering of training programs with novel programs to fill our deficiency in translational research training, will have recruited talented and committed trainees into all programs, and will begin to measure the fruits of this training through objective criteria of academic performance and research productivity.

G2i2. Background and Significance

As the UR-CTSI seeks to break down the road-blocks to research translation (Figure G2i1), the Education and Training Key Function will take on a central role in mobilizing and organizing institutional faculty and resources. In many institutions, education and training is a logistical issue, in which personnel are trained to carry out the research. The UR-CTSI will be organized so that the trainee will be the catalyst to form multidisciplinary research teams focused on the trainee's area of interest (Figure G2i.1). In this way, education and training becomes a key strategy to integrate heretofore separate research groups into the multidisciplinary research teams needed to address complex translational research issues.

Figure G2i.1. Conceptual Rationale for the Rochester CTSI Education and Research Key Function



To carry out this key strategy, the Education and Training Key Function will espouse six premises which form the rationale for development of UR-CTSI education and training programs.

Premise #1: Multidisciplinary research skills are increasingly needed to address clinical/translational research problems. Figure G2i.1 illustrates the breadth of skills needed to carry out bench to human and human to bedside translational research, including basic (preclinical) sciences, experimental therapeutics, population sciences, and health services research.

Premise #2: Clinical/translational research careers increasingly focus on one part of the spectrum of clinical/translational research. Experience with over 120 trainees in the Rochester Clinical Research Curriculum (K30) Program has shown us the predilection for careers in a more increasingly defined subset of clinical/translational research, such as patient-oriented translational research, patient-oriented experimental therapeutics, population-based research, health services/outcomes research, and ethics/law/policy research. These line up well with the NIH definition of the components of clinical research.

Premise #3: New didactic courses are needed for trainees to learn the theory and methods of translational research. In general, curricula are frequently segregated into basic science and clinical research, with few courses emphasizing translation between the two. The key functions of the UR-CTSI identify topics for didactic courses relevant to translational and/or clinical research.

Premise #4: Successful conduct of clinical/translational research requires a wide variety of practical skills. These often entail training in the use of the wide-range of clinical and translational research resources often needed to address complex issues. One approach to assure acquisition of this range of skills is to also organize this around the CTSA key functions, so that trainees can identify, access, and effectively use these newly organized resources in the UR-CTSI.

Premise #5: Multidisciplinary clinical/translational research training will require a team of co-mentors in addition to a primary mentor, to provide the trainees with the breadth of research skills needed in modern translational research. At the same time, the UR-CTSI brings together faculty from a wide range of disciplines focused on the trainee's research topic, and promotes productive interaction in which the trainee is the "glue" to the research team and the driver of their research agenda. This strategy has worked well in the Rochester K30 Program as a means to form effective multidisciplinary research teams.

Premise #6: The development of high quality research mentors is crucial in the sustaining and expanding of translational research at URMC. The interaction between the well-prepared trainee and the experienced, skillful research mentor will remain a cornerstone of all research training. The quality of mentorship varies widely, and new faculty receive little guidance about their mentorial roles and responsibilities. Their readiness for training of multidisciplinary translational researchers is often limited. A translational research mentor development program is a key, long-term investment to assure quality translational research training at URMC.

G2i3. Training Environment at the University of Rochester Medical Center.

G2I3a. Institutional Overview. The University of Rochester, Strong Memorial Hospital, and its affiliated hospitals have a long tradition of excellence in the training of both clinicians and clinical researchers. The School of Medicine ranks 8th among U.S. medical schools in the percentage of graduates between 1982 and 1991 who are current members of medical school faculties (AAMC, 1996). This institution has a wide range of excellent pre- and postdoctoral programs in the basic biomedical sciences, including PhD programs in the School of Medicine in Anatomy, Biochemistry, Biophysics, Epidemiology, Genetics, Health Services Research, Microbiology and Immunology, Neuroscience, Pathology, Pharmacology, Physiology, and Toxicology. A full complement of residencies and postdoctoral clinical fellowship programs provide postdoctoral training opportunities in clinical medicine and clinical research.

G2i3b. MD Curriculum.

1) Overview. In 1998, the MD curriculum at the University of Rochester School of Medicine underwent a comprehensive reform, in response to accreditation bodies' concerns about its lecture-based didactic curriculum. The new curriculum was given a translation-oriented the name, "The Double Helix Curriculum", in that it integrates basic science and clinical medicine throughout a four-year course of instruction. The curriculum begins with four weeks of Mastering Medical Information which entails instruction in epidemiology, biostatistics, bioinformatics and evidence-based medicine in contrast to most curricula which begin with a basic science such as anatomy. The second lecture of Medical School is a description of hypothesis-driven research. The summer between Year I and Year II is unscheduled and provides opportunities for short-term research electives. Years III and IV have flexibility in clinical rotations, allowing research electives to be taken.

2) Summer Research Fellowships. Most medical students participate in a scholarly project between Year I and Year II. The Office of Medical Student Enrichment offers support for these summer research preceptorships, and a Committee for Student Research reviews proposals submitted by students for these funds. A Student Research Handbook includes instruction on preparing a hypothesis-directed research proposal. In 2005, 55 students were supported for short-term research projects, mostly between Years I and II.

3) Year-Out Program. University of Rochester medical students (100 students per class) frequently take a year out to participate in a wide array of elective experiences. Students receiving institutional support to take a year out to perform research, either full-time in a research laboratory or as part of a Master's degree program were: 19 for 2002-3, 19 for 2003-4, 16 for 2004-5, and 20 for 2005-6. The MPH Program (Clinical Investigator Track) is elected by 2-3 students per year.

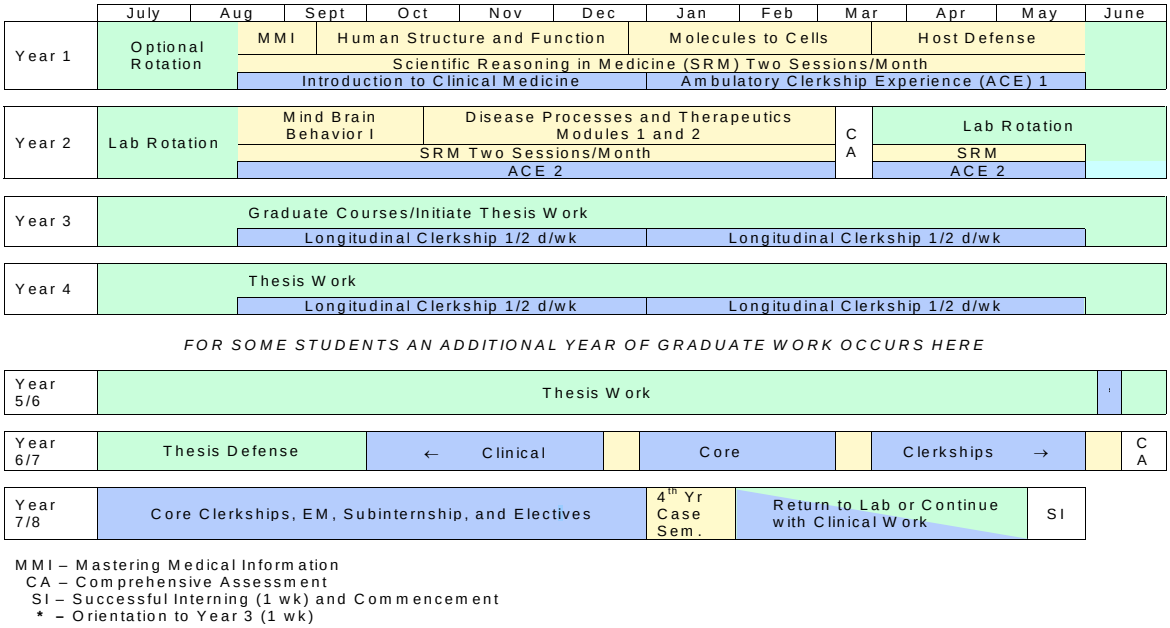
G2i3c. MD-PhD Program; Medical Scientist Training Program. (MSTP)

1) Background. The University of Rochester has trained MD-PhD students for almost 50 years. From the late 1950's, MD-PhD trainees were funded either by the School or the Clinical Investigator Training Program. Substantial institutional resources have been expended to augment the support available from the NIH and to ensure the continued success of the MD-PhD training programs. Over ninety students have graduated from our training program since the initial MSTP award some 30 years ago. The majority of former trainees have selected academic careers and many have assumed positions of leadership within their institutions. The career trajectories of students reveal that of 38 students graduating with the MD-PhD between 1987 and 1999, 34 remain in academia with 12 independently funded through R01 or K award mechanisms at the Instructor or higher academic level and 13 still in fellowship training. Thus, the MSTP program at Rochester fulfills the principal goal of training physician-scientists and academic leaders. It is supported by a MSTP grant from NIH.

2) MD-PhD Curriculum. The MD-PhD curriculum provides students with a longitudinal integration of basic and clinical sciences, punctuated by a period of rigorous graduate research training. Figure G2i.2 provides an outline for the major curricular components of the program. For most students, it is anticipated that this program can be readily completed in eight years, and that a proportion of students will complete the program in seven years. Opportunities for conducting research rotations in the first years of the program, a shortened second medical school year, targeted clinical activities during graduate training, and significant flexibility in returning to medical school at the conclusion of graduate training all contribute to timely completion. Of special relevance to the Predoctoral Clinical Research Training Program are several opportunities for student interaction. First, throughout Years I and II, a special seminar on "Scientific Reasoning in Medicine" is held twice a month. This MSTP-specific seminar has three goals: 1) to provide an opportunity for students to meet with a range of outside research faculty; 2) to learn about a research topic that links basic science to a

medical problem; and 3) to engage students in critical literature evaluation in a journal club format. Second, there are monthly MSTP dinners which provides informal faculty presentations. Third, students attend regional and national MD-PhD student conferences. Finally, the MD-PhD students have an annual retreat in which they present their work. The MSTP Program has admitted 8 students per year since 2002. Dean Guzick expanded the program at that time, through use of Institutional funds. Therefore, of the current 41 students, only 11 are supported by the MSTP grant, with the remainder funded by the School of Medicine or by research grants of mentors.

Figure G2i.2: MD-PhD Curriculum



3) Clinical Research Training in the MD-PhD Program. A recent development in the Rochester MSTP Program has been the admission of students interested in disciplines traditionally recognized as clinical research rather than basic science. Traditionally, MSTP students receive their PhD training in basic science laboratories, though many thesis projects involve human tissues or patient-oriented research. Since 2002, five students have been accepted to the MSTP Program with interests in PhD training in Biostatistics, Epidemiology, and Health Services Research. These students form an important precedent for developing an MD-PhD Program in Translational Biomedical Science.

G2i3d. Rochester Clinical Research Curriculum (K30) Program.

1) Overview of Didactic Curriculum. The Rochester Clinical Research Curriculum (RCRC) Program has been supported by a K30 Award since its inception in 1998, with successful renewal through 2010. It forms a foundation for further development of clinical/translational research training. The goal of the RCRC is to develop a model two-year curriculum for the training of clinical investigators. Most RCRC trainees are senior fellows or junior faculty (See Tables G5C.3, 4, 5). The components of the RCRC include didactic coursework on clinical research, an enhanced series of RCRC Skill-building Workshops, and a well-established weekly Clinical Research Seminar Series. This core curriculum, in turn, is based on a series of educational objectives and competencies which are considered essential for the preparation of the competent clinical/translational researcher. The original RCRC curriculum, based on 19 educational objectives, including 6 knowledge, 8 skill, and 5 attitudinal objectives, has been revised for the CTSA (See Table G2i.3). Since this curriculum is competency-based, it provides flexibility for clinical research trainees from a variety of backgrounds to receive credit for prior courses or experiences, so that time and effort might instead be spent acquiring new knowledge and skills. Each educational objective/competency has a measurable outcome, facilitating evaluation of the trainee's progress. Trainees completing educational objectives and degree requirements receive a Master's Degree in Public Health in the Clinical Investigator Track. Figure G2i.3 shows the trainee's program on a month-by-month basis and illustrates a two-year curriculum with required coursework, mentored research experience, elective coursework, and skill-building workshops.

Figure G2i.3: Rochester Clinical Research Curriculum/Master of Public Health (Clinical Investigation) Program

YEAR	July	August	September	October	November	December	January	February	March	April	May	June
1	RCRC Workshop: Introduction to Clinical Research	RCRC Workshop: Introduction to Research Informatics	*PM 421 Intro. to US Health Care System*				*PM 470: Environmental Health 1.5 hours per week*					MENTORED RESEARCH
			PM 415: Principles of Epidemiology				*PM 450: Management & Evaluation of Health Service Organizations*		***PM 424 :PC SAS for Clinicians***			
			BST 463: Introduction to Biostatistics				***BST 464 Statistical Methods for Biomedical Applications or BST 465 Design of Clinical Trials***					
	Clinical Research Field Visits		***PM 426 Social and Behavioral Medicine***				***PM 484: Medical Decision and Cost Effectiveness Analysis***					
	Departmental Orientation/ Selection of Research Mentors	RCRC Workshop: IND 501 Ethics in Research	***PM 482 Clinical Evaluation & Outcomes Research***				***Track Elective***					
			RCRC Workshop: Recruitment and Retention of Research Subjects				RCRC Workshop: Workshop in Scientific Communication					
	Clinical Research Seminar											

YEAR	July	August	September	October	November	December	January	February	March	April	May	June
2	Mentored Research/ Thesis Preparation		Track Elective				Track Elective					MENTORED RESEARCH
			Mentored Research/ Thesis Preparation				Mentored Research/ Thesis Preparation					
	RCRC Workshop: Advanced Informatics		RCRC Workshop: Technology Transfer/Working With Industry				RCRC Workshop: Practical Skills in Grant Writing RCRC Workshop: Research Program Administration					
	Clinical Research Seminar											

LEGEND: *Required for MPH in Clinical Investigation (MPH-CI) Only*
Required for both Rochester Clinical Research Curriculum (RCRC) and MPH-CI
Required for RCRC Only

2) Skill-Building Workshops. The didactic coursework forms the core of RCRC instruction on the theory and methods of clinical research, yet this didactic component is considered necessary, but not sufficient to assure productivity in the trainee. There remain a number of competencies required for success which cannot be assured in the mentor-mentee relationship, nor do they lend themselves to a theoretical or methods-oriented course. To modify this, a two-year sequence of skill-building workshops is provided (Table G2i.1).

Table G2i.1: Skill-building Workshops Offered as Part of the Rochester Clinical Research Curriculum

Workshop	Duration	Competencies Addressed
Introduction to Clinical Research	4 weeks, Yr I	Overview of the RCRC Program
Introduction to Medical Informatics	4 weeks in Yr I 4 weeks in Yr II	Basic research informatics skills Advanced skills in bioinformatics
Ethics in Research	8 weeks in Yr I	Ethical conduct of research
Recruitment and Retention of Research Subjects	14 weeks in Yr. I	Recruitment and retention of research subjects Responsible conduct of research
Scientific Communication	14 weeks in Yr I	Scientific presentation and writing
Technology Transfer/ Working with Industry	14 weeks in Yr II	Intellectual property Opportunities in private sector
Grant Writing	14 weeks in Year II	Grant application and review
Research Program Administration	8 weeks in Year II	Regulatory aspects of research

3) Clinical Research Seminar Series. This series of research seminars serves the entire URMC and has several purposes. First, it brings together mentors and trainees from diverse fields and disciplines to serve as the "glue" for the RCRC. Second, there should be mechanisms by which new technologies, especially those in the basic sciences, are introduced to clinical researchers. Third, it is essential that there be a forum for outstanding clinical researchers to be brought to the University of Rochester to not only share the newest advances in clinical research theory and methods, but also to serve as additional role models for trainees. Fourth, RCRC Scholars should have an opportunity to present their work to their peers, to identify ideas and methods which would enhance their work, and to simulate cross-disciplinary approaches. With these purposes in mind, the Clinical Research Seminar has been successfully held Tuesdays from 12:15 to 1:30 PM for approximately 36 weeks per year, and will easily evolve into a Clinical/Translational Research Seminar.

4) RCRC Performance. The Program has recruited 124 RCRC trainees who meet the selection criteria in its first seven years of operation (See Tables G5C.3-10). Of these, 52 have successfully completed the Program and seven dropped out (one for medical reasons and one died). The remaining trainees continue in various stages of the program, with many having completed their coursework and requiring only the completion of their research project to graduate. Most RCRC trainees are graduates of U.S. professional schools with additional training in U.S. residency and postdoctoral fellowship programs (Table G5C.10). The trainees have been essentially evenly divided by gender (51% female). Minority representation has been acceptable (but not superior), with 4% of RCRC Scholars of Hispanic ethnicity and 11% African Americans, for a total of 15% from underrepresented minorities. RCRC graduates generally remain in academic positions even if they leave Rochester. Only 5 of the 124 Scholars (including withdrawals) are not affiliated with major academic medical centers (Table G5C.10). All graduates participated in a research project to complete requirements for their MPH-CI Track.

The research applications from RCRC graduates have met with considerable success (Table G5C.8). A total of 75 federal and 161 non-federal grant applications have been submitted with the RCRC Scholar as PI, resulting in 33 federal and 116 non-federal grants being funded. These data are somewhat misleading since several of the unsuccessful applications were resubmitted successfully. Not counting the pending applications, this amounts to 44% of federal and 72% of non-federal grants being funded. These funded federal grants include 12 K23, 1 K24, 2K07, 1K01 and 1 R25 grants. Funded grants amount to $22,183,830 in total costs for all years of which $11 million is from NIH (Table G5C.7). A total of 45 RCRC scholars currently hold grants as Principal Investigators (G5C.8). Research productivity as measured by publications has been excellent. RCRC trainees list 349 first-authored publications and 224 co-authored papers since their training began (Table G5C.6). These data support the effectiveness of the RCRC in developing clinical research skills in the trainees and providing them with mentored opportunities to be productive. Their career trajectories, though early in the process, appear excellent based on acquisition of career development awards and other research grant funding. Our conclusion is that the RCRC has attained its productivity objectives in terms of the quality and quantity of clinical investigators initially proposed as program goals. These evaluation methods are further described in Section E.

G2i3e. Other Training Programs at the University of Rochester. A final measure of the training ongoing at the URMC is the number of institutional training grants funded by the Public Health Service at the University. Table G2i.4 lists 32 T32 training grants, 3 R25 faculty development programs, and 3 other PHS training grants currently at URMC. These training grants support 111 predoctoral and 95 postdoctoral trainees (all years). The breadth of training programs includes the School of Nursing, the Eastman School of Dentistry (2) and the College of Arts, Science and Engineering (3). Institutional training grants have frequently been sources of clinical research trainees for the RCRC, but also the RCRC has been instrumental in development of 13 of the T32, K12, and R25 Programs. In addition, the URMC currently sponsors 43 individual K awards (K01, K08, K23 and K24 Awards)(Table G2i.5). The Clinical Research Program has been involved with these awards in two ways. First, 10 K awardees enrolled in the RCRC for the first two years of their award. Second, RCRC trainees have written successful applications in the Grant Writing Workshop for 16 of the 43 K Awards. This emphasizes not only the richness of training activities at URMC, but also the substantial interactions between them that involve clinical research.

G2i4. Institutional Commitment: Statement by David S. Guzick, MD, PhD, Dean

G2I4a. Commitment to the Research Education and Training Program. As the Principal Investigator of the CTSA application, I have a clear commitment to education and training as a critical component of the Rochester CTSI. We have placed education and training as a key strategy to integrate the entire application. Trainees will not only serve as the next generation of clinical and translational researchers, but, over the short-term, serve to coalesce the multidisciplinary research teams needed for translational research. During my tenure as Dean, I have been fully supportive of the Rochester Clinical Research Curriculum (K30) Program, and, as Director of a K12 Program in Women's Health, referred trainees to it. I have supported efforts of the Academic Research Track, and have provided tuition waivers to students taking a year-out in research. I have used school funds to expand the MD-PhD Program to eight positions per year. I consider the Research Education and Training Component of the CTSI to be a logical next step in a progression of research training programs here at the School of Medicine.

G2i4b. Specific Commitment to the Predoctoral Training Program (T32). The Predoctoral Training Program is an essential addition to our training of translational researchers, especially MD and MD-PhD trainees who can be identified early in their Medical School careers. I am pleased to support this program by endorsing the commitments of administrators and mentors to the successful development and maintenance of this program. I will assure that trainees have adequate laboratory space and other support for their programs. I will continue to support the Academic Research Track (ART) program which will serve as a pipeline for students interested in the MD-MS program. I will oversee recruitment of ART students with a special interest in increasing the number of students from under-represented minority groups. More specifically, I will support with stipends and tuition-waivers an additional four medical students who wish to complete the MD-MS program either in Translational Research or in Clinical Investigation. Moreover, in addition to the one new PhD student added per year in Years II-V of the Translational Biomedical Research Programs, I will support an additional two students per year for up to four years, to create a critical mass to this program. Finally, in addition to the one additional MD/PhD student supported in Years II-V, I will support an additional two MD-PhD students with stipends and tuition, again to bolster the critical mass of the PhD Program in Translational Biomedical Research.

G2i4c. Specific Commitment to the Research Career Development Program (K12). The transition from fellow/junior faculty to independent investigator is well recognized as the most perilous step in career development. As a previous Principal Investigator of a K12 Program, I am fully aware of the benefits of this career development program. My commitment includes support for administrative faculty and mentors' efforts to supervise these CTSI Scholars. I will be especially interested in a strong recruitment effort, especially of scholars from underrepresented minorities. Moreover, I will assure that 75% effort (or at least 50% effort from certain specialties) of CTSI scholars be spent on research and career development activities. I will work with the chairs of their respective departments to assure their time is protected and that their remuneration is consistent with others of like rank in their departments. Laboratory and office space needs will be accommodated to support their career development.

In summary, I am in a unique position as Dean and Principal Investigator of the UR-CTSA to have first-hand knowledge and appreciation of the Research Education and Training Key Function. I have proposed both philosophical and tangible measures of support, and intend to react positively to needs of the Education and Training Program as they arise.

David S. Guzick, MD, PhD
Dean, School of Medicine and Dentistry

G2i5. Overview of Research Education, Training, and Career Development Programs

G2i5a. Organization. The Research Education and Training Key Function is organized to integrate opportunities and resources across several training programs (existing K30, T32, K12)(Figure G2i.4). The governance will be centralized in a Directorate consisting of the Director, Co-Directors, and administrative staff (see below). This Directorate will be supported by five cores: Administration, Curriculum, Mentor Development, Recruitment and Admissions, and Evaluation. The centralization of these support functions will enhance efficiency while assuring adequate availability of personnel and resources to carry out the essential functions. CTSA Education and Training Programs will integrate with other educational programs at URMC, especially other graduate programs in the Schools of Medicine and Nursing as well as the Eastman Dental Center. Similarly, programs for medical students will be collaborated with, including the Academic Research Track and the Medical Scientist Training (MD-PhD) Program.

Essentially three programs are proposed, including modification of our successful Rochester Clinical Research Curriculum Program (K30) as well as initiation of two new programs, a Predoctoral (T32) Program in Clinical/Translational Research and a Mentored Career Development (K12) Program for fellows and junior faculty. Each of these programs will have access to a number of training modules, including short-term clinical/translational research preceptorships, didactic programs leading to the PhD degree or to Master's degrees, Skill-building Workshops, and an ongoing, institution-wide CTSI Seminar Series. This sharing of training modules offers optimal flexibility, so that, for example, a CTSI Scholar could elect short-term research rotations, a Master's Program, or a Doctoral program, depending on his/her needs. Finally, new doctoral and master's programs are added to existing programs. A new PhD in Translational Biomedical Science is proposed, to provide opportunities for advanced learning in patient-oriented translational research or experimental therapeutics. Similarly, two new Master's degrees are proposed, a Masters of Science in

Translational Research (MSTR) and a Masters of Science in Clinical Investigation (MSCI). These new programs and degrees represent major additions to training programs at URMC.

G2i5b. Governance. The Research Education and Training Directorate will report to the CTSI Director and Executive Committee through representation on the CTSI Administrative Committee by its Key Functions Director. This will assure integration of education and training with other key functions. The Directorate will consist of a Director (Thomas A. Pearson, MD, MPH, PhD), two Co-Directors (Paul LaCelle, MD, PhD and Robert Holloway, MD, MPH), and Directors of the degree programs. The Directorate will meet monthly, and receive reports from Cores and Program Directors. Program governance functions will be carried out by the training support cores, in terms of resources and finances (Administrative Core), curricular content (Curriculum Core), faculty effort and preparation (Mentor Development Core), trainee recruitment, review, and admission (Recruitment and Admission Core), and program evaluation (Evaluation Core). These training support cores will be convened regularly, as needed. For example, the Administrative Core will convene weekly, but the Recruitment and Admissions Core will convene during receipt and review of applications.

1) Administrative Core. This group provides organizational support for this key function, including the Directorate, other Cores, and the UR-CTSI's three education and training programs. It shall be led by Thomas Fogg, MA, CTSI Administrator, and supported by a halftime administrative assistant. This core will schedule meetings for the Directorate and Cores, develop a training and education website for internal communications and external recruitments, administer budgets for K30, K12 and T32 components, prepare annual progress reports, etc.

2) Curriculum Committee. This group will review and approve all didactic coursework, including K30, K12, and T32 curricula, as well as short courses, etc., prior to direct submission to the Graduate Studies Board. All courses will have learning objectives, syllabi, and means for trainee evaluation. All courses will be evaluated annually and will also be reviewed every three years for course content and objectives. This core will also recommend replacements of instructors if any should need to be replaced. This will be chaired by Paul LaCelle, MD, PhD. Other members of the Core will include Director of the Masters in Clinical Investigation and Masters in Translational Research Programs and the Director of the PhD Program in Translational Biomedical Science.

3) Mentor Development Core. This core will be responsible for the Mentor Development Program (see Section G2i.7). It will be chaired by Thomas A. Pearson, MD, MPH, PhD, Senior Associate Dean for Clinical Research, and include Peter Szylagyi, MD, MPH, Professor of Pediatrics; Donna Giles, PhD, Associate Professor of Psychiatry; Vivian Lewis, MD, Professor of Obstetrics and Gynecology; and Stephen Dewhurst, PhD, Professor of Microbiology. Those faculty have long and successful careers in mentoring trainees.

4) Recruitment and Admissions Core. This core will handle all tasks related to advertising the programs, processing applications, reviewing the applications, communicating with the successful and unsuccessful applicants, and maintaining records of completion of requirements for degrees. (See Sections G2i.3, 10 for Recruitment of Trainees).

5). Evaluation Core. This core will carry out the Evaluation Plan required for this core, (See Section G2i.9).

G2i5c. Key Function Leadership.

1) Director. Thomas A. Pearson, MD, MPH, PhD is the Albert D. Kaiser Professor and Chair of the Department of Community and Preventive Medicine and Professor of Medicine at the University of Rochester School of Medicine. Dr. Pearson has been active both as a classroom teacher and as a research mentor since 1983. He is the recipient of a Preventive Cardiology Academic Award from NHLBI from 1983-1998 and a Nutrition Academic Award from NHLBI from 1998-2003. At the University of Rochester, he is Course Director for "Practical Skills in Grant Writing," one of the RCRC Skill-building Workshops. He is also Course Director for the first course in the MD curriculum, "Mastering Medical Information". Dr. Pearson also has a long experience with clinical research training in addition to his direction of the K30 Program. He is the Principal Investigator for an Institutional National Research Service Award (T32) entitled: "Research Training in Preventive Cardiology," which has been renewed through 2010 and an R25 programs supported by NCI. Since 1983, he has served as mentor for 49 clinical research trainees, a large number of whom have gone on to have distinguished clinical research careers.

Dr. Pearson is uniquely positioned to provide leadership to the Research Education and Training Program. First, he is officially a Basic Science Chair (interfacing regularly with chairs of PhD-granting disciplines), and is also a Clinical Chair (interfacing with clinical disciplines). Second, he is Chair of the department which offers

the MPH-degree and the proposed MS-CI degree. In that capacity, he is ultimately responsible for the didactic training programs currently most closely tied to clinical research at the University of Rochester. As Senior Associate Dean for Clinical Research, he directs the Office for Clinical Research which organizes and coordinates clinical research on an institutional basis. Finally, as Principal Investigator of the K30 award, he can assure access for predoctoral and K12 trainees to courses and workshops of that postdoctoral program.

Figure G2i.4: Organizational Chart for the Research Education and Training Key Function

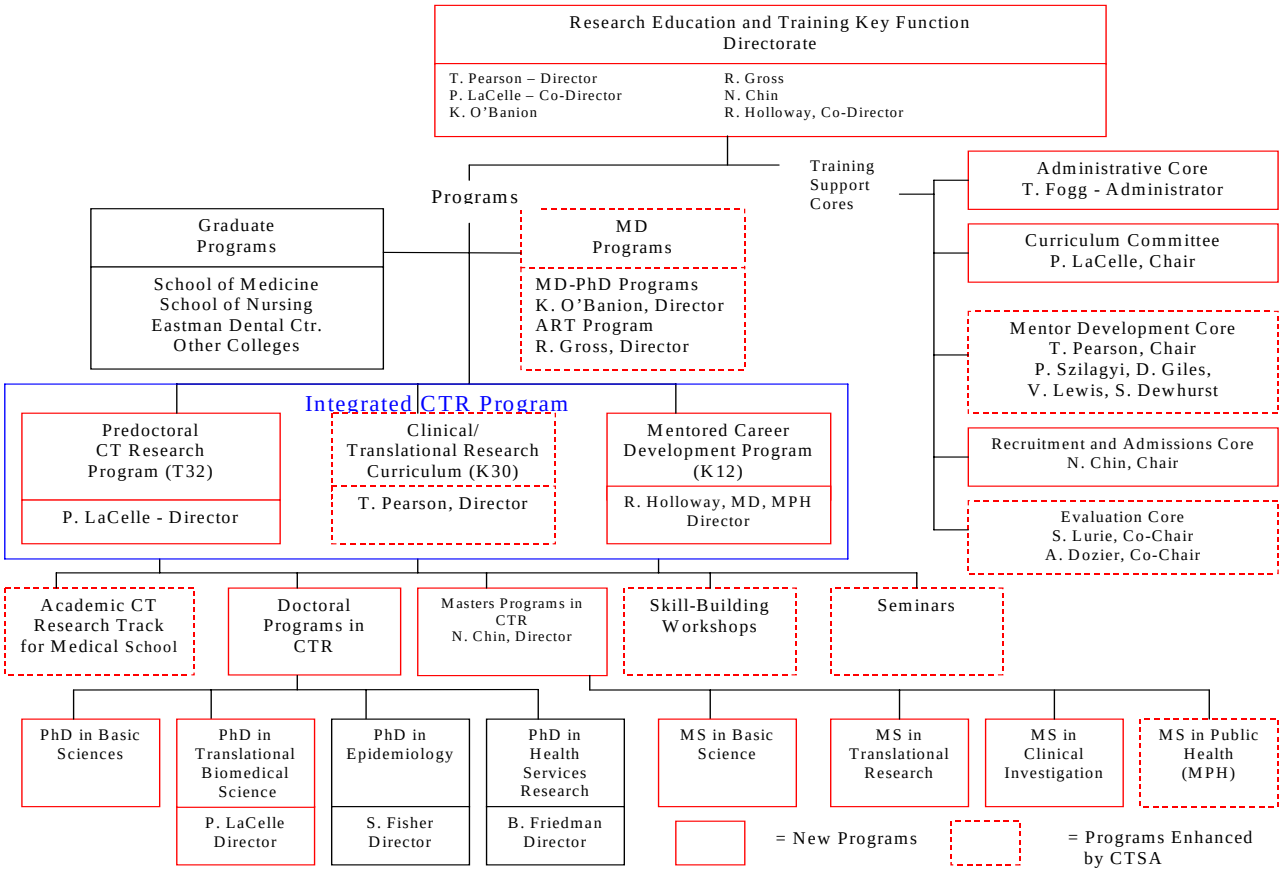


Table G2i.2. Participation in Training Modules by Clinical/Translational Research Training Program

Module	MD-MS (ART Program)	PhD in Translational Biomedical Research	MD-Ph In TBR	CT Research Education (K30)	CTR Career Development (K12)
MS in Clinical Investigation	X or	X and	X and	X or	X and/or
MS in Translational Research	X	X	X	X	X
Lab Rotations	1	Several	Several	-	-
Mentored Research	X	X	X	X	X
Skill-building Workshops	X	X	X	X	X
Seminars in CTR	X	X	X	X	X
Training in Responsible Conduct of Research	X	X	X	X	X

2) Co-Director for the T32 Program: Paul LaCelle, MD, PhD will direct the T32 Predoctoral Program. Dr. LaCelle is the Senior Associate Dean for Graduate Education in the School of Medicine and Dentistry, and chairs the Committee on Graduate Studies. As such, he has authority for all predoctoral training

(Master's and Doctorate). Dr. LaCelle is also Professor of Pharmacology and Physiology, with a distinguished record of graduate student supervision and basic science research.

3) Co-Director for the K12 Program: Robert Holloway, MD, MPH will direct the K12 Career Development Program. Dr. Holloway is Associate Professor and Associate Chair for Academic Affairs in the Department of Neurology, with a joint appointment in Community and Preventive Medicine. He is also Associate Director of the Clinical Trials Coordination Center. He is currently supported by a K24 award from NINDS and is a co-investigator on the K30 award. Dr. Holloway has a distinguished track record of mentoring fellows in experimental therapeutics and in research on clinical trials, cost-effectiveness, and research ethics in the field of Parkinson's disease.

G2i6. Training Modules

G2i6a. Overview. This section will describe seven training modules which will be combined to support the Predoctoral (T32), Clinical/Translational Research Curriculum (K30) and Clinical/Translational Career Development (K12) programs (Table: G2i.2). Each will be described separately here and then combined to describe the Programs in Section G2i8.

G2i6b. MS in Clinical Investigation Didactic Coursework. All degree programs will be organized according to educational objectives and acquired competencies (Table G2i.3). The MSCI degree is designed to be a two-year program, though the second year largely consists of mentored research. The MSCI will replace the MPH in the Clinical Investigation Track of the K30 Programs, though the MPH in the Generalist Track will continue. This is necessary to provide a new required course (e.g. Health Informatics) and elective courses which could not be accommodated within the restrictions required by its accrediting body (e.g. Council on Education in Public Health). "BST525: Introduction to Health Informatics" will be a full-semester course taught by Dongwen Wang, PhD from Biostatistics and Computational Biology. It will replace two RCRC Workshops in informatics. This degree will require 32 credits (Table G2i.4). The remainder of the MSCI degree will consist of Skill-Building Workshops (including "Instruction in the Responsible Conduct of Research"), research experiences mentored by a clinical researcher leading to a scholarly work worthy of publication in a peer-reviewed journal, and seminars in clinical/translational research.

Table G2i.4: Didactic Coursework for Masters Degrees (* = New Courses)

MS in Clinical Investigation

Course	Credits	Semester
BST 463: Introduction to Biostatistics	4	I
PM 415: Introduction to Epidemiology	3	I
PM 482: Clinical Evaluative Sciences	3	I
*BST: Introduction to Health Informatics	3	I
Elective	3	I
PM 424: PC SAS for Clinicians	2	II
BST 465: Design of Clinical Trails	3	II
PM 484: Medical Research and Cost-Effectiveness Analysis	4	II
PM 415: Advanced Epidemiologic Methods	3	II
Elective	4	II
Total	32	

MS in Translational Research

Course	Credits	Semester
BST 463: Introduction to Biostatistics	4	I
PM 415: Introduction to Epidemiology	3	I
*Pathways to Disease	3	Summer
*BST: Introduction to Health Informatics	3	I
*Introduction to Translational Research Methods	3	I
PM 424: PC SAS for Clinicians	2	II
BST 464: Statistical Methods for Biomedical Applications	3	II
*Experimental Therapeutics	4	II
PM 417: Molecular Epidemiology	3	II
Elective	4	II
Total	32	

G2i6c. MS in Translational Research: Didactic Coursework. This degree will be entirely new, supported by the CTSA. It will also target specific educational objectives and acquired competencies (Table G2i.3). The emphasis will be on the mastery of basic principles of human pathophysiology, the technologies that measure these either as a predictor or as an outcome in translational research, and the development of therapeutics to correct the pathophysiology (Table: G2i.4). Unlike the MSCI degree, the MSTR will have four new courses developed for it. The "Pathways to Disease" course will be organized by Paul LaCelle, MD, PhD

and will serve as a review of human disease processes, to be taught over eight weeks in the summer before the first year. BST 525: "Introduction to Health Informatics" will also be required. A new course, "Translational Research Methods," will be directed by Steven Welle, PhD and the Laboratory Support Center Director. It will introduce the trainees to the development and use of major translational technologies. The fourth course, "Experimental Therapeutics" will be co-directed by Robert Holloway, MD, MPH and Karl Kieburtz, MD, MPH. It will describe the scientific basis for drug discovery and development. The MSTR will also allow two electives for the trainee to specialize in a disease or methodologic area of interest.

The remainder of the MSTR degree will consist of Skill-building Workshops (including "Instruction in Responsible Conduct of Research"), research experience mentored by a translational researcher leading to a scholarly work worthy of publication in a peer-reviewed journal, and weekly seminars in clinical translational research and in their area of translational science.

Table G2i.3: Objectives/Acquired Competencies for Education and Training in Clinical/Translational Research

Educational Objectives/Acquired Competencies	Measurable Outcomes	Degree Program		
		MSTR	MSCI	PhD
Knowledge				
1 Learn the principles and theories which serve as the basis of biostatistics and quantitative data analysis.	1 Completion of Introduction to Biostatistics or equivalent course.	x	x	x
2 Understand the ways to measure the distribution of traits and diseases in populations, the determinants of those distributions, and study designs for this purpose.	2 Completion of Principles of Epidemiology or equivalent course.	x	x	x
3 Be able to design and analyze studies relevant to patient-oriented clinical research	3 Completion of an Advanced Epidemology course or equivalent.		x	x
4 Appreciate study designs, settings, and databases available to evaluate clinical interventions.	4 Completion of Clinical Evaluative Sciences or equivalent course.		x	x
5 Comprehend the concepts underlying the quantitative analysis of medical decisions.	5 Completion of Medical Decision and Cost-Effectiveness Analysis or equivalent.		x	x
6 Understand the design and conduct of human experiments.	6 Completion of Clinical Trials or equivalent course.	x	x	x
7 Identify social and behavioral factors which impact on human health and the use of health services.	7 Completion of Social and Behavioral Medicine or equivalent course.		x	x
8 Understand basic pathophysiologic mechanisms leading to human disease.	8 Completion of Pathophysiology course or equivalent.	x		x
9 Know the theory and application of major new methodologies to measure biological perameters important in human health.	9 Completion of Translational Technologies course or equivalent.	x		x
10 Appreciate the development and evaluation of therapies for treatment of disease.	10 Completion of course in Experimental Therapeutics or equivalent.	x		x
Skill				
1 a. Identify a hypothesis, select the appropriate study design, and collect data to test the hypothesis.	1 a. Carry out a clinical research project under the supervision of a mentor or mentorial committee, including proposal development, data collection, data management, and data analysis.			x
b. Develop hypothesis with a data set and perform appropriate statistical tests of the hypothesis.	b. Carry out hypothesis test within pre-existing data set.		x	
c. Acknowledge and be able to use resources for evaluation of a diagnostic and therapeutic agent.	c. In Experimental Therapeutics course, develop protocol for evaluation of a diagnostic and therapeutic agent.	x		x
2 Use multiple types and sources of medical informatics to facilitate research.	2 Completion of Bioinformatics course or equivalent.	x	x	x
3 Use database management and statistical software to organize and analyze data.	3 Analysis of trainees' data using computers with SAS or equivalent software under supervision.	x	x	x
4 Gain skills in communicating results of research in abstract and presentation forms.	4 a. Write and submit at least two abstracts of trainees' work to regional/national meetings.	x	x	x
	b. Present research findings at a minimum of one Clinical Research Seminar or Departmental Research Conference.	x	x	x
	c. Present research results orally or as a poster at a minimum of one national scientific conference.	x	x	x
5 Acquire skills in writing and critiquing research manuscripts.	5 a. Critique at least one manuscript submitted to mentor or advisor for review.	x	x	x
	b. Publish at least two manuscripts in peer-reviewed journals within two years of training.	x	x	x
6 Develop abilities in writing and critiquing of research grant proposals.	6 a. Write at least one complete research grant suitable for submission.	x	x	x
	b. Critique at least one research grant and write-up comments for peer review.	x	x	x
7 Manage the fiscal, personnel, facilities and regulatory assets of a funded clinical research program.	7 Complete a Clinical Research Skills workshop on Research Project Management and receive a Research Project Administration Compliance Number.	x	x	x
8 Identify institutional resources needed to carry out high- quality research.	8 Use the Clinical Research Resource Inventory to identify and access collaborative resources available for clinical research.	x	x	x
Attitudes				
1 Appreciate ethical issues involved with research in human subjects.	1 a. Completion of Ethical Conduct of Research Workshop.	x	x	x
	b. Complete instruction on protection of human subjects in research to qualify for an HSPP number.	x	x	x
	c. Completion of IRB application and section in research grant application.	x	x	x
2 Understand the regulations and rationale for inclusion of women, minorities, and children research.	2 a. Completion of Clinical Research Skills Workshop on Recruitment and Retention of Research Subjects.		x	x
	b. Completion of section of research grant application on inclusiveness.	x	x	x
3 Comprehend the types of clinical research which offer career opportunities.	3 Completion of field visits to observe research in each of five types of clinical and translational research.	x	x	x
4 Appreciate the opportunities and challenges of multidisciplinary research involving two or more basic, clinical, or population sciences.	4 Inclusion of two or more disciplines as mentors or members of the MPH-CI Thesis Committee.	x	x	x
5 Understand the opportunities and obstacles to performing research within the private sector.	5 Completion of Clinical Research Skills Workshop on relations with industry and Technology Transfer/Working with Industry.	x	x	x

G2i6d. PhD Program in Translational Biomedical Research: Didactic Coursework. The PhD Program will, philosophically, seek to create the translational investigator with a broad theoretical and methodologic underpinning. This should enable the trainee to apply basic scientific observations to patient-oriented problems and to have the breadth of methodological skills to design, conduct, analyze, and interpret studies at the bench/bedside interface. The didactic coursework required for this breadth is essentially that required for both the MS-CI and MS-TR degrees (Tables G2i.3 and G2i.4). This yields a didactic curriculum requiring two years of coursework, but limited to 52 credits. The saving of 12 credit hours allows the trainee additional credits for laboratory rotations or initiation of the PhD thesis project before the end of the second year. **G2i7. Mentored Research Component**

G2i7a. Overview.

A research experience under the supervision of an experienced mentor will be a cornerstone of each Training Program (T32, K30, K12). However, the selection, direction, and intensity of the research experiences will differ between Programs and will be described only with each Program (See Section G). This section will describe a Mentor Development Program at URMC, the criteria for selection of 30 mentors representing multidisciplinary research clusters, and their evaluation.

G2i7b. A Program for Mentor Development at URMC.

In the Fall of 2004, Vivian Lewis, MD, Professor of OB/GYN, developed a web-based, anonymous survey of URMC faculty below the rank of Professor to describe the level of mentoring the faculty perceived as having. A total of 307 faculty (143 women, 164 men) completed the survey. Less than half of the faculty had an annual meeting with their mentor about scholarly productivity or grant applications. Only 43% of men and 53% of women identified a mentor, suggesting a need for a program to develop URMC mentors.

As part of the UR-CTSI, a Mentoring Committee will develop and implement a Mentor Development Program. The Committee will be chaired by Thomas A. Pearson, MD, MPH, PhD, and includes Donna Giles, PhD; Peter Szilagyi, MD, MPH; Vivian Lewis, MD; and Stephen Dewhurst, PhD, who not only are recognized as superb mentors in their own rights, but represent departments (Psychiatry, Pediatrics, OB-GYN, and Microbiology, respectively) with well-developed Mentoring Programs already in place. The overall objective of this Mentor Development Program is to improve and standardize the mentoring available to CTSI Scholars.

Table G2i.5: Thirty Multidisciplinary Research Clusters at the University of Rochester

Cluster	No. of Mentors	No. of Preceptors	Disciplines Represented	Representative Mentor
Antiviral Immune Responses	3	4	Epidemiology; Immunology; Infectious Disease; Microbiology; Neonatology; Virology	Dewhurst, Stephen
Antiviral Therapy	4	4	Biochemistry; Infectious Disease; Molecular Biology	Treanor, John
Arthritis	5	4	Biomedical Engineering; Immunology; Orthopoedics; Orthopoedics; Radiology; Rheumatology	Rosier, Randy
Autoimmunity	4	2	Immunology; Immunology; Microbiology; Neurology; Oncology; Rheumatology	Mosmann, Tim
Biomedical Imaging	5	3	Bioengineering; Physics; Physics; Physics; Radiation Oncology; Radiology	Yu, Yan
Biomedical Informatics	2	1	Biomedical Informatics; Biostatistics; Medical Informatics	Wu, Hulin
Biomedical Optics in Ophthalmology	3	4	Cognitive Science; Computer Science; Ophthalmology; Optics; Psychology	Yoon, Geun-Young
Bone Biology	5	1	Biomedical Engineering; Biophysics; Endocrinology; Epidemiology; Orthopoedics; Pathology	O'Keefe, Regis
Cancer Control and Prevention	4	-	Behavioral Science; Dermatology; Epidemiology; Psychology	Fisher, Susan
Cardiovascular Clinical Trials	3	4	Biostatistics; Cardiology; Epidemiology; Health Services Research; Laboratory Medicine; Pharmacology; Physiology	Moss, Arthur
Center for the Study and Prevention of Suicide	3	1	Anthropology; Epidemiology; Psychiatry; Psychology	Conwell, Yeates
Childhood Asthma Prevention	2	3	Biomedical Engineering; Environmental Medicine; Health Services Research; Neonatology; Pediatrics	Szilagyi, Peter
Clinical Trials in Neurology	2	1	Neurology; Biostatistics	Shoulson, Ira
Healthcare Communication/Telemedicine	6	3	Dermatology; Family Medicine; Health Services Research; Nursing; Pediatrics;	Pentland, Alice
Healthcare Disparities	3	-	Cardiology; Epidemiology; Family Medicine; Health Services Research; Pediatrics	Fiscella, Kevin
Hematologic Malignancies	5	7	Biostatistics; Cytogenics; Epidemiology; Hematology; Hematopathology; Molecular Biology; Molecular Pathology; Oncology; Pathology	Fisher, Richard
Liver Biology and Hepatitis	3	2	Immunology ; Pathology; Surgery; Toxicology	Topham, David
Metabolic Syndromes	3	4	Cardiology; Endocrinology; Epidemiology; Health Economics; Obstetrics and Gynecology; Oncology; Pathology; Pharmacology; Physiology	Gerich, John
Mitochondrial Research	10	6	Anesthesiology; Biochemistry; Biology; Cardiology; Genetic Engineering; Genetics; Molecular Biology; Neurobiology; Neurology; Pathology; Pharmacology; Physiology; Pulmonology	Gross, Robert
Neurodegenerative Diseases	4	1	Biochemistry; Molecular Biology; Neurobiology; Neurology; Neurosurgery	Griggs, Robert
Neuromuscular Diseases	3	3	Biostatistics; Endocrinology; Neurology; Pharmacology; Physiology; Psychiatry	Moxley, Richard
Oral Infectious Disease and Clinical Trials	2	2	Dentistry; Health Services Research	Billings, Ron
Presbycusis	3	3	Bioengineering; Biology; Informatics; Neurobiology; Neuroscience; Otolaryngology; Psychology	Frisina, Robert
Preventive Cardiology	5	5	Behavioral Science; Cardiology; Epidemiology; Health Services Research; Hematology; Neurology; Pathology	Pearson, Thomas
Respiratory Infections	6	2	Infectious Disease; Microbiology; Pediatric Infectious Disease; Pediatric Pulmonology; Toxicology	Iglewski, Barbara
Sensory Integration and Plasticity	5	9	Bioengineering; Biomedical Engineering; Cognitive Science; Neurobiology; Neurophysiology ; Neuroscience; Physics; Visual Science	Paige, Gary
Traumatic Brain Injury	2	3	Cognitive Science; Emergency Medicine; Health Services Research; Neurology; Surgery	Bazarian, Jeffrey
Ultrafine Particles and Nanobiology	3	2	Chemical Engineering; Neonatology; Pulmonology; Toxicology	Frampton, Mark
Vaccine Development and Testing	7	2	Immunology ; Infectious Disease; Microbiology; Pediatric Infectious Disease; Virology	Reichman, Richard
Vascular Biology	6	5	Biochemistry; Biomedical Engineering; Biophysics; Cardiology; Functional Genomics; Hematology; Molecular Biology; Physiology; Vascular Surgery	Taubman, Mark

Proposed here is a two-part Mentor Development Program. The first part entails a didactic portion available online on our Intranet describing the components and development of a successful mentor-mentee relationship, including the roles and responsibilities of the mentor and the roles and responsibilities of the mentee. The second part will be a Research Career Development Plan (RCDP) as a joint effort of the mentor and mentee. This would be similar to "mentoring contracts" or other agreements used in some institutions. The Research Career Development Plan will include: the CTR Scholar's career development goals and objectives; the CTR Scholar's curriculum vitae; a critical self-appraisal by the Scholar of his/her training needs; description of how the mentor or a mentorial committee meets the mentee's needs and their role in meeting those needs; a two or more year plan of activities in clinical care, teaching, didactic coursework, other training, and skill development; overall research plan; and advice regarding growth within their institution and profession. It is hoped that by developing the RCDP, the mentor will also identify areas in which he or she might improve their own mentoring skills. The RCDP will be required of all incoming CT Scholars and their mentors. The Key Function Directorate and Mentoring Committee will request and review the RCDP at the initiation of the mentorship. At the end of Year I and Year II, progress being made by each mentor-mentee relationship will be monitored; poorly performing mentors may be recommended for replacement by the Mentoring Committee.

G217c. Organization of Multidisciplinary Research Teams, Mentors, and Preceptors.

In preparation for this award, each Department Chair and Center Director whose unit conducted clinical research was visited by Program Leadership to describe the Program. The clinical and translational research activities of their units were reviewed, including involvement of fellows or faculty in the K30 Program, and the acquisition of K,R, T or other training/career development awards by departmental faculty. The Chairs and Center Directors were then invited to nominate clusters of researchers from within or outside of their departments who work on a multidisciplinary area of research. This generated more than 65 potential research clusters which were then reviewed by the Key Function Director and reduced to 30 to emphasize translational research.

A "Multidisciplinary Research Cluster" is defined as an area of research at URMC in which there are at least two mentors (see definition below), preferably from different disciplines or departments. The multidisciplinary research cluster is envisioned as a research team which would provide the CTSI Scholar with excellent mentoring, access to ongoing research during short-term research experiences, and collegial and material support for their clinical research project. A mentor is required to be an established investigator from either clinical, translational or basic research disciplines who has: 1) federally-funded research support and an active program of investigation, and 2) a track record of supervision and mentoring of students, fellows, or junior faculty. A number of promising, more junior faculty in these research clusters did not have both of these criteria. These junior faculty are included as members of the research clusters and are designated as preceptors. These preceptors are considered to be our mentors of the future, and will be encouraged to participate in the Mentor Development Program and to serve on the CTR Scholars Mentorial Committee as a preceptor.

Table G2i.5 provides a brief overview of the 30 mentors representing each of 30 research clusters identified as research teams with at least two mentors and resources which would facilitate the career development of a CTR Scholar (See Tables G5D1-3 for descriptions of each mentor and their research). In turn, the CTSI Scholar may activate the cluster by bringing these multidisciplinary individuals together to focus on the Scholar's specific project. This large and talented group of investigators underscores the adequacy of the URMC faculty to support the CTSI with multidisciplinary translational research teams performing cutting-edge research. The Directorate and Admissions and Recruitment Core will serve to link interested CTSI Scholars with these clusters. It is expected that their organization and description on the CTSI website will facilitate linkage of Scholars and mentors/clusters.

G2i7d. Evaluation of Mentors.

A member of the Mentor Development Committee will be assigned to each trainee of a CTSI T32, K30, or K12 Program and will meet with them at least two times a year. One of these meetings will include the mentor. The trainee will complete a form which reviews performance toward their Research Career Development Plan, and includes the trainee's evaluation of their mentor. These reports will be brought to the Mentorial Committee and, if any deficiencies are identified, the Key Function Director or other Mentor Development Committee members will meet with the mentor. If deficiencies persist, the Scholar may need to identify another mentor.

G2i7e. Skill-Building Workshops. (See also Table G2i.4 and Section G2i.4).

A two-year long sequence of skill-building workshops and seminars is provided. The workshops are generally scheduled each week at times convenient for those with laboratory or clinical responsibilities (e.g. 4-6 PM). They provide instruction in several of the CTSA Key Functions.

a. "Introduction to Clinical Research." Instructor: T. Pearson, MD, MPH, PhD. (July, Year I) This series constitutes three two-hour seminars which introduce the CTSI Scholar to clinical and translational research in the CTSI.

b. "Ethics in Research" (IND 501). Course Director: S. Trafton, JD. This eight-week workshop is required of all postdoctoral research trainees at the University of Rochester. This course covers a broad range of topics and issues related to professional standards of conduct, including: human subjects in research, animal subjects in research, conflict of interest, academic honesty and misconduct in scholarship, data management, responsible authorship and intellectual property. Two small group sessions are convened for face-to-face discussion of this important material. This workshop should be completed by the beginning of Semester 1 in Year I, and is the initiation of the Scholar to Instruction on the Responsible Conduct of Research. (See Section B.5.f for entire Plan).

c. "Workshop on Recruitment and Retention of Research Subjects." Instructor: A. Dozier, RN, PhD. (Semester 1). This fourteen week workshop is designed to follow the Ethics in Research workshop and focuses on strategies to recruit and retain subjects known to be "hard to recruit", such as individuals from disenfranchised communities, the elderly, etc. This workshop is part of the Scholar's Instruction on the Responsible Conduct of Research.

d. "Workshop in Technology Transfer/Working with Industry." Instructor: Marjorie Hunter, JD, Director of the Office of Technology Transfer. (Semester 1). This workshop's overall goals are to introduce trainees and faculty to the relationships between the university-based research and private industry, including intellectual property issues. This 11-week workshop prepares the university-based researcher for productive interactions with industry.

e. "Workshop in Scientific Communication." Instructor: Pat Braus, MPH (Semester 2). This workshop series addresses the principal elements of scientific presentation and communication such as: abstract preparation, poster development, PowerPoint instruction, manuscript review and critique, oral presentations, working with the media/public relations

f. "Practical Skills in Grant Writing" (PM438). Instructor: T. Pearson, MD, MPH, PhD. (Semester 2) This 16-week workshop instructs the trainee in the types and sources of research support, the procedures by which applications are reviewed, the structure of a research proposal, clear organization and communication of research ideas, development of budgets and resources, and the critique of a proposal. Scholars will write a research grant application for NIH electronic submission with the assistance of their research mentors.

g. "Workshop on Research Program Administration." Instructors: G. Liders and S. Griffin-Roth (Semester 2, Year II). Federal Agencies are increasingly asking for instruction to assure compliance with federal regulations regarding clinical research and use of federal funds. A new Workshop is planned to 1) educate and certify CTSI Scholars as to their knowledge of federal regulations regarding research and 2) provide practical skills regarding the post-award management of the financial, human resources, facilities, and regulatory aspects of a federally-funded research project. This program will be available on-line on a web portal. At the successful completion of this Workshop, each Scholar will be certified in Research Project Administration Compliance (RPAC).

h. "Workshop on Community Participatory Research." Instructors: Nancy Bennett, MD and Noelle Andrus, PhD (Semester I, Year II). This Workshop will be developed by the Community Engagement Key Function and will educate CTSI Scholars how to constructively interface with their target committees. This will include topics of community organization, mobilization, cultural competency, etc.

i. "Workshop on Academic Development." Instructors: Peter Szilagyi, MD, MPH, Vivian Lewis, MD, and Timothy Dye, PhD (Summer before Year 2). This new workshop will discuss a range of topics helpful in development of an academic career. Major areas of emphasis will include being an effective teacher and enrollment in the Mentor Development Program.

G2i7f. Clinical Research Seminar Series and Clinical Research Scholar's Dinner Meeting.

The Clinical Research Seminar has been successful with excellent attendance on Tuesdays from 12:15 to 1:30 PM for approximately 36 weeks per year. Eminent clinical researchers from within the University as well as from U.S. and International institutions will present. Over the course of a year, this seminar provides

CTSI Scholars with a broad exposure to clinical research topics and role models. CTSI Scholars are expected to attend one other seminar in their specialty.

Courses, workshops, and seminars are open to the entire University community and are not especially developed for CTSI Scholars. Funds have been requested to convene a dinner meeting six times a year for all CTSI Scholars in T32, K30, and K12 Programs and their mentors as well as Key Function Directors. This will serve to make the group cohesive and interactive to promote multidisciplinary research.

G2i7g. Instruction in Responsible Conduct of Research.

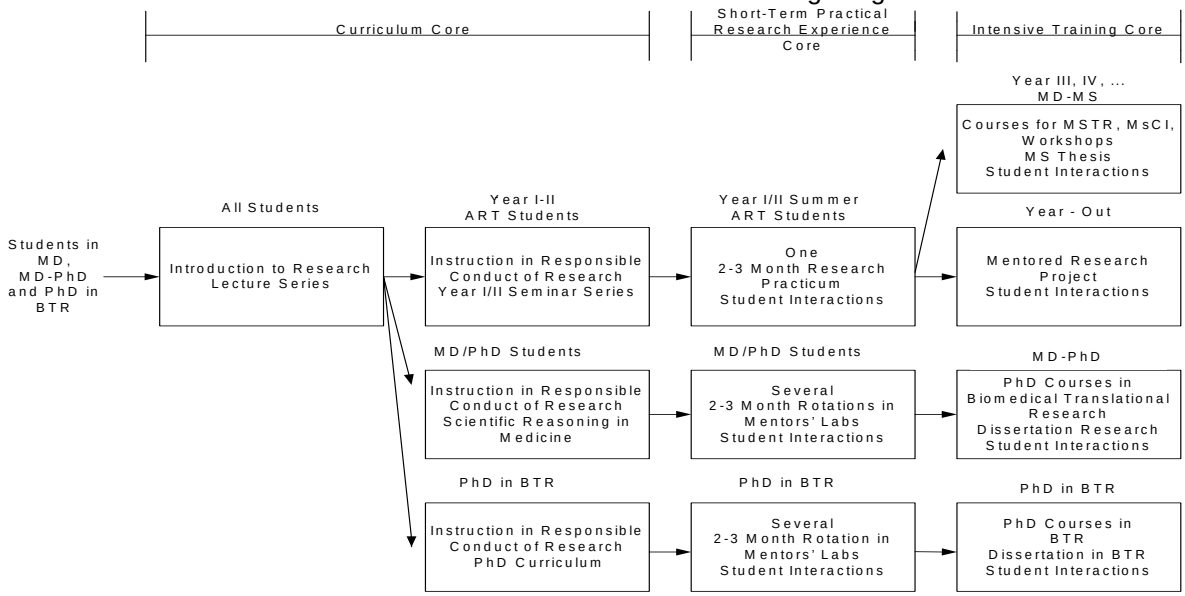
Currently, all research trainees, including CTR Scholars at the University of Rochester, are required to complete and pass the eight week on-line workshop: "Ethics in Research" (See G2i7b). This course is considered a minimum requirement for this broad and important topic. Several enhancements will be required. First, regarding ethical treatment of research subjects, all CTSI Scholars will complete the on-line course: "Protection of Human Subjects in Research" and receive their Human Subjects Protection Program (HSPP) number, as required to direct a study involving human subjects. A second Workshop: "Recruitment and Retention of Research Subjects" will be required, again dealing with research ethics in studies involving human subjects. Third, the RCRC Workshop: "Research Program Administration" has several components specifically dealing with compliance with ethical standards in research, conflict of interest, etc. CR Scholars must complete the program and receive a Research Program Administration Compliance Certification. Finally, the first Clinical Research Seminar of each month is given by the Office of Human Subjects Protection to update attendees as to new ethical and regulatory issues in clinical research.

G2i8. Training Programs

G218a. Predoctoral (T32) Training Program in Clinical and Translational Research.

1) Overview of Predoctoral Clinical Research Program. This section will describe the opportunities for students to be introduced to clinical research and then to proceed to progressively more intensive instruction in the principles and methods of clinical research. Figure G2i.5 illustrates the modules to be described in this Section. For each module, the number of students supported by the CTSI will be noted.

Figure G2i.5: Overview of the Rochester Predoctoral Clinical Research Training Program.



2) The Curriculum Core for Predoctoral Students.

(a) Introductory Lecture Series (10-11 students per year).

The Curriculum Core will include a series of six introductory lectures describing research and research opportunities at URMC to be presented in the first four weeks of Medical School. This serves as a recruitment strategy for students into the T32 Program. All Year I MD, MD/PhD and PhD students would be invited to attend; students pursuing the Academic Research Track (see below) would be required to attend. The six, one-hour lectures (with discussion time) would kick off with a review of the Student Research Handbook in a lecture entitled: "Hypothesis-driven Research," given by Dr. Pearson. The next five lectures, in a noon

luncheon format, would introduce students to five general areas of research: basic science, translational research, patient-oriented research (experimental therapeutics, epidemiology) health services research, and educational research. Seminar presenters would be URMC leaders in their respective areas of research. The intent is to broaden the students' perspectives so that they can choose from the entire range of basic, translational and clinical research ongoing at the URMC.

(b) Academic Research Track (ART) Core Curriculum (10-11 students per year).

For students enrolling in the ART Curriculum, separate curricula will be provided in Year I and in Year II. The purpose is to provide a broad exposure to research topics as a means to enrich their core curriculum, especially building on topics introduced in the Double Helix Curriculum. In each year, ART faculty will develop three modules relevant to research career development (Table G2i.6). Each module will include 2-4 lectures, so that each year will have one ART seminar per month, or 10 seminars per academic year. Guest lecturers from outside URMC will present one lecture per semester on a related topic. Topics include leadership of a research team, finding a mentor, grant writing, and ethics. These seminars will also be open to MD-PhD and PhD in Biomedical Translational Research students.

Table G2i.6: Modules for Academic Research Track Seminars in Year I and in Year II of Medical School

Topic	Coordinator
Year I	
Being Mentored, Being a Mentor, Leading a Research Term	Ronald Epstein, MD, Professor of Family Medicine
Formulating a Research Question, Research Models, and Conceptualization	Kathleen Hoeger, MD, Associate Professor of OB/GYN
Measures and Analysis of Samples in Clinical Research	Jeffrey Lyness, MD, Associate Professor of Psychiatry
Year II	
Ethical Issues in Research	Kerry O'Banion, MD, PhD, Assoc. Professor of Neurobiology and Anatomy
Data Analysis and Presentation	Craig Mullen, MD, PhD, Professor of Pediatrics
Acquisition of Support for Research: Sources and Process	Thomas Pearson, MD, MPH, PhD, Professor of Community and Preventive Medicine
Student Presentations of Proposals for Year-Out Projects	Robert Gross, MD, PhD, Professor of Neurology

(c) MD-PhD Program: Year I/II Program (3-4 students per year)

MD-PhD students have the opportunity to complete their requirements for training in the Responsible Conduct of Research, similar to ART students. The ART Year I-II Seminar Series is also available to MD-PhD students.

All MD/PhD students participate in an additional class, "Scientific Reasoning in Medicine (SRM)", that meets for eight sessions each semester. The format for these sessions is a faculty presentation at noon on Friday followed by a student-run journal club the following Monday at noon. Faculty are chosen from all disciplines within URMC and are asked to present on research issues with clear clinical relevance. The journal club provides a forum for critical evaluation of primary scientific literature related to the research topic. Dr. O'Banion, Director of the MD-PhD Program, organizes this course and attends most sessions. SRM is also required of students in the second year of the program. Thus MD-PhD students are introduced to the science of more than 30 faculty in their first two years, including clinical research. Other opportunities to learn about faculty research interests include departmental seminars, MD-PhD organized seminars, interactions with faculty who teach in the medical curriculum, and student-initiated meetings with graduate program advisors and individual faculty.

3) Short-term Practical Research Experience Core (all T32 students, 50+ students per year).

(a) Overview.

All predoctoral students, including those MD students in the Academic Research Track and the MD/PhD Program as well as students in the PhD in Translational Biomedical Science Program, have the summer between Year I and II free of coursework. Most short-term experiences will occur then, but several may be taken at any point in graduate school. All students are encouraged to participate in at least one research elective. MD/PhD students are expected to participate in a "laboratory rotation" in the area in which their PhD degree would be obtained.

(b) Goals of the Short-term Practical Research Experiences.

The establishment of goals for the Short-term Practical Research Experience allows these rotations to be designed more formally, effectively, and specifically for clinical and translational research projects. The goals for the Short-term Practical Clinical Research Experience are:

(1) To encourage the predoctoral student to concentrate on a disease, diagnostic test, therapy, etc. in contrast to the more superficial coverage in an MD curriculum.

(2) To join a research team to appreciate the roles and contributions of the multidisciplinary members of the team.

(3) To develop a Research Mentoring Plan with an experienced research mentor who can serve as teacher, advisor and role model.

(4) To understand the organization and content of a research protocol for purposes of conducting a clinical research study.

(5) To participate in more than one phase of the clinical research project (e.g. subject recruitment, data collection, intervention, data analysis, etc.).

(6) To develop a proposal to address a research question and complete the project within or shortly after the time-frame of the experience. The research project should have scope and feasibility such that it can be completed shortly after the end of the rotation.

(7) To consider the research team or the research question for pursuance in an intensive clinical research training program (e.g. Year-out, Master's degree or PhD).

(c) Implementation of Short-term Practical Research Experience Core.

Students will usually be enrolled in one of the three programs shown on Figure G2i.5 (ART, MD-PhD, PhD in TBS) These students would be expected to have participated in the curriculum core, ART or SRM courses, and the Responsible Conduct of Research/HSPP training. It is proposed that first priority for funded short-term preceptorships be given to students who have completed these preparatory courses and seminars. However, if a preceptorship is still available, students who have not been in one of these programs can be accepted as a means of encouraging their enrollment in one of the programs.

Once the practical research experience has commenced, the student should participate as a member of the research team. He/she should have access to the clinical research protocol and should be able to participate in at least two different facets of the project (e.g. laboratory analysis, recruitment, data collection, endpoint assessment, data analysis). The student should have an approved proposal which can be carried out during the two month period. Often, this will entail one aspect of a larger study which can be carried out for completion by the student. The mentor should monitor the student's progress to assure completion of the project. Some projects may constitute pilot studies for a Year-Out Project, Master's Thesis or PhD Dissertation.

(4) Integration and Interaction between Students in Short-term Research Experiences.

Students will be encouraged to integrate fully into the departments and centers for the duration of the eight-week experience. This includes Seminar Series, Journal Clubs, Visiting Professor Lectures, etc. Some students may attend regional or national conferences related to their research. Their emphasis will be on their membership in a research team.

Nonetheless, interactions between the students enrolled in the 8-week experience will be encouraged by get-togethers with Administrative Core members during the course of the experience. Proposed are seminars every two weeks, including an introductory session with students and mentors in which the mentor will present a brief description of the research team and the student will describe the proposed project. At the end of the 8-week period, students will be asked to prepare and submit a written report of their research experience to the Administrative Core, and to complete an evaluation form for the short-term experience.

Students will be encouraged to write up their projects for submission as abstracts for presentation at scientific meetings or for publication in a peer-reviewed journal. Students will be expected to present their work at the annual Medical Student Research Poster Day.

d. Intensive Training Core.

To meet the needs of the students, four options are available for intensive training in clinical research: 1) Masters Track; 2) Year-Out Program for MD students, and 3) MD/PhD Program in conjunction with the MSTP Program, and 4) PhD Program in TBR. A total of 8-11 students will participate in the Master's or Year-Out Programs per year. An additional 1-4 students will be supported in the MD/PhD Program and 1-4 students in the PhD in TBR (See Budget Justification for number of students in each program).

(1) MD-MS Track

Students can enroll in either the MS in Clinical Investigation or MS in Translational Research Programs (See Tables G2i.2 and G2i.3) for objectives, competencies, and courses). Students would also participate in Skill-Building Workshops and Clinical/Translational Research Seminars. A scholarly project (thesis) is required, entailing the identification of a research mentor and, under that faculty member's supervision, the completion of the project. A committee of three faculty would approve the thesis project prior to initiation and sign-off on the thesis/scholarly work.

(2) Non-degree Clinical Research Program for One Year (Year-Out) Program.

(a) Overview.

Medical students in the Academic Research Track may choose to spend one academic year as part of a clinical research team as their intensive training component. This has been especially popular among medical students interested in an in-depth experience in a subspecialty area, in preparation for residency training in highly competitive postgraduate programs.

(b) Goals of Non-degree Programs for One Year

Design of effective programs as well as recruitment and selection of students for stipends necessitates the establishment of goals for this Year-Out Program. The following goals are proposed:

(1) To provide the opportunity for the medical student to delve deeply into a clinical research question, disease process, etc.
(2) To contribute to a research team with defined role and expectations of performance.
(3) To establish a Research Mentoring Plan with a mentor in the setting of a clinical research project.
(4) To develop a more extensive research proposal/protocol and carry out the proposed work within the one-year time-frame. This proposal should entail most phases of a research project (e.g. subject recruitment, data collection, endpoint assessment, analysis, etc).
(5) To present results in a departmental research conference and in a conference for the Predoctoral Clinical Research Training Program.
(6) To present results in at least one regional or national clinical research conference.
(7) To write a manuscript related to the research project of quality publishable in a peer-reviewed journal.
(8) To prepare a written progress report of the Year-Out Program and its accomplishments.

Students in the ART Program should consider mentors and research teams for a Year-Out Program during the Short-term Practical Research Experience and during the Year II phase of the ART Seminar Series. The last series of seminars in Year II entails student presentations of proposals for their Year-Out or Master's Programs. This proposal should be the product of mentor-mentee discussions, with clear expectations of a timeline and productivity outcomes. The ART Program Executive Committee reviews and recommends these proposals to the Predoctoral Program Director so the student can plan the Year-Out effectively and count on stipend support. Additional preparations may include submission to the Institutional Review Board and identification of research resources prior to the initiation of the Year-Out.

The didactic programs in the Rochester Clinical Research Program would be available for the student. Of particular use to the student may be the Skill-Building Workshops in the RCRC, such as "Recruitment and Retention of Research Subjects," "Scientific Communication," "Technology Transfer/Working with Industry," "Research Program Administration," and "Practical Skills in Grant Writing." All students are expected to attend the weekly Clinical Research Seminar. Students should attend at least one national scientific meeting in their area of science during the year.

The 3-6 students enrolled in the Year-Out Program will be encouraged to participate in the teaching of more junior students. Potential opportunities would be as tutors of Year I students, presenters/discussants during the Year I/II ART Seminar Series, and presenters during the Short-term Practical Research Seminars held in the summer. A roughly monthly group meeting of Year-Out students is proposed to assure progress. At the end of the Year-Out Program, students will be convened and each will present a 15-20 minute synopsis of their research and its findings to the other students and the faculty. Students would be encouraged to present their work at the annual Medical Student Research Poster Day.

(3) MD-PhD Programs: Medical Scientist Training Program in Clinical Research

(a) Overview

The Medical Scientist Training Program (MSTP) at the University of Rochester has recently been expanded by Dean Guzick to support up to eight MD-PhD students per year. Most of these students are not supported by funds from the NIH MSTP grant, but from institutional funds. The purpose of the MD-PhD Program in Clinical and Translational Research therefore is to support at least one student per year to complete requirements for a PhD degree in Translational Biomedical Research. This would require a dissertation involving patient-oriented research conducted with human subjects or on tissues of human origin which the student directly interacts with and is linked to human subjects. An overview of the Program is shown on Table G2i.2.

(b) Didactic Coursework for PhD in Translational Biomedical Science

The MD-PhD statement would complete the one and one-half year of courses required for the PhD in TBS (Tables G2i.3, G2i.4). This should leave opportunities for several short-term research experiences.

(c) Implementation of MD-PhD Programs in Translational Biomedical Science.

The seven- (or eight-year) program leading to MD and PhD degrees is shown on Table G2i.6. A short-term research experience in the department in which the PhD degree is sought occupies the summers before Year I and Year II. The "Scientific Reasoning in Medicine" and other MD-PhD Program events are limited to MD-PhD students. Also, students are encouraged, but not required, to participate in their PhD departmental seminars in Years I and II. MD-PhD students with interest in dissertation research involving interaction with human subjects will be identified for support at this point. PhD coursework occupies Years III and IV with requirements varying by PhD program. Also required are four semesters of Longitudinal Clinical Elective, half day per week, usually performed during Years III and IV. A qualifying examination is required following PhD coursework, but prior to initiation of dissertation research. Dissertation research may be initiated in Year IV, V, and VI, culminating with a dissertation thesis defense. Additional clinical experience can be arranged with consent of the MD-PhD Program Director for Years IV-VI. MD-PhD Program events (retreats, seminars, dinners) require participation throughout Years III-VI. Years VI-VII (or VII-VIII) entail return to the MD curriculum but with continued participation in MD-PhD Program events.

d. PhD Program in Translational Biomedical Science.

The trainee matriculating into the PhD Program in TBS will complete 1.5 years of coursework (See Tables G2i.3, G2i.4) and several short-term research experiences in Years I and II (64 credits). A qualifying examination must be passed at the end of Year II. Years III-V (if needed) would be carried out in his/her mentor's laboratory. A multidisciplinary thesis committee will judge the merits of the thesis. The PhD student would be expected to participate in Skill-building Workshops, the Clinical/Translational Research Seminar, seminars in the department of his/her mentor, etc.

Table G2i.6: MD/PhD Program in Translational Biomedical Science: Timeline

Year	Summer	Fall Semester	Spring Semester
I.		MD Curriculum Scientific Reasoning in Medicine ART Seminars (optional) Departmental Seminars (optional)	MD Curriculum Scientific Reasoning in Medicine ART Seminars (optional) Departmental Seminars (optional
II.	Short-term Research Experience	MD Curriculum Scientific Reasoning in Medicine ART Seminars (optional) Departmental Seminars (optional)	MD Curriculum Scientific Reasoning in Medicine ART Seminars (optional) Departmental Seminars (optional)
III. *	Pathways to Disease Course	PhD Coursework Departmental Seminars (required) MD/PhD Program Events Longitudinal Clinical Experience Clinical Research Seminar	PhD Coursework Departmental Seminars (required) MD/PhD Program Events Longitudinal Clinical Experience Clinical Research Seminar
IV. *	Short-term Research Experience	PhD Coursework Departmental Seminars MD/PhD Program Events Longitudinal Clinical Experience Clinical Research Seminar Research Experience	PhD Coursework Departmental Seminars MD/PhD Program Events Longitudinal Clinical Experience Clinical Research Seminars Research Experience Qualifying Examination Dissertation Research
V. *	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Program Events	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Programs Events	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Program Events
VI. * (if needed)	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Program Events	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Program Events	Dissertation in Patient-Oriented Research Longitudinal Clinical Elective MD/PhD Program Events Thesis Defense
VII.	MD Curriculum Clinical Clerkships MD/PhD Program Events	MD Curriculum Clinical Clerkships MD/PhD Program Events	MD Curriculum Clinical Clerkships MD/PhD Program Events
VIII.	MD Curriculum Clinical Electives MD/PhD Program Events	MD/Curriculum Clinical Electives MD/PhD Program Events	MD Curriculum Clinical Electives MD/PhD Program Events

2. Clinical/Translational Research Curriculum (K30) Program

The K30 Program is described in Section C2iC4 and will retain many of its current features (e.g. Skill-Building Workshops, Clinical/Translational Seminar Series). Major revisions in the didactic content have been made, however, with new efficiency for students in selecting career tracks of specific interest, such as the MPH (for population/health services/ethical policy interests) (see Figure G2i.3), MSCI (for experimental therapeutics and clinical trial interests), and MSTR (for translational research interests) (Tables G2i.3, G2i.4). Each Program would entail two years of didactic coursework, skill-building workshops, seminars, and mentored research in their respective programs. Each would require scholarly work worthy of publication in a peer-reviewed journal as judged by a Committee of three faculty.

3. Clinical/Translational Research Curriculum Development Program (K12)

a. Overview

The K12 Program will entail 3-5 years of training in which a fellow/junior faculty member would complete their didactic coursework, including that required for MPH, MSCI, MSTR, or PhD in TBS, participate in the series of Skill-Building Workshops, and weekly seminar series, develop and implement a translational research program, and emerge as an independently-funded investigator. This section will identify the educational modules (previously detailed) that would constitute a K12 Program. Emphasis is placed on flexibility of modules to meet scheduling needs while maintaining rigor in educational requirements. Each year, 2-3 new CTSI Scholars would enter the K12 Program.

b. Didactic Coursework

The CTSI Scholar could elect to pursue MSTR, MSCI, and MPH degrees, as detailed in Tables G2i.3, G2i.4. In addition the student could enroll in the PhD-TBS Program for completion during their five-year program (Table G2i.3, G2i.4).

c. Skill-Building Workshops and Clinical Translational Research Seminars

These components of the Rochester Clinical/Translational Research Curriculum will be required of K12 scholars.

d. Research Experience

(1) Practicum Research Experience (Year II).

The CTSI Scholars will initiate planning for a one-year research experience during their first year of training. The CTSI Scholar should have selected his/her primary mentor by mid year and have at least two co-mentors approved by the Mentor Development Committee. Therefore, the CTSI Scholars should have met with their mentors throughout the second semester of the first year to map out a practicum research experience, a Research Mentoring Plan, and an individual Career Development Plan. The Practicum would be done at the laboratory of their mentors.

The short-term research experience is envisioned to be one of two types of projects. First, the CTSI Scholar may wish to join a research cluster (usually that of the mentor) and identify a research question of limited scope that can be completed within the one-year practicum phase. Typically, these would entail active involvement as part of the research team in data collection and analysis as a co-investigator. One circumscribed aspect of the research would be identified, such as data collection or analysis from specific subgroups, application of new assays to existing specimen repositories, or statistical analyses of the research team's already collected data to address a new question. The goals of this experience would be to work as a research team member, observe the function of such a team, develop a hypothesis-driven protocol, gain experience in data collection and patient accrual, plan and carry out a data analysis, prepare Human Subjects Protection forms, and write up results worthy of presentation and publication.

A second practicum experience may be the joining of an ongoing research project or research team for the purpose of collection of pilot data in preparation for the Research Project. This experience would entail the earlier development of hypothesis and methods for the Research Project, which would then identify specific needs for pilot data. The outcomes of this practicum experience would be a well-prepared preliminary results section within the Research Project proposal. It should provide the CTSI Scholar with experience in protocol development, preparation of Human Subjects Protection forms, recruitment and data collection involving research subjects, and planning and carrying out data analysis.

The Scholar will submit his/her practicum clinical research experience plan to the key function director by April 15. A form to standardize the plan's content will be developed. It will be reviewed by the Director/Co-Director for completeness or need for further data. If complete, it will be submitted to two

Directorate members for their review and will be discussed in the next Directorate meeting, usually within 2-4 weeks. If found inadequate, the Scholar will need to respond to criticism and revise the plan. If acceptable, the Scholar will be expected to implement the plan immediately at the beginning of Year II. Most of the time of Year II is devoted to this practicum research experience. At the end of Year II (approximately June 1), the Scholar will submit a report outlining performance on the practicum experience. We propose to use a form to identify specific research methods and skills learned, as well as provide the opportunity for the Scholar to describe his/her activities. Presentations and publications resulting from this year will be identified.

(2) Research Project (Years III-V).

During Year II, the CTSI Scholar works with two or more mentors using a Research Mentoring Plan, has relatively little didactic coursework, and is engaged in an ongoing research project within an active research team. Moreover, one of the didactic experiences during this year is the workshop: "Practical Skills in Grant Writing," which is convened in January of Year II and ends in mid May, with the workshop requiring a completed grant application with budget, background and significance, pilot studies, research plan, IRB application, etc. Each application is reviewed in the workshop by three faculty and one peer. This then is the ideal time for the Scholar to convene a mentorial committee to assist him/her in the development of a Research Project protocol. The Scholar will develop the protocol throughout Year II and complete it by the end of the grant writing workshop. It should be approved by his Mentorial Committee, especially the primary and secondary mentors, prior to submission to the Directorate.

The Directorate will assign two reviewers for the grant application, who will submit their written critiques to the Program Director and who will present the project to the entire Directorate. The Directorate may approve or disapprove the application; disapproved applications will require revision and resubmission.

A Mentoring Committee member will be assigned to each Scholar to monitor progress of the Research Project. This entails meetings every three months or so. The CTSI Scholar, mentor, Program Director or Co-Director, and monitor will meet with the Scholar at the end of each year of support. Prior to this, a written progress report should be available for review. The Scholar's Progress Report and the notes from this meeting will be presented to the Directorate and will be signed off prior to sending the Progress Report to the NIH Program Office. Problems with progress will be identified and addressed. Evidence of inadequate progress toward project aims may entail a vote of inadequate progress, resulting in a probationary review at three months. If not corrected, the Directorate may terminate the Scholar's support.

The CTSI Scholar, mentor, Program Director or Co-Director, and faculty monitor may consider, after 1-2 years of the Project, that the Scholar can "graduate" from the Program. This may be due to completion of the Research Project, acquisition of independent funding, change in career plans, or other reasons. They will review a report from the Scholar identifying the intent to complete the program, and the Directorate can accept or reject this request.

e. Availability and Recruitment of CTSI Scholars.

(1.) Pool of Potential Applicants at the University of Rochester.

Experience during the Rochester Clinical Research Curriculum (K30) Program has shown that applicants originate from two sources: postdoctoral fellows in clinical training programs and junior faculty members early in their academic careers. In both instances, the RCRC has become an asset in recruiting trainees and junior faculty from outside the Medical Center to the University of Rochester. While most candidates appear to be from within the URMC, many of their recruitments actually entailed an offer to pursue an MPH-CI degree and enroll in the K30 Program as an important factor in their decision to come to the University of Rochester. The enrollment of a sizable number (20) of Scholars per year in the RCRC is facilitated by the ability of fellows and faculty to take two courses per semester tuition-free, with tuition paid from the URMC benefits pool. Despite this advantage, a number of highly qualified potential Scholars each year elect not to pursue the K30 Program, often due to lack of salary or tuition support. These candidates would directly benefit from the CTSI K12 Program.

The URMC has a large pool of trainees from which to draw. A total of 656 house officers train in 75 Programs in 17 clinical departments. These departments also have 48 Senior Instructors and 218 Assistant Professors. Thus, a total of over 800 persons are potentially eligible for the K12 Program. While it is realized that many house officers and fellows have no intention to pursue a research career, this identifies a huge pool from which to recruit and select two or three CR Scholars per year. The CTSI will be advertised to these potential participants at the initiation of their faculty appointment, and to their Chairs/Center Directors. Another successful strategy has been the integration of the Clinical Research Curriculum as part of funded institutional

training programs. The University of Rochester currently lists 38 Training Programs including 33 T32 training grants and 6 other grants (K12, R25) (Table G2C12). The T32 training grants support 111 predoctoral and 95 postdoctoral trainees. Finally, a number of RCRC Scholars are participating by virtue of their successful acquisition of NIH Mentored Career Development Awards (K01, K08, K23, K24) and other related awards. Table G5C11 lists the Institution's 43 Mentored Career Development Awards (9 K01, 11 K08, 19 K23, 4 K24).

2. Plans for Recruitment of Clinical Translational Research Scholars .

The Admissions and Recruitment Core will carry out an active program to identify and recruit the most qualified trainees and junior faculty from all departments in the URMC and from outside URMC. The Directorate members will be charged with identifying candidates. Dr. Pearson, as Senior Associate Dean for Clinical Research, will have access to Department Chairs and Center Directors from across the URMC, as well as the upstate CTR consortium (UNYTRN). All URMC training program directors will be sent a letter of recruitment on an annual basis. The CTSI will be featured prominently in the URMC Website: www.urmc.rochester.edu. Advertisements in medical journals or at clinical research meetings will target a national pool of Scholars.

All new postdoctoral clinical and research fellows will be informed of the CTSI during their orientation period in June-July of each year. Fellows will be given a questionnaire identifying their interest in the K12 Program. The Clinical Research Seminar Series is widely advertised to all fellows and the CTSI will be advertised at these URMC-wide sessions. All research fellows are required to enroll in the Ethics in Research online module. As they do, they will be sent a note inviting their application to the K12 Program. Dr. Pearson, as Senior Associate Dean for Clinical Research, is frequently invited to update Clinical Departmental Leadership about clinical research, and the CTSI will be re-emphasized during these sessions. Similarly, all training programs directed at the partnering institutions will be sent a program brochure annually. Dr. Pearson will present to appropriate audiences at these institutions.

3. Selection Criteria and Process.

The Recruitment and Admissions Core will solicit applications beginning in the second semester of the academic year, and require application materials be completed by April 15. The Core will review all applications and make recommendations to the Directorate about trainee acceptance based on the following criteria:

(1) Status as U.S. citizen or permanent resident.
(2) Doctoral degree in a Health Discipline (MD, DO, DDS, PhD in Nursing, or PhD in Health related discipline).
(3) Graduate or Medical School academic research experience.
(4) Letters of recommendation from three previous mentors/colleagues.
(5) A three- to four-page statement indicating a high level of interest in clinical research, and the potential for and commitment to a productive career in clinical research. Commitment of 75% of full-time professional effort (50% in some technical medical specialties).
(6) A letter from a mentor or chair stating his/her goals for the Scholar (if appropriate).
(7) No prior receipt as Principal Investigator of RO1, R21, Center or Mentored Career Development (K) grants.

The admissions process will entail completion of application materials for the Career Development Program, which includes curriculum vitae, transcripts, proof of citizenship or permanent status, and personal statements required for the Master's degrees. The letter of nomination from a research mentor should outline the candidate's qualifications, and commitment for the award. Finally, the candidate's 3-4 page description of his/her career objectives should describe the way in which the K12 would meet those objectives, prior experience in research, other evidence of commitment to a research career, and a broad overview of the type of clinical research (e.g. translational research, experimental therapeutics, population-based research, outcomes health care research, ethics/law/policy research) to be pursued, and prior interactions with his/her mentor. Detailed plans for the practicum experience and research project would be considered premature at this point, prior to the core curriculum and career development portions of the Program.

All trainees will be given a ranking on the basis of their credentials, and the top 1-4 trainees will be accepted, depending on funds. Applicants will be strongly encouraged to apply for the Master's degree programs; all Master's applicants must meet criteria and be formally admitted to that program. Women and under-represented minorities will be encouraged to apply, and every effort made to assure diversity of the

trainee cohort. Trainees will be notified of their acceptance by June 1 so that they can participate in CTSA activities immediately upon beginning their didactic year.

G2i9. Education and Training Program Evaluation

G2I9a. Evaluation Committee.

The evaluation of the Education and Training Key Function will be carried out by a group of faculty and staff with a primary career interest in program evaluation. Ann Dozier, RN, PhD and Stephen Lurie, MD, PhD will co-chair the Committee. Staff includes Mrs. Carla Boff who is responsible for the student database within the Department of Community and Preventive Medicine.

G2i9b. Evaluation of Didactic Coursework.

Each course and workshop required for the Master's and PhD degrees will be evaluated by course participants at the end of the course. Written evaluation forms are distributed online and submitted to Pattie Kolomic, Graduate Education Coordinator, for summarization. Copies of the evaluation summaries are sent to the Curriculum Committee Chair (Dr. Chin). These are used by the Directorate for course review and improvement or, if necessary, replacement of the Course Director.

G2i9c. Evaluation of CTSI Scholar Learning Objectives and Competencies.

Evaluation of the CTSI Scholar in the didactic curriculum and research practicum is facilitated by the establishment of 23 learning objectives and acquired competencies at the beginning of the CTSI (Table G2i.3). Each objective has one or more measurable outcomes. At the completion of the didactic core curriculum, each Scholar completes the CTSIA evaluation form. Completion of knowledge objectives entails receipt of an A or B for the coursework. Scholar progress is reviewed twice annually by the Recruitment/Admissions Office and individuals with a course grade less than a B are placed on probation. Receipt of more than one grade below B will result in dismissal or retaking the course for an acceptable grade.

Attainment of skill objectives is monitored by reporting on the CTSI evaluation form the title of the research project, the mentor, publications, presentations, abstracts, and grant activity. These are entered into the CTSI Scholar database. The attitude objectives are also assessed on the CTSA evaluation form by completion of workshops and field visits. Of particular interest will be a description of the Research Project developed. The number of mentors, the different disciples represented, and the different institutions represented will be recorded.

G2i9d. Evaluation of CR Scholar Career Development.

At completion of the didactic phase, the information on the CTSA evaluation form is entered into the CTSI Scholar database. In addition, each of the CTSI Scholar's Mentorial Committees will submit an evaluation of the Scholar's strengths, weaknesses and recommendations for growth. A curriculum vitae is also collected at that time. Ms. Boff will request and obtain written informed consent to follow-up with each Scholar on an annual basis, requesting an updated C.V. From this, the following data would be extracted and entered into the database: current position and affiliation, new publications, abstracts, presentations, grants submitted and received, awards and accomplishments.

In addition, beginning at the time of completion, the Evaluation Committee will track publications generated since admission to the CTSI, through extensive searches of MEDLINE, assisted by the Miner Library. The number of first and coauthored papers will be summarized. One paper per year (if present) will be selected from the journal judged to be most respected and the impact factors of that journal entered into the database. The average impact factors for each CTSI Scholar will be calculated, along with the number and first authorship of papers.

Similarly, the grant activity of each CTSI Scholar will be requested. The grants submitted and approved as Principal Investigator will be ascertained. The funding rate will be determined and entered into the database along with the number of grants funded as principal and collaborating investigator.

Each Scholar's career development then will be summarized in the existing CTSI Scholar database. Outcome measures to be tracked include: continued academic appointment; promotion in position since the CTSI; grant applications submitted, awarded, and funding rate; number of total and first authored publications; and impact factors of best publication. While these outcome measures could not be compared with a control group, they do provide some absolute benchmarks that can be agreed upon as evidence for career success following the CTSI training. Each year's data will be presented to the Directorate for review and discussion.

G2i10. Recruitment of Trainees from Underrepresented Minorities and Women.

To increase the number of minorities and women in the RCRC, institutional efforts from the University and individual efforts from the Program Director will be required. The University of Rochester has taken a proactive role in identifying highly qualified minority students from a variety of levels who are encouraged to pursue biomedical careers. The School of Medicine has been successful in recruiting minority students and women, such that the medical school student body consists of 50% women and 14% minorities. The Eastman Dental Center has a Minority Student Summer Research Training Program, a 10-week intensive research training program for minority students matriculating into dental schools. The Clinical Research Seminar Series will seek to have speakers who deal with topics relevant to women's health and minority health. Outside speakers sponsored by the Program have included distinguished investigators who are members of minority groups.

Dr. Pearson and the Program Executive Committee will also expend considerable personal effort to recruit women and minorities. Women and minorities are represented in the Program leadership and faculty. Dr. Pearson will meet with Department and Center Directors annually to identify and encourage mentors to make potential female and minority applicants aware of the Program. He will personally contact those individuals identified, with the mentor's permission. CTSI brochures will encourage participation by women and minorities.

Collaboration with the UNYTRN, a network of at least ten upstate New York Institutions will also expand the number of trainees from which to select women and minority candidates.

G2i11. Integration of Education and Training Key Functions with CTSA.

As mentioned, the education and training key function serves as the catalyst for formation of research teams around the trainee, thereby involving many other key functions. New courses in bioinformatics, translational technology , and community engagement are specifically proposed, as educational linkages to those key functions. Current didactic coursework and workshops include biostatistics, study design, regulatory compliance, ethics, and evaluation. Numerous opportunities exist for partnering with UNYTRN members in the areas of education. Continuing education seminar series provide numerous opportunities for presentation and discussion of methodology/technology, regulatory compliance, ethics, etc. Of course, well-trained students will positively benefit all the key functions as they bring their new knowledge and skills to the solution of complex questions.

G2i12. Innovation

The Educational and Training Key Function brings a number of revised innovative programs to the Rochester CTSI. The innovations are listed in Table G2i.7 by the new program proposed and the way that it represents an innovation. The innovations identify Education and Training as one of the key change agents to transform clinical and translational research at URMC.

Table G2i.7: Innovations in the Education and Training Key Function

New Component	How it is Innovative
Training as Translational Strategy	Use of trainees to bring together multidisciplinary translational research teams
Degree Programs	Curriculum focused in Key Functions of Translational Research
Masters in Clinical Investigation	Revisions adding new course, focus on clinical research
Masters in Translational Research	New Degree program, 4 new courses, new Mentors
PhD in Translational Biomedical Research	New degree program, hybridizes Clinical Investigation and Translational Research, new Mentors
Courses	New courses in Bioinformatics, Pathophysiology, Translational Research Methods, Experimental Therapeutics
Skill-Building Workshops	Research Project Administration Workshop, Academic Development, and Community Engagement
Mentors	New Mentor Development Program for Translational Research Faculty
Predoctoral Program	Flexible tracks for MD-MS, Year-out or MD-PhD programs
Career Development Program	Career Development Program integrating Degree Programs and transition to independent investigator status
Seminar Series	Greater representation of translational research

G2J. UPSTATE CONSORTIUM

G2J1. Specific Aims

The overall goal of this key function is to organize and develop the Upstate New York Translational Research Network (UNYTRN), involving ten major institutions performing biomedical research in the Upstate New York region. To assist faculty at URCTSI and member institutions, its mission is to access technologies, facilities, services, and expertise available at member institutions, to foster collaborations, and to reduce resource duplication. UNYTRN will emphasize bidirectional transfer of information between the bench scientists and the bedside investigators within the Network, and foster CTSA key functions on a regional basis.

To carry out this goal, the UNYTRN will achieve the following specific aims:

1. Organize a consortium of at least ten biomedical research institutions in the Upstate New York region into a regional network for translational research. This organization will include administration and governance of the UNYTRN through an independent foundation, the Foundation for Healthy Living, so that all partners will be able to take advantage of the Network's shared resources.
2. Develop inventories of 1) translational research ongoing at the member institutions, and 2) research resources and methodologies accessible for collaborative research by UNYTRN faculty and trainees.
3. Engage UNYTRN translational research faculty in a needs assessment focusing on barriers to performance of high quality translational research at their institutions and in the region.
4. Create and/or expand translational research resources that will effectively support all member institutions of the UNYTRN, using Working Groups to plan and implement the following resources:
   a. Assistance with regulatory compliance, including training programs on regulatory issues to assist investigators in the preparation and submission of regulatory documents.
   b. Regional support for Institutional Review Boards (IRBs) including education and certification of clinical investigators on ethical conduct of research, training of IRB members, and creation of a "central" IRB for coordinated review of multi-institutional UNYTRN projects.
   c. Regional marketing, recruitment, and retention of study subjects through the training of project coordination and recruitment staff to improve efficiency of recruitment and retention of research subjects.
   d. Establishment of regional databases and bioinformatics resources for collection, management and storage of data from research projects by UNYTRN members.
   e. Development of a UNYTRN network of faculty to serve as consultants for study design and analysis, to assure all UNYTRN faculty have adequate support for protocol development and analysis.
   f. Accessibility for UNYTRN faculty to the resources of the Clinical and Translational Science Institute (CTSI) and its General Clinical Research Center (GCRC) at the University of Rochester for: 1) performance of translational research studies and Phase I-IIa clinical trials; and 2) organization and support of GCRC satellites with facilities and trained staff to carry out translational research studies locally.
   g. Establishment of a program of translational research pilot studies which involve investigators from two or more UNYTRN institutions, to encourage investigators to use the multidisciplinary faculty of the UNYTRN in development and implementation of translational research projects.
5. Provide opportunities for training, career development and continuing education in the principles and practice of translational research, to include postgraduate training programs and short courses/summer institutes for formal training of new investigators in translational research methods, and an annual regional translational research symposium.
6. Evaluate success of the UNYTRN by documenting attainment of preordained objectives and deliverables.

The UNYTRN will support the Rochester CTSI as a translational research center serving Upstate New York, but go beyond to support development of CTSA Programs at other member institutions, to create a "Regional Home for Clinical Research."

G2J2. Background and Significance

G2J2a. Removing the Road Blocks to Translational Research through Regional Collaboration.

The translation of basic research findings to clinical medicine and population health has been identified as a major challenge to the biomedical research community. At least seven roadblocks from bench to human research and from human research to clinical medicine will be addressed by the UNYTRN and, as such, provide the rationale for the structure and function of the UNYTRN proposed herein.

Barrier #1 In many institutions of higher learning, the relatively larger numbers of basic biomedical scientists and their potentially translatable discoveries would likely exceed the capacity of currently available translational research facilities and faculty. This provides the rationale to expand, on a regional basis, the quantity and quality of facilities, staffs, and investigators who can carry out high quality translational research.

Barrier #2 Paradoxically, sophisticated and resource-intensive facilities and/or technology required for translational research are frequently underutilized overall, utilized by individual investigators rather than multidisciplinary translational research teams, or utilized only by investigators from a single institution. This provides the rationale to increase the accessibility of translational research resources to investigators on a regional basis.

Barrier #3 Single institutions, especially smaller ones, may not have the critical masses of basic scientists, translational researchers, or clinical investigators to assure the number and variety of collaborators needed to assemble multidisciplinary translational research teams. This also emphasizes the importance of inclusion of small or medium-sized institutions within a regional consortium.

Barrier #4 Basic biomedical scientists, translational researchers, and clinical investigators frequently are not aware of each other's research and have little opportunity for interaction. A common problem within most biomedical research programs is communication between laboratories, departments, schools, etc. as to the areas of interest and expertise of investigators, the availability of research facilities and equipment, and centralized resources to support research activity. These issues could be addressed by a consortium in which faculty, facilities, and resources within the region are inventoried to meet translational research needs.

Barrier #5 Some resources essential for translational research are costly for single institutions, especially small- and medium-sized ones, and could be more efficiently provided by a centralized body rather than duplication of efforts by single institutions.

Barrier #6 Increasing regulation of the ethical, financial, and administrative aspects of clinical and translational research has increased requirements for personnel and expertise which may be unavailable or inefficient for single institutions. This forms the rationale for centralized training programs and other mechanisms to support regulatory compliance on a regional basis.

Barrier #7 There is a critical shortage of investigators with formal training in the principles and practice of translational research. This provides the rationale for regional training programs to refill the pipeline of new investigators who would serve to link basic and clinical investigations.

The UNYTRN will specifically address these barriers perceived to be major causes of reduced translational research activity. The advancement of UNYTRN's goals will largely deal with the identification and removal of these and other barriers so that future CTSA proposals from Upstate New York can be confident in their ability to carry out high quality translational research.

G2J3. Prior Experience

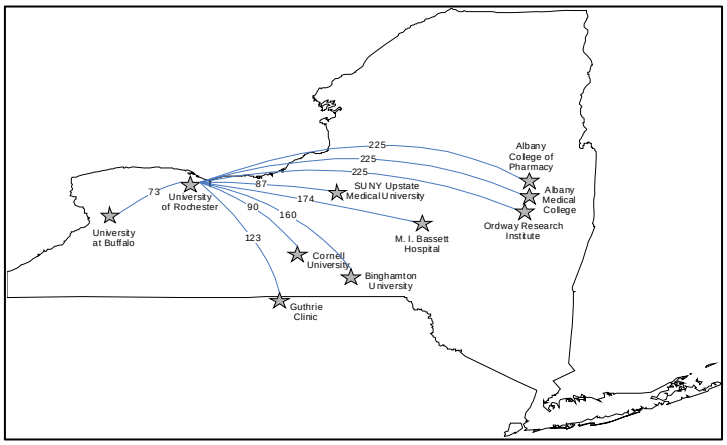
G2J3a. Evidence of Ongoing Regional Excellence in Biomedical Research.

1) UNYCoR. UNYTRN will be affiliated with the Upstate New York Coalition for Biomedical Research (UNYCoR) (See letter of support from Barbara Humphrey, UNYCoR Executive Director). Therefore, one distinctive feature of UNYTRN is that it is not a new consortium formed ad hoc in response to the CTSA Program, but rather the focusing of an already organized and functioning coalition for biomedical research. UNYCoR is a consortium whose members include leading biomedical academic and research institutions spanning Upstate New York from Albany to Buffalo, as well as south to the Pennsylvania line. In April, 2001, six of Upstate New York's biomedical research-intensive institutions formed UNYCoR, a unique partnership designed to accelerate biomedical research success through the development of collaborative research partnerships and the sharing of core research facilities and expertise. URMC was one of these. Further information about UNYCoR is available at: http://www.upstate.edu/unycor/about.shtml.

UNYCoR member institutions that will also be members of UNYTRN currently bring in approximately $750 million in extramural funding annually, including over 1,000 grants totaling more than $356 million from the National Institutes of Health (See Table G2J1). These institutions have made significant investments in sophisticated technology, established centers of biomedical research and training, and provided high levels of clinical care to millions of patients, including successfully taking basic science findings and translating them into innovative therapies and patient care. Working alone, many of our UNYCoR institutions are world-renowned. Standing together, they possess the potential to turn Upstate New York into a world-class center for biomedical and translational research with a robust biomedical economy.

2) Other UNYTRN Partnering Institutions.

Figure G2J1: UNYTRN Member Institutions (with driving distances in miles between Rochester and each institution indicated)



The UNYTRN proposes to build upon the organizational experience of UNYCoR to develop an affiliated network focused on translational research. Ten members are initially proposed, all located within easy driving distance of Rochester, New York (Figure G2J1). As demonstrated below, each currently proposed UNYTRN member brings a wealth of experience, resources and facilities to the consortium. By virtue of its members, UNYTRN has several distinguishing features which it brings to the National CTSA Program. First, several of its members are smaller institutions for whom membership in a research consortium would be especially valuable in terms of access to additional faculty and technologies. Thus, UNYTRN will demonstrate the role of a CTSA in fostering translational research in smaller research organizations. Second, UNYTRN represents virtually all of the biomedical research organizations in Upstate New York, and therefore is truly a regional center, with members all within several hours travel. It also has the potential to be population-based, for purposes of epidemiologic studies. Third, UNYTRN has access to several populations which are understudied. Upstate New York has a large rural population. The University at Buffalo and the Cornell Cooperative Extension have nationally recognized research programs in rural health. Bassett Healthcare and the Guthrie Clinic are models of vertically integrated rural healthcare systems. Another understudied population in Upstate New York are Native Americans, with at least four tribal organizations of the Iroquois Nation served by SUNY Upstate Medical Centers, University of Buffalo, and University of Rochester. Finally, the Deaf and Hard of Hearing (D/HOH) community is remarkably understudied. Rochester has perhaps the highest prevalence of deaf people in the U.S. and has initiated the National Center for Deaf Health Research to organize and partner with that community in clinical research projects.

The other proposed members of the UNYTRN are briefly described (see letters of support):

(1) Albany College of Pharmacy was founded in 1881 with the vision of educating professional pharmacists in a formal academic environment, rather than by the customary apprentice system. Today, over 80 full-time faculty teach more than 110 courses for both the Doctor of Pharmacy and Bachelor of Science programs in Pharmaceutical Sciences and Biomedical Technology. ACP is home to the Pharmaceutical Research Institute (PRI), led by Shaker A. Mousa, Ph.D., a renowned senior research scientist from DuPont Pharmaceuticals Co. PRI is a non-profit research and development institute dedicated to cutting-edge research, pharmaceutical services and education in partnership with industry and academic and research centers in New York State, nationally and worldwide.

(2) Albany Medical College Albany Medical Center is the only academic health sciences center in the 25 counties of eastern New York and western New England. The Medical Center incorporates the 631-bed Albany Medical Center Hospital, one of upstate New York's largest teaching hospitals; the Albany Medical College, which was founded in 1839 as one of the nation's first private medical schools; the Albany Medical Center Faculty Group Practice, staffed by about 225 full-time clinical faculty members of the Medical College; and the Albany Medical Center Foundation, Inc., one of the largest fund-raising organizations in the region.

(3) Bassett Healthcare is a network of four hospitals and 21 health centers serving central New York State. It includes the Bassett Research Institute, which has a productive history of major healthcare advances, including seminal research in “early ambulation” after surgery, the world’s first human bone marrow transplantation, and pioneering work on the biosynthetic pathways of albumin. Bassett Healthcare also has a long tradition of research in rural populations, including a unique private health census of a rural Upstate New York population.

(4) Binghamton University is part of the State University of New York (SUNY) system. The newest department within the Watson School of Engineering is the Department of Bioengineering, founded in 2001. The University’s newly-formed Institute of Biomedical Technology seeks to identify fundamental areas of research

that provide interfaces between academia and industry and to promote the development and expansion of a biotechnology industry in New York's Southern Tier.
(5) Cornell University's Division of Nutritional Sciences includes programs in the College of Agriculture and Life Sciences and the College of Human Ecology. Cornell University has over 500 faculty engaged in biological and biomedical research at its upstate campuses in Ithaca and Geneva. Nationally designated interdisciplinary centers and specialty areas include nanobiotechnology, structural biology, biomedical engineering, biophysics, computational biology, and veterinary medicine. A $600-million "New Life Sciences Initiative" includes construction of a 270,000 sq. ft. facility that will house key academic initiatives and an 80,000 sq. ft. animal facility. New departments of Biomedical Engineering and of Biological Statistics and Computational Biology and a new Cornell Institute of Molecular and Cell Biology have been established.
(6) Guthrie Health includes the Guthrie Healthcare System, a community-based, not-for-profit healthcare system serving New York's southern tier and North Central Pennsylvania, and the Guthrie Research Institute. Guthrie's Clinical Research Department supports a wide spectrum of patient-oriented research, including investigator-initiated studies and industry-sponsored clinical trials.
(7) Ordway Research Institute is a freestanding corporation with a mandate to translate basic science observations into therapeutics, is committed to fostering inter-institutional, competitively-funded research. Research themes of the Institute expand on existing regional programs of excellence. The Center for Medical Science houses Ordway researchers and those from Wadsworth Center/New York State Department of Health and the Albany College of Pharmacy, making it the first research laboratory facility in the region to serve multiple research institutions. The building reflects the idea that a nationally-competitive, critical mass of research scientists in the Capital District can be assembled by meaningful collaboration among the region's academic and government research facilities.
(8) SUNY Upstate Medical University is one of Central New York's premier biomedical research centers. Extramural funding for research continues to double every 4-5 years. More than 500 active research projects span a wide range of disciplines. 225,000 square feet of research facilities include a new $50 million Institute for Human Performance and over $30 million of newly renovated state-of-the-art research laboratories and core support facilities. The 350-bed University Hospital serves a 15-county area, treats and discharges more than 16,000 patients annually.
(9) The University at Buffalo (UB), also part of the SUNY system, is the largest public University in New York. The University has established a variety of specialized research centers, including Centers for Advanced Photonics & Electronic Materials (CAPEM), Computational Research (CCR, Unified Biometrics (CUBS), Research and Education in Special Environments (CRESE), Microbial Pathogenesis, and the Institute for Lasers, Photonics and Biophotonics. UB is also the host institution for the New York State Center of Excellence in Bioinformatics & Life Sciences, a $250 million state initiative that will provide support for this grant. This AAU institution has five affiliated hospitals, including the Roswell Park Cancer Institute, a School of Public Health and a College of Pharmacy.

3) Ongoing Sponsored Research at UNYTRN Member Institutions.

Table G2J1: NIH Sponsored Projects at UNYTRN Institutions (FY2004)

Institution	*# of Projects (FY2004)*	*Total NIH Funding ($, FY2004)*
Albany College of Pharmacy	1	288,570
Albany Medical College	51	13,796,938
Bassett Healthcare	4	1,042,031
Binghhamton University	17	4,630,750
Cornell University Ithaca	207	62,177,730
Guthrie Health	1	258,650
Ordway Research Institute	8	2,557,535
SUNY Upstate Medical University	59	17,718,460
University at Buffalo (incl. Roswell Park)	287	96,614,301
University of Rochester	427	157,549,144
Total	**1,062**	**356,634,109**

Table G2J1 provides a summary of NIH-sponsored research projects underway at UNYRTN member institutions. When considered as a whole, UNYTRN would have ranked as the 10th largest NIH-funded institution in Fiscal Year 2004.

G2J3b. Examples of Ongoing Regional Collaboration.

UNYTRN members have collaborated on a number of specific translational research studies, funded by NIH, USDA, and private industry, as well as regional conferences, and training in the Rochester K30 Program. A few examples of larger initiatives are provided here.

1) University of Rochester Human Subject Research Enhancement Program. The URMC was awarded a three-year grant from the National Center for Research Resources to enhance the functioning of existing IRB programs and integrate education and monitoring functions on a regional basis (S07 RR18136-02, PI: David S. Guzick, MD PhD). Three regional collaborators, all UNYTRN partners, joined the URMC in this effort: Bassett Healthcare, Cornell University and Guthrie Health. Educational programs were developed and made available to the collaborating institutions. Three audiences were targeted: IRB members, investigators, and research administrators. Media appropriate for each audience were developed and presented in a variety of formats.

2) NYS Center of Excellence in Bioinformatics & Life Sciences at the University at Buffalo. This $250 million Center of Excellence was designated by the Governor in 2002 to coordinate drug discovery research throughout the state. The Center is coordinating work in neurodegenerative disease, cancer, cardiothoracic disease, and pathogenesis, and has high throughput functional genomics, systems biology, and high performance computing assets that are readily available to UNYTRN. Recently, Center of Excellence members from UB, URMC, Cornell, Syracuse, Columbia University, Rockefeller, and Ordway joined with investigators from Yale and New Jersey to successfully formulate an NIH-funded Regional Center in Biodefense. This $50 million basic science and clinical research program utilizes URMC as a primary location for vaccine trials (John Treanor, MD as Director).

3) Translational Research Conferences. SUNY Upstate Medical University has organized four Translational Research Conferences for the benefit of Upstate New York researchers. These have taken place in 2002, 2004 and 2005 with a fourth scheduled in April, 2006. Speakers have included noted translational researchers from Upstate New York institutions, noted NIH research leaders, and other leading researchers and scientific leaders from major pharmaceutical companies.

4) UNYCHRQ Initiative on Palliative Care. The Foundation for Healthy Living and its UNYCHRQ network (see below) has organized an Upstate initiative to improve palliative care services. A working group has been active with Timothy Quill, MD, of URMC as its Chairperson. This illustrates the viability of a parallel consortium for healthcare quality improvement.

G2J3c. Progress in Organization of UNYTRN.

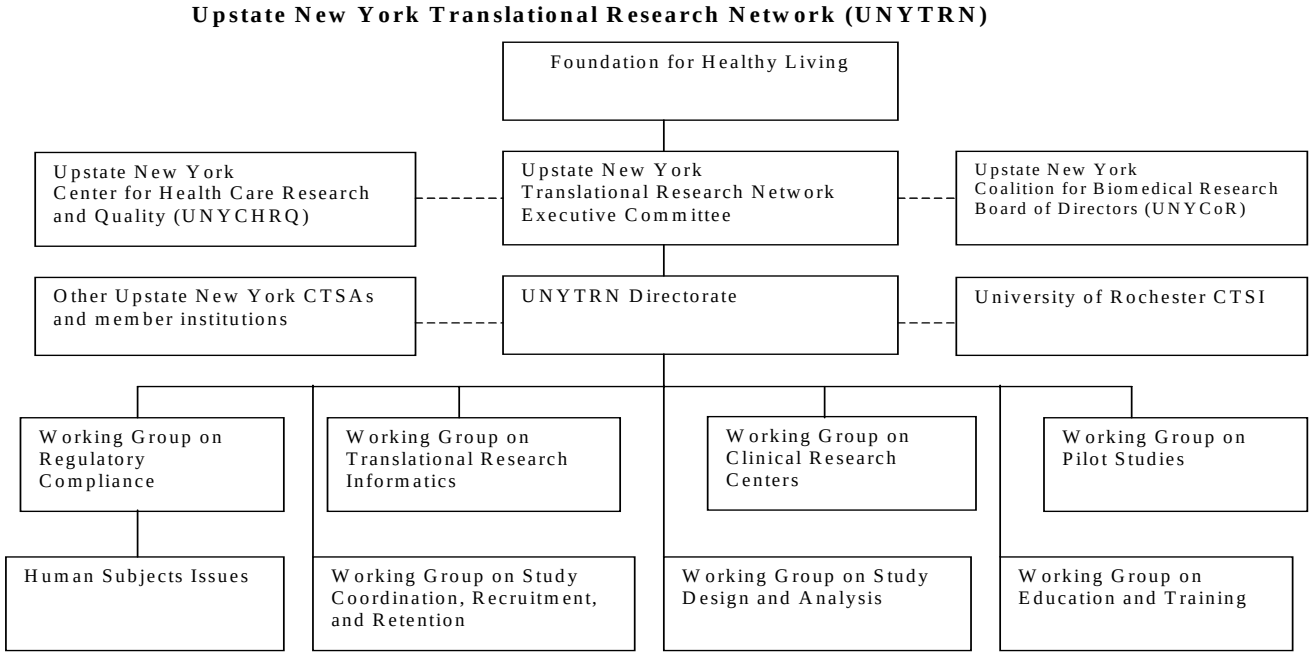
Important in the development and maintenance of an Upstate consortium is an organization in which all members can share ownership, rather than being subservient to another academic institution. In the Fall of 2005, Steven Szebenyi, MD, approached Drs. Guzick and Pearson of URMC about translational, clinical, and health sciences research projects that might be done involving all of Upstate New York and its healthcare institutions. Dr. Szebenyi is Executive Director of the Foundation for Healthy Living, formed by funds donated by a Managed Care Organization. The Foundation for Healthy Living has committed $3 million to improve health in Upstate New York through research. These funds have resulted in creation of the Upstate New York Center for Healthcare Research and Quality (UNYCHRQ). UNYCHRQ consists of all academic institutions in Upstate New York involved in health research, including health services research and public health. In preparation for this proposal, Foundation for Healthy Living has accepted responsibility as convener and organizer of UNYTRN and has committed substantial funds of its own to the Network (See letter of support from Dr. Szebenyi).

G2J4. Methods

G2J4a. Organization of the Upstate New York Translational Research Network. (Specific Aim 1).

1) Overall Organization. A primary objective of this Key Function is to organize the UNYTRN so as to optimize the involvement of all members. Toward this end, UNYTRN is organized into committees and working groups (Figure G2J2, UNYTRN Organizational Chart), each with the purpose of carrying out this proposal's specific aims. Note that the working groups align themselves closely with CTSA key functions.

Figure G2J2: Organizational Chart



UNYTRN will take advantage of the five years of organizational activities by UNYCoR. In addition, UNYTRN will include academic medical centers not previously part of UNYCoR (e.g. M.I. Bassett Hospital and Guthrie Clinic). Thus, there will be an interaction and communication between UNYTRN and UNYCoR, as the translational research aim of UNYTRN is a subset of the larger biomedical research aim of UNYCoR. Similarly, the organizational and administrative functions of the UNYTRN Directorate will be carried out by Foundation for Healthy Living which is providing in kind support. UNYCHRQ is another network of Foundation for Healthy Living which has a broader mission including healthcare access and public health education.

2) Executive Committee: Role and Functions. An Executive Committee will be the governing body of UNYTRN, and will consist of representatives of all ten UNYTRN members (Table G2J2). The members' representatives have been selected by the Senior Officials of each member institution, as the institution's voice to and from UNYTRN (see Biosketches and Letters of Support). They represent a wide spectrum of disciplines and research interests, all relevant to translational research. The Committee will meet quarterly face-to-face as a governing board. Monthly conference calls will complement these meetings. A website will be established. Minutes will be recorded and distributed. Quarterly reports from the eight Working Groups will be reviewed and acted upon. The Executive Committee will be a forum for discussion and resolution of differences between partnering institutions. The Executive Committee will evaluate UNYTRN's progress toward fulfillment of the proposed specific aims and deliverables (Table G2J7) and modify or add aims as opportunities allow. The Executive Committee will review the administration of any NIH grants to the UNYTRN and receive budgetary reports on disbursement of UNYTRN grant funds. This Committee would select a new Network Director if a vacancy were to occur.

Table G2J2: Proposed Members of the UNYTRN Executive Committee

Name	Institution	Role in Institution
Steven E. Szebenyi, MD (Director)	Foundation for Healthy Living	Executive Director
Thomas Pearson, MD MPH PhD	University of Rochester	Senior Associate Dean for Clinical Research Director of the Office of Clinical Research
Paul Davis, MD	Ordway Research Institute	Director and CEO
Vincent P. Verdile, MD	Albany Medical College	Albany Medical College
Thomas Brenna, PhD	Cornell University	Professor, Division of Nutritional Sciences
Bruce Holm, PhD	University at Buffalo	Senior Vice Provost
John Lucas, PhD	Upstate Medical University	Vice Provost for Research
Ken McLeod, PhD	Binghamton University	Professor and Chair, Department of Bioengineering
Dwight Stapleton, MD	Guthrie Clinic	Director, Clinical Research
William Streck, MD	M.I. Bassett Hospital	President and CEO
Mary Andritz, PharmD	Albany College of Pharmacy	Dean

Each member of the Executive Committee is briefly described below. (See letters of intention to enter into a research consortium).

Steven E. Szebenyi, MD, M.M.M., is Executive Director of the Foundation for Healthy Living. He is an MD graduate of the Johns Hopkins University School of Medicine and board-certified internist. Prior to his current position, he held faculty positions at the M.I. Bassett Hospital and Albany Medical College. He has extensive experience as director of clinical and research programs for patients with HIV/AIDs.

Thomas A. Pearson, MD, MPH, PhD, is the Albert D. Kaiser Professor and Chair of the Department of Community and Preventive Medicine and Professor of Medicine at the University of Rochester School of Medicine. He is also the Senior Associate Dean for Clinical Research. He has been Adjunct Professor of Nutrition in the Division of Nutritional Sciences at Cornell University since 1990. He was Director of Research at the M.I. Bassett Hospital for nine years. He currently serves as Program Director for the Rochester Clinical Research Curriculum, supported by a K30 Award from NIH, and Associate Director of the Rochester CTSI.

Mary Andritz, PharmD, FASHP, is Dean of the Albany College of Pharmacy. She has been a board member of the New York State Council of Health-system Pharmacists (NYSCHP) Research and Education Foundation for over 15 years, and was the recipient of the NYSCHP 2006 Board of Directors Award. She is a member of numerous professional organizations, including the American Association of Colleges of Pharmacy and the New York State Pharmacy Conference.

J. Thomas Brenna, PhD, is a Professor and Director of Undergraduate Studies in the Division of Nutritional Sciences at Cornell University. Dr. Brenna is an internationally recognized expert on polyunsaturated fatty acid metabolism and biomedical mass spectrometry. His research group has been R01 funded continuously since 1992; he is, or has been, PI for NIGMS, NEI, and NICHD grants, as well as from the National Science Foundation and industry.

Paul Davis, MD, is Chief Executive Officer for the Ordway Research Institute and Associate Dean for Clinical Research at Albany Medical College. A board-certified endocrinologist, Dr. Davis has a distinguished career in development and evaluation of new therapeutic agents.

Bruce Holm, PhD, is the Senior Vice Provost at the University at Buffalo, with particular responsibility for biotechnology and other high technology projects. In this role, Dr. Holm is the chief administrator in the Provost's Office for the Buffalo Center of Excellence in Bioinformatics, the Strategically Targeted Academic Research (STAR) Center for Disease Modeling and Therapy Discovery, and the Center for Advanced Biomedical and Bioengineering Technologies (CAT).

John Lucas, PhD, is Vice Provost for Research and Research Development and Professor of Biology, at SUNY Upstate Medical University. Dr. Lucas created the Clinical Trials Office at his institution; sponsored and hosted two regional OHSP conferences on human subject protections (2000, 2001); and worked with the State University of New York (SUNY) Research Foundation to create a SUNY-wide (30 campus) working group on human subject protections. He is one of the charter members of UNYCoR and serves as its Scientific Director.

Ken McLeod, PhD, is Professor and Chair of the Department of Bioengineering at Binghamton University, and also Director of its Bio-complexity Research Institute. Dr. McLeod's primary research interests are understanding the mechanism of interaction of biophysical factors in the processes of tissue development, healing, and adaptation. He inaugurated the Bioengineering Program at Binghamton University.

William Streck, MD, is the President and CEO of Bassett Healthcare in Cooperstown, NY, and Clinical Professor of Medicine at Columbia University's College of Physicians and Surgeons. He is a graduate of the University of Rochester School of Medicine. He has been nationally recognized for innovations in rural healthcare.

Dwight Stapleton, MD, is Chief of Cardiology and Medical Director for Clinical Research at Guthrie Health in Sayre, PA. His research interests include pharmacologic trials in heart failure and other cardiologic conditions. Guthrie Healthcare and the URMC have a formal agreement to collaborate in clinical research and regional healthcare.

Vincent P. Verdile, MD, is Dean of the Albany College of Medicine. He is a fellow of the American College of Emergency Physicians, and past chair of the Department of Emergency Medicine at Albany Medical Center. He has authored more than 60 academic publications.

3) The UNYTRN Directorate (See Letters of Support from Foundation for Healthy Living). In addition to the Executive Committee with institutional representatives, another group is required for the day-to-day administration of the UNYTRN. A UNYTRN Directorate will be organized at the Foundation for Healthy Living.

The office will consist of the Executive Director of the Foundation for Healthy Living and administrative staff. Thomas Fogg, Administrator of the Rochester CTSI will serve as liaison to the Directorate. Other CTSAs could do likewise. They will work on behalf of UNYTRN to carry out its specific aims. The Directorate will receive recommendations from the Executive Committee for actions on behalf of UNYTRN and carry them out, as appropriate, or provide feedback as to barriers to their implementation. It will serve as the clearing house for communication via written, telephonic, or electronic means between member institutes, with the Executive Committee, with UNYCoR, and with other CTSAs. It will administer a subcontract from the Rochester CTSA, disburse funds, provide progress reports, etc. It will support the eight Working Groups by organizing their meetings and conference calls, preparing and distributing minutes, etc. The Director, Administrator, and Administrative Assistant will meet weekly or as needed, joined telephonically or face-to-face by Mr. Fogg as representative of Rochester CTSI.

4) Development of the UNYTRN Website. Coincident with the initiation of the CTSA, development of the UNYTRN web site will begin. This activity is expected to require five months to complete. It is envisioned that the site will have a public side and a protected side available to members only. The public side will contain information about UNYTRN, its mission, member institutions, a timeline of significant activities, and contact information to facilitate communication. In addition, links will be established to allow users to access conveniently the web sites of each UNYTRN member institution and UNYCoR. Similarly, the sites of partnering UNYCoR and UNYCHQR networks will feature links to the UNYTRN web site. The protected side of the site will be instrumental in coordinating the activities of the Directorate, Executive Committee and eight Working Groups. It will serve as a repository for meeting minutes, and as a convenient means to post important information concerning planned activities. It will also serve as a medium to provide access to data collected by the project team, such as a CRISP-like database of translational research projects at UNYTRN member institutions, and an inventory of resources available to support research projects in the region (described below).

G2J4b. Development of Translational Research Resource Inventories. (Specific Aim 2)

1) Uses of Inventories of Translational Research Resources. A natural starting point for planning a regional program of translational research is the identification of personnel, programs, facilities, and technologies within the region which might be available to translational researchers. UNYCoR has already identified a number of basic research resources available for its members. The complete assessment of current programs in translational research will be essential for expansion of translational research and to encourage basic translational researchers to apply their laboratories and methodologies to human diseases. Moreover, clinical researchers should be encouraged to identify models of disease mechanisms and new basic science methods and technologies for application to their area of clinical research. The development of multidisciplinary research teams is an obvious strategy to quickly develop translational research. Therefore, in addition to identifying ongoing translational research with UNYTRN members, basic laboratories and clinical research programs of the UNYTRN will also be inventoried.

A number of uses are proposed. First, a resource inventory will serve as the initial phase of a needs assessment (Table G2J5). Areas of urgent need are obvious targets for future proposals. Second, the inventory will serve as a directory for multidisciplinary interaction, both within institutions and between institutions. The UNYTRN will serve as a clearinghouse for requests for collaborating investigators and specialized technical and methodologic resources. The inventory should be accessible by UNYTRN members and their faculty and students, without consultation of the UNYTRN office. Finally, an inventory of resources and ongoing translational research will serve as one means to evaluate the development of translational research, entailing collaboration between member institutions, as a measure of success of the UNYTRN.

2) UNYTRN Database. Readily achievable is a database of most translational research projects funded by the Public Health Service. This will use the CRISP database, which lists currently funded research projects searchable by institution, investigator, and keywords (Table G2J3). The abstract of each individual project can also be accessed. An advantage of this database is its availability as a public resource. Proprietary information should not be included in

Table G2J3: Number of Projects in CRISP Database, by Institution

Institution	*# of Projects in CRISP Database, FY2005*
Albany College of Pharmacy	1
Albany Medical College	43
Bassett Healthcare	4
Binghhamton University	17
Cornell University Ithaca	230
Guthrie Health	0
The Ordway Research Institute	9
SUNY Upstate Medical University	67
University at Buffalo (incl. Roswell Park)	281
University of Rochester Medical Center	475
Total	1,127

the abstracts or keywords. The disadvantage of the database is the potential exclusion of projects and programs funded by groups not in the CRISP database, including non-PHS federal funders (e.g. National Science Foundation, Department of Agriculture, etc.). Moreover, it lists all types of research, not just translational research. Nonetheless, the projects in the CRISP database do provide a useful, if incomplete, database to serve as a starting point, upon which additional translational research projects can be added.

3) Inventory of Research Resources Available to UNYTRN. The organizations identified in the CRISP database and those participating in UNYTRN will be surveyed every two years for translational research resources which might be available for collaborators within UNYTRN. The survey instrument will be similar to that of the Clinical Research Resource Inventory used at the University of Rochester, with additions/modifications from the Executive Committee. The types of resources surveyed are listed in Table G2J4. These resources will be available on the UNYTRN website which will be searchable by these types of resources, including persons to contract. A repeat of this survey should serve as a means for evaluation of UNYTRN success in fostering collaboration within and between member institutions.

Table G2J4: Research Resources To Be Included in the UNYTRN Database

Research Technologies	Study Coordinators
Patient Databases	Staff for Subject Recruitment/Retention
Accessible Populations	Data Collection and Management Staff
Banks of Tissues, Cells, Serum/Plasma	Data Analysis Staff
Research Clinics/Inpatient Units	

G2J4c. Assessment of Needs for Translational Research within UNYTRN. (Specific Aim 3)

1) Surveys of UNYTRN Investigator Research. The investigators identified in the CRISP database will be asked to complete a Web-based questionnaire on barriers to their carrying out high quality translational research. Specific needs for collaborators, consultants, technology, specialized research units (e.g. GCRC), staff, data, and pilot funds will be solicited. Member institutions will motivate their faculty members to participate. The data will be organized by institution, with these data shared with each member institution. Data aggregated across all institutions will be available to the Executive Committee as part of their needs assessment and Network evaluation.

2) Formal Needs Assessment for Translational Research Programs and Resources. The CRISP database and survey of research resources available to UNYTRN members will be completed by the end of the first year of the grant period. The data will then be organized to identify UNYTRN capacity in key subject and resource areas. Furthermore, the extent of collaborations between UNYTRN institutions will be documented. Finally, the results of the investigator survey will be distributed, grouping areas of need identified by UNYTRN investigators.

The Executive Committee will assess the available data to identify resource inadequacies. First, needs identified by investigators may be fulfilled by other UNYTRN institutions. In this instance, the remedy would be additional education and training in the use of the UNYTRN database and facilitation of collaboration by the UNYTRN leadership. Second, there may be areas where resources for investigators are unavailable. The Executive Committee would develop a list of priorities for resource acquisition and identify whether UNYTRN or individual members might pursue funding opportunities, including the URMC through its CTSI Methodology Development Key Function.

G2J4d. Translational Research Resources Planned for UNYTRN. (Specific Aim 4)

1) Overview. The resources proposed for development as part of the UNYTRN are those that would benefit from centralization of the service or expertise. These services are generally needed by all institutions involved in translational and clinical research, to meet regulatory, training, or research design and conduct needs. The UNYTRN will organize eight Working Groups which will meet at least quarterly to develop plans for their assigned area of consideration. Each UNYTRN institution will be invited to appoint a faculty member or administrator to represent them in each Working Group. Some members may not choose to appoint persons to each group, as the member institution's needs dictate. Each Working Group will have a chairperson appointed (Table G2J5) (see Letters of Support). The Working Group will meet face-to-face or by conference call as needed to plan for the research resource assigned. The following sections describe the resources to be developed.

Table G2J5: Proposed UNYTRN Working Groups and Their Chairpersons

Working Group	Chairperson(s)	Institution
Regulatory Compliance	Gunta Liders, MA	University of Rochester
Human Subjects Issues	Gary Chadwick, PharmD John Lucas, PhD	University of Rochester SUNY Upstate Medical University
Study Coordinator/Recruitment and Retention	Laurie Kopin, RN, ANP William Flesher, RN, MPH	University of Rochester Guthrie Clinic
Translational Research Informatics	Bruce Holm, PhD	University at Buffalo
Study Design and Analysis	Alan Hutson, PhD	University of Buffalo
Clinical Research Center	John Gerich, MD Kimberly O'Brien, PhD	University of Rochester Cornell University
Pilot Studies	Allan Green, D.Phil Paul Davis, MD	MI Bassett Hospital Ordway Research Institute
Education and Training	Thomas Pearson, MD, MPH, PhD Maurizio Trevisan, MD	University of Rochester University at Buffalo

2) Regional Assistance with Regulatory Compliance. Investigators are often frustrated by the array of regulations involving research which has applications to human subjects. Proposed, as a solution to this problem, is a regional Working Group on Regulatory Compliance. This will be chaired by Gunta Liders, Director of the Office of Research and Program Administration at the URMC and leader of the Rochester CTSA Key Function Group on Regulation and Compliance. This Working Group will be charged with a needs assessment for regulatory issues on a regional basis, to assure implementation of the FDA Good Clinical Practice Regulations and the ICH Good Clinical Practice Consolidated Guideline.

One proposed approach to this problem would be training programs accessible by regional principal investigators and by research administrators. The courses could be modeled after those already offered at the University of Rochester. The Sponsored Programs Compliance Training Program for Principal Investigators is available online at the University's Office of Research and Program Administration's web site. The major topics of the program are seen in Table G2J6. The Working Group will consider modification of this or other programs for use by individual UNYTRN institutions or for UNYTRN-wide use.

Table G2J6: Contents of a Training Program on Sponsored Programs Compliance

Responsible Conduct of Research	Cost Principles
Environmental Health and Safety	Award Terms and Conditions
Protection of Research Subjects	Salaries and Effort Accounting
Conflict of Interest	Documenting Allocability
Publication, Data and Intellectual Property	Monitoring Project Spending
Scientific Integrity	Equipment
University Sign-off Procedures	Project Closeout
Financial Management/Audit	

A second consideration by this Working Group would be a training program for grants administrators. The CLASP Program (Continuous Learning for Administrators of Sponsored Programs) is currently a classroom-based program which could be offered on a regional basis, after modification to make it applicable to all required UNYTRN members. It currently is taught in five modules: Sponsored programs overview, Pre-award functions (including proposal/budget development and costing issues); Accounting for sponsored programs and post-award administration; Effort reporting and cost-sharing; and Project closeout.

3) Regional Support for Institutional Review Boards. This Working Group will consider regional needs for support of Institutional Review Boards and will be co-chaired by Gary Chadwick, PharmD, MPH, and John Lucas, PhD. Dr. Chadwick is a Co-director of the Regulatory Knowledge and Support Key Function of the Rochester CTSI. This Program might be modeled after a regional program previously funded by the Division of Research Resources. The Working Group will consider a centralized program for the education and certification of clinical investigators on the ethical conduct of research, with a potential for a regional curriculum and certifying examination. For example, the current Human Subjects Protection Program at the University of Rochester uses Dr. Chadwick's book, Protecting Study Volunteers in Research, and offers a certifying examination required for all Principal Investigators at the University of Rochester. Recertification is required every three years, allowing updates or newer federal regulations to be communicated. Alternatively, SUNY Upstate Medical University offers CITI (Collaborative IRB Training Initiative). A second consideration of the IRB Working Group will be the training of IRB members. The possibility of training IRB members on a

regional basis will be considered, using classroom or distance learning technologies. A final consideration of this Working Group would be the development of a Regional IRB for review of multi-institutional grants involving UNYTRN institutions. This Central UNYTRN IRB would need to have its approval accepted by member institutions' IRBs. The composition of this Board then would need to have representatives from the UNYTRN institutions.

4) Project Coordination and Subject Recruitment Staff Training. Research project coordinators are essential members of the translational research team who benefit from training and continuing education. This Working Group will consider a regional training and continuing education program for research coordinators, research nurses, etc. William Flesher, RN, MPH and Laurie Kopin, RN, ANP will Co-chair this Working Group. Several regional resources are already available. The Office of Human Subjects Protection at the University of Rochester provides training programs for clinical research coordinators every six months or so. The K30 Program at the University of Rochester offers a course: "Recruitment and Retention of Human Research Subjects." Either of these courses would be made available to UNYTRN members for training of their research nurses and study coordinators. The Working Group will also consider development within the UNYTRN network of a regional program to recruit subjects for translational research studies. This could entail marketing of protocols with ongoing recruitment. The desirability, feasibility, and implementation of such a recruitment network will be considered.

5) Translational Research Informatics. Informatics has become an increasingly rate-limiting step in basic science, translational, and clinical research. The ability to store, handle, analyze, and visualize disparate data sets from studies ranging from robotic genomic and proteomic experiments to large-scale population health studies requires specialized instrumentation and expertise. High performance, multi-paradigm computing, three-dimensional, dynamic data visualization, storage area networks, data fusion, data mining, bioinformatics algorithm development, ontology, metasystematics (a program management paradigm), and biostatistics analysis must all be coordinated to successfully pursue translational research.

The goal of this Working Group will be to identify and organize the human and infrastructure resources necessary to carry out UNYTRN projects. The Working Group will coordinate with the NYS Center of Excellence in Bioinformatics & Life Sciences, also directed by Working Group Chair Bruce Holm, and the Rochester CTSI Bioinformatics Key Function to achieve these goals and develop mechanisms for utilization and reimbursement of the considerable Biomedical Informatics resources that are already available to UNYTRN. In addition to developing a systems approach for informatics resource utilization and, where necessary, development, this Working Group will also address the coordination of the large number of degree/offering, continuing education, and other training programs that exist within the UNYTRN academic institutions in areas of computational biology, biostatistics, bioinformatics, and clinical informatics.

6) Assistance with Research Design and Analysis. Single institutions frequently have a limited number of faculty and staff with expertise and formal training in experimental therapeutics, clinical trial design, epidemiology and biostatistics. These colleagues also tend to be fully occupied with projects within their institutions. Yet, clinical research in general and translational research specifically requires increasingly specialized expertise, which a single institution is unlikely to have. Examples of such specialized skills are Phase I trial design, multicenter trial design and management, epidemiologic study design, survey sampling, and an array of specific statistical design and analysis issues. The goal of this Working Group would be to identify investigators with methodologic expertise in study design and analysis who may be available to serve as consultants on UNYTRN projects. Alan Hutson, PhD of the University of Buffalo will chair this group and will interface with the analogous Rochester CTSI Key Function. The Working Group will use the UNYTRN Database and Resource Inventory and ask its members to verify availability of faculty for collaboration. Reimbursement issues for consultation would also be discussed, both for initial consultations and ongoing projects. The involvement of these valuable colleagues in UNYTRN training programs, continuing education symposia, etc. will also be discussed

7) General Clinical Research Center (GCRC). For studies at the bench-human interface such as investigations of metabolic pathways, novel markers, etc., as well as for the initial trials (Phase I, IIa) of new therapies and devices, an inpatient unit or designated outpatient research clinic is critically important. Presently, the University of Rochester has the only federally funded GCRC within the region, and the goal here would be to identify ways to support Clinical Research Center functions regionally either by increasing access to the Rochester GCRC or through the support of satellite Clinical/Translational Research Centers. John Gerich, MD, Director of the Rochester GCRC and Kimberly O'Brien, PhD of Cornell University will Co-chair this

Working Group. The first issue for discussion would be the accessibility of GCRC facilities and resources at the University of Rochester for use by UNYTRN members' faculty. Information about the Rochester GCRC resources should be shared with UNYTRN members. The review and approval process would be discussed, including involvement of UNYTRN faculty in the process. A mechanism for prioritizing GCRC resources among UNYRTN member institutions and other non-member institutions will be discussed and developed as deemed appropriate. Issues of cost sharing would be raised. The potential supplementation of GCRC funds specifically for multidisciplinary, multi-institutional translational research in furtherance of UNYTRN proposals as a means to expand access and services would be considered.

A second major topic for discussion would be the development of satellite CRC's in UNYTRN institutions supported by the Rochester GCRC. A new nutrition/human metabolism unit has just been constructed at the Division of Nutritional Sciences at Cornell University. Similar CRC facilities are available in the University at Buffalo-affiliated hospitals, the M.I. Bassett Hospital, and SUNY Upstate Medical University. Other UNYTRN institutions may wish to develop such units. The development of these units would be facilitated by accessibility of the GCRC program at the University of Rochester to help organize and support these CRC satellites to carry out translational research locally at the UNYTRN institutions. First, facilities and staff would be supported by GCRC expertise. Second, a network of core laboratories will be discussed. Third, a tiered approach might consider the type of study and the study population targeted. For example, a nutritional intervention might be piloted at the nutrition/human metabolism unit at Cornell University in normal subjects and, if promising, be used in a clinical (disease-positive) population at the Rochester GCRC. Such a network of satellites is expected to expand the utilization and capabilities of both the Rochester GCRC and the CRC satellites.

8) Pilot Studies for Multi-institutional Translational Research. The UNYTRN plans to break down barriers between institutions due to communication, access to faculty and services, regulations, training, and specialized facilities. However, the removal of these barriers may not be enough to induce UNYTRN members to collaborate. Any such system has inertia brought on by unfamiliarity, distance, etc. The availability of funds for pilot studies which use the UNYTRN network would be an important incentive to take those first steps to build multidisciplinary, multi-institutional teams which take advantage of unique resources at the member institutions. The goal of this Working Group would be to develop a program for translational research pilot studies with the UNYTRN. Allan Green, DPhil of the M.I. Bassett Research Institute and Paul Davis, MD of Ordway Research Institute will Co-chair this group. As member institutions may have their own internal funds for pilot studies, this program to fund one pilot study per year which would require meaningful involvement of faculty and facilities from two or more UNYTRN institutions. The pilot studies would need to fulfill criteria for translational research, and have the potential to develop into full proposals for external support. The application process, eligibility criteria, review of applications, expenditure of funds, progress reporting, and tracking of each project's impact would be developed by the Working Group. One pilot study per year will be supported by the Rochester CTSI. Three additional pilot studies may be funded by the Foundation for Healthy Living, as their contribution to UNYTRN.

G2J4e. Training, Career Development, and Continuing Education. (Specific Aim 5)

The shortage in faculty with translational research expertise necessitates a program for training and career development. Four approaches to alleviate the shortage will be considered by the Education and Training Working Group: 1) Curriculum leading to a degree in translational research offered on a regional basis; 2) Career development awards supported by multiple UNYTRN institutions; 3) Short courses for UNYTRN faculty and students; and 4) Continuing education programs for UNYTRN members. The Working Group will consider each of these options as potential solutions to the shortage of investigators performing translational research. Drs. Pearson (URMC) and Trevisan (Dean, SUNY Buffalo School of Public Health) will co-chair this Working Group.

1) Translational Research Curriculum Leading to a Master's Degree. The Working Group will identify Master's and Doctoral Degree Programs in the region which might prepare an investigator for a career in translational research. One model might be the modification of the Rochester Clinical Research Curriculum (K30) to provide core instruction in clinical and translational research. The opportunities for regional collaboration in such a program will be explored. In general, the Program should include two years of instruction with a core didactic curriculum, skill-building workshops, and a period of research under a research mentor. Various models will be considered, such as centralized coursework or workshops using distance-learning technologies, with mentored research and thesis preparation in the trainee's sponsoring institution.

2) Career Development Awards for Translational Research. The UNYTRN might also provide regional support for career development awards, such as K08, K23, or K12 awards. These 3- to 5-year training awards could be considered for individual applications (K08, K23) or as part of an institutional award (K12). In these programs, the didactic curriculum might be completed at a central Clinical Research Curriculum, the team of mentors might consist of faculty for multiple UNYTRN institutions, and the research project performed at the trainee's home institution. The Working Group will determine the feasibility and desirability of a regional program for translational research career development.

3) Short Courses Relevant to Translational Research. Each UNYTRN member will be surveyed for courses that might be of interest to trainees in translational research. The accessibility of these courses by distance-learning or web-based technologies will be explored. Of interest would be a core curriculum of lectures on research methods and of research skill-building workshops, such as intellectual property protection, grant writing, or research project administration. Another scenario would be the provision of a centralized course given over a few days such as a summer institute or research conference. This potential to partner with other CTSAs for this purpose should be explored.

4) Continuing Education Programs. The UNYTRN institutions will be invited to post their seminar series relevant to translational research on the UNYTRN website. Investigators who may wish to attend conferences at other institutes should be encouraged to do so. The sharing of faculty between UNYTRN institutions would be highly desirable. UNYTRN will support at least one regional symposium of translational research each year. This has been done annually for the past four years under the sponsorship of UNYCoR and the Upstate Medical University. UNYTRN will partially support this conference, in future years. This Translational Research Conference will be encouraged to highlight UNYTRN investigators, as well as bring in guest speakers from outside the region.

G2J4f. Evaluation of the UNYTRN. (Specific Aim 6).

This Key Function has designated deliverables for each of its specific aims (Table G2J7). The extent to which each of these deliverables is successfully produced will be the basis for the Key Function's success.

Table G2J7: Summary of Deliverables from UNYTRN and Their Use in Further CTSA Proposals

Specific Aim	Deliverable from UNYTRN	Potential Use in Further CTSA Proposals
1. Organization of UNYTRN	a. Four quarterly meetings of Executive Committee documented with minutes b. Seven monthly conference calls per year documented with minutes c. Monthly meetings of Directorate, documented with minutes d. Development of UNYTRN Website	a. Executive Committee for membership b. Directorate for administration c. Website for communication of UNYTRN resources and administration with CTSA
2. UNYTRN Resource Inventories	a. Web-based CRISP database of projects in member institutions b. Completed survey with >80% response for translational research resources	a. Communication tool to identify collaborators and technologies usable by CTSA b. Baseline for recurrent surveys in translational research in member institutions, UNYTRN-wide, and between institutions
3. Needs Assessment for Translational Research	a. Survey of investigators on barriers and needs b. List of collaborations between UNYTRN members c. Assessment of research institutions and needs surveys to identify unmet needs	a. Baseline for surveys to measure changes in barriers and needs b. Baseline for recurrent surveys to assess level of collaboration between UNYTRN members and CTSA c. Targets for requests for resources based on needs
4. Planned Translational Research Resources	a. Convention of 8 Working Groups at least quarterly as documented by minutes	a. Use of some or all Working Groups to direct CTSA resources
4a. Regulatory Compliance	a. Regulatory Compliance Training Program for Principal Investigators b. Regulatory Training Program for research administrators c. Consideration of an office for assistance in regulatory affairs	a. Support of program for principal investigators b. Support of program for administrators
4b. Support for IRBs	a. A centralized program for education and certification of PIs in human subjects protection b. A centralized program for training of IRB members c. A regional IRB for multi-institutional projects	a. Support of program for education and certification of PIs in human subjects protection b. Support of program to train IRB members c. Assembly of regional IRB for use by CTSA
4c. Project Coordinator Training	a. A regional program to train and certify research coordinators b. Regional program to provide research coordinators with continuing education c. Consideration of a network for human subjects recruitment	a. Support of research coordinator training program for CTSA b. Support of research coordinator continuing education program for CTSAs c. Support of subject recruitment network for CTSA
4d. Translational Research Informatics	a. Identify the research informatics resources currently available within the UNYTRN b. Develop mechanisms for utilization and reimbursement of informatics resources c. Prioritize needs for informatics resources and training	a. Assembly of regional informatics network for collaboration with bioinformatics Key Function b. Coordination of training in bioinformatics
4e. Research Design and Analysis	a. Directory of faculty and staff within UNYTRN available for consultation b. Consideration of systems to compensate providers of design/analysis services	a. Support for design and analysis services between UNYTRN members and CTSAs b. Baseline for level of use of design/analysis services
4f. General Clinical Research Center	a. Improved access to Rochester GCRC by UNYTRN members b. Development of procedures for review and approval of GCRC proposals from UNYTRN members. c. Support for satellite GCRCs in members without a GCRC	a. Additional resources for Rochester's GCRC to accommodate UNYTRN requests b. Baseline for level of use of GCRC by UNYTRN members as evaluation of UNYTRN activity c. Support for CTSA faculty and personnel to develop satellite GCRCs
4g. Pilot Studies	a. A program to fund pilot translational research studies requiring multi-institutional collaboration within UNYTRN b. Development of policies and procedures to receive and review applications	a. Funds to support pilot studies b. Methods to evaluate success of pilot studies in encouraging externally-funded research
5. Education and Training	a. Masters Degree Program in Translational Research b. Career Development Awards (K08, K23 or K12) for UNYTRN Faculty c. List of short courses/summer institutes relevant to translational research d. Support for Regional Translational Research Award Symposium (SUNY-Upstate)	a. Support for Regional Clinical Research Curriculum expansion b. K08, K23, or K12 Awards using multiple UNYTRN Programs c. Support of short courses or summer institutes. d. Annual Regional Translational Research Symposium e. Collaboration with other CTSA's on short courses or summer institutes.

G3. TRACKING AND EVALUATION

G3A. Specific Aims

The overall goal of the Tracking and Evaluation Plan is to assess the progress toward achievement of the short-term and long-term goals of the CTSI. To achieve this goal, evaluation activities will essentially have three objectives. The first is to evaluate the organizing activities of the CTSI, to map the transformation of clinical and translational research at URMC. The second is to document progress toward implementation of goals of each of ten key functions. Finally, the CTSI as a whole, encompassing the entire spectrum of URMC clinical and translational research, will be assessed to document institutional change, cooperation and collaboration among key functions and other program components. The reorganization into a cohesive, unified research unit should create a functional academic home for clinical and translational research. To achieve these goals and objectives, the Tracking and Evaluation Plan will have the following specific aims:

1. To develop a logic model as the conceptual framework for self-evaluation activities, to assess not only CTSI organizational processes and key function activities, but also short-term and ongoing outputs and long-term outcomes of the CTSI as a whole.
2. To incorporate Evaluation and Tracking into the planning of each key function, including measurable short-term and long-term outcomes.
3. To identify valid measures of organizational activities, short-term and ongoing outputs, and long-term goals, and a means to prioritize them in assessing overall CTSI success, in addition to those of key functions.
4. To develop and implement data collection methods for the pre-specified measures, including IRB approval of protocols requiring g consent by trainees, CTSA scholars, and mentors.
5. To assess, on an annual basis, the achievement of CTSI goals through review and analysis of collected evaluation data, to feed results back to CTSI and Key Function leadership, and to implement modifications to improve performance in these areas falling short of goals.
6. To participate in the National CTSA Evaluation Plan. The UR CTSI Logic Model may serve as a model for efforts to evaluate such a National CTSA Programs.

At the end of the initial period of CTSA funding, the Evaluation and Tracking Support Group will have an ongoing systematic program assessing the quantity and quality of activities in each key function. Moreover, there will be a clear description of the transformational process which allowed creation of the UR CTSI and the formation of ten key function groups. Finally, solid information on short0term outputs of the CTSI, with some early evidence of progress concerning long-term outcomes, will be made available to CTSI leadership for program modification and improvement. The UR CTSI should contribute to a National CTSA evaluation Program, given its experience in assessment of institutional change in similar projects.

G3B. Organization of Tracking and Evaluation: The Evaluation and Tracking Support Group

G3B1. Overview

Evaluation and Tracking has been given high priority in the UR CTSI and afforded a role similar to that of a key function (Figure G1E1, CTSI Organizational Chart). An Evaluation and Tracking Support Group has been formed to carry out the specific aims relevant to this area. The Director, Ann Dozier, RN, PhD, will serve on the CTSI Administrative Committee, along with other Key Function Directors. A CTSI Co-Director, Thomas A. Pearson, MD, MPH, PhD, and a CTSI Administrator, Thomas Fogg, will be members of the Support Group, providing access to the CTSE Executive Committee and CTSI Director. Figure G1E1 identifies the Evaluation and Tracking Support Group as relating to each key function, to assist in their respective evaluation plans. The organizational chart also shows a supporting relationship to the CTSI Administrative Committee, for evaluation of the UR CTSI as a whole unit, as well as to the National CTSA consortium for involvement in the National CTSA Evaluation Plan.

G3B2. Personnel Constituting the Evaluation and Tracking Support Group.

Ann Dozier, RN, PhD will serve as Director of the Evaluation and Tracking Support Group. Dr. Dozier is Director of the Research Services Group within the Department of Community and Preventive Medicine and, in this capacity, has access to a data collection and management group which can develop questionnaires; perform mail, telephone and emails surveys; create data abstraction tools; enter and clean data; and analyze results. Dr. Dozier's primary research interest is in the evaluation of research and healthcare organizations and she brings 15 years of experience as both a consultant and, more recently, a tenure track faculty member. Much of her current grant support [e.g., Rochester Prevention Research Center, Images of a Healthy Worksite

(NHLBI), K30 Program] is related to her evaluation activities. Therefore, she brings not only senior expertise in the theory and practice of program evaluation, but also a research group with expertise and experience in similar projects (See G3B3).

Thomas A. Pearson, MD, MPH, PhD is Co-Director of the UR CTSI and Director of the Education and Training Key Function. Dr. Pearson will represent the CTSI Director in the Evaluation and Tracking Support Group and assure that any requests for evaluation data are received in a timely manner at a high rate of response. Dr. Pearson is Principal Investigator of the Rochester Prevention Research Center and the National Cardiovascular Health Intervention Network, two large multi-institutional program funded by the CDC. He brings expertise in developing evaluation plans for such national programs.

Stephen Lurie, MD, PhD is Director of Education Evaluation in the Office of Medical Education. His major interest is in the evaluation of educational programs and psychometrics, and he serves the UR CTSI as Director of the Evaluation Core of the Education and Training Key Function. He brings expertise in this area to the Evaluation and Tracking Support Group.

Thomas Fogg, MS is Administrator for the UR CTSI and will provide a liaison to the key function groups, for whom he will provide administrative support. Mr. Fogg also has been Senior Planner in the Office of Clinical Research and in this capacity has considerable expertise in Logic Models for the planning and evaluation of complex, multi-institutional programs, such as the Rochester Prevention Research Center. In addition, Mr. Fogg has overseen the Research Resource Inventory and its updates in 2003 and 2005.

Carla Boff will serve as Special Project Coordinator for the Support Group. Mrs. Boff has been responsible for the tracking of 124 Scholars in the Rochester Clinical Research Curriculum (K30) Program, with high rates of follow-up response. She will be responsible for continued tracking of K30 Scholars, and also T32 trainees and K12 Scholars.

Joseph Duckett will serve as data analyst for the Support Group. A member of the Research Services Group, Mr. Duckett will assist key function directors in development of data collection and abstraction instruments and, if appropriate, supervise the collection, management, and reduction of the data into usable summary form.

Tina McCoy will serve as Administrative Assistant to the Group. She will organize meetings, receive requests, prepare evaluation reports, etc. for the Support Group. She currently supports the Office of Clinical Research and the K30 Program.

G3B3. Functioning of the Evaluation and Tracking Support Group

The Group will meet weekly to plan activities and assess progress. The Director will attend monthly meetings of the CTSI Administrative Committee and will meet at least quarterly with each key function director to ascertain needs for evaluation and tracking. Each key function will have its own evaluation plan. It is expected that she will provide a regular report to the CTSI Administrative Committee. The Support Group will contribute significantly to the Annual Report required by the Project Office, including T32, K30, and K12 trainee tracking, progress by key function groups toward their goals, as well as tracking CTSI studies supported by the GCRC. This Group will annually update the Research Project Data in the Research Resource Inventory, to track research sponsored by both federal and non-federal sources. The Research Resource Inventory will also survey, on a biennial basis, key research resources by all 83 research units at the URMC (See Tables G1A1, G1A2, G5A2 and G5B1).

G3C. Prior Experience in Program Evaluation and Tracking

G3C1. Overview.

The Evaluation and Tracking Support Group has been created by bringing together individuals within URMC who have been responsible for these activities in individual programs. Like the rest of the UR CTSI, creating a single, centralized Support Group enhances the evaluation and tracking capacity for URMC as a whole and assures the fidelity of evaluation across key functions. This section will provide several examples of ongoing experience in evaluation and tracking relevant to the CTSI.

G3C2. The Research Resource Inventory as an Evaluation Tool.

G3C2a. Methods.

A Clinical Research Resource Inventory has been carried out in 1998, 2003 and 2005 to catalog and make accessible resources and activities related to clinical and translational research at the URMC. These data have also been used to support clinical research strategic planning, and as an Intranet-based directory of clinical research faculty and resources at the URMC for use by investigators and trainees. As an

evaluation tool, they provide several measures of the growth in URMC research, the types of research ongoing, and the type and quantity of major research resources, space and personnel (See below).

Essentially two surveys have been conducted. The first was intended to obtain a list of all clinical research projects currently being conducted and to categorize them according to type of clinical research. The survey was distributed to all principal investigators (PCs) as listed in either the University's Office of Research and Project Administration's (ORPA) list of externally-sponsored projects or in the Office of Human Subjects containing individualized information for verification, modification or addition. A second phase of similar forms was sent to departmental administrators to add any names not listed on the ORPA/OHSP lists. Response rates have been excellent. By the end of the inventory in August, 2003, a response rate of 94% had been obtained. In August 2005, response rate of 90% of PIs was obtained. A second survey inventoried clinical research resources at the URMC. This inventory collected information on space for clinical research, available study populations, clinical research personnel, patient databases, specimen repositories, etc. The survey was sent to 33 Departments and Centers, of which five Basic Science Departments responded that they had no clinical research activity. Among the 28 remaining Departments and Centers, 20 responded for the whole department and 8 large Departments responded by Divisions and other submits, for a total of 83 units responding. The response rate by July 30, 2003 was 100%. In 2005, 81 units were surveyed with a 98% response.

G3C2b. Clinical Research Faculty and Projects at URMC (2003).

The Clinical Research Resource Inventory enumerated Principal Investigators at URMC in 2003 and 2005 of whom 36% were not involved in clinical research and 64% were so involved. (If a faculty member performed both kinds of research, they were classified in the clinical researcher group.) These investigators identified ongoing research projects, of which 33% were not clinical research and 67% were clinical research or clinical research training in both years. As an example of the rich database available for evaluation and tracking, the numbers of projects classified by type of clinical research are shown in Table G3.1. A steady growth of the number of projects is seen between 1998 and 2005, with especially consistent growth in patient-oriented research.

Table G3.1: Number of URMC Research Projects by Category in the Clinical Research Resource Inventory Database for 1998, 2003, and 2005

Clinical/Translational Research Project Category	Number of Projects		
	1998	2003	2005
Patient-oriented Research	330	445	626
Population-based Research	80	151	134
Health Services and Outcomes Research	58	120	108
Health Ethics, Law, and Policy Research	*NA	8	6
Total Clinical/Translational Research	468	724	874

*NA = Not Available

G3C2c. Clinical and Translational Research Resources (CRRI) at URMC Identified by the Clinical Research Resource Inventory.

The Clinical Research Resource Inventory lists a wide array of clinical research resources as identified by the 83 units in URMC in 2003 and 2005 which perform clinical research. Space available for clinical research can be identified on the URMC campus and off campus. A feature of the 2003 and 2005 surveys was to identify populations and databases that would include persons from under-represented minority groups. A wide array of specialized technologies was identified (special instruments, imaging, etc). Staff working in subject recruitment and follow-up, data collection, and data entry, management and analysis has been tracked, showing steady growth (Table G3.2). The results document not only a vast array of staff, technology, space, study subjects, and databases available to CTSI investigators, scholars and trainees, but also the extent to which it is organized and accessible. The entire CRRI is available to faculty and trainees on a Clinical Research Intranet Website. Serial (e.g., every two years) surveys provide for a unique means to assess clinical and translational research growth on an institution-wide basis and this provides a powerful tool for identification and evaluation of gaps in progress and infrastructure.

Table G3.2: Number of URMC Staff by Clinical Research Functions in the Clinical Research Resource Inventory for 1998, 2003, and 2005

Staff Function	Number of Fulltime Equivalents		
	1998	2003	2005
Data Collection	74.8	136.7	112.2
Data Entry, Management, and Analysis			
Doctorally prepared	26.0	45.5	61.4
Not Doctorally prepared	69.6	138.6	121.4
Subject Recruitment and Follow-up	140.1	139.5	152.3

G3C3. Evaluation of the Rochester Clinical Research Curriculum (K30) Program

The CTSI Education and Tracking Key Function will build on prior experience with the K30 Program, which required rigorous evaluation and tracking of its trainees. Evaluation and tracking was carried out by Mrs. Boff and Mrs. Kolomic.

Each trainee has had 17 educational objectives or competencies required by the RCRC. Each RCRC Scholar submits an evaluation form certifying attainment of their learning objectives and competencies at completion of the Program. All trainees must have received an A or B to be credited with the didactic coursework. Completion of skill-building workshops allows completion of 6 skill objectives and 5 attitude objectives.

The evaluation plan also intends to track RCRC graduates at the end of their training and two years later. A smaller number of RCRC matriculates have completed the program long enough to qualify for a two-year follow-up. Nonetheless, it is possible to derive some conclusions about their career pathways to date. First, of 124 RCRC Scholars, only 7 have withdrawn from the Program and only 5 lack follow-up data. RCRC graduates remain in academic positions even if they leave Rochester; only 5 Scholars are not affiliated with major academic medical centers (See Table G5.8). All graduates participated in a research project to complete requirements for their MPH-CI Degree. Second, there has been frequent and successful research grant activity from RCRC graduates. A total of 75 federal and 160 non-federal grant applications were submitted, resulting in 33 federal and 115 non-federal grants being funded. These are somewhat misleading since several of the successful applications were resubmissions. Not counting the pending applications, this amounts to 62% of federal (33/53) and 80% (115/143) of non-federal grants being funded. These funded federal grants include 2 K07, 12 K23, 1 K24, and 1 R25 grants. Funded grants to RCRC Scholars amount to $22,183,830 in total research costs for all years, including $11,047,525 from NIIH and $11,136,295 from other sources. A total of 45 RCRC Scholars currently hold grants as Principal Investigators. Third, research productivity as measured by publications has been excellent. RCRC Scholars list 344 first-authored publications and 224 coauthored papers since matriculation in the RCRC.

These data support the effectiveness of the RCRC in developing clinical research skills in the Scholars and providing them with mentored opportunities to be productive. Their career trajectories, though early in the process, appear excellent based on acquisition of career development awards and other research grant funding. Our conclusion is that the productivity objectives in terms of the quality and quantity of clinical investigators can be effectively tracked as measures for program effectiveness toward short-term and long-term education and training objectives.

G3C4. Evaluation of the Rochester Prevention Research Center (PRC)

The Rochester PRC is one of 33 Prevention Research Centers funded by the Centers for Disease Control. This Program requires Community Participatory Research and a rigorous evaluation of all programmatic elements based on a Logic Model. The PRC National Community Committee selected, among the 33 PRC's, the Rochester Logic Model as the most clear and useful, and proposed it as a model for evaluation of the National PRC Program. Dr. Dozier is the leader of the Rochester PRC evaluation group and has developed a rigorous plan for evaluation of the entire program and its components, including measures of institutional change. This provides evidence of our capability to develop and use logic models and to contribute to evaluation of a national program.

G3D. Methods to Carry Out Specific Aims

G3D1. Development of a Logic Model for Self-Evaluation (Specific Aim 1)

G3D1a. Overview

The UR CTSI logic model is shown in Figure G4.1 and had been developed to support the overall mission of the UR CTSI. This narrative describes each component of the logic model, linking them to other parts of the UR CTSI application. Each logic model component can and will be related to a National CTSA Evaluation Plan. Indeed, the UR CTSI logic model would be prototype for this.

G3D1b. Contextual and Motivating Conditions.

The model recognizes the increasing demand by the U.S. public and its lawmakers for translational research. The logic model takes into consideration clinical and translational research at the URMC in its present situation, including obvious deficits in space and equipment, lack of translational research training, no coordinated engagement of the community, etc. On the other hand, the URMC has considerable programmatic activity in this area, both research and training. The URMC leadership is committed to fundamental organizational change to transform clinical and translational research and to create a physical and intellectual home for it at the URMC.

G3D1c. Inputs

A wide variety of organizations, both internal and external to the URMC, will provide guidance, personnel, resources, and requests to the UR CTSI. These stakeholders include the University of Rochester leadership, the academic environment at the URMC, a large number of national and regional partners including the NIH program Office, the National CTSA Program, an External Advisory Board, regional institutions participating in the Upstate New York Translational Research Network (UNYTRN, see Section G2J), and community partners, including a Community Advisory Board and a variety of community-based organizations. These inputs will assist the UR CTSI in achieving its vision of excellence and relevance.

G3D1d. Organizing Activities of the UR CTSI

One set of short-term process measures will be the organizing activities of the UR CTSI. These deal with transforming the structure of the clinical and translational research at the URMC through the implementation of the key functions into a single, functional unit, as a major goal for the CTSA Program.

G3D1e. Key Functions of UR CTSI

These activities directly relate to the key functions, as proposed by each of their Directors. These have been grouped into larger types of measurable activities, including recruiting and training CTR Scholars, the support of investigators, the stimulation of new and multidisciplinary research, the development and sharing of methodologies, the engagement of the local community, the stimulation of regional collaboration, and the strengthening of UR CTSI capacity through resource acquisition.

G3D1f. Short-Term and Ongoing Inputs

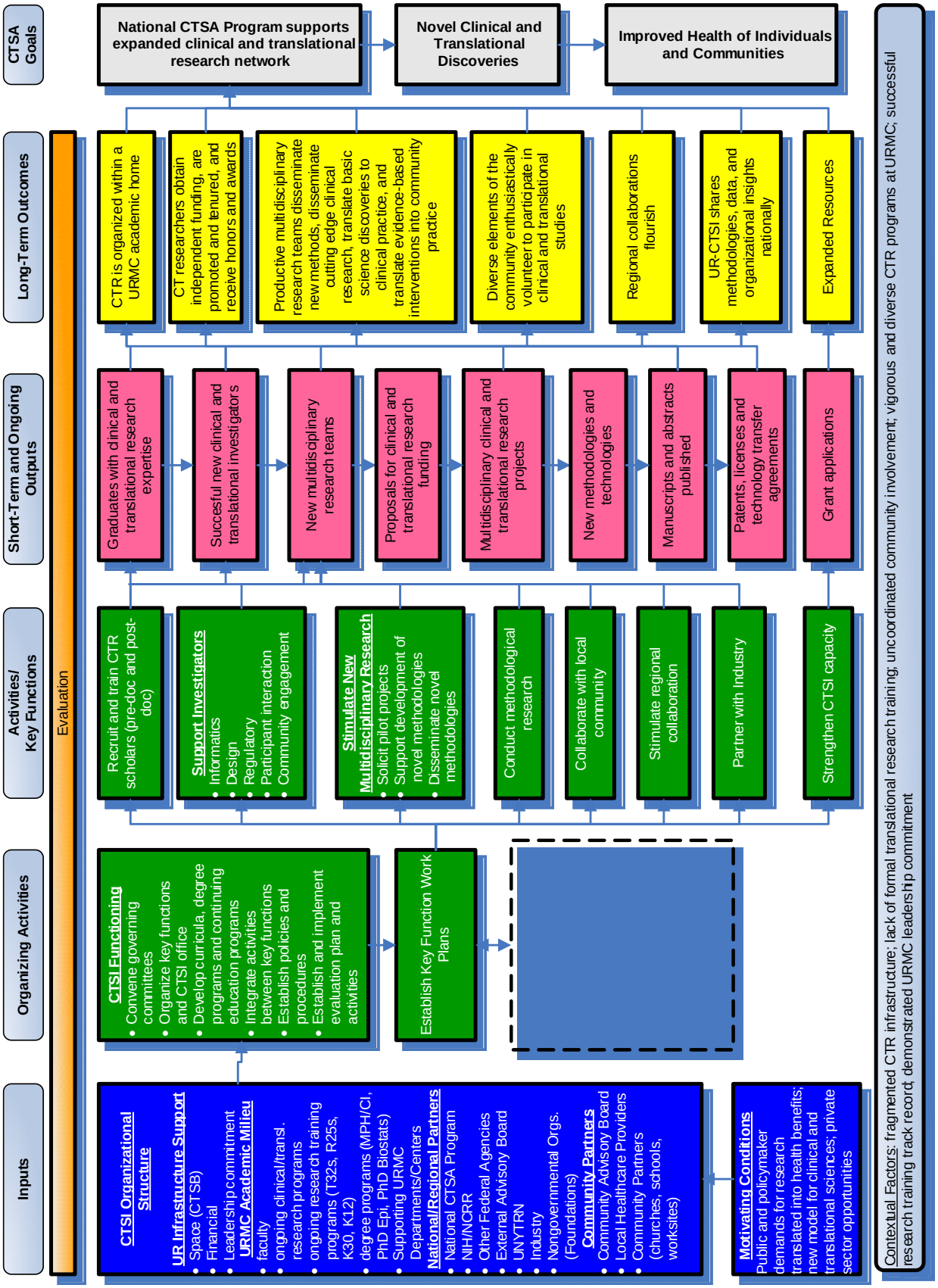
Of particular relevance to an evaluation plan are short-term outputs of the UR CTSI. Seven large categories of end products are envisioned. First, the numbers of graduates with CTR-related degrees should increase. Second, an increasing number of investigators should be performing CTR, through their training, recruitment and retention. Third, the number of research teams with multiple disciplines involved should increase at the URMC. Fourth, the number of proposals requesting external support on CTR research by multidisciplinary teams should increase. Fifth, the number of active multidisciplinary clinical and translational research projects should expand. This should be reflected in additional projects and resources in the Research Resource Inventory. Sixth, the number of submitted and published abstracts and manuscripts of CTR should also increase over the relatively short term. Finally, the number of research discoveries which elicit patents, licensing agreements and other technology transfer actions should signal a successful pipeline of translated research.

G3D1g. Long-Term Outcomes

These endpoints are more challenging to measure, but nonetheless serve as the most valid assessment of sustainable program effectiveness, as compared to process or short-term output measures. The first measure is that of establishment of a real home for clinical and translational research. This may be measured in a number of ways, including physical clustering of resources and personnel, assessment of ease in accessing CTR resources and staff, etc. A second measure is the development of independence in careers of CTR trainees through obtaining of their own research funding, appointment, promotion and tenure in academic faculties, and honors and awards (e.g. members in the National Academy of Sciences/Institute of Medicine). Third, the long-term functioning of these multidisciplinary clinical and translational research teams needs to be

Figure G3.1: University of Rochester Clinical and Translational Science Institute Logic Model

The mission of the University of Rochester Clinical and Translational Sciences Institute is to bring innovations in diagnosis, treatment and prevention of disease to patients and communities through collaborative, multidisciplinary clinical and translational research, and train a new generation of leaders in the clinical and translational sciences.



assessed. An assessment of short-term outputs may provide trends as useful evidence of research activity, publication and technology transfer. Specific measures of methods development (e.g. publications, patents), dissemination (e.g. publication, education), translation to clinical practice (FDA investigational new drug classification, approval of drugs and devices, etc.), and translation to clinical practice (e.g. guidelines, utilization surveys, sales) will be needed. Fourth, the involvement of the local community in clinical research might be assessed by local opinion surveys, but the "bottom line" will be the number and diversity of volunteers for clinical and translational research protocols. Fifth, measures of regional collaboration should be possible through the number of formal contractual relationships within members of the Upstate New York Translational Research Network, as well as multi-institutional use of core facilities such as the new GCRC and educational and training programs. Sixth, the involvement of UR CTSI in the sharing of data, resources and software should be a measure of involvement in a National CTSA Program. This includes involvement of URMC faculty in the National CTSA Steering Committee and its Subcommittees.

Finally, a common measure of success involves the extent of funding for clinical and translational research at the URMC. These should include the number and size of projects in the new GCRC. Moreover, with the Research Resource Inventory, there should be an expansion in the number and cost of clinical and translational research projects, not at the expense of basic research. Indeed, the ability of the Research Resource Inventory to track not only the number of investigators and the amount of externally sponsored research, but also the type of research, the formation of multidisciplinary teams, and the acquisition of research space, staff and equipment should provide important information on the transformation of URMC research.

G3D1h. UR CTSI Goals

The overall goal of the UR CTSI should remain clear, namely the participation in and contribution to a successful national program promoting clinical and translational research which yields clinical and translational discoveries which directly improve the health of individuals and communities. The UR CTSI logic model provides a framework to assess the extent to which these goals are addressed through the UR CTSI.

G3D2. Evaluation and Tracking Plans for Individual Key Functions (Specific Aim 2)

G3D2a. Overview

Each key function director and working group is charged with developing objectives. Measurable outcomes have then been derived for each objective. Evaluation of each of the ten key functions will be described here, in addition to the incorporation of evaluation plans into each key function section. Thus, Evaluation and Tracking has been built into the key functions for the purposes of performance monitoring and feedback, and this evaluative information will also be used to assess performance of the UR CTSI as a new organization.

G3D2b. Novel Clinical and Translational Methodologies Key Function

Table G3.3 describes the three overall goals of the Novel Methodologies Key Function and the six areas for which measurable outputs might be collected. The measurable outcomes then require several specific steps. First, a Methodology Review Panel would be organized to enumerate, grade and fund proposals for new methodologies, including those by new investigators and those from under-represented minorities. The Panel would also track those funded proposals as to their success in achieving their aims, including use of the methodology, publications describing or employing it, and intellectual property outcomes. Likewise, the Panel would assess the success of travel grants in bringing new methodologies to the URMC. Second, an annual survey of CTSI investigators, such as those in the Research Resource Inventory, would assess the level of knowledge, satisfaction and need for methodologies at the CTSI and the URMC. The level of citation of CTSI methods would be monitored in CTSI conferences, newsletters and websites. Third, the GCRC Advisory Committee would incorporate methodology assessments in their protocol review. This would include assessments of improvements in research quality that would occur if other methodologies were available in the CTSI. Finally, the Research Resource Inventory would enumerate every two years the presence, number and type of research methodologies at the URMC. An upward trend may be further explained by examination of the aforementioned evaluation results.

Table G3.3. Measurable Outcomes for Novel Methodologies Key Function

Aim/Objective	Measurable Outcome
Develop new methodologies	
1. Solicit and review proposals	1. Organize and convene at least quarterly a Methodology Review Panel 2. Count proposals received 3. Count proposals received annually which meet three criteria for approval 4. Count proposals submitted and approvable annually by new investigators and under-represented minorities
2. Provide support for promising proposals	1. Count proposals funded and level of quality according to three criteria 2. Identify <25% of programs from a single department or center 3. Track use of CTSI methodologies in other CTSI research proposals and funded grants every six months 4. Track publications describing funded methodologies every six months 5. Track publications describing applications of funded methodologies 6. Track patents, licenses, or other intellectual property actions related to funded methodologies 7. Assess feasibility and validity of methodology on six-month intervals
3. Provide travel grants to investigators to learn new methodologies	1. Count number of applications for travel grants 2. Assess whether methodology for which travel was performed was initiated at CTSI, and if not, reasons 3. Assess use of learned methodology in CTSI at six-month intervals
Facilitate interactions regarding new methodologies and CT researchers	
1. Provide information about new methodologies in widely available sources	1. Conduct annual survey of knowledge and satisfaction with new technologies to Research Resource Inventory PI list 2. Track number of references to new methodologies n CTSI newsletter, website and conferences 3. Track number of CTSI weekly conferences devoted to novel technologies
2. Review new technologies as part of new GCRC Advisory Committee considerations	1. Count number of GCRC protocols with methodology reviews per year 2. Count number of GCRC protocols which could be enhanced by new technologies/methodologies
Assess research needs of CTSI faculty and address them	
	1. Conduct an annual survey of satisfaction with existing technology and need for new technologies 2. Solicit at least one proposal per year to develop a methodology identified as needed at UR-CTSI 3. In biennial Research Resource Inventory, serially enumerate number and type of research methodologies at URMC

Table G3.4 Aims/Objectives and Measurable Outcomes for Pilot and Collaborative Studies Key Function

Aim/Objective	Measurable Outcome
1. Organization of a Pilot and Collaborative Translational and Clinical Sciences Program	1. Organization of Pilot Project Coordination Committee and convening it once a quarter 2. Organization of Application Review Committees with specific expertise 3. Hiring of a Senior Health Project Coordinator to collect and track outcome measures 4. Convene an external site visit panel in Year 3 to review performance
2. Facilitate production of preliminary data to support research proposals	1. Count applications for trainee pilot projects, minority support fellowships, investigator-initiated pilot projects, and RFA-responsive pilot awards 2. Identify fundable projects based on project review priorities including collaboration and target research areas 3. Fund 6-10 projects per year of the highest merit 4. New funding from pilot data will be primary outcome 5. Publications, application of methods/technologies, technology transfer, or other products of pilot studies will be secondary outcomes of longitudinal follow-up surveys 6. Cross-disciplinary collaborations involving the new methods will be tracked
3. Support proof-of-concept studies seeking clinical applications for basic science findings	1. Same as #1-6 above 2. Count applications for the collaboratively funded projects between Pilot Programs, Community Engagement, and Development of Novel Methodologies Key Functions 3. Assess funded applications for collaboratively funded project same as #4-6 above
4. Stimulation of new cross-disciplinary collaborations, within the Institution and externally	1. Count applications for Interdisciplinary conference grants and Traveling fellowship grants 2. In funded projects, assess #4-6 as above

G3D2c. Pilot and Collaborative Translational and Clinical Studies Key Function

This key function has essentially one organizational goal: to create and Pilot and Collaborative Translational and Clinical Sciences Program, and three functional goals, as shown on Table G3.4. Completion of organizational goals will require four steps shown on the Table. The three functional goals will entail solicitation, review, awarding and longitudinal tracking of seven different award mechanisms, of which there are hopes to support 6-10 projects per year. The Coordination Committee supported by the Senior Project Coordinator will collect and review annual progress reports in the last month of funding. The projects will be followed up annually thereafter for well-defined metrics of new research support related to pilot data as the primary outcome, as well as publications and applications including patents, licenses and other products of research. An assessment of creation of multidisciplinary research teams emanating from the pilot studies will also be collected. A strong feature is the aforementioned data available for their review and consideration.

G3D2d. Biomedical Informatics Key Function

The Biomedical Informatics Key Function has an organizational aim of developing the Biomedical Informatics Program (BIP) at the URMC, for which three outcomes can be assessed (Table G3.5). The four objectives of this key function will be evaluated by process measures of the use of informatics resources and personnel. Surveys of users will provide specific quantitative information. More qualitative assessments will be derived from workshops, users' meetings and help lines. More difficult to assess are the integration and sharing of informatics in context-specific uses, and two specific applications are proposed to map their use by CTSI faculty and trainees. Similarly, integration of informatics into clinical information systems and applications for improving clinical care will be awarded by two specific applications. A Data and Technology Sharing plan is proposed with commitment to actively participate in the National CTSA Informatics Steering Committee.

Table G3.5. Aims/Objectives and Measurable Outcomes for Biomedical Informatics Key Function

Aim/Objectives	Measurable Outcomes
1. Organize a Biomedical Informatics Program (BIP) at URMC	1. Organization of directorate for BIP 2. Convene BIP Advisory Committee at least twice a year 3. Hire and train coordinator and developers
2. Facilitate and coordinate use of existing biomedical informatics resources	1. Keep records of all services provided, including a. Online resources b. Web portal functions c. In person consultations d. Specialized services 2. Implement system logs to track online and web portal usage 3. Seek user feedback on specific informatics services by a. Regular surveys of PI's b. User meetings and workshops c. Online feedback forms d. Help lines
3. Integrate existing biomedical informatics services with additional services to provide context-specific support	1. Enumerate use of services in key context areas a. Mathematical models for clinical trial simulation b. Facilitation of clinical trial subject recruitment and process monitoring
4. Facilitate data sharing and knowledge reuse through adoption and development of standards and protocols	1. Enumerate use of integration of data and knowledge reuse into clinical information systems to separate patient-specific recommendations 2. Enumerate integration of best practice recommendations into clinical settings to improve behavioral interventions
5. Coordinate with NIH CTSA Informatics Steering Committee	1. Implementation of Data and Technology Sharing Plan 2. Participation in CTSA Informatics Steering Committee meetings and activities

G3D2e. Design, Biostatistics and Clinical Research Ethics Key Function

This key function will organize the Biostatistics, Epidemiology and Clinical Research Ethics Program whose aims will be carried out by an Executive Committee. The Committee will review all CTSI requests for biostatistics, epidemiology and ethics support using four criteria (Table G3.6). This creates the opportunity to assess the level of investigator or trainee preparation in these areas, as an assessment of K30, T32 or K12 training. This is especially a rare opportunity to assess education in research ethics, such that assessments of conflict of interest, human subject issues, etc. will be made as part of the service and also serve as a measure of ethics knowledge and skill. Those protocols given priority for support will be tracked for effort assigned to the project as well as a questionnaire to the investigator about the services received. For developing protocols, their success in obtaining funding will be tracked. For activated protocols, the presentations, peer-reviewed publications, further grant acquisitions and technology transfer actions will be tracked longitudinally. Some assessment of the utility of the support service in the success or failure of the project will be made. The unit will also seek to develop and evaluate new methodologies, using similar outcome measures.

Table G3.6. Aims/Objectives and Measurable Outcomes for Biostatistics, Epidemiology & Clinical Research Ethics

Aims/Objectives	Measurable Outcomes
1. Organize the CTSI Biostatistics, Epidemiology and Clinical Research Ethics Program	1. Organize and convene the Executive Committee
2. Provide detailed consultations for development of study protocols	1. Enumerate number of protocols reviewed by executive committee 2. Tracking of resources assigned to projects 3. Counting number of conflicts of interest or other ethical problems with protocols as means to assess adequacy of ethics education 4. Completion of questionnaire by investigator receiving support 5. Follow-up for application and funding of grants
3. Provide biostatistical and epidemiologic support during conduct of studies	1. Track status of ongoing projects with enumeration of effort expended 2. Completion of a questionnaire by investigator receiving support 3. Electronic follow-up to track peer-reviewed publications, presentations, and inventories related to project 4. Assessment of whether resources given each project were effective in project success
4. Collaborate in interim and final analyses of study data	
5. Collaborate in preparation of manuscripts and presentations	
6. Develop novel research methods to address special research problems	1. Methodological development reported to Director of Unit 2. Presentation, publication, and technology transfer of methods tracked
7. Study ethical issues of research including stakeholder perceptions, impact of cost-effectiveness analyses, and conflict of interest policies	1. Track presentations, publications , grant applications, and funding in Research Ethics

G3D2f. Regulatory Knowledge and Support Key Function

This key function will organize a Regulatory Knowledge and Support Program by naming a Director of Regulatory Compliance Support and opening of Office of Regulatory Compliance Support (ORCS), with a faculty advocate and User Advisory Board (Table G3.7). Training of CTSI investigators will be evaluated by levels of Ethics Certification and also the need for consultations by the ORCS. A series of quality improvement audits will provide a strong monitoring tool for compliance in protocols. A Regulatory Compliance Web Portal can be tracked for completion by 100% of CTSI trainees and, if made mandatory, CTSI faculty and staff. User surveys will assess satisfaction and identify issues for alteration. Conflict of interest management will also be tracked. Finally, the Regulatory Knowledge and Support Program should be a national model, worthy of sharing with UNYTRN and with the National CTSA Regulatory Support Steering Committee.

Table G3.7: Aims/Objectives and Measurable Outcomes for Regulatory Knowledge & Support Key Function

Aims/Objectives	Measurable Outcomes
1. Organize the CTSI Regulatory Knowledge and Support Program	1. Name Director of Regulatory Compliance and Support 2. Organize and staff the Office of Regulatory Compliance and Support 3. Create the User Advisory Board
2. Train CTSI researchers in science and ethics of human subjects research	1. Ensure 100% of PI's have HSPP certification 2. Enumerate number of requests for consultations to Office of Regulatory Compliance and their outcomes 3. Enumerate number of unresolved issues referred to Research Review Process Improvement Team 4. Assess number of protocols for which the Faculty Advocate was needed for 5. Enumerate number of workshops on regulatory compliance in CTSI seminar series and elsewhere, and attendance at each
3. Regulatory Compliance Monitoring and Improvement	1. Conduct quality improvement/good clinical practice guideline audits to evaluate level of regulatory compliance 2. Follow-up audits will enumerate number of deficiencies corrected and remaining
4. Computer-assisted Regulatory Document Assistance	1. Finalization of the Regulatory Compliance Web Portal 2. Ensure 100% of CTSI trainees (K30, T32, K12) complete Web Portal 3. Assess number of faculty PI's who receive certification in regulatory compliance 4. If mandatory, require 100% of PI's of special programs to complete programs as prerequisite for grant submission 5. Survey of users' satisfaction and needs for improvement
5. Conflict of Interest Management	1. Tracking submission of conflict of interest disclosures 2. Enumerate COI management plans with CTSI faculty
6. Development and Sharing Best Practices	1. Enumerate programs with UNYTRN 2. Actively participate in the National CTSA Regulatory Support Steering Committee

Table G3.8: Aims/Objectives and Measurable Outcomes for Participant and Clinical Intervention Resources

Aims/Objectives	Measurable Outcomes
1. Reorganize the GCRC into the new GCRC as part of the CTSI	1. Reorganize the CTRC Advisory Committee 2. Reallocate and track GCRC resources to new CTSI Key Functions 3. Name a new CTRC Associate Program Director for Translational Research 4. Create an Office of Clinical Research Coordination
2. Expand support for patient-oriented translational research	1. Relocate to new, upgraded space to support GCRC functions 2. Enumerate users of GCRC from UNYTRN and other users in the region 3. Assess personnel, space, and finance needs with new configuration of GCRC 4. Convene Advisory Committee every six months to assess utilization or poor performance of GCRC components to develop for corrective actions
3. Assist in recruitment of basic scientists	1. Update basic science research resource inventory 2. Enumerate basic scientist-clinical researcher partnerships in GCRC submissions 3. Enumerate number of pilot study proposals from basic scientists or their collaborators.
4. Expedite initiation of protocols	1. Track number of applications, approvals, and active protocols and the resources allocated to each 2. Attendance at monthly lunchtime seminar for new investigators 3. Enumerate use of Patent Advocate on development of protocols 4. Assess duration of time from contact with GCRC to protocol submission
5. Encourage and facilitate participation of subjects in studies	1. Track use of funds for local transportation 2. Track use of childcare by research subjects
6. Assist investigators in identifying and recruiting subjects	1. Assess use of research coordinators by investigators 2. Assess cost-effectiveness of CRCO in supplying study coordinators from a pool
7. Promote introduction of novel research technologies	1. Enumerate number and attendance at monthly seminars on research methods

G3D2g. Participant and Clinical Interactions Resources

This key function entails the restructuring of the GCRC to a shared support unit of the CTSI (Table G3.8). While some resources are relocated (e.g. Biostatistics, Bioinformatics), there is also the opportunity to emphasize translational research, as is done with a new GCRC Associate Director for Translational Research. Also, the emphasis on resources allows investment in a Research Coordinator Program. The GCRC will be relocated in a new, upgraded space, allowing some expansion in protocols, which will be tracked for applications, approvals, and activities as previously in the GCRC. All protocols will be annually reviewed for productivity and, if not, the Advisory committee may not renew their funds. Expansion of GCRC may also involve external institutions from the UNYTRN, or basic scientists now partnering with CTR investigators. Protocol review and approval will be facilitated by a Patient Advocate skilled at protocol development. The new GCRC should be more research subject-friendly. Additional help will be afforded in participant recruitment, including childcare.

G3D2h. Community Engagement

One of the organizational goals of the community Engagement Key Function is to organize this within a new Center for Community health, including the creation of a Community Advisory Board and several offices to carry out its specific aims (Table G3.9).

Participatory evaluation will be used to the extent possible, with outcomes and measures defined through a process that includes community participants and investigators. The table below outlines a series of preliminary outcomes and measures that will be refined through the participatory process. Both qualitative and quantitative approaches will be employed, including tracking logs; participant and community surveys; pre-post assessments of participant knowledge, intention and attitude; and focus groups/key informant interviews. Results will be presented to the CTSI Administrative committee. Feedback and CQI methods will be used throughout the project to assure implementation of needed modifications.

Table G3.9. Evaluation Goals and Measures of Community Engagement Key Function

Evaluation Indicator	Assessment Method
Specific Aim A: Promote community participation in the development of clinical and translational research	
Participation and diversity of members/key groups	Member participation log
Participant satisfaction with engagement	Feedback Survey; qualitative methods
Advisory Groups effectiveness	PSAT*; qualitative methods
Effect on research activities (e.g. prioritization, feedback, design)	Meeting Minutes, participant and investigator surveys
Knowledge and awareness of clinical research among groups	Pre/post assessments
Effectiveness of participatory research partnerships	PSAT*; qualitative methods
Specific Aim B: Promote participation of community health care providers in research	
Number of participating practices / practitioners	Baseline, then annual survey of practices in PBRNs
Number of researchers/practitioners trained on PBRNs	Database of trainees.
Identification of barriers/facilitators to participating in research	Annual survey of MDs in and out of PBRNs
Satisfaction with participation/involvement	Feedback about consultation service by users (survey)
Number of patients recruited in PBRN-related studies	Database maintained by the ROCH-PBRN
Number and types of PBRN-related studies/grants/ research dollars generated and number of manuscripts	Database maintained by the ROCH-PBRN
External evaluation: overall effectiveness, improvements	Provider Advisory Board- annual meeting/feedback
Specific Aim C: Improve the ability of researchers to understand and incorporate community perspectives	
Number of courses offered/participants attending/completing	Track course offerings and participants
Course modifications made	Track changes made; focus group
Satisfaction among course participants	Participant feedback survey; journal entries
Number of departments with "community" trained research staff	Track participants
Number of "community competent" researchers and research staff	Pre/post assessments; qualitative methods
Changes made to trained researchers' protocols	Track changes and survey
Specific Aim D: Increase the level and diversity of subject participation in clinical and translational research	
Deployment of marketing messages	Track distribution of materials (number, location), and numbers of presentations (diversity of audiences)
Determine extent of exposure among general public to clinical research messages	Community surveys (telephone, mailed, in-person) in future years
Assess change in attitude and interest among general public	Community surveys (as above); qualitative methods
Assess investigator access to and use of resources	Track utilization of bibliography, templates, toolkits, expert/user groups
Participation in user and expert groups	Track participation
Satisfaction among user group and expert group members	Feedback Survey; qualitative methods
Number of research projects collaborating with CTSI	Track research project participation
Number of individuals enrolled and retained in clinical research among CTSI participating researchers	Track research participants screened, enrolled and retained (first timers; repeat subject participants; ethnic/other cultural subgroups; gender; other specifically-targeted groups based on research conducted (deaf, homosexual, disease specific))
Scholarly productivity relative to recruitment and retention	Track proposal, manuscript, and abstract submissions

*The Partnership Self-Assessment Tool (PSAT) developed by the Center for the Advancement of Collaborative Strategies in Health, New York Academy of Medicine, is a tool used to assess the effectiveness of community partnerships (41-44).

G3D2i. Translational Technologies and Resources

This key function will organize a Laboratory Support Center and provide trainees and investigators with subsidies for technology used, as well as investing in new technology in specified areas. Evaluation measures include process measures of amount of technology and its level of use (Table G3.10). Other outcomes include presentations, publications, licensing and patents, grant applications, and sponsored research awards. An internal/external review board will be brought in every two years to review the laboratory Support center, and cores will continue to be reviewed on an annual basis by the Core's Steering Committee.

Table G3.10. Aims/Objectives and Measurable Outcomes of the Translational Technologies and Resources Key Function

Aims/Objectives	Measurable Outcomes
1. Establish a Laboratory Support Center	1. Name a Director 2. Quantity support for selected core facilities 3. Level of inquiries for use of cores will be documented 4. Number of investigators and level of support documented annually 5. Assessment every two years by an Internal and External Advisory Committee 6. Annual review of existing cores by Cores Steering Committee
2. Establish translational technology access subsidy	1. Number of applications for subsidy per year 2. Monitoring of expenditures and project progress a. Annual Progress Reports b. External funding applied for and/or received c. Presentations, Publications, Technology Transfer
3. Upgrade the CTSI Physical Infrastructure	1. Monitor support for imaging and use by investigators 2. Monitor support for genomics and use by investigators 3. Monitor support for proteomics and use by investigators 4. Tracking of productivity by presentations, publications, and technology transfer

G3D2j. Education and Training Program Evaluation

G3D2j(1). Evaluation Committee.

The evaluation of the Education and Training Key Function will be carried out by a group of faculty and staff with a primary career interest in educational program evaluation. Ann Dozier, RN, PhD will chair the Committee. Staff includes Carla Boff who is responsible for the Student Database within the Department of Community and preventive Medicine.

G3D2j(2). Evaluation of Didactic Coursework.

Each course and workshop required for the Masters and PhD Degrees will be evaluated by course participants at the end of the course. Written evaluation forms are distributed online and submitted to Pattie Kolomic, Graduate Education Coordinator, for summarization. Copies of the evaluation summaries are sent to the Curriculum Committee Chair (Dr. Chin). These are used by the Directorate for course review and improvement or, if necessary, replacement of the Course Director.

G3D2j(3). Evaluation of CR Scholar Learning Objectives and Competencies.

Evaluation of the CTR Scholar in the didactic curriculum and research practicum is facilitated by the establishment of 23 learning objectives and acquired competencies at the beginning of the curriculum (Table G3.11). Each objective has one or more measurable outcomes. At the completion of the didactic core curriculum, each Scholar completes the CTSA evaluation form. Completion of knowledge objectives entails receipt of an A or B for the coursework. Scholar progress is reviewed twice annually be the Recruitment/Admissions Office and individuals with course grades less than a B are placed on probation. Receipt of more than one grade below B will result in dismissal or retaking the course for an acceptable grade.

Attainment of skill objectives are monitored by reporting on the CTR Evaluation Form of the title of the research project, the mentor, publications, presentations, and abstracts, and grant activity. These are entered into the CTR Scholar Database. The attitude objectives are also assessed on the CTSA Evaluation Form by completion of workshops and field visits. Of particular interest will be a description of the Research Project

developed. The number of mentors, the different disciplines represented, and the different institutions represented will be recorded.

G3D2j(4). Evaluation of Responsible Research Conduct Training

All CTR Scholars will have successfully completed: the Research Ethics Workshop, the Workshop on Recruitment and Retention of Research Subjects, and modules on human subjects, ethics, etc. in several other courses and workshops. All CTR Scholars should have completed self-study and passed examinations for the Human Subjects Protection Program (HSPP), as well as the Regulatory compliance Web Portal. Their protocols submitted for consultation on design, knowledge and ethics will be reviewed for ethical concerns. All projects will be reviewed by RSRB unless exempt. CTR Scholars will be considered well prepared upon completion of this series of modules on responsible conduct of research.

G3D2j(5). Recruitment of Under-represented Minorities and Women

All trainees in the MD Programs (ART, Year-Out and MD-MS), the T32 Program (phD and MD PhD Programs in Translational biomedical Science), the K30 Program, and the K12 Program will be assessed annually according to gender, ethnicity, and race as self reported. Extensive efforts will be made to recruit women and under-represented minorities. Current efforts would be considered adequate if at least half the trainees are women and 25% or more are from under-represented minorities, while preserving the high quality of students.

G3D2j(6). Evaluation of CR Scholar Career Development.

The CR Scholar database has been established with the CTSA evaluation form at the completion of the didactic phase. A curriculum vitae is also collected at that time. Mrs. Boff will follow-up with each Scholar on an annual basis, requesting an updated C.V. From this, the following data would be extracted and entered into the database: current position and affiliation, new publications, abstracts, presentations, grants submitted and received, awards and accomplishments.

In addition, beginning at the time of completion, the Evaluation Committee will track publications generated since admission to the CTSI, through extensive searches of MEDLINE, assisted by the Miner Library. The number of first and coauthored papers will be summarized. One paper per year (if present) will be selected from the journal judged to be most respected and the impact factors of that journal entered into the database. The average impact factors for each CR Scholar will be calculated, along with the number and first authorship of papers.

Similarly, the grant activity of each CR Scholar will be requested. The grants submitted and approved as principal Investigator will be ascertained. The funding rate will e determined and entered into the database along with the number of grants funded as principal and collaborating investigator.

Each Scholar's career development then will be summarized on the existing CR Scholar database. Outcome measures to be tracked include: continued academic appointment; promotion in position since the CTSA; grant applications submitted, awarded, and funding rate; number of total and first authored publications; and impact factors of best publication. While these outcomes measures could note be compared with a control group, they do provide some absolute benchmarks that can be agreed upon as evidence for career success following the CTSI training. Each year's data will be presented to the CTSI Administrative Committee for review and discussion.

G3D2j(7). Evaluation of Mentors.

A member of the Mentor Development Committee will be assigned to each trainee of a CTSA T32, K30, or K12 Programs and will meet with them two times a year. One of these meetings will include the mentor. The trainee will complete a form which reviews performance toward their Research Career Development Plan, and includes the trainee's evaluation of their mentor. These reports will be brought to the Mentor Development Committee and, if any deficiencies are identified, the Key Function Director or other Mentor Development Committee members will meet with the Mentor. If deficiencies persist, the Scholar may need to identify another mentor.

Table G3.11: Objectives/Acquired Competencies for Education and Training in Clinical/Translational Research

Educational Objectives/Acquired Competencies	Measurable Outcomes	Degree Program		
		MSTR	MSCI	PhD
Knowledge				
1 Learn the principles and theories which serve as the basis of biostatistics and quantitative data analysis.	1 Completion of Introduction to Biostatistics or equivalent course.	x	x	x
2 Understand the ways to measure the distribution of traits and diseases in populations, the determinants of those distributions, and study designs for this purpose.	2 Completion of Principles of Epidemiology or equivalent course.	x	x	x
3 Be able to design and analyze studies relevant to patient-oriented clinical research	3 Completion of an Advanced Epidemology course or equivalent.		x	x
4 Appreciate study designs, settings, and databases available to evaluate clinical interventions.	4 Completion of Clinical Evaluative Sciences or equivalent course.		x	x
5 Comprehend the concepts underlying the quantitative analysis of medical decisions.	5 Completion of Medical Decision and Cost-Effectiveness Analysis or equivalent.		x	x
6 Understand the design and conduct of human experiments.	6 Completion of Clinical Trials or equivalent course.	x	x	x
7 Identify social and behavioral factors which impact on human health and the use of health services.	7 Completion of Social and Behavioral Medicine or equivalent course.		x	x
8 Understand basic pathophysiologic mechanisms leading to human disease.	8 Completion of Pathophysiology course or equivalent.	x		x
9 Know the theory and application of major new methodologies to measure biological perameters important in human health.	9 Completion of Translational Technologies course or equivalent.	x		x
10 Appreciate the development and evaluation of therapies for treatment of disease.	10 Completion of course in Experimental Therapeutics or equivalent.	x		x
Skill				
1 a. Identify a hypothesis, select the appropriate study design, and collect data to test the hypothesis.	1 a. Carry out a clinical research project under the supervision of a mentor or mentorial committee, including proposal development, data collection, data management, and data analysis.			x
b. Develop hypothesis with a data set and perform appropriate statistical tests of the hypothesis.	b. Carry out hypothesis test within pre-existing data set.		x	
c. Acknowledge and be able to use resources for evaluation of a diagnostic and therapeutic agent.	c. In Experimental Therapeutics course, develop protocol for evaluation of a diagnostic and therapeutic agent.	x		x
2 Use multiple types and sources of medical informatics to facilitate research.	2 Completion of Bioinformatics course or equivalent.	x	x	x
3 Use database management and statistical software to organize and analyze data.	3 Analysis of trainees' data using computers with SAS or equivalent software under supervision.	x	x	x
4 Gain skills in communicating results of research in abstract and presentation forms.	4 a. Write and submit at least two abstracts of trainees' work to regional/national meetings.	x	x	x
	b. Present research findings at a minimum of one Clinical Research Seminar or Departmental Research Conference.	x	x	x
	c. Present research results orally or as a poster at a minimum of one national scientific conference.	x	x	x
5 Acquire skills in writing and critiquing research manuscripts.	5 a. Critique at least one manuscript submitted to mentor or advisor for review.	x	x	x
	b. Publish at least two manuscripts in peer-reviewed journals within two years of training.	x	x	x
6 Develop abilities in writing and critiquing of research grant proposals.	6 a. Write at least one complete research grant suitable for submission.	x	x	x
	b. Critique at least one research grant and write-up comments for peer review.	x	x	x
7 Manage the fiscal, personnel, facilities and regulatory assets of a funded clinical research program.	7 Complete a Clinical Research Skills workshop on Research Project Management and receive a Research Project Administration Compliance Number.	x	x	x
8 Identify institutional resources needed to carry out high- quality research.	8 Use the Clinical Research Resource Inventory to identify and access collaborative resources available for clinical research.	x	x	x
Attitudes				
1 Appreciate ethical issues involved with research in human subjects.	1 a. Completion of Ethical Conduct of Research Workshop.	x	x	x
	b. Complete instruction on protection of human subjects in research to qualify for an HSPP number.	x	x	x
	c. Completion of IRB application and section in research grant application.	x	x	x
2 Understand the regulations and rationale for inclusion of women, minorities, and children research.	2 a. Completion of Clinical Research Skills Workshop on Recruitment and Retention of Research Subjects.		x	x
	b. Completion of section of research grant application on inclusiveness.	x	x	x
3 Comprehend the types of clinical research which offer career opportunities.	3 Completion of field visits to observe research in each of five types of clinical and translational research.	x	x	x
4 Appreciate the opportunities and challenges of multidisciplinary research involving two or more basic, clinical, or population sciences.	4 Inclusion of two or more disciplines as mentors or members of the MPH-CI Thesis Committee.	x	x	x
5 Understand the opportunities and obstacles to performing research within the private sector.	5 Completion of Clinical Research Skills Workshop on relations with industry and Technology Transfer/Working with Industry.	x	x	x

G3D2k. Evaluation of the Upstate Consortium, UNYTRN.

This Key Function has designated deliverables for each of its specific aims (Table G3.12). The extent to which each of these deliverables is successfully produced will be the basis for the Key Function's success.

Table G3.12 Summary of Deliverables from UNYTRN and Their Use in Further CTSA proposals

Specific Aim	Deliverable from UNYTRN	Potential Use in Further CTSA Proposals
1. Organization of UNYTRN	a. Four quarterly meetings of Executive Committee documented with minutes b. Seven monthly conference calls per year documented with minutes c. Monthly meetings of Directorate, documented with minutes d. Development of UNYTRN Website	a. Executive Committee for membership b. Directorate for administration c. Website for communication of UNYTRN resources and administration with CTSA
2. UNYTRN Resource Inventories	a. Web-based CRISP database of projects in member institutions b. Completed survey with >80% response for translational research resources	a. Communication tool to identify collaborators and technologies usable by CTSA b. Baseline for recurrent surveys in translational research in member institutions, UNYTRN-wide, and between institutions
3. Needs Assessment for Translational Research	a. Survey of investigators on barriers and needs b. List of collaborations between UNYTRN members c. Assessment of research institutions and needs surveys to identify unmet needs	a. Baseline for surveys to measure changes in barriers and needs b. Baseline for recurrent surveys to assess level of collaboration between UNYTRN members and CTSA c. Targets for requests for resources based on needs
4. Planned Translational Research Resources	a. Convention of 8 Working Groups at least quarterly as documented by minutes	a. Use of some or all Working Groups to direct CTSA resources
4a. Regulatory Compliance	a. Regulatory Compliance Training Program for Principal Investigators b. Regulatory Training Program for research administrators c. Consideration of an office for assistance in regulatory affairs	a. Support of program for principal investigators b. Support of program for administrators
4b. Support for IRBs	a. A centralized program for education and certification of PIs in human subjects protection b. A centralized program for training of IRB members c. A regional IRB for multi-institutional projects	a. Support of program for education and certification of PIs in human subjects protection b. Support of program to train IRB members c. Assembly of regional IRB for use by CTSA
4c. Project Coordinator Training	a. A regional program to train and certify research coordinators b. Regional program to provide research coordinators with continuing education c. Consideration of a network for human subjects recruitment	a. Support of research coordinator training program for CTSA b. Support of research coordinator continuing education program for CTSAs c. Support of subject recruitment network for CTSA
4d. Translational Research Informatics	a. Identify the research informatics resources currently available within the UNYTRN b. Develop mechanisms for utilization and reimbursement of informatics resources c. Prioritize needs for informatics resources and training	a. Assembly of regional informatics network for collaboration with bioinformatics Key Function b. Coordination of training in bioinformatics
4e. Research Design and Analysis	a. Directory of faculty and staff within UNYTRN available for consultation b. Consideration of systems to compensate providers of design/analysis services	a. Support for design and analysis services between UNYTRN members and CTSAs b. Baseline for level of use of design/analysis services
4f. General Clinical Research Center	a. Improved access to Rochester GCRC by UNYTRN members b. Development of procedures for review and approval of GCRC proposals from UNYTRN members. c. Support for satellite GCRCs in members without a GCRC	a. Additional resources for Rochester's GCRC to accommodate UNYTRN requests b. Baseline for level of use of GCRC by UNYTRN members as evaluation of UNYTRN activity c. Support for CTSA faculty and personnel to develop satellite GCRCs
4g. Pilot Studies	a. A program to fund pilot translational research studies requiring multi-institutional collaboration within UNYTRN b. Development of policies and procedures to receive and review applications	a. Funds to support pilot studies b. Methods to evaluate success of pilot studies in encouraging externally-funded research
5. Education and Training	a. Masters Degree Program in Translational Research b. Career Development Awards (K08, K23 or K12) for UNYTRN Faculty c. List of short courses/summer institutes relevant to translational research d. Support for Regional Translational Research Award Symposium (SUNY-Upstate)	a. Support for Regional Clinical Research Curriculum expansion b. K08, K23, or K12 Awards using multiple UNYTRN Programs c. Support of short courses or summer institutes. d. Annual Regional Translational Research Symposium e. Collaboration with other CTSA's on short courses or summer institutes.

G3D3. Identify and Prioritize Valid Resources of Organizing Activities, Short-term and Ongoing Outputs, and Long-Term Goals (Specific Aim)

G3D3a. Overview.

The measures of UR-CTSI progress are alluded to in the logic model (Figure G3.1) and will be expanded upon here. They will refer to the organizing activities, short-term and ongoing outputs, and long-term outcomes of the logic model. The Evaluation Key Function proposes these at this state of planning but will further refine them as planning and implementation of the CTSI proceeds.

G3D3b. Organizing Activities.

Even prior to Year I, organizing of CTSI Executive and Administrative Committees, its Administrative Core, and the Evaluation and Tracking Support Group will be high priorities (See Table G4.1). For the ten key functions, the first aim/objective in Tables G3-8, 10 and 12 are organizational goals of most key functions. They too would be priorities for the first quarter of Year I. For Education and Training, this would entail development of curricula and approval of degree programs, by the faculty identified as course directors for the new Master's and PhD programs. The CTSI Executive and Administrative Committees would establish policies and procedures as needed to carry out CTSI key functions and to encourage key function interactions.

A test of key function organization and activities would be the development of work plans prior or to early in Year I. These would be read by the CTSI Administrative Committee and serve as an indicator of organization progress.

Finally, the organization of external partners would commence possibly in Quarter 2 or 3 of Year I. These include recruitment and convention of the External Advisory Committee, the Community Advisory Board, and the UNYTRN Executive Committee. Each of these external bodies would then mature in parallel to UR CTRI and provide advice and support during this process of growth and change.

G3D3c. Short-term and Ongoing Outputs

These indicators would be the most likely to provide evidence of change over the initial period of CTSI funding (Figure G3.1). Some valid measures of long-term and ongoing outputs under consideration are:

(1) Graduates with clinical and translational research expertise.

This would be measured by the number of graduates from the MSTR and MSCI Programs, as well as the PhD in Translational Biomedical Research and MD-PhD graduates with this PhD concentration. Moreover, CTSI Scholars in the K30 (20-25/year) and K12 (3-4/year) would be assessed as to their didactic coursework in the new curriculum and to their scholarly project, which would be classified according to the research methods used. These graduates would be compared to those in the RCRC database to map progress in type of clinical/translational research being learned.

(2) Successful new clinical and translational investigators.

The success of graduates from #1 will be tracked by the Evaluation and Tracking Support Group on an annual basis and the data entered into the RCRC/CTSI database. These measures are reviewed in Section G3D2j(6), and include position, affiliation, presentations, abstracts, publications, grants submitted and received, awards and accomplishments. These provide a quantitative measure of "success".

(3) New multidisciplinary research teams.

It is possible to identify the number of investigators on a research proposal from departments and centers other than that submitting the proposal. This can be done for Master's and PhD these committees and K award mentorial committees.

(4) Proposals for clinical and translational research funding.

The number of proposals which self-identify as clinical/translational research at the time of submission can be tracked. This would be important as a denominator of the quality and innovation of CTR proposals also, assessing with the proportion funded.

(5) Multidisciplinary clinical and translational research projects.

The number of active projects, either sponsored and registered in the Office of Research and Program Administration (ORPA) or approved to use human subjects by the Office of Human Subjects Protection (OHSP), would be enumerated by email updates of the Research Resource Inventory. These can be further assessed as to type of CT research.

(6) New Methodologies and Technologies.

Similarly, the biennial Research Resource Inventory will assess each of the 83 centers, departments, and divisions during clinical and translational research to assess major research resources, including major equipment, technical staff, access the populations, time and cell banks, etc. These serial surveys should allow

identification of new methodologies including those created by the Novel Methodologies Key Function (See G5B2 for list of current research technology at URMC).

(7) Manuscript and abstracts published.

The URMC will develop a centralized electronic biosketch as one informatics advance planned by the Senior Associate Dean for Academic Affairs. While this is being developed for appointment and promotion purposes, it also provides an assessment tool for mapping CTSI investigators' progress. More specifically, publications associated with CTSI pilot studies, GCRC-funded projects, CTSI-developed methodologies, and CTSI Education and Training Programs will be collected annually as evaluation measures of those specific key functions.

(8) Patents, Licenses, and Technology Transfer Agreements.

The Office of Technology Transfer will provide information annually on patent applications and approvals, number and size of licenses of products with industry, and other technology transfer agreements from CTSI-support research. These indicate translation of discoveries to practical application. The financial worth of these activities can also be tracked.

(9) Grant Applications.

In addition to the active projects registered with ORPA or OHSP, the number of federal and non-federal grant applications, their monetary value, the number funded (and their value) is tracked on a quarterly basis, from ORPA databases. It is expected that the number of applications in general, the proportion from Clinical and Translational Research, and the rate of approval and funding would continue to increase, recognizing the external influences on the rate of funding. Nonetheless, when including non-federal and private sector funding, an expansion of the quantity and quality of CT research might still be assessed.

G3D3d. Long-term Outcomes.

There are outcomes which may require more than one funding cycle to assess but would serve as more stable indicators of a successful UR CTSI. Some long-term measures might be:

(1) CTSI is the Academic Home for Clinical and Translational Research at the University of Rochester.

This may be measured in several ways, including an assessment of the proportion of CT research which is linked to UR CTSI either physically or collaboratively. The proportion of education and training at the Master's and Doctoral levels could also be tracked to the CTSI. The level of activity in the CTSB in terms of education, research, community engagement would be another measure.

(2) CT Researchers obtain independent funding, promotion, tenure, honors, and awards.

Funding would be tracked in the Research Resource Inventory. CTSI investigator's biosketeches could be abstracted for the other measures. For CTSI Scholars, all of these would be tracked on a yearly basis.

(3) Productive multidisciplinary research teams.

The continuation of short-term and ongoing outputs in G3D3c would, over a large period of time, provide a measure of this omnibus indicator of a successful CTSI.

(4) Volunteering for participation in clinical and translational research studies.

The number of protocols which meet their recruitment goals both in number of subjects meeting entry criteria, but also their diversity goals (women, under-represented minorities) can be tracked by ORPA or RSRB, as an indicator of success in community engagement.

(5) Regional collaborations flourish.

UNYTRN allows other regional CTSAs to collaborate in a non-competitive manner, and reaches out to smaller institutions for inclusion in cutting edge research. UNYTRN evaluation measures should indicate the success of this Upstate New York Consortium (See Table G312).

(6) UR-CTSI shares methodologies, data and expertise nationally (See Specific Aim 6).

This entails the participation of the URCTSI in the National CTSA Program including involvement with the Steering Committee and the Key Function Committees. The active involvement and successful leadership contributions to the National CTSA can be measured. The success of the UR-CTSI data sharing, resource sharing, and software sharing plans can be assessed annually in terms of number and type of sharing and any failures to do so.

(7) Expanded Resources.

The Research Resource Inventory will continue to be updated annually for principal investigators, projects and research funding. Every two years, the resources will be updated. It is expected that the positive increase in quantity and quality of CTR resources and infrastructure would continue.

G3D4. Develop and Implement Data Collection Methods. (Specific Aim 4)

A variety of qualitative and quantitative methods are used to collect the wide range of data endpoints proposed here. The measurable outcomes for the ten key functions describe many of the data sources and data collection methods proposed. Two methods will be described in more detail.

G3D4a. Tracking of CTSI Trainees in K30, K12, and T32 Programs.

Prior to a data collection, proposals for obtaining informed consent and collecting career development data will be submitted to the Institutional Review Board for approval. Upon this approval, written informed consent will be obtained from all CTSI trainees (including T32 trainees not in degree programs and past K30 participants) requesting permission to contact them longitudinally, indicating the type of data to be collected, and the use of the data. A commitment to complete confidentiality and right to withdraw or refuse at any time will be emphasized. A copy of the IRB consent will be given to the trainee. Annual progress reports will be shared with the RSRB, renewal of RSRB protocol approval will be required at regular intervals, and changes in protocol will need submission to and approval by the RSRB. Persons not providing consent will not be contacted, though some passive data collection such as MEDLINE searches for literature may use publicly available sources of information.

G3D4b. Research Resource Inventory.

This useful evaluation tool will be administered longitudinally using the methods described in G3C2. ORPA and OHSP databases will be used to update projects annually, usually in July of each year. Surveys of research resources will be carried out every two years over the 83 centers, departments, and divisions. The data will be available as an online intranet service for investigators to identify collaborators/mentors, technologies/methodologies, and other clinical resources such as databases; serum cell, or tissue repositories, technical staff, etc. High response rates have been the rule and the data are of great use in planning looking forward, as well as evaluation looking backward.

G3D5. Assess Achievement of UR CTSI Goals, Feedback to CTSI and Key Function Leadership, and Implementation of Modifications. (Specific Aim 5)

The Evaluation and Tracking Support Group will be represented by Drs. Dozier and Pearson and Mr. Fogg on the CTSI Administrative Committee. It is expected that the director of the Support Group would provide a monthly report on evaluation activities and progress toward achievement of CTSI goals. The logic model will serve as the self-evaluation plan with individual key function evaluation plans contributing to the whole.

On an annual basis, the CTSI Administrative Committee will have an Evaluation Retreat of at least one day's duration. This would best be done in late summer, early fall after the Research Resource Inventory is available and individual key function surveys might be completed at the end of the prior academic year. This would afford the opportunity to comprehensively examine the wide range of indicators for both the UR-CTSI as a whole and each key function as a functional sub-unit. This would provide immediate feedback to CTSI and key function leadership and allow formulation of the next year's work plans by the key functions which incorporate modifications and corrections in their next year's work plan. These modifications could be reviewed at the following year's retreat as to their success or failure. The retreat would allow comprehensive planning to occur, unlike monthly two-hour meetings which provide information and problem solving. NIH Program staff may participate in such planning, as deemed appropriate.

G3D6. Participate in the National CTSA Evaluation Plan. (Specific Aim 6)

The UR-CTSI intends to actively and fully participate in a National CTSA Evaluation Plan in several ways. First, effort by four members of the Evaluation and Tracking Support Group (Drs. Dozier, Pearson, Lurie and Mr. Fogg) has taken into account the need to participate in the plan. Four trips to NIH have been budgeted (if necessary, these could be expanded) to participate in UR CTSI National Plan. UR CTSI Evaluation and Tracking Support Group has considerable expertise in evaluation of large, complex academic programs, including the creation of logic models. The logic model shown on Figure G3.1 would easily serve as a template for a National CTSA Evaluation Plan, for example. Third, individual evaluation tools proposed by the UR CTSI would also be shared. These include the Research Resource Inventory, but also a number of smaller survey instruments and resources of research quality and quantity.

The UR CTSI will seek IRB approval and other internal approvals for collection of data from individual faculty and trainees as part of a National CTSA Evaluation. It will also work with partners in our regional consortium (UNYTRN), our External Advisory Committee, and our Community Advisory Board to encourage participation even if not employed by the URMC.

The UR CTSI intends to comply with its plan for sharing of data, technology, and software as described in Section G1. These shared entities would be available for the National CTSA Evaluation under this agreement.

G4. IMPLEMENTATION PHASE AND MILESTONES

The implementation phase of the UR CTSI will begin prior to notification that the award has been granted. Three months prior to the expected award date, the CTSA PI will convene the first Executive Committee meeting, and embark upon a series of organizational tasks that will activate each of the CTSI committees, the CTSI Administrative Core and key program functions. This represents a substantial commitment of institutional time and resources. The planned implementation steps for each such component are described below, and are illustrated in Figure G4.1. The roles and responsibilities of each committee, and its membership or the process for choosing members, are described in section G1E of this application ("Governance").

Figure G4.1. Year 1 Milestones for Establishment of UR CTSI

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Convene Executive Committee	X				
Convene Administrative Committee	X				
Organize Administrative Core	X				
Organize Evaluation and Tracking Support Group	X				
Approve annual work plans	X				
CTSI evaluation Plan submitted		X			
CTSI evaluation Plan approved			X		
Evaluation Plan reporting begins			X		
Convene Committee on Industry and Foundation Relations			X		
Recruit External Advisory Committee Members			X		
Convene External Advisory Committee				X	

G4A. Governing Committees and Cores

As previously described in this application, the UR CTSI is planned with a specific organizational structure to support its goals and activities. An organizational chart is included as Figure G1E1 in Section G1. The implementation plan for each organizational unit is described below.

G4A1. Executive Committee. As noted, the Executive Committee will begin meeting prior to the award date, and after that date will meet on a weekly basis. Its first tasks will be to develop committee meeting guidelines, detailed roles and responsibilities for each committee and the CTSI Administrative Core, and create an annual work plan and proposed evaluation plan for the Committee. These documents are described below in this section. Another matter to be taken up by the Executive Committee immediately after the notice of award is the selection and recruitment of members of the External Advisory Committee. The Committee will seek suggestions from the Senior Vice President for Health Sciences, create a list of candidates of its own choosing, and will also accept nominations from members of the Administrative Committee. After discussion, the Committee will reduce this list to a set of 6 to 8 initial candidates, who will be approached regarding participation. If a particular candidate declines, the Committee will select another from the pool of nominees.

The Executive Committee will be responsible for coordination with the NIH Program Office responsible for the CTSA program. It is anticipated that the Executive Committee will engage in several teleconferences each year with its assigned program officer and other NIH staff, for the purpose of providing informal status reports,

G4A2. Administrative Committee. This committee will also begin to meet prior to the award date, and after that point will meet monthly. Meetings may be more frequent early in the grant period, and *ad hoc* meetings will be arranged as necessary. As noted elsewhere, it will be made up of members of the Executive Committee, plus the CTSI key program function directors. The CTSA PI will serve as chair, and will convene the first meeting. Initial organizational steps will include the consideration of meeting guidelines and committee roles and responsibilities proposed by the Executive Committee, as described below. The Administrative Committee will also develop an annual work plan, which will be submitted to the Executive Committee for approval. In addition, the Committee will develop a proposed evaluation plan, which will go the Evaluation Tracking and Support Group for use in developing the overall CTSI Evaluation Plan.

G4A3. Administrative Core. The CTSI Administrative Core also will be organized prior to the award date, and will support the initial activities of the governing committees. This represents another material commitment of institutional resources prior to the funding period. Throughout the funding period, the Core will support each of the CTSI committees and key program functions. Working with each entity, the Core will facilitate the

development of work plans and evaluation plans, and will coordinate their review by the Executive Committee. In addition, the Core will facilitate the development of meeting guidelines and roles and responsibilities documents, working closely with the Executive Committee and each CTSI committee. The Core will also develop a proposed work plan for the year, which will be reviewed and approved by the Executive Committee. It will submit a proposed evaluation plan to the Evaluation Tracking and Support Group for use in developing the overall CTSI Evaluation Plan.

The Administrative Core will also be responsible for the development and maintenance of two CTSI websites. The first will be a public website, available through the URMC's site on the worldwide web. This site will explain the mission and vision of the UR CTSI, describe facilities available to support research, explain how to request access to CTSI capabilities, and provide contact information. It will serve as a platform for disseminating discoveries made with the support of the UR CTSI, by providing news and information and links to further information available elsewhere on the web, as described in Section G2c ("Biomedical Informatics"). Finally, it will be a primary vehicle for supplying information to the lay public regarding clinical and translational research. As described in Section G2G ("Community Engagement"), this will include not only descriptions of research underway at the CTSI, past accomplishments and future plans, but also information regarding how research helps the community, and how the community can become involved. The URMC will provide web server services and support without cost to the grant, illustrating one form of institutional support for the CTSI.

The second will be a password-protected private website, available only to CTSI faculty, staff and committee members. This site will include an announcement section, a calendar of events for the CTSI, a document library containing key documents regarding the CTSI (including meeting agendas, minutes, documents to be reviewed at meetings, policies, proposed policies, organization charts, publications related to CTSI research, lists of available CTSI resources, etc.), a task list for tracking key activities, and a discussion board where threaded discussions regarding CTSI matters can take place. A version of this website is already in use to support and facilitate the preparation of this grant application. Again, this represents a commitment of institutional resources well in advance of the funding period.

The CTSI Administrative Core will also manage the planning of the Clinical and Translational Sciences Building, working closely with the URMC space planning and finance offices, under the oversight of the CTSI Executive Committee. Preliminary plans for the building have already been developed and are described in this application (Section G1). The CTSI Administrative Core will manage the creation of a detailed needs document based upon input from all CTSI units, and will coordinate with other URMC offices in the development of a detailed project plan. This project clearly will exceed levels of effort supported under the grant, and is a form of institutional contribution to the establishment of the UR CTSI. In addition, the above-mentioned University Resources have contributed and will contribute very substantial amounts of time and effort to the planning and construction of the Clinical and Translational Sciences Building, representing a significant investment of resources separate and apart from those that will be supported by the CTSA.

G4A4. Evaluation and Tracking Support Group. The Evaluation and Tracking Support Group (ETSG) will be convened by the CTSI PI three months prior to award of the grant, another commitment of institutional resources prior to the award date. This group will depend upon the CTSI Administrative Core for staff support, and will work closely with it in the development of the CTSI Evaluation Plan and in tracking and reporting performance data. As noted above, the ETSG will receive approved work plans and proposed evaluation plans from each governing committee, the Administrative Core, and each key function. From this input, the ETSG will develop specific measures for each element of the work plans. In the process of developing measures, it is likely that the ETSG will identify gaps in individual work plans, or instances where work plans fail to cohere. In such cases, the ETSG will, with the advice of the Executive Committee, work with the entity or entities responsible for the particular work plans to resolve the problem.

G4A5. Committee for Industry and Foundation Relations. This Committee will meet on a quarterly basis, beginning four months after the initiation of the grant. Meetings may be more frequent early in the grant period. The CTSI PI will convene the first meeting. As for all CTSI committees, initial activities will include consideration of meeting guidelines and roles and responsibilities, and the development of a work plan.

G4A6. External Advisory Committee. The CTSI PI will convene the External Advisory Committee during the third quarter of the grant period. In-person meetings will be planned in Rochester on an annual basis. Between in-person meetings, the Executive Committee, working through the Administrative Core, will communicate progress to the Committee through Evaluation Reports and other updates. The Committee will review proposed meeting guidelines and roles and responsibilities and recommend refinements. The CTSI PI

and key program function directors will present a status report to the External Advisory Committee at each meeting. The Committee will make recommendations for the continued progress of the CTSI. The Executive Committee will assign each recommendation to a particular committee or key program function for follow-up, and will report back to the External Advisory Committee on the status of each at each meeting. The ETSG will track the status of each recommendation over time and periodically report to the Executive Committee.

G4B. Operating Guidelines and Practices

The UR CTSI will operate according to its logic model, written guidelines and practices that will facilitate efficient operations and successful pursuit of its goals. The key support documents are described below.

G4B1. Annual work plans. The Executive Committee will task itself and each of the CTSI standing committees (with the exception of the External Advisory Committee), the CTSI Administrative Core, and CTSI key program functions with the development of an annual work plan. Initially, these documents will lay out plans for each entity for the first year of the grant period in detail, listing overarching goals, necessary inputs, planned activities, outputs that will result from the activities, and expected outcomes that will result, as shown in Figure G4.2. Inputs are defined as resources or organizational relationships that will support the CTSI. Activities are discrete tasks that lead to specific outputs. Outputs are concrete deliverables, such as reports, publications, curricula or the like. Outcomes are intangible consequences that are expected to result from outputs and which will support the desired goals. Each organizational unit will also be responsible for producing a less detailed five-year work plan that includes only goals, outcomes and outputs for years 2 through 5 of the grant period. Prior to the beginning of each program year, each unit will produce a detailed annual work plan. The Executive Committee will review and approve each proposed work plan.

The target date for completion of initial work plans is the projected award date. Not only will this allow all organizational units to commence the funding period with a clear idea of their goals and objectives, it also will provide the Evaluation Tracking and Support Group (ETSG) sufficient time to prepare the Evaluation Plan by its deadline. Clearly, this entire planning effort represents a substantial commitment of institutional time and resources prior to the funding period.

Figure G4.2. Model Work Plan

<table>
<tr><td colspan="5">Goal: the desired ultimate endpoint</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td colspan="3">Outcome 1</td><td colspan="2">Outcome 2</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td>Output 1.1</td><td colspan="2">Output 1.2</td><td colspan="2">Output 2.1</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td>Activity 1.1.4</td><td colspan="2">Activity 1.2.4</td><td colspan="2" rowspan="2">Activity 2.1.2</td></tr>
<tr><td>Activity 1.1.3</td><td colspan="2">Activity 1.2.3</td></tr>
<tr><td>Activity 1.1.2</td><td colspan="2">Activity 1.2.2</td><td colspan="2" rowspan="2">Activity 2.1.1</td></tr>
<tr><td>Activity 1.1.1</td><td colspan="2">Activity 1.2.1</td></tr>
<tr><td colspan="5"></td></tr>
<tr><td>Input 1</td><td>Input 2</td><td>Input 3</td><td>Input 4</td><td>Input 5</td></tr>
</table>

G4B2. Evaluation Plan. After approval by the Executive Committee, the Evaluation and Tracking Support Group (ETSG) will use the annual work plans and proposed evaluations plans submitted by the governing committees, the Administrative Core and the key program functions to create an Evaluation Plan. As detailed in Section G3, the Evaluation Plan will be crafted to be fully consistent with the UR CTSI Logic Model (Figure G3.1; see Section G3 for a full description). For each output and outcome listed in the work plans, the Evaluation Plan will include one or more specific measures, specifying the exact nature of the data to be collected, the data source, how the data will be collected, who will collect it, and when it will be collected. The ETSG will create a database in which to store the data, and develop reports indicating the status of each measure and how it compares to its targeted value. The ETSG will present this information to the Executive and Administration Committees on a quarterly basis.

The first draft of the Evaluation Plan will be presented to the Executive Committee for review in the third month after the beginning of the grant period. A final approved document will be in place no later than five months after the beginning of the grant period, and regular progress reporting will begin at that time.

G4B3. Meeting Guidelines. The Executive Committee will prepare preliminary meeting guidelines for all CTSI standing committees. Guidelines will encompass decision-making processes, agenda structure and expectations regarding meeting minutes. Each committee will review the preliminary guidelines in light of its own needs, and will recommend refinements if necessary. The Executive Committee will approve all changes.

G4B4. Roles and Responsibilities. The Executive Committee will prepare preliminary roles and responsibilities for each CTSI standing committee and the CTSI Administrative Core. These documents will describe the scope of responsibilities for each unit, specify the sorts of decisions that each will be empowered to make, and describe the inter-relationships between each entity. Each unit will review the preliminary documents and recommend refinements if necessary, subject to final approval by the Executive Committee.

G4C. Key Program Functions

G4C1. Development of Novel Clinical and Translational Methodologies. As for all of the key functions, the first step for Novel Clinical and Translational Methodologies key function will be to develop an annual work plan and proposed evaluation plan. The Executive Committee will approve the work plan prior to the notice of award. This work will be carried out by the Co-Directors. Concurrently, the Co-Directors will convene a new review panel for proposals to develop novel methodologies, the Novel Methodologies Review Panel. This group will begin meeting immediately upon receiving the notice of grant award, and will meet on at least a quarterly basis and more frequently if warranted by the volume of proposals. Among its first tasks will be to develop a novel methodologies and travel awards proposal solicitation notice, application process and scoring rubric, and release the solicitation. These tasks will be accomplished within the first quarter of the grant period. Initial proposals will be due in the second month of the second quarter, and awards will be made prior to the end of the quarter. This solicitation and review process will repeat in subsequent years.

The work plan for this key function also includes the development of a number of means to communicate information regarding novel methodologies that are judged to be underutilized or underpublicized. The Co-Directors, working with other members of the CTSI Administrative Committee, will plan a Novel Methodologies Seminar Series to begin in the second quarter of the program year, with the expectation that such seminars will be held on a quarterly basis thereafter. Seminar topics will be solicited from the Administrative Committee and from CTR trainees and independent investigators. In the third quarter a semiannual “nuts and bolts” forum series will be established. Topics will be established using the same means described for the Seminar Series. Additionally, the Co-Directors will establish a quarterly newsletter to publicize information regarding new methodologies. This will be initiated in the first quarter of the program year, and initially will be released through several existing e-mail listservs available at the University of Rochester. Newsletters will be archived on the CTSI website, and this will provide a means to solicit subscribers to a new listserv specifically for the newsletter. The website will also include an archive of information regarding methodologies drawn from seminars and “nuts and bolts” forums.

In the fourth quarter of the program year, the Co-Directors will initiate a needs assessment among clinical and translational investigators at the University of Rochester. Through a survey of investigators and trainees, supplemented by interviews with selected members of both groups, the Co-Directors will gather information regarding methodological needs and opportunities. The information gathered will be used in the following proposal solicitation cycle.

Figure G4.3. Year 1 Milestones for Development of Novel Clinical and Translational Methodologies

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Convene Novel Methodologies Review Panel	X				
Develop proposal solicitation, application and scoring process		X			
Newsletter		X	X	X	X
Solicitation Cycle			X		
Novel Methodologies Seminars			X	X	X
Nuts and Bolts Forum				X	
Needs assessment					X

G4C2. Pilot and Collaborative Translational and Clinical Studies. The Co-Directors of this key function will take as their first task the development of an annual work plan and a proposed evaluation plan (Figure

G4.4). The work plan will be reviewed and approved by the Executive Committee before the notice of award. At the same time, the Co-Directors will convene two committees that will assist in the work of this key function. The first is the Pilot and Collaborative Translational and Clinical Studies Coordination Committee, which with the Co-Directors will provide overall leadership for the key function. The second is the Application Review Committee, which will be responsible for reviewing funding proposals as described below. The initial meetings of this group will be for the purpose of training the members in the proposed solicitation process and gathering their input. Initial meetings of both groups will take place in the first quarter, and will continue on at least a quarterly basis throughout the funding period.

Two funding cycles per year are planned. Each will begin with a multidisciplinary research conference on a specific topic chosen by the Coordination Committee. The first of these will be held in the third month of the first program year. Initial pilot project solicitation will occur the following month. Pre-review of initial applications will take place in the fifth month of the program year, followed by full applications in the seventh month. Awards will be announced in the eighth month, with funding starting immediately afterwards. The second multidisciplinary research conference will be held in the ninth month of the program year, beginning the next solicitation cycle.

Awardees will submit an annual progress report to the Coordination Committee at the end of the one-year funding cycle. The Co-Directors will submit a report on the progress of all projects and other key function activities to the CTSI Administrative Committee on a biannual basis.

Figure G4.4. Year 1 Milestones for Pilot and Collaborative Translational and Clinical Studies

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Convene Coordination Committee	X				
Convene Application Review Committee	X				
Multidisciplinary Research Conference 1		X			
Solicitation Cycle 1			X		
Biannual Progress Report 1			X		
Multidisciplinary Research Conference 2				X	
Solicitation Cycle 2					X
Biannual Progress Report 2					X

G4C3. Biomedical Informatics. The first task of the Co-Directors of the Biomedical Informatics key function will be to create an annual work plan and a proposed evaluation plan (Figure G4.5). The CTSI Executive Committee will review and approve the work plan prior to the award date. Simultaneously, the Co-Directors will convene the Biomedical Informatics Program Advisory Committee. In the first quarter, a coordinator will be identified to organize existing bioinformatics resources at the UR, as outlined in Section G2C. In addition, a team of software developers will be identified in the first quarter to begin work on the development of the new and integrated systems described in Section G2C.

The Biomedical Informatics software development team will be responsible for the development of a UR CTSI website. The initial version of the site will be available in the first quarter, and major updates will be made each quarter throughout the first grant year. Subsequently, information will be continuously maintained. This team will also be responsible for routine consulting services to investigators and trainees; this service will be initiated in the first quarter of the funding period.

In the second quarter of the funding period, the Co-Directors will organize efforts to collect information on use of existing informatics resources. This data collection process will continue indefinitely. In addition, specific feedback on informatics services will be sought through surveys, user meetings and workshops on a continuous basis.

The Co-Directors will kick off an effort to analyze the demand for informatics services by clinical and translational researchers in the second quarter of the grant period. This will involve the establishment of focus groups, and the conduct of surveys, interviews and other data collection efforts. These efforts will lead to an analysis of user requirements with respect to informatics services. In the third quarter of the grant period, the Co-Directors will develop a plan for incremental integration of existing informatics resources and development of new functions. The plan will be based in large part on the user requirements analysis completed in the second quarter. It will be developed in collaboration with the Biomedical Informatics Program Advisory

Committee and presented to the CTSI Executive Committee for its approval. Also in the third quarter, the Co-Directors will develop a plan to implement systems to facilitate intra- and inter-organizational electronic communication based on standards for process knowledge representation and data encoding. Annual work plans for program years 2 through 5 will be based on these plans.

Figure G4.5. Year 1 Milestones for Biomedical Informatics

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual Work Plan and evaluation plan	X				
Convene Biomedical Informatics Program Advisory Committee	X				
Organize existing informatics resources and development team		X			
Implement UR CTSI website		X			
Major UR CTSI website updates			X	X	X
Initiate routine consulting services			X		
Gather usage data for existing informatics resources			X		
Initiate user feedback mechanisms			X		
Analysis of informatics user requirements			X		
Plan for incremental integration of existing resources and new functions				X	
Plan for systems to facilitate electronic communications				X	

G4c4. Design, Biostatistics and Clinical Research Ethics. The Co-Directors of the Design, Biostatistics and Clinical Research Ethics key function will collaborate to draft an annual work plan, to be submitted and approved by the CTSI Executive Committee prior to the notice of award (Figure G4.6). At the same time, the Co-Directors will draft a proposed evaluation plan. Such plans will be submitted at the beginning of every program year. Early in the first quarter, the Co-Directors will organize the expanded Shared Support Unit for Research Design, Biostatistics, Epidemiology and Ethics. This will involve developing a process through which investigators and trainees will submit requests for services, an prioritization process through which the Shared Support Unit Executive Committee will review requests and prioritize them, an assignment process through which investigators and trainees will be linked with appropriate consulting resources, and a monitoring process through which the Executive Committee will review ongoing projects for resource use and progress.

Throughout the grant funding period, researchers associated with this key function will develop novel research methods to handle problems unique to clinical and translational science, and also conduct research regarding ethical issues involved in clinical and translational science. At the end of each year, researchers involved in these areas will submit to the CTSI Executive Committee a status report and research plan for the upcoming year.

Figure G4.6. Year 1 Milestones for Design, Biostatistics and Clinical Research Ethics

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Organize Shared Support Unit for Research Design, Biostatistics, Epidemiology and Ethics		X			
Submit research status report and annual plan					X

G4C5. Regulatory Knowledge and Support. The first task for the Regulatory Knowledge and Support key function will be to recruit a candidate for the Director of the Office for Regulatory Compliance and Support (ORCS) (Figure G4.7). The CTSI Executive Committee will work with the Directors of the University's Office of Human Subjects Protection and the Office of Research and Project Administration to identify potential candidates. The Executive Committee will make the final decision regarding selection of a candidate. This process is expected to be complete by the end of the first quarter of the grant period. Shortly thereafter, the Director will submit an Annual Work Plan for the key function to the CTSI Executive Committee. Subsequent plans will be prepared and submitted for approval at the beginning of each program year. The Director will convene the Regulatory Knowledge and Support User Advisory Board, and working with that board, identify a Faculty Advocate who will work with the ORCS. These activities will be complete by the end of the second quarter of the grant period.

A quality improvement/good clinical practice auditor will commence work at the beginning of the grant period. Initially, this person will work under the direction of the University's Office for Human Subject Protection. Supervision will transition to the Director of the ORCS after the first quarter of the grant period. In a similar fashion, patient subject advocates will initially report to the faculty level research subject advocate, with supervision transitioning later to the ORCS Director. Finally, a research administrator will be identified, will initially report to the Director of the Office for Research and Project Administration, and will transition to supervision by the ORCS Director after the first quarter of the funding period.

In the second quarter of the grant period, the ORCS Director will initiate an effort to develop online tools and outreach for investigators. The first generation of such tools will be available in the third quarter, with additional releases in the fourth quarter. In the second quarter of the grant period, the ORCS Director will initiate support for an ongoing conflict of interest program for investigators making use of CTSI resources, and a program for developing and sharing best practices on an institutional, regional and national basis.

Figure G4.7. Year 1 Milestones for Regulatory Knowledge and Support

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Identify Office of Regulatory Compliance Support staff		X			
Recruit Director of the Office of Regulatory Compliance Support		X			
Annual Work Plan			X		
Convene Regulatory Knowledge and Support User Advisory Board			X		
Identify faculty advocate			X		
Initiate development of online tools for investigators			X		
Release online tools for investigators				X	X
Initiate conflict of interest compliance program			X		
Initiate program for sharing best compliance practices			X		

G4C6. Participant and Clinical Interaction Resources. As noted in Section G2F, the GCRC will move into new space in the University of Rochester School of Medicine and Dentistry, in a location convenient for subjects and close to the site of the planned Clinical and Translational Sciences Building. This move is not dependent on the result of this grant application, but it will be a substantial effort during the early phases of the funding period. The GCRC Program Director will submit an Annual Work Plan to the CTSI Executive Committee prior to the notice of award (Figure G4.8) . Additionally, the Program Director will draft a proposed evaluation plan. At the beginning of the grant period, Dr. Stephen Welle will be appointed as a new GCRC Associate Program Director responsible for liaison with other CTSI key functions and the Medical School research deans.

In the first quarter of the funding period, the GCRC Program Director will initiate a new monthly seminar series on the initiation of a patient-oriented research protocol. Also in this period, the GCRC Administrator will lead the implementation of new services to encourage participation in research, such as childcare and transportation services. In the second quarter of the grant period, the GCRC will establish a Clinical Research Coordinator Office. Also in the second quarter, the GCRC will initiate a monthly seminar series on the introduction of novel techniques for use in patient-oriented studies, under the newly-appointed GCRC Associate Program Director. In the third quarter of the funding period, a GCRC mentoring program will be initiated by the GCRC Program Director in collaboration with the Department Chair of Medicine and training program directors from the Medicine/Pediatrics residency program.

Figure G4.8. Year 1 Milestones for Participant and Clinical Interaction Resources

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and proposed evaluation plan	X				
Plan and carry out GCRC move	X	X	X	X	X
Appoint new GCRC Associate Director		X			
Initiate seminar series on initiation of patient-oriented research protocols		X			
Implement new research subject services		X			
Initiate seminar series on novel techniques for patient-oriented studies			X		
Initiate GCRC mentoring program				X	

G4C7. Community Engagement. The Director of the Community Engagement key function will submit an annual work plan to the CTSI Executive Committee, which will review and approve it at the beginning of the funding period (Figure G4.9). Also prior to the notice of award, the Director will lead the development of a draft evaluation plan. Subsequent annual work plans will be due at the beginning of each program year. The Director will lead the process of establishing community criteria for CTSI research working with the Community Advisory Board of the University's Center for Community Health. This process will be complete by the fourth quarter of the grant period. Dr. Daniel Blumenthal, a consultant to the UR CTSI, will training CTSI investigators in community-based participatory research, beginning in the first quarter of the grant period. The staff of the Community Engagement key function will begin to establish partnerships with local community groups in order to create a community forum regarding clinical and translational research in the second quarter of the grant period. Training will be provided to community group members in the basics of clinical and translational research.

The Co-Directors of the Community Engagement key function will establish the Rochester Office for Practice-Based Research Networks in the second quarter of the grant period. In the third quarter, the Co-Directors will lead the development of a training program for investigators, field staff and practitioners in practice-based research. In the fourth quarter, they will lead staff in the development of a list of interested practitioners and initiate a program of regular communications with them, in order to facilitate subject recruitment through clinical practices.

Key function staff, working with the Director and Co-Directors, will develop a skill-building workshop in community and population health, community structures and health priorities, and recruitment and retention. Development will begin in the first quarter and will be complete in the fourth quarter of the funding period. The workshop will be available throughout program years 2 through 5, and will be continuously evaluated and improved.

Early in the grant period, the Director will lead a number of initiatives to increase participation of traditionally under-represented groups in research. This will involve building awareness of clinical research within the local community; designing and testing recruitment and retention initiatives targeted to specific communities; and creating a community-based research resource center for investigators. These efforts will begin in the second quarter of the grant period.

Figure G4.9. Year 1 Milestones for Community Engagement

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Establish community criteria for CTSI research					X
Initiate training in community-based participatory research		X			
Begin to engage community organizations as partners		X			
Establish Rochester Office for Practice-Based Research Networks			X		
Initiate training program in practice-based research				X	
Initiate communications program with interested practitioners					X
Complete development of skill-building workshop in community research					X
Begin efforts to increase participation of under-represented groups in research			X		

G4C8. Translational Technologies and Resources. At the beginning of the funding period, Drs. Howard Federoff and Stephen Welle will initiate recruitment for the Director of the Laboratory Support Center. The CTSI Executive Committee will choose the successful candidate. This process will be complete by the end of the first quarter of the funding period. The Director will be responsible for creating an annual work plan for this key function, which will then be updated at the beginning of each program year (Figure G4.10). The Director will lead the process of establishing the Center, including convening a committee to review requests for support, development of a website to organize information about core lab support available at the University of Rochester, organizing seminars and workshops on available resources, and developing a course on translational technologies. On an annual basis, the URMC Cores Steering Committee will interview core lab directors regarding the quality of services provided by the Laboratory Support Center. By the third quarter of

the funding period, the Director will have in place a simple web-based process to allow investigators to submit applications for core lab support.

Beginning with the start of the grant period, the CTSI will support new technical staff members to assist investigators with the use of imaging, genomics and proteomics resources. These activities will initially be coordinated and monitored by Dr. Welle, but the responsibility will transition to the Director of the Laboratory Support Center by the third quarter of the funding period.

Figure G4.10. Year 1 Milestones for Translational Technologies and Resources

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Coordinate technical staff in imaging, genomics and proteomics		X			
Recruit Director of the Laboratory Support Center		X			
Submit annual work plan			X		
Convene proposal review committee			X		
Develop informational website			X		
Organize seminars/workshops on core technologies			X		
Evaluate quality of Laboratory Support Center services					X
Implement web-based support application process				X	

G4C9. Research Education, Training and Career Development. The Director of this key function will submit an annual work plan to the CTSI Executive Committee prior to the beginning of the funding period (Figure G4.11). In addition, the Director will draft a proposed evaluation plan. Subsequently, these plans will be updated at the beginning of each program year, in each case subject to the approval of the Executive Committee. Well prior to the beginning of the funding period, the Director will have initiated the process of gaining necessary approvals for the initiation of new Masters degree programs in Clinical Investigation and Translational Science, and a new PhD program in Translational Biomedical Sciences. In addition, new didactic courses and workshops necessary for these programs will have been designed and approved by the University. Thus, well prior to the entry of the first new trainees, the necessary didactic infrastructure will be in place to support the proposed T32 and K12 programs. This effort will require substantial commitment of institutional resources prior to the beginning of the funding period.

Simultaneously with the beginning of the funding period, the Directorate of this key function will organize the five training support cores described in Section G2I. The Administrative Core will lead the process of developing a website support recruitment by the middle of the second quarter of the funding period; advertisements will be placed in appropriate venues at the same time. Applications for training program slots will be due in the middle of the third quarter of the funding period, and decisions will be made in the beginning of the fourth quarter. This pattern will repeat each year.

The Mentor Development Core will be tasked with creating an online Mentor Development Program. This will be complete by the beginning of the fourth quarter of the project period. As trainees enroll in the program, the Mentor Development Core will match trainees with mentors and will monitor the progress of the mentor-mentee relationship.

Figure G4.11. Year 1 Milestones for Research Education, Training and Career Development

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Organize five training support cores		X			
Begin recruitment			X		
Applications due				X	
Decisions made					X
Mentor development program in place					X

G4C10. Upstate Academic Consortium. The Director of this key function, with the assistance of the Directorate of the Upstate New York Translational Research Network (UNYTRN), will submit an annual work plan to the CTSI Executive Committee, which will review and approve it at the beginning of the grant period. The Director will also submit a draft evaluation plan (Figure G4.12). This process will repeat each year of the funding period. The UNYTRN Directorate, working through its Executive Committee, will convene eight

research working groups during the first quarter of the funding period. Each working group will submit quarterly reports throughout the funding period.

A UNYTRN website will be developed and will go live during the second quarter of the funding period, under the leadership of UR CTSI and UNYTRN administrative staff. An inventory of ongoing translational research projects and research resources available at UNYTRN institutions will be created by UR CTSI and UNYTRN administrative staff by the third quarter of the funding period. The eight UNYTRN working groups will work together to produce a comprehensive translational research needs assessment, to be complete during the fourth quarter of the funding period. This needs assessment will inform annual work plans for the group in program years 2 through 5.

Figure G4.12. Year 1 Milestones for the Upstate Academic Consortium

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Annual work plan and evaluation plan	X				
Convene eight research working groups		X			
UNYTRN website available			X		
Translational Research Inventory available				X	
Translational Research Needs Assessment available					X

G4D. Evaluation and Tracking Support Group

As noted in Section G3, Evaluation, the foundation of the UR CTSI Evaluation Plan has already been created in the form of a logic model (Figure G3.1) and suggested performance measures for each key function. The Evaluation Tracking and Support Group (ETSG) will build on this foundation, beginning its work in earnest well prior to the anticipated award date (Figure G4.13). Its first steps will be to draft and submit a proposed annual work plan to the Executive Committee for review and approval. It will also develop a draft evaluation plan covering its own activities, outputs and outcomes, and will distribute this in draft form to all key function directors for their use as a template in drafting key function evaluation plans. Draft key function and other evaluation plans will be submitted to the ETSG. The ETSG will then critique the draft plans and work with key function directors to bring them up to required standards. Before the end of the first quarter of the funding period, the ETSG will submit a comprehensive CTSI evaluation plan, based on the individual evaluation plans, to the Executive Committee for its review and approval. Performance tracking activities will begin immediately afterward. Evaluation reports will be submitted to the Executive Committee at the beginning of each quarter. The ETSG will also be responsible for updating the URMC Research Resource Inventory an on annual basis.

Figure G4.13. Year 1 Milestones for the Evaluation Tracking and Support Group

Milestone	***Pre-NOA***	***Q1***	***Q2***	***Q3***	***Q4***
Development of logic model	X				
Annual work plan and evaluation plan (for ETSG)	X				
CTSI evaluation Plan submitted		X			
CTSI evaluation Plan approved			X		
Evaluation Plan reporting begins			X		
Update Research Resource Inventory				X	

Table G5A1: Average Annual Total Sponsored Costs Allocated by Category $ by Sponsor Type - Fiscal Year 2005

	Sponsor Type				
Category	*NIH*	*Federal - Non-NIH*	*Industry*	*Other*	*Grand Total*
Patient-Oriented Translational Research	16,290,620	313,811	2,905,129	2,745,596	22,255,157
Patient-Oriented Experimental Therapeutics	17,189,191	485,155	19,683,216	6,451,129	43,808,692
Population-Based Research	8,678,703	3,261,822	4,875,875	3,376,621	20,193,022
Health Services and Outcomes Research	2,029,002	1,708,179	514,507	2,136,574	6,388,263
Ethics and Health Policy Research	33,303	-	-	142,119	175,422
Subtotal - Clinical Research	44,220,820	5,768,968	27,978,728	14,852,040	92,820,555
Basic Research	78,657,039	4,050,414	2,095,409	11,629,193	96,432,055
Subtotal - Research	122,877,859	9,819,382	30,074,137	26,481,232	189,252,610
Clinical Research Education/Training	3,765,176	959,656	514,174	633,393	5,872,399
Basic Research Education/Training	6,864,657	579,637	35,438	369,627	7,849,360
Clinical Education/Training	298,531	2,369,582	10,289	3,462,867	6,141,269
Subtotal - Education/Training	10,928,364	3,908,876	559,901	4,465,887	19,863,029
Clinical Research Conference	64,025	-	-	141,755	205,780
Basic Research Conference	959,547	20,341	-	60,924	1,040,813
Clinical Conference	-	388,284	-	23,842	412,126
Subtotal - Conference	1,023,573	408,625	-	226,521	1,658,719
Other - Not Research, Education or Training	1,850,760	494,285	67,241	2,943,166	5,355,451
Total	136,680,555	14,631,168	30,701,279	34,116,806	216,129,809

These figures represent average annual costs allocated across categories, using percentages supplied by principal investigators.

Table G5A2: Sponsored Projects by Category, 2005

Category	*No.*
Patient-Oriented Translational Research	182.7
Patient-Oriented Experimental Therapeutics	443.3
Population-Based Research	134.0
Health Services and Outcomes Research	107.8
Ethics and Health Policy Research	5.5
Subtotal - Clinical Research	873.3
Basic Research	440.1
Subtotal - All Research	1,313.4
Clinical Research Training	39.7
Basic Research Training	46.3
Clinical Training	51.4
Subtotal - Training	137.5
Clinical Research Conference	6.5
Basic Research Conference	5.6
Clinical Conference	2.6
Subtotal - Conference	14.6
Other - not research, training or conference	60.5
Total	1,526.0

These figures represent the number of active projects in each category. Where principal investigators allocated projects to more than one category, those projects are counted proportionally in each category.

Table G5B1: Clinical and Translational Research Resources, 2005

Resource Type	
General	No.
Accessible Study Populations (# populations)	156
Patient Databases (# databases)	141
Specimen Repositories (# repositories)	27
Specialized Technology	105
Other Resources	51

Space	Sq. Ft.
Off Campus Clinical Research Space	29,600
On Campus Clinical Research Space	66,626

Staff	FTEs
Subject Recruitment and Follow-Up Staff	152.25
Data Collection Staff	112.17
Data Management and Analysis Staff	61.41
Data Entry, Management and Analysis Staff	121.44

Training Programs	No. of Units Offering
Degree and Certificate Programs	31
Formal Coursework for Faculty	13
Formal Coursework for Postdoctoral Students	23
Formal Coursework for Graduate Students	20
Formal Coursework for Medical Students	16

Table G5B2. Research Resource Inventory: Specialized Technologies

Department or Center	Resource Description
Anesthesiology	Quantitative sensory testing instruments
Biomedical Engineering	Computer simulations (20 sun processors)
Biomedical Engineering	Fluorescence microscopy
Community and Preventice Medicine	Population Data Laboratory
Community and Preventive Medicine	Personal Digital Assistant software for nicotine dependence counseling
Community and Preventive Medicine	Large Database statistical tools (SAS)
Dermatology	High resolution digital image acquisition
Eastman Department of Dentistry	Kyrkanides-cephalometric quantatative evaluation of craniofacial skeletons
Eastman Department of Dentistry	Tallents-pharyngometry, ankylosis testing
Eastman Department of Dentistry	Koo-realtime PCR
Eastman Department of Dentistry	Billings-Teledentistry, saliva collection techniques for toddlers and adolescents
Eastman Department of Dentistry	Berkowitz-saliva collection in preschool children
Eastman Department of Dentistry	Ren, Malmstrom-portable gas chromatography
Environmental Medicine	Air Pollution Exposure Chamber (in CRC)
Imaging Sciences	MRI
Imaging Sciences	Magnetic Resonance
Imaging Sciences	Computerized Tomography
Imaging Sciences	Angiography
Imaging Sciences	MR Breast
Imaging Sciences	Ultrasound- sonoelastography
Medicine	Infusion center services (provided by CRC)
Medicine	Clinical Inhalation Facility
Medicine	FACs Scanner
Medicine	Specimen processing
Medicine	Capsule Endoscopy
Medicine	Pulmonary Function Testing
Medicine	MADIT - invasive and non-invasive electrocardiology
Medicine	LQTS- molecular genetics, non-invasive electrocardiology
Microbiology and Immunology	GLP Lab for Antibody Measurement for pediatrics and adult vaccines
Neurobiology and Anatomy	Labs specialized in quantifying human sensory and motor behavior.
Neurobiology and Anatomy	HINT
Neurobiology and Anatomy	DP & TOAE and contraleteral suppression
Neurobiology and Anatomy	Caloric Irrigator
Neurobiology and Anatomy	Clinical audiometer
Neurology	Digital EEG Database
Neurology	muscle testing
Neurology	sub zero freezer
Neurology	centrifuge
Neurology	Motion Perception Psychophysics
Neurology	Expertise in geriatric psychiatry
Neurology	Transcranial doppler ultrasonography
Opthalmology	Wavefront Sensors- Meliora Hall, Meridian Centre
Opthalmology	Vision retraining computers
Opthalmology	Keratometer
Opthalmology	Pachimeter
Opthalmology	Visual field machine
Opthalmology	Slit lamp camera
Opthalmology	ORBScan
Opthalmology	Goldmann tonometer
Opthalmology	Optical Coherence Tomographer- Anterior Segment
Orthopaedics/ Center for Musculoskeletal Research	KXRF Scanner
Orthopaedics/ Center for Musculoskeletal Research	Dexa scanner
Otolaryngology	Full capability for complete auditory testing.
Pathology and Laboratory Medicine	Review of hematologic tissue samples

Table G5B2. Research Resource Inventory: Specialized Technologies (continued)

Department or Center	Resource Description
Pathology and Laboratory Medicine	Prostate tissue microarray (TMA) not linked to clinical data but that can be used for "translational" research
Pathology and Laboratory Medicine	Histologic and moprphologic analysis by pathologists of tissues from patients in clinical studies
Pathology and Laboratory Medicine	Mutation analysis, SNP identification and detection, customized genotyping, patient DNA banking, patient cell-line establishment
Pathology and Laboratory Medicine	Immunohistochemistry, molecular studies on tissue
Pediatrics	Research quality assurance
Pediatrics	Amplitude Integrated EEG (aEEG)
Pediatrics	On-line/web survey methods expertise
Pediatrics	Study coordination
Pediatrics	Survey Research/Data methods group with experience in hard-to-reach populations
Pediatrics	Project management
Pediatrics	Pediatric Flexible Fiberoptic Bronchoscopy
Pediatrics	Neurocognitive tests
Pediatrics	High Frequency Ventilation
Pediatrics	Ioherxol msr of Glomerularfiltration Rate
Pediatrics	Carotid Thickness Ultrasound
Pediatrics	Amb BP Monitorins
Pediatrics	Forced oscillation
Pediatrics	Perform developmental evaluations
Pediatrics	Characterizing children with ASD
Pediatrics	Pediatric Pulmonary Function Laboratory
Pediatrics	Infant Pulmonary Function Testing
Pediatrics	Inhaled Nitric Oxide
Pediatrics	Body Cooling Apparatus for Brain Injury Prevention
Pediatrics	Extracorporeal Membrane Oxygenation
Pediatrics	Telehealth PCs, software, and cameras
Pediatrics	Respiratory Inductive Plethysmography
Physical Medicine and Rehabilitation	PT/OT Equipment
Physical Medicine and Rehabilitation	ITB Interthecal Baclofen
Physical Medicine and Rehabilitation	Biodex
Psychiatry	Event Related Potentials
Psychiatry	Polysomnography
Psychiatry	Some materials on film in sign language
Psychiatry	Psychophysiological Measures (eg: EEG,EKG,EMG, EOG, EGG, GSR/ESA)
Psychiatry	Statistical Analysis (SAS)
Psychiatry	Sleep Laboratory Technology
Psychiatry	Power Spectal Analysis
Radiation Oncology	Other linear accelerators and high-dose rate machines
Radiation Oncology	Massage table
Radiation Oncology	Actigraphs
Radiation Oncology	Bioelectrical Impedance Device
Radiation Oncology	Handigrip dynamometer
Radiation Oncology	Ambulatory impedence monitor
Radiation Oncology	Brain Lab Novalis Linear Accelerator
Radiation Oncology	Web registration/randomization of participants to CCOP studies
Radiation Oncology	Acupressue/acustimulation bands
Surgery	Esophageal Function Lab
Urology	Bladder scans and uroflow
Urology	Bladder Instillations
Urology	CMG's
Urology	CMG's
Urology	Cystoscopy

Table G5B3. Research Resource Inventory: Accessible Study Populations

Department or Center	Resource Description	Resource Size
Anesthesiology	Patients with diverse chronic pain conditions	1000 persons
Cancer Center	Cancer/Hematological Malignancies	7000 persons
Center for Aging and Developmental Biology	Alzheimer's Disease Center Autopsy Program	75 persons
Center for Aging and Developmental Biology	Genetic Profiles - Alzheimer's Disease Center	461 persons
Community and Preventive Medicine	Mid-life and older smokers	3000 persons
Community and Preventive Medicine	Strong Memorial Hospital Patients	38000 persons
Community and Preventive Medicine	Medical students	300 persons
Community and Preventive Medicine	Physicians and Residents	100 persons
Community and Preventive Medicine	African American obese adolescents and families	100 persons
Community and Preventive Medicine	Dominican Republic Community Members	2300 persons
Community and Preventive Medicine	Adolescents (includes 100 smokers)	9000 persons
Community and Preventive Medicine	Adults exposed to radiation as infants	7500 persons
Community and Preventive Medicine	U.S. Air Force cohort	5000000 persons
Community and Preventive Medicine	Healthy Workers	3600 persons
Community and Preventive Medicine	Males with Cardiomyopathy	700 persons
Community and Preventive Medicine	Laryngeal Cancer Patients	350 persons
Department of Pediatrics	Patients requiring pediatric critical care	850 persons
Department of Pediatrics	Pateints after pediatric cardiac surgery	200 persons
Eastman Department of Dentistry	Billings 12-48 month old children with caries	100 persons
Eastman Department of Dentistry	Kyrkanides-children and adults with diseases of the oral maxiofacial skeleton	300 persons
Eastman Department of Dentistry	Malmstrom-General dentistry, dental emergency patients, oral surgery	0 persons
Eastman Department of Dentistry	Watson-Sjogren's Syndrome, head and neck radiation xerostomia, drug induced xerostomia	65 persons
Eastman Department of Dentistry	Berkowitz-24-60 month old children with ECC, OR population	200 persons
Eastman Department of Dentistry	Weiss-Adults with periodontal disease, implants patients	312 persons
Eastman Department of Dentistry	Ren-General dentistry, dental emergency patients	300 persons
Eastman Department of Dentistry	Tallents-TMD/symptomatic and assymptomatic,pharyngometric/pain populations, tooth ankylosis poulations	447 persons
Emergency Department	Adult ED patients	67000 persons per year
Emergency Medicine	Children seen in the the pediatric Emergency Department	26000 persons per year
Environmental Medicine	Patients: Occupational/ Environmental Problem	0 persons
Environmental Medicine	Patients: Finger Lakes Occupational Health Services	0 persons
Family Medicine	A stratified random sample of 100 general interninsts and family physicians	100 persons
Family Medicine	Physicians participating in a study who volunteer to meet with standardized patients	51 persons
Family Medicine	Women living in Western New York with symptomatic fibroids	70 persons
Family Medicine	Immigrant Somali women	36 persons
Family Medicine	Adult patients hospitalized in New York, California, and Florida	15000000 persons
Family Medicine	Nationally representative sample of people 65+ (elderly)	20000 persons
Imaging Sciences	Womean	8000 persons
Medicine	Renal Transplant	100 persons
Medicine	Pediatric- LQTS	2513 persons
Medicine	RA	2500 persons
Medicine	PsA	600 persons
Medicine	Patients who have received cardiac services	89216 persons
Medicine	AS	300 persons
Medicine	Adult- MADIT II	450 persons
Medicine	Geriatric- MADIT II	782 persons
Medicine	Fibro Myalgia	100 persons
Medicine	End stage Renal Disease	200 persons
Medicine	Chronic Renal Disease	2000 persons
Medicine	Endocrine clinical practice patient charts	10000 persons

Table G5B3. Research Resource Inventory: Accessible Study Populations (continued)

Department or Center	Resource Description	Resource Size
Medicine	Caucasian	1000 persons
Medicine	Latino	100 persons
Medicine	Heart Failure	80 persons
Medicine	Patients with HIV infection	900 persons
Medicine	Hospital Medicine Inpatient Service	75 persons
Medicine	Nursing Home Population	500 persons
Microbiology and Immunology	Infants, children, adolescents	20000 persons
Neurobiology and Anatomy	Normal across ages (>18)	150 persons
Neurobiology and Anatomy	Inner ear disorders	0 persons
Neurology	Epilepsy Center patients	4000 persons
Neurology	Patients with neurological conditions.	1000 persons
Neurology	Children with Dystonia or Cerebral Palsy	30 persons
Neurology	Children and Adults with Chorea	24 persons
Neurology	Alzheimer's Disease	910 persons
Neurology	Patients with all forms of cerebrovascular disease	750 persons
Neurology	Children with Batten Disease	56 persons
Neurology	Neonatal Seizure Database	180 persons
Neurology	Monroe Community Neurogeriatric Clinic	50 persons
Neurology	Depression	74 persons
Neurology	Mild Cognitive Impair	184 persons
Neurology	Other dementia	330 persons
Neurology	Multiple sclerosis	2000 persons
Neurology	Episodic ataxias	15 persons
Neurology	Non-dystrophic myotonias	20 persons
Neurology	Periodic paralysis	30 persons
Neurology	Facioscapulohumeral Muscular Dystrophy Patients and Family Members	467 persons
Neurology	Myotonic Dystrophy Patients and Family Members	558 persons
Neurology	Anderson-Tawil Syndrome	10 persons
Neurosurgery	Surgical patients	2400 persons per year
Opthalmology	Dry Eye	500 persons
Opthalmology	Refractive Surgery	187 persons
Opthalmology	Migraine	1670 persons
Opthalmology	Cataract	3439 persons
Opthalmology	Macular Degeneration	2101 persons
Opthalmology	Diabetic Retinopathy	0 persons
Opthalmology	Glaucoma	4307 persons
Otolaryngology	Research Audiology, 18-90 years, relatively healthy	1000 persons
Pediatrics	Harris Poll On-Line Panel	persons
Pediatrics	children and adolescents with type 2 diabetes	100 persons
Pediatrics	Inpatient sick newborns	1170 persons
Pediatrics	children and adolescents with type 1 diabetes	900 persons
Pediatrics	Childcare/school registration	4014 persons
Pediatrics	Rochester Area Primary Care Child Health	800000 persons
Pediatrics	Children with ASD	0 persons
Pediatrics	Asthma	300 persons
Pediatrics	School Age Children	150 persons
Pediatrics	Infants with congenital HHV6	75 persons
Pediatrics	Children with acute respitory infections	700 persons per year
Pediatrics	HIV Exposed (not infected) infants	20 persons
Pediatrics	NICU Follow up via Mail Questionnaire to age 10	20000 persons
Pediatrics	NICU follow up via Clinic to 18 months	350 persons
Pediatrics	American Academy of Pediatrics, Pediatric Research in Office Settings	1500 persons
Pediatrics	Children with developmental disabilities	500 persons
Pediatrics	Wheezing infants	240 persons
Pediatrics	Children with inborn errors of metabolism	200 persons
Pediatrics	Children with physical disabilities (CP & Spina Bifida)	0 persons
Pediatrics	Children with various birth defects	500 persons
Pediatrics	Inpatient normal newborns	2400 persons
Pediatrics	HIV Infected Children	30 persons

Table G5B3. Research Resource Inventory: Accessible Study Populations (continued)

Department or Center	Resource Description	Resource Size
Pediatrics	Children exposed prenatally to MeHg	0 persons
Pediatrics	Cystic Fibrosis	150 persons
Pediatrics	Children and adults with dual diagnosis	0 persons
Pediatrics	Technology dependent children	70 persons
Pediatrics	Infants born premature	177 persons
Physical Medicine and Rehabilitation	Occupational Therapy (OT)	0 persons
Physical Medicine and Rehabilitation	Acute Rehabilitation	0 persons
Physical Medicine and Rehabilitation	Neuropsych	0 persons
Physical Medicine and Rehabilitation	MS	0 persons
Physical Medicine and Rehabilitation	Amputee	0 persons
Physical Medicine and Rehabilitation	Liver Transplant	0 persons
Physical Medicine and Rehabilitation	CVA	0 persons
Physical Medicine and Rehabilitation	Spinal Cord Injury	0 persons
Physical Medicine and Rehabilitation	Physiatrist patients	0 persons
Physical Medicine and Rehabilitation	Physical Therapy (PT)	0 persons
Psychiatry	Deaf Individuals	50 persons
Psychiatry	Cohort of families identified by depressed probands and by control probands	350 persons
Psychiatry	Older adults in aging services care management	250 persons
Psychiatry	Children in foster care, ages 11-14	180 persons
Psychiatry	Adults discharged from ED after presentation for suicide attempts or ideation	120 persons
Psychiatry	Psychiatric inpatients, children and adolescents	22 persons
Psychiatry	Sign Language Interpreters	0 persons
Psychiatry	Adults with sleep disorders	100 persons
Psychiatry	6-9 year old urban children with elevated behavioral and emotional problems; and parents	200 persons
Psychiatry	Older primary care patients	756 persons
Psychiatry	General Adult Population, Hispanic Patients	200 persons
Psychiatry	Emergency psychiatary, adults, children and adolescents	100 persons
Psychiatry	Dementia	3000 persons
Psychiatry	Psychiatric Inpatients, adults	66 persons
Psychiatry	Older adults with mental illness (Alzheimer's affective and psychotic disorders)	200 persons
Psychiatry	Children and Adolescents with psychiatric and behavioral disorders	500 persons
Psychiatry	General adult population (primarily depression, anxiety and personality disorders)	1000 persons
Psychiatry	Severely mentally ill adults (primarily schizophrenia and othe rpsychotic disorders)	1000 persons
Psychiatry	Legal Community	0 persons
Psychiatry	Domestic Violence Providers	38 beds
Psychiatry	Rochester City Court	0 persons
Psychiatry	Monroe County Family Court	200 persons per month
Psychiatry	Adults with substance use disorders	1000 persons
Psychiatry	Older normals	4000 persons
Radiation Oncology	Patients seen in radiation oncology	20000 persons
Radiation Oncology	Our study populations are obtained from other departments and CCOP sites	0 persons
Surgery	Adult and Pediatric Plastic Surgery Patients	0 persons
Surgery	Trauma, Burn, Critical Care Surgery Patients	0 persons
Surgery	Breast Cancer Patients	0 persons
Surgery	GI/ GI Oncology Surgery Patients	0 persons
Surgery	Cardiac Surgery Patients	0 persons
Surgery	Vascular Laboratory and Surgery Patients	0 persons
Surgery	Esophagus and Foregut Surgery Patients	0 persons
Surgery	Liver, Kidney, and Heart Transplant Patients and Solid Organ Donors	0 persons
Surgery	Lung Cancer and Emphysema Patients	0 persons

Table G5B4. Research Resource Inventory: Patient Databases

Department or Center	Resource Description	Resource Size
Anesthesiology	Patients with diverse chronic pain conditions	1000 records
Center for Aging and Developmental Biology	Genetic Profiles - Alzheimer's Disease Center	461 records
Center for Aging and Developmental Biology	Alzheimer's Disease Center Database	952 records
Community and Preventice Medicine	Area Resource File	
Community and Preventice Medicine	The Third National Health and Nutrition Examination Survey (NHANES III)	
Community and Preventice Medicine	Robert Wood Johnson Foudation Employer Health Insurance Survey, 1993	
Community and Preventice Medicine	Community Tracking Study	
Community and Preventice Medicine	Census of Population and Housing Public Use Microdata Samples (1% samples)	
Community and Preventice Medicine	National Nursing Home Survey	
Community and Preventice Medicine	National Home and Hospice Care Survey (NHHCS)	
Community and Preventice Medicine	Health and Retirement Study 1998	
Community and Preventice Medicine	Medicare Current Beneficiary Survey (MCBS)	
Community and Preventice Medicine	Behavioral Risk Factor Surveillance System (BRFSS)	
Community and Preventice Medicine	American Hospital Association's Annual Survey	
Community and Preventice Medicine	National School-Based Youth Risk Behavior Survey (YRBS)	
Community and Preventice Medicine	Medicare State and County Enrollment for 1998	
Community and Preventice Medicine	Robert Wood Johnson Family Health Insurance Survey, 1993	
Community and Preventice Medicine	Alpha-Numeric HCPCS File	
Community and Preventice Medicine	Provider of Service Files	
Community and Preventice Medicine	Strong Care	
Community and Preventice Medicine	SPARCS	
Community and Preventice Medicine	Medical Expenditure Panel Survey	
Community and Preventice Medicine	National Hospital Ambulatory Medical Care Survey	
Community and Preventice Medicine	National Health Interview Survey (NHIS)	
Community and Preventice Medicine	Health Data on Older Americans, 1999	
Community and Preventice Medicine	Healthcare Cost and Utilization Project: Kid's Inpatient Database	
Community and Preventice Medicine	National Survey of American Families	
Community and Preventice Medicine	National Longitudinal Survey of Adolecent Health	
Community and Preventice Medicine	Health Data on Older Americans, 1992	
Community and Preventice Medicine	Health Cost and Utilization Project: State Inpatient Sample Database	
Community and Preventice Medicine	Health Cost and Utilization Project: Nationwide Inpatient Sample (HCUP-NIS)	
Community and Preventice Medicine	Medical Expenditure Panel Survey (MEPS)	
Community and Preventice Medicine	National Hospital Discharge Survey (NHDS)	
Community and Preventice Medicine	National Ambulatory Medical Care Survey (NAMCS)	
Community and Preventice Medicine	National Maternal and Infant Health Survey (NMIHS)	
Community and Preventice Medicine	National Survey of Family Growth, Cycles I, II, and III	
Community and Preventice Medicine	National Longitudinal Survey of Youth (NLSY79)	
Community and Preventive Medicine	Medical students	300 records
Community and Preventive Medicine	Finger Lakes Perinata Data Base	100000 records
Community and Preventive Medicine	Adolescents (includes 100 smokers)	9000 records
Community and Preventive Medicine	Dominican Republic Community Members	2300 records
Community and Preventive Medicine	African American obese adolescents and families	100 records
Community and Preventive Medicine	Smoker's Registry	773 records
Community and Preventive Medicine	Clinical Financial Database (SMH)	38000 records per year
Community and Preventive Medicine	Mid-life and older smokers	3000 records
Community and Preventive Medicine	Physicians and Residents	100 records
Department of Pediatrics	Census (currently kept by hand)	800 records
Dermatology	Psoriasis subjects	200 records
Eastman Department of Dentistry	Tallents-MRI assymptomatic/symptomatic	447 records
Eastman Department of Dentistry	Berkowitz-RO3 database-ECC outcomes, Hersha data base-ECC prevalence	179 records

Table G5B4. Research Resource Inventory: Patient Databases (continued)

Department or Center	Resource Description	Resource Size
Eastman Department of Dentistry	Watson-Sjogren's Syndrome, head and neck radiation xerostomia, drug induced xerostomia	65 records
Eastman Department of Dentistry	Kyrkanides-craniofacial dysmorphology data	300 records
Eastman Department of Dentistry	Billings-Caries risk, older adults	1800 records
Emergency Department	ED database	67000 records per year
Emergency Medicine	Emergency Department database	26000 records per year
Environmental Medicine	Finger Lakes Occupational Health	
Environmental Medicine	New York State Clinical Network Database	
Environmental Medicine	Strong Occupational Medicine Clinic	
Family Medicine	Immigrant Somali women	36 records
Family Medicine	Women living in Western New York with symptomatic fibroids	70 records
Family Medicine	Adult patients hospitalized in New York, California, and Florida	15000000 records
Family Medicine	Nationally representative sample of people 65+ (elderly)	20000 records
Family Medicine	Physicians participating in a study who volunteer to meet with standardized patients	51 records
Family Medicine	A stratified random sample of 100 general interninsts and family physicians	100 records
Medicine	Hospital Medicine Inpatient Service	75 records
Medicine	Cardiology Pronto Database	89216 records
Medicine	Organ Transplant Tracking Record (OTTR)	500 records
Medicine	Ventricular Assist Device (VAD) Database	150 records
Medicine	Patients with HIV infection	900 records
Medicine	Hepatitus C	66 records
Medicine	Pulmonary	2100 records
Medicine	ELA	2400 records
Medicine	E Pager	9900 records
Medicine	LQT 3	1600 records
Medicine	LQTS Genetics	350000 records
Medicine	Autoimmune Hepatitis	11 records
Medicine	LQTS Population	350000 records
Medicine	MADIT CRT	8200 records
Medicine	RAPID	1700 records
Medicine	MADIT II	321000 records
Microbiology and Immunology	Elmwood Pediatric Group	20000 records
Neurobiology and Anatomy	HRSC Database	150 records
Neurology	HIPAA protected, private practice	1000 records
Neurology	SEC Data Manager	4000 records
Neurology	Batten Disease	56 records
Neurology	National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscual Dystrophy Patients and Family Members	1025 records
Neurology	Internal database	300 records
Neurology	Starting new database collection tool August 2005	
Neurology	TRIADD (Clinical-research database for Memory Disorders Clinic and Program in Neurobehavioral Therapeutics)	2400 records
Opthalmology	Demographics and outcomes data for refractive surgery.	2500 records
Otolaryngology	Otolaryngology - Surgical practices	20000 records
Otolaryngology	Audiology - Clinical practices	30000 records
Pathology and Laboratory Medicine	Clinical Labs Information System	1000 records
Pathology and Laboratory Medicine	Renal biopsies back to 1961 (Filemaker)	5000 records
Pediatrics	NYS Perinatal Data System	400000 records
Pediatrics	Congenital HHV6 Infection	75 records
Pediatrics	NVSN-CDC Surveillance	2839 records
Pediatrics	Children with physical disabilities (CP & Spina Bifida	

Table G5B4. Research Resource Inventory: Patient Databases (continued)

Department or Center	Resource Description	Resource Size
Pediatrics	Children exposed to MeHg	
Pediatrics	NEOS- high risk infant follow up database	20000 records
Pediatrics	Newborn intensive care unit admissions	14000 records
Pediatrics	CHS- Health School Age	170 records
Pediatrics	NICHD Neonatal Research Network Databases	55000 records
Pediatrics	IDX	
Pediatrics	Congenital	3000 records
Pediatrics	Extracorporeal life support organization (ELSO)	20000 records
Pediatrics	NYS Perinatal Data System- Neonatal Module	5000 records
Pediatrics	Previous Multi-Center Trial Dataset (STOP-ROP)	649 records
Pediatrics	NYS Perinatal Data System	400000 records
Pediatrics	HHV6 Primary Infection	350 records
Pediatrics	Cystic Fibrosis Foundation Patient Registry	150 records
Pediatrics	Cohort of children with asthma from RCSD	1000 records
Pediatrics	Previously enrolled asthma subjects from office and school based studies	500 records
Pediatrics	Children with ASD	
Pediatrics	Epidemiologic Study of Cystic Fibrosis	150 records
Pediatrics	Children and adults with dual diagnosis	
Pediatrics	Childcare/school registration	4014 records
Pediatrics	Community Surveillance Peds	13000 records
Physical Medicine and Rehabilitation	Spinal Cord Injury	
Physical Medicine and Rehabilitation	Sastisity	
Physical Medicine and Rehabilitation	CVA	
Psychiatry	Community controls	86 records
Psychiatry	Alpha; The hospital-based patient admission database	5000 records
Psychiatry	Gynecology patients	242 records
Psychiatry	Inpatients with depression over age 50	250 records
Psychiatry	Strong Ties pharmacy database	1000 records
Psychiatry	Older adults with depression	400 records
Psychiatry	Completed suicides over age 50	110 records
Psychiatry	Completed suicides under age 50	50 records
Psychiatry	Active duty Air Force personnel	350000 records per year
Radiation Oncology	U6904; Sleep Study	8 records
Radiation Oncology	U8199; Acustimulation for nausea	125 records
Radiation Oncology	Patients seen in radiation oncology	20000 records
Radiation Oncology	Polarity therapy for fatigue	16 records
Radiation Oncology	Radiation oncology symptom inventory	1500 records
Radiation Oncology	U8993; Paxil for depression	125 records
Radiation Oncology	Exercise and fatigue	39 records
Radiation Oncology	Modafinil for fatigue	75 records
Radiation Oncology	Predicting Side Effects of Cancer Treatment; Acupressure bands for nausea	90 records
Surgery	Esophageal and Thoracic Surgery Patient Database	
Surgery	Organ Transplant Tracking Record (OTTR)	
Surgery	Trauma Registry	
Urology	Urology Billing Database	

Table G5B5. Research Resource Inventory: Specimen Repositories

Department or Center	Resource Description	Resource Size
Center for Aging and Developmental Biology	Alzheimer's Disease Center Genetic Profiles	3200 samples
Center for Aging and Developmental Biology	Alzheimer's Disease Center Brain Tissue Repository	2200 samples
Community and Preventive Medicine	Human saliva	200 samples
Dermatology	Squamous Cell Carcinoma	250 samples
Eastman Department of Dentistry	Watson-Salivary gland bank, saliva bank	25 samples
Eastman Department of Dentistry	Tallents-mandibles of rabbits with unilateral artheritis 5/experimental, 5 controls	10 samples
Medicine	MADIT	2200 samples
Medicine	THROMBO	
Medicine	Specimens related to specific studies	
Microbiology and Immunology	Blood	10000 samples
Microbiology and Immunology	bacteria, respiratory	3000 samples
Neurology	brain	
Neurology	spinal fluid	
Neurosurgery	Brain Tissue Bank under development	
Pathology and Laboratory Medicine	Surgical Pathology slides/blocks	500000 samples
Pathology and Laboratory Medicine	Cord blood samples (stored for several weeks on healthy and ill newborns)	
Pathology and Laboratory Medicine	Autopsy slides/blocks	25000 samples
Pathology and Laboratory Medicine	Fresh tissue from various tumor types	
Pathology and Laboratory Medicine	Frozen peripheral blood stem cells from deceased patient with hematologic malignancies.	
Pathology and Laboratory Medicine	Excess blood samples, wide variety of diseases, both serum and anti-coagulated whole blood	
Pediatrics	CNS- Serum, frozen cells	900 samples
Pediatrics	Broncho Alveolar Lavage Specimens from Premature Infants	18 samples
Pediatrics	Lung Tissue Specimens	51 samples
Pediatrics	NVSN- Nasal Swabs	2839 samples
Pediatrics	Congenital HHV6 Serum, Urine, DNA, Saliva	225 samples
Pediatrics	HHV6 Primary Infection, serum, saliva, DNA	1500 samples
Pediatrics	Lymphoblastoid cell lines from families with cleft lif/cleft palate	500 samples
Pediatrics	Community Surveillance	4000 samples
Urology	Urological Tissue Bank	573 samples

Table G5B6. 2004-2005 GCRC Ancillary Costs by Principal User

SPID	Investigator	Protocol Title	Ancillary Costs Used
955	Schifitto	Predicting Progression of Neuro AIDS	$9,975
968	Reichman	A5178 Suppressive Long-Term Antiviral Management of Hepatitis C Virus (HCV) and HIV-1 Coinfected Subjects (SLAM-C)	$7,806
747	Reichman	ACTG A5001: Longitudinal Linked Randomized Trials (ALLRT) Protocol	$6,325
893	Reichman	ACTG A5142: A Phase III, Randomized, Open-Label Comparison of Lopinavir/ Ritonavir plus Efavirenz vs. Lopinavir/Rotinavir plus Savudine Extended Release (or Zidovudine) plus Lamivudine vs. Efavirenz plus Stavudine Extended Release (or Zidovudine) plus Lamivudine for the Initial Therapy of HIV-1 Infection	$6,014
998	Frampton	Exposure to Ultrafine Carbon Particles in Diabetes (UPDIABETES)	$5,178
1008	Mapstone	Cognitive, Behavior, and Hormones in Perimenopause	$4,208
976	Schifitto	The Effects of Minocycline Co-Adminisrative Alone and in Combination with Valproic Acid on Atazanivir/Ritonavir Plasma Concetnration and Tenofovir Intracellular Concentrations in HIV-1 Infected Men and Women.	$3,912
965	Gerich	Hormonal and Substrate Regulation of Renal and Hepatic Gluconeogenesis in Nondiabetic Volunteers and in Subjects with Type 2 Diabetes Mellitus (T2DM)	$3,770
1051	Zareba	Familial Coronary Disease: Biomarkers and Genetic Factors	$3,405
981	Reichman	ACTG A5211: Phase II, Randomized, Double-Blind Study of the Safety and Efficacy of SCH 417690 (An Orally Administered HIV-1 Entry Inhibitor) in HIV-Infected, Treatment-Experienced Subjects	$3,250

Table G5B7 Principal Users of the GCRC

INPATIENT DAYS

Investigator	Department	2002-2003 Category A	2002-2003 Category D	2003-2004 Category A	2003-2004 Category D	2004-2005 Category A	2004-2005 Category D	2005-2006 Category A	2005-2006 Category D
Moxley	Neurology	168		6				6	
Walsh	Infect Dis					110		3	
Francis	Hem/Onc			26		72		1	
Gerich	Endocrine	46		55				26	
Sahler	Hem/Onc	26							
Zabera	Cardiology	6		23		2		15	
Ward	Anesthesiology					23		31	
Thornton	Neurology			2		17		17	
Richard	Neurology	15							
Goodman	Neurology		15						
Schifitto	Neurology							40	

Table G5B8. Recent Inpatient Utilization of the GCRC

Year	Category A	Category B	Scatter Bed A	Scatter Bed B	Category D	Category C	Average Length of Category A Inpatient Stay
2002-2003							
Used:	280	0	0	0	15	29	2.09
Awarded:	300	0	0	0	144	0	
2003-2004							
Used:	117	0	0	0	0	0	1.21
Awarded:	315	0	0	0	71	0	
2004-2005							
Used:	249	0	0	0	0	0	1.86
Awarded:	200	0	0	0	20	0	
2005-2006							
Used:	268	0	0	0	9	0	1.22
Awarded:	314	0	0	0	0	0	

Category A: Research patients or normal controls.

Category B: Patients receiving established medical care and participating in a research project
All research costs are paid by the GCRC or from the investigator's research support.

Category D: Industry-initiated research project. All charges paid by industry directly to institution.

Category C: Non-research patients who are boarded on discrete Centers.

Table G5B9. Principal Users of the GCRC

OUTPATIENT DAYS

Investigator	Department	2002-2003 Category		2003-2004 Category		2004-2005 Category		2005-2006 Category	
		A	D	A	D	A	D	A	D
Treanor	Infectious Disease	1699	2085	2120	685	1587	0	2963	0
Reichman	Infectious Disease	736	23	1130	5	1010	3	498	0
Shelly	Infectious Disease	639	0	437	0	0	0	0	0
Demeter	Infectious Disease	245	0	316	0	200	0	0	0
Hall	Pediatrics	298	0	326	0	98	1	0	0
Keefer	Infectious Disease	359	0	228	0	115	0	359	0
Caserta	Pediatrics	124	0	256	0	309	0	97	0
Betts	Infectious Disease	0	299	0	90	0	173	0	54
Schifitto	Neurology	139	0	264	0	105	0	124	2
Asselin	Pediatrics	218	0	92	0	76	0	0	0

Table G5B10. Recent Outpatient Utilization of the GCRC

Year		A	B	D
2002-2003	< 1 hour	3418	0	777
	1 – 3 hours	1258	0	248
	3 – 6 hours	242	0	190
	6 – 10 hours	323	0	32
	> 10 hours	33	0	0
	Total (USED)	5274	0	1247
	Awarded	3811	0	1082
2003-2004	< 1 hour	2032	0	254
	1 – 3 hours	1063	0	428
	3 – 6 hours	218	0	194
	6 – 10 hours	137	0	43
	> 10 hours	12	0	0
	Total (USED)	3462	0	919
	Awarded	4070	0	780
2004-2005	< 1 hour	3033	0	37
	1 – 3 hours	1230	0	95
	3 – 6 hours	229	0	138
	6 – 10 hours	131	0	44
	> 10 hours	30	0	0
	Total (USED)	4653	0	314
	Awarded	2997	0	1340
200-2006	< 1 hour	4283	0	27
	1 – 3 hours	1989	0	210
	3 – 6 hours	285	0	27
	6 – 10 hours	91	0	34
	> 10 hours	21	0	10
	Total (USED)	6642	0	308
	Awarded	5359	0	0

G5C1. Previous Clinical Associate Physician (CAP) and Minority Clinical Associate Physician (MCAP) Award

Name	Dates of Support	Specialty	Current Professional Activities	Academic Affiliation	Current NIH Funding	Role On Grant
Quaidoo, Emmanuel	7/1/96 – 6/30/98	Immunology	Clinical Assistant Professor	UR	None	
Tawil, Rabi	7/1/95 – 6/30/98	Neurology	Associate Professor Neurology, Pathology and Laboratory Medicine	UR	1N01AR002250-000 2R01AR046806-05 1U54NS048843-019002 5R01AR049077-04 5U54RR019482-03 1R01NS045686-01A1	Co-Investigator Co-Investigator Co-Investigator Co-Investigator Co-Investigator Co-Investigator
Demeter, Lisa	4/1/94 – 3/31/97	Infectious Disease	Associate Professor Medicine, Microbiology & Immunology	UR	5R01AI041387-07 1R01AI065217-01A1 3U01AI027658-18S2 3U01AI047980-05S1 5P01HD040540-05	PI PI Co-PI Co-Investigator Co-Investigator
Frampton, Mark	4/1/89 – 3/1/92	Pulmonary	Professor Medicine and Environmental Medicine	UR	5T32HL066988-05 5R01ES013394-02 5R01ES011853-04	PI PI PI

G5C2. Recent Medical Students Supported by GCRC Resources

Protocol Number	Name of Medical Student	GCRC PI/ Mentor	Dates of Support
785	Melissa Covington	Steven Schwid, MD	6/01 - 8/01
842	Tamar Smith	John Gerich, MD	6/01 -8/01
796	Tara Jane Maha	Arthur Papier, MD	6/02 - 9/02
707	Richard Moxley, IV	Eric Logigian, MD	7/02 -9/02
842	Anne Barlett	John Gerich, MD	6/03 - 8/03
707	Richard Moxley, IV	Eric Logigian, MD	7/03 - 9/03
974	Anne Buchanan	Jennifer Griggs, MD	7/04 -9/04
850	John Scherer	Steven Schwid, MD	7/04 - 9/04
974	Meagan Ford	Jennifer Griggs, MD	7/05 - 9/05

Table G5C3. Number and Status of RCRC (K30) Scholars, by Year of Entry (through March 2006)

Year Entered	*Number Entered*	*Completed*	*Withdrawn*	*Continuing*	*Degrees Conferred*
1999	15	11	1	3	9
2000	14	12	1	1	11
2001	20	13	1	6	11
2002	14	6	2	6	6
2003	17	7	0	10	7
2004	19	3	2	14	3
2005	17			17	
2006	8			8	
	124	52	7	65	47

2006 data through March 15 only

Table G5C4 Characteristics of RCRC (K30) Scholars, 1999-2006

Sex		
	Male	61
	Female	63
Ethnicity		
	Hispanic/Latino	5
	Not Hispanic/Latino	119
Race		
	Black/African American	14
	Asian	13
	White	97
Prior Degrees		
	MD or DO	98
	DDS or DMD	8
	PhD or Psy.D.	15
	MD/PhD	2
	DDS/PhD	1

Table G5C5. Professional Affiliation of RCRC (K30) Scholars, 1999-2006

Discipline or Specialty	*#*
Basic Science	3
Dentistry	9
Dermatology	3
Emergency Medicine	8
Environmental Medicine	1
Family Medicine	10
Medicine	27
Neurology	2
Nursing	3
Obstetrics and Gynecology	3
Ophthalmology	1
Orthopaedics	1
Pathology	1
Pediatrics	32
Psychiatry	2
Psychology	5
Radiation Oncology	1
Radiology	9
Surgery	3

Table G5C6: Publications for RCRC (K30) Participants

Publication Year	*First Author*	*Not First Author*	*Total*
1999	13	6	19
2000	10	7	17
2001	29	16	45
2002	37	21	58
2003	63	42	105
2004	82	51	133
2005	80	64	144
2006	35	17	52
Total	349	224	573

2006 data through March 15 only.

Table G5C7. Grants Awarded to RCRC (K30) Participants
Total $

Year Awarded	*NIH*	*Other*	*Total*
1999	-	59,208	59,208
2000	571,262	672,909	1,244,171
2001	2,175,288	70,665	2,245,953
2002	544,009	495,928	1,039,937
2003	3,426,452	915,819	4,342,271
2004	2,917,845	3,615,864	6,533,709
2005	837,199	3,484,678	4,321,877
2006	575,480	1,821,225	2,396,705
Total	11,047,535	11,136,295	22,183,830

2006 data through March 15 only.

Table G5C8: Research Grant Activity as Principal Investigator for RCRC (K30) Scholars

			Submitted		*Funded*		*Pending*	
Name	**Year Entered**	**Year Complete**	*Federal*	*Non-Federal*	*Federal*	*Non-Federal*	*Federal*	*Non-Federal*
Adams, M. Jacob	2000	2003	2	1	1			
Aligne, Andrew	1999	2001		7		6		
Arnold, Georgianne	2004		2	3	2	3		
Basu, Swati	2003	2005		2				2
Bazarian, Jeffrey	1999	2003	5	2	1		2	
Biglan, Kevin	2000	2005	1	3	1	3		
Block, Robert	2004		1	1			1	1
Brotanek, Jane	2001	2004		1		1		
Carroll, Jennifer	1999	2002	1	4	1	2		1
Cimpello, Lynn	2001		1	2		1	1	
Conner, Kenneth	1999	2003	9	5	5	2	3	1
Dosa, Nienke	1999	2003		2		2		
Eirich, Melissa	1999		2	4				
Everett, Clifford	2000	2005	1					
Figueroa-Mosely, Colmar	2005			2		2		
Forbis, Shalini	2000	2004		3		3		
Fox, Mark	2001	2005	2	2	2	1		
Friedman, Deborah	2002		1	5	1	5		
Ginde, Savita	2001			1				
Godfrey, Emily	2000	2004		1		1		
Goldsmith, Lowell	2001	2002		1				1
Gottlieb, Ronald	1999	2002	2	2	1	2		
Hadee, Taj	2005			1		1		
Hazel-Fernandez, Leslie	2003			1		1		
Hendren, Samantha	2005			3		3		
Hoeger, Kathleen	2003		2	1	1	1		
Horan, John	1999	2003	1	8		7	1	
Katz, Alan	2001	2004	1	2		1		1
Kelts, Elizabeth	2003	2005		1		1		
Kodjo, Cheryl	1998	2001	2	4	2	3		
Kopycka-Kedzierawski, Dorota	2000	2003	1	2		1	1	1
Lerner, Norma	1999		8	4	4	2	2	
Levy, Deborah	2003		1				1	
Loy, Rebekah	2006			1		1		
Maddow, Charles	2002			1		1		
McIntosh, Kenya	2004			1				1
Mihalopoulos, Nicole	2003	2005		4		4		
Mustian, Karen	2004		3	3	2	2	1	1
North, Stephen	2004		1	3		1	1	2
Noyes, Ekaterina	2000	2002	2	2	1	1	1	
Pietropaoli, Anthony	2003		1		1			
Pope, Charlene	2001	2003	1	2				
Quinn, Jill	2005			1				1
Rand, Cynthia	2002	2005		1				
Ren, Yan Fang	2001	2005	2	7		7	2	
Ritchlin, Christopher	2002		1	24	1	22		1
Robinson, Arvin	2001	2005		2		1		
Salloum, Rabih	2004			2				2
Shah, Manish	2002		9	4	3	2	3	
Stevens, Timothy	2001	2005	3	3	1	2	2	1
Syed, Labib	2002	2005		1		1		
Tanski, Susanne	2001		3	5	1	4		
Wilson, Matthew	2003			3		3		
Wing, Richard	2003			1		1		
Wu, Justine	2004			2		2		
Yawman, Daniel	2002	2005		2		1		
Yussman, Susan	2000	2004	3	5	1	5		
			75	161	33	116	22	17

G5C9. RCRC Graduates: MPH thesis Title and Mentor (through March 2006)

Name	MPH Thesis Title	Mentor
Adams, M. Jacob	Cardiovascular Function in Long-Term Survivors of Hodgkin's Disease Treated with Chest Radiotherapy	Thomas A. Pearson, MD MPH PhD
Aligne, Andrew	Association of Dental Caries with Passive Smoking	Mark Moss, DDS
Basu, Swati	Study of the Length of Stay and Mortality Associated with Febrile Neutropenia in Children With Cancer.	Diana Fernandez, MD PhD
Bazarian, Jeffrey	Lateral Automobile Impacts and the Risk of Tramatic Brain Injury	Susan Fisher, PhD
Biglan, Kevin	The Impact of Non-Motor Symtoms on Quality of Life In Parkinson's Disease	Robert Holloway, MD
Brotanek, Jane	Bridging Two Worlds: Latino Asthma Practices and Standard Medical Therapy	Ann Dozier, PhD
Carroll, Jennifer	Explanatory Models of Mental Illness in Refugees from Somalia	Timothy Dye, PhD
Chirieac, Doru	Hyperlipidemia in Secondary Prevention: Its Unrealized Potential	Thomas A. Pearson, MD MPH PhD
Chirieac, Madalina	Gender Differences in Depression and Chronic Pain in Older Adults	Sarah Trafton, JD
Church, Douglas	Using Upper Airways to Predict OSA Severity	Susan Fisher, PhD
Conde, Anthony	Meta-Analysis: Positron Emision Tomography (PET) Vs. Computed Tomography Imaging (CT-Scan) In the Diagnosis, Staging and Restaging of Head and Neck Cancers With Histopathological Confirmation.	Diana Fernandez, MD PhD
Conner, Kenneth	Risk Factors for Suicide and Medically Serious Suicide Attempts Among Alcoholics: Analyses of Canterbury Suicide Project Data	Kerry Knox, PhD
Dosa, Nienke	Pioneer-Survivors: Insights on Childhood Resilience by Adults with Spina Bifida	Nancy Chin, MPH PhD
Everett, Clifford	Colles Fracture: Validation of a Radiologic Grading System	Katia Noyes, MPH PhD
Fadl, Yazid	History of Hypertension and Enhanced Thrombogenic Activity in Post-Infarction Patients	Arthur Moss, MD
Forbis, Shalini	Illiterate Parents: Barriers to Accessing Healthcare for Their Children.	Nancy Chin, MPH PhD
Fox, Mark	What Can Transplantation Learn From Public Health	Thomas A. Pearson, MD MPH PhD
Glantz, John	Medical Induction of Labor: Rate variation and Relation to Case	Timothy Dye, PhD
Godfrey, Emily	Factors Influencing Reversible Contraception Use in Women Aged 35 and Over: An in-Depth Interview Study	Nancy Chin, MPH PhD
Goldsmith, Lowell	Analysis of Satisfaction with Prenatal Care in Monroe County	Thomas A. Pearson, MD MPH PhD
Gottlieb, Ronald	CT in Detecting Urinary Tract Calculi: Influence on Patient Imaging and Clinical Outcomes	Robert Holloway, MD
Gust, Anthony	Evaluation of an Internet-Based, Interactive Tutorial for Teaching Dermatologic Terminology to Medical Students.	Scott McIntosh, PhD
Harris, Lewanza	Mistrust in Medical Institutions as a Barrier to Pneumococcal and Influenza Vaccinations in Black Communities.	Nancy Chin, MPH PhD
Horan, John	Survival After HLA-Identical Allogeneic Peripheral Blood Stem Cell and Bone Marrow Transplant for Hematologic Malignancies:A Meta-Analysis of Randomized Controlled Studies	Susan Fisher, PhD
Jacob-Parks, Carolyn	Counseling Adolescent Mothers on Breastfeeding.	Scott McIntosh, PhD
Kaba, Kristen	Effects of Lipids and Lipoprotein Particle Size on Hemostatic Factors in Patients with Myocardial Infarction	Kerry Knox, PhD
Katz, Alan	Circulating Cytokine Levels and Their Correlation with Fatigue in Breast Cancer Patients Treated with Chemotherapy	Susan Fisher, PhD
Kelts, Elizabeth	Adolescents' Sexual Habits and Emergency Contraception Awareness.	Ann Dozier, PhD
Kodjo, Cheryl	Intrinsic and Extrinsic Risk Factors for Carrying A Weapon at School	Thomas A. Pearson, MD MPH PhD
Kopycka-Kedzierawski, Dorota	Cost-Effectiveness Model of Caries Risk Assessment in Children	Susan Fisher, PhD
Mihalopoulos, Nicole	Behavior Change and Cardiovascular Risk Factors in Adolescents	Jonathan D. Klein, MD MPH
Moutsiakis, Demetrius	Why is Participation by Blacks in HIV/AIDS Vaccine Trials so Low?	Sarah Trafton, JD
Noyes, Ekaterina	Pramipexole vs Levodopa as Initial Treatment for Parkinson's Disease: A Randomized Clinical-Economic Trial Cross Cultural Communication in Preventive Cardiology	Jack Zwanziger, Ph
Pope, Charlene	Teen Voices: Barriers to Communication of Smoking Cessation Advice	Deborah Ossip-Klein, PhD
Popelka, Sandro	Relationship of Age to Tooth Loss in a Chronic Care Facility.	Sally Trafton, JD
Rand, Cynthia	Source of Reproductive Healthcare in a University Setting: Implications for Quality of Care.	Ann Dozier, PhD
Ren, Yan Fang	Health Care Seeking Behavior Of Dental Emergency Patients.	Susan Fisher, PhD
Roberts, Timothy	Longitudinal Effect of Intimate Partner Abuse on High-Risk Behavior Among Adolescents	Susan Fisher, PhD
Robinson, Arvin	Positron Emission Tomography (PET) in the Staging and Management of Malignant Lymphoma.	Robert Holloway, MD
Sinkin, Robert	Effect of Managed Care on Perinatal Transports for the Publicly Funded in Upstate NY	Timothy Dye, PhD
Smith, Claudine	Barriers to Management of Diabetes Mellitus Type 2 In An African American Community: A Qualitative Inquiry.	Nancy Chin, MPH PhD
Stevens, Timothy	RSV Hospitalization Among Infants Born 32-35 Weeks Gestation.	Susan Fisher, PhD
Syed, Labib	Annual Mammograms in Women Between 40-50 Years Old or Not? A Qualitative Assessment.	Sarah Trafton, JD
Tabak, Carolyn	The Association of Glycemic Index and Load with Pediatric Obesity: A National Perspective	Michael Weitzman, MD
Vyas, Anant	Do Statins Have Anti-Arrhythmic Properties?	Thomas A. Pearson, MD MPH PhD
Watson, David	Airway Size, Jaw Pain, and Daytime Sleepiness in Children with Rheumatic Disease.	Katia Noyes, MPH PhD
Weiss, Oren	The Effect of the Interleukin-1 Genotype on the Outcome of Regenerative Peridontal Therapy with Bone Replacement Grafts	Susan Fisher, PhD
Wittman, Brenda	Body Mass as a Predictor for Overall and Disease-Free Survival and Toxicity of Chemotherapy in Pediatric Patients with T-Cell ALL or NHL Treated on the Pediatric Oncology Group 9404 Protocol: A Retrospective Cohort Study.	Katia Noyes, MPH PhD
Yawman, Daniel	The Use of Spanish by Medical Students and Residents at a University Hospital.	Scott McIntosh, PhD
Yussman, Susan	Complementary and Alternative Medicine Use by Adolescents with Special Health Care Needs	Sarah Trafton, JD
Zareba, Grazyna	Risk Factors Associated With Increased Mercury Levels In Mothers and Children From the Seychelles Child Development Study.	Sarah Trafton, JD
Zottola, Paul	Simultaneous Evaluation of Clinical Attachment Level and Probing Depth Measurements: A Novel Approach to Outcomes Assessments	Susan Fisher, PhD

Table G5C10. Prior Training and Current Positions of Rochester Clinical Research Curriculum Participants

STUDENT NAME	MINORITY STATUS	PREVIOUS INSTITUTIONS and DEGREES	RESIDENCY TRAINING	FELLOWSHIP TRAINING	PRESENT POSITION
Adams, M. Jacob*	M White	AB, 1993, Washington University MD, 1997, Johns Hopkins University	Pediatrics University of Rochester	Fellow, Preventive Cardiology University of Rochester	Assistant Professor, Epidemiology
Aligne, Andrew C*	M White	BS, 1987, UCLA MD, 1992, UCLA	Pediatrics University of Wisconsin	Fellow, Pediatrics University of Rochester	Private Practice
Arnold, Georgianne	F White	BS, 1979, Indiana University MS, 1983, Indiana Purdue University MD, 1986 SUNY Upstate Medical University			Associate Prof. Pediatrics University of Rochester
Basu, Swati*	F Asian	MBBS, Bombay University	Pediatrics Beth Israel Medical Center Grant Medical College	Pediatrics Beth Israel Medical Center	PhD Student Epidemiology University of Rochester
Bazarian, Jeffrey J*	M White	BA, 1987, Brown University MD, 1987, University of Rochester	Internal Medicine University of Rochester Completed 1990		Assistant Professor, Neurology Emergency Medicine University of Rochester
Biglan, Kevin M*	M White	BS, 1992, Albright College MD, 1996, Jefferson Medical College	Internal Medicine Lankenau Hospital Neurology Thomas Jefferson University	Experimental Therapeutics University of Rochester	Assistant Professor, Johns Hopkins University School of Medicine
Block, Robert	M White	MD, 1991, Uniersity of Medicine & Dentistry of New Jersey			Clinical Instructor - General Internal Medicine - University of Rochester
Bowen, Kevin L	M White	BS, University of Iowa MD, University of Iowa MBA, Simon School - University of Rochester	Anatomic and Clinical Pathology, University of Virginia	Fellow, Hematopathology William Beaumont Hospital Michigan	MPH Graduate Student, University of Rochester
Brotanek, Jane M*	F White	BA, 1994, Yale College MD, 1998, NYU School of Medicine	Pediatrics St. Vincent's Medical Center	Fellow, Pediatrics University of Rochester	Fellow, Academic Pediatrics University of Rochester
Brown, Lanette	F African/ American	BS, 1993, Denison Uniersity MD, 2004, University of Rochester			Fellow Preventive Cardiology University of Rochester
Bush, Gretchen	F White	DDS, Case Western, 2001 BS, RIT, 1997	General Practice Dentistry University of Rochester	Fellow, General Dentistry University of Rochester	Fellow, General Dentistry University of Rochester
Caprio, Thomas	M White	BS, 1996 Nazareth College of Rochester MD, 2000, SUNY Buffalo		Research Fellow in Geriatrics and Gerontology University of Rochester	Research Fellow in Geriatrics and Gerontology University of Rochester
Carroll, Jennifer K*	F White	MA, 1991, Wellesley College MD, 1996, Univiversity of Connecticut	Family Medicine University of Rochester	Fellow, Family Medicine University of Rochester	Asst Professor, Family Medicine Boston University
Chesley, Eric B	M White	BA, 1991, University of Utah DO, 1998, Western Univ. of Health Sciences	Pediatrics Children's Hospital	Fellow, Pediatrics University of Rochester	Fellow, Pediatrics University of Rochester
Chirieac, Doru V*	M White	MD, University of Medicine Romania	Pathology University Hospital, Romania	Fellow, Pathology University of Rochester	Fellow, Pathology University of Rochester
Chirieac, Madalina C*	F White	MD, University of Medicine Bucharest		Fellow, Endocrinology University of Rochester	Research Coordinator, Monroe County Long Term Care
Church, Douglas Chad*	M White	DDS, Lamar University	TMJD Eastman Dental School University of Rochester		Asst Professor, Dentistry University of Rochester
Cimpello, Lynn Babcock	F White	MD, 1995, UMDNJ-Robert Wood Johnson Medical School	Pediatrics Yale New Haven Hospital	Fellow, Pediatric Emergency Medicine Montefiore Medical Ctr.	Sr. Instructor in Medicine University of Rochester
Conde, Anthony*	M Hispanic	BS, University of Miami MD, 2000, Lance School of Medicine	Preliminary Surgery, Hershey Medical Center Nuclear Medicine, SUNY Buffalo Diagnostic Radiology, University of Rochester		MD/MPH Diagnostic Radiology Residency University of Rochester
Conner, Kenneth R*	M White	Psy.D., 1993, Wright State University GPA: 3.83			Assistant Prof Psychiatry University of Rochester
Cook, Stephen R	M White	BS, 1992, Niagara University MD, 1996, Univ of Buffalo School of Medicine	Pediatrics Children's Hospital of Buffalo	Fellow, General Pediatrics University of Rochester	Clinical Instructor, Pediatrics School of Medicine and Biomedical Sciences, Buffalo
Dele-Michael, Abiola	M African- American	BS, 2001, Cornell University			Medical Student, MA-MS Prog. University of Rochester
Dickerson, Ty	M White	MD, 1998 University of Iowa BS, 1991,University of Iowa	Pediatric Residency, SUNY Syracuse, NY		Asst Professor, Pediatrics SUNY Upstate Syracuse
Dosa, Nienke*	F White	MD, 1994 SUNY-MSC Syracuse BA, 1983 Yale University	SUNY- Syracuse Pediatrics	Fellow-General Academics University of Rochester	Ass't Professor, Pediatrics SUNY Upstate Syracuse
Eirich, Melissa	F White	MD, 1992 Northeastern Ohio University BS, 1998, Kent State University	Allegheny General Hospital Emergency Medicine	Carolinas Medical Center	Assistant Professor Emergency Medicine University of Rochester

Table G5C10.
Prior Training and Current Positions of Rochester Clinical Research Curriculum Participants (continued)

STUDENT NAME	MINORITY STATUS	PREVIOUS INSTITUTIONS and DEGREES	RESIDENCY TRAINING	FELLOWSHIP TRAINING	PRESENT POSITION
Everett, Clifford, R*	M White	BA, Regis College, 1990, GPA: 3.617	Physical Medicine and Rehab Mayo Clinic		Assistant Professor Orthopedics
Fadl, Yazid*	M White	BA, 1994, Carnegie Mellon University MD, 1998, Temple University School of Medicine	Internal Medicine, University of Rochester	Fellow, Preventive Cardiology University of Rochester	Fellow, Cardiology Washington University Barnes Hospital, St. Louis
Figueroa-Mosely, Colmar	M African American	BA, 1993, Carnegie Mellon University MA, 1996, University of Alabama at Birmingham PhD, 1997, University of Alabama at Birmingham		Cancer Center Fellow University of Rochester	Ass't Professor, Radiology Oncology University of Rochester
Finigan, Elizabeth	F White	BS, 1984, University of Massachusetts MD, 2000, Medical College of Wisconsin			Family Medicine University of Rochester
Forbis, Shalini*	F Asian	MD, 1997 Medical College of Ohio BS, 1992 Ohio State University	Pediatrics Medical College of Ohio	Fellow, Pediatrics University of Rochester	Children's Health Clinic Ohio
Fox, Mark D*	M White	BA, 1994, Georgetown University MD, 1997, Vanderbilt School of Medicine	Internal Medicine and Pediatrics University of Rochester	Preventive Cardiology Fellow University of Rochester	Associate Director Bioethics Center University of Oklahoma
Friedman, Deborah I	F White	BA, Georgia Institute of Technology MD, Tulane University	Resident - Neurology, Baylor College of Medicine Intern - Good Samaritan Hosp.	Neuro-Ophthalmology , Univ. Southern California	Associate Professor Ophthalmology & Neurology University of Rochester
Garcia, Madelyn	F Hispanic	BA, 1994, New York University MD, 1999, University of Pennsylvania	Pediatrics Hasbro Children's Hospital University of Rochester		Resident Pediatric Emergency Medicine University of Rochester
Ginde, Savita Y	F Asian	BA, 1992, Univ of Pennsylvania MD, 1997, American Univ. of the Caribbean	Family Medicine Dartmouth	Fellow, Reproductive Health Family Planning University of Rochester	Senior Instructor, Health Sciences Center, University of Colorado
Glantz, John*	M White	MD, 1976 University of California, Las Angeles BA, 1976 University of California, San Diego	Obstetrics & Gynecology North Carolina Memorial Hospital	Fellow, OB/GYN University of Rochester	Assistant Professor, OB/GYN University of Rochester
Godfrey, Emily M*	F White	BS, University of Wisconsin-Madison 1991, GPA: 3.642	Family Practice Suburban Hospital Family Practice, Chicago, IL	Fellow, Family Medicine University of Rochester	Faculty Obstetrics & Gynecology Stroger Hospital - Cook County
Goldsmith, Lowell A*	M White	AB, 1959, Columbia University M.D., 1963 State University of NY	Medicine UCLA Medical Center	Dermatology, Harvard University	Professor of Dermatology, University of North Carolina
Gottlieb, Ronald H*	M White	BA, Univ. of Pennsylvania, 1976 MD, Duke Univ Medical School, 1980	Radiology, North Shore University Hospital		Faculty, Dept. of Radiology, University of Rochester
Gust, Anthony J*	M White	BS, 1998, Penn State University MD, 2002, University of Virginia	Internal Medicine University of Rochester	Fellow, Radiology University of Rochester	Departmental Fellow Dermatology University of Rochester
Hadee, Taj	F African American	BS, 1990 Tufts University MD, 1997, SUNY at Buffalo School of Medicine	Pediatric Residency McGraw-Northwestern University	Fellow, Family Medicine University of Rochester	Fellow, Family Medicine University of Rochester
Harris, Lewanza*	F African American	BS, 1993, Xavier University of Louisiana MD, 1998, University of Rochester	Surgery Morehouse School of Medicine		Resident, Family Medicine University of Rochester
Hendren, Samantha	F White	BA, 1991, Rice University MD, 1996, Yale University School of Medicine	Surgery University of Pennsylvania	Colorectal Surgery University of Toronto	Ass't Professor of Surgery University of Rochester
Hazel-Fernandez, Leslie	F African American	BA, 1991, Hunter College MA, 2003 , University of Rochester PhD, Current, University of Rochester		Fellow, Preventive Cardiology University of Rochester	Fellow, Preventive Cardiology University of Rochester
Hernandez, Nilda	F Hispanic	BA, 1993, Case Western Reserve University		Fellow, Preventive Cardiology University of Rochester	Dropped Out, 2001
Hoeger, Kathleen M	F White	BS, Stanford University MD, Jefferson Medical College	Thomas Jefferson University	University of Virginia	Assistant Professor Obstetrics & Gynecology University of Rochester
Holmes, Alison	F White	BS, 1993, Haverford College MS, 1995, Washington University MD, 2000, Stanford University			Ass't Professor Community & Family Medicine Dartmouth Medical School
Horan, John*	M White	MD, 1993 New Jersey Medical School BA, 1984 Colgate University	Pediatrics University of Rochester	Fellow, Hematology/Oncology University of Rochester	Assistant Professor Hematology/Oncology University of Rochester
Jacobs-Parks, Carolyn*	F African American	MD, 1999 SUNY-Syracuse BA, Johns Hopkins		Fellow, Adolescent Medicine University of Rochester	Fellow, Adolescent Medicine University of Rochester
Jandzinski, Dana I	F White	BA, 1993, Case Western Reserve Univ. MD, 1998, SUNY Buffalo	General Surgery St. Joseph's Hospital Radiology University of Rochester	Fellow, Radiology University of Rochester	Fellow, Radiology, University of Rochester

Table G5C10. Prior Training and Current Positions of Rochester Clinical Research Curriculum Participants (continued)

STUDENT NAME	MINORITY STATUS	PREVIOUS INSTITUTIONS and DEGREES	RESIDENCY TRAINING	FELLOWSHIP TRAINING	PRESENT POSITION
Jensen, Peter M	M White	DDS, 1979 University of Detroit	General Practice Dentistry University of Rochester		Associate Professor, Dentistry University of Arizona
Kaba, Kristen N*	M African American	PhD, University of Tulbingen, Germany Pharmacy, Univ of Tulbingen, Germany		Post - Doctoral Fellow, Biochemistry & Biophysics, University of Rochester	Clinical Affairs Manager Eastman Kodak Company
Katz, Alan W*	M White	BA, 1981, SUNY Binghamton MD, Sacles School of Medicine, Tel-Aviv	Oncology, Sheba Medical Ctr	Radiation Oncology, University of Rochester	Instructor, Radiation Oncology University of Rochester
Kelts, Elizabeth, A*	F White	BS, Biological Sciences, Colorado State MD, University of Rochester	Family Medicine University of Rochester	Fellow, Reproductive Health & Family Planning University of Rochester	Fellow, Reproductive Health & Family Planning University of Rochester
Kodjo, Cheryl M*	F African American	BA, 1991, Princeton University MD, Columbia	Pediatrics, Montefiore Medical Center	Fellow, Adolescent Medicine University of Rochester	Senior Instructor, Pediatrics & Adolescent Med., University of Rochester
Kohli, Sadhna	F Asian	PhD, 1997			
Kopycka-Kedzierawski,* Dorota	F White	DDS, State Univ. of Lublin School of Medicine	AEGD Eastman Dental Center		Assistant Professor, Eastman Dental Center
Kuderer, Nichole	F White	MD, 2002, Albany Medical College	Internal Medicine University of Rochester		Fellow, Hematology/Oncology University of Rochester
Lerner, Norma	F White	MD, 1975 Brown University BA, 1971 Jackson College, Tufts Univ	Pediatrics Boston City Hospital Senior Resident, Pediatrics	Fellow, Children's Hosp-Phil Fellow, Sloan Kettering	Associate Professor Peds/Hem/Oncology University of Rochester
Levy, Deborah R	F White	BA, 1996, Univ of Pennsylvania MD, 2000, Tel Aviv University	Massachusetts General Hosp. Internal Medicine University of Rochester	Post-Doctoral Fellow, Preventive Cardiology University of Rochester	Post-Doctoral Fellow, Preventive Cardiology University of Rochester
Liebman, Scott	M White	BA, 1993, Cornell University MD, 1997, SUNY Syracuse	Internal Medicine Mount Sinai Hospital	Nephrology University of Colorado	Ass't Professor Nephrology University of Rochester
Loy, Rebekh	F White	BS, 1971, University of California, Irvine PhD, 1975, University of California, Irvine			Associate Professor Neurology University of Rochester
Maddow, Charles L	M White	BA, 1994, Univ of Pennsylvania MD, 1998, Temple University	Emergency Medicine, University of Chicago		Sr. Instructor, Emergency University of Rochester
Maher, Mary	F White	BSN, 1977, D'Youville College MSN, 1994, Case Western Reserve University			Ass't Professor Nursing Nazareth College
McIntosh, Kenya	F African American	BS, 1996, Atlanta University MD, 2004, University of Rochester			MPH Student University of Rochester
Merner, David	M White	BA, 2005, University of Rochester			MD/MPH Student, University of Rochester
Middleton, Tamar	F African American	MD, 2000, Morehouse School of Medicine BA, 1985 Agnes Scott College	Columbus Family Practice Columbus Georgia	Fellow Reproductive Health University of Rochester	Fellow Reproductive Health University of Rochester
Mihalopoulos, Nicole L*	F White	BA, 1995, University of Utah MD, 1999, Tulane University MPH, 2003, Tulane University	Internal/Preventive Medicine, Tulane University	Fellow, Adolescent Medicine University of Rochester	Fellow, Preventive Cardiology University of Rochester
Mikityansky, Igor	M White	BS, 1997, Hunter College MD, 2002, University of Rochester	University of Rochester Radiology	R25 Fellow, Radiology	Post Doc Fellow Radiology, University of Rochester
Moutsiakis, Demetrius*	M White	MD, SUNY-Stony Brook BA SUNY StonyBrook	SUNY- Stonybrook Medicine Stony Brook, NY	Fellow, Pharmacology SUNY-StonyBrook	Fellow, Radiology University of Rochester
Murray, Theresa E	F White	BA, 1991, University of Virginia MD, 1995, University of Virginia	Pediatrics University of Iowa Hospitals	Fellow, Neonatology University of Rochester	Fellow, Neonatology University of Rochester
Mustian, Karen	F White	BS, 1991, East Carolina University MA, 1993, East Carolina University PhD, 2003, University of N. Carolina at Greensboro			Research Ass't Professor of Oncology University of Rochester
Narang, Shalu	F Asian	BA, 1997, New York University MD, 2001, St. George's University	Pediatrics Maimonides Medical Center		Pediatric Hematology/Oncology Fellow University of Rochester
Nead, Karen Gnuse	F White	BA, 1992, Middelbury College MD, 1997, Univ of Rochester	Internal Medicine, Pediatrics University of Rochester		Assistant Professor, Pediatrics Yale University
North, Stephen	M White	MD, 2000 University of North Carolina BA, 1993, University of Wisconsin	Family Practice University of Rochester	Fellow, Adolescent Medicine University of Rochester	Fellow, Adolescent Medicine University of Rochester
Noyes, Ekaterina I*	F White	BS, Saratov State University, 1995 PhD, 2000 Biophysicians & Biochemistry,2000 University of Rochester		Fellow, Health Services Research University of Rochester	Assistant Professor, Health Services Research University of Rochester
O'Connor, Alec	M White	BA, 1992, University of California at Berkeley MD, 1996, Indiana University	Internal Medicine University of Rochester		Ass't Professor of Medicine University of Rochester
O'Gara, Kevin	M	MD, 1996 University of Rochester	Pediatrics	Emergency Medicine	Emergency Medicine

Table G5C10. Prior Training and Current Positions of Rochester Clinical Research Curriculum Participants (continued)

STUDENT NAME	MINORITY STATUS	PREVIOUS INSTITUTIONS and DEGREES	RESIDENCY TRAINING	FELLOWSHIP TRAINING	PRESENT POSITION
Pietrasik, Grzegorz	M White	MD, 1999, Medical University of Warsaw	Internal Medicine John Stroger Hospital of Cook County		Fellow, Heart Research University of Rochester
Petronaci, Carol-Lynn	F White	BA, 1980, Cedar Crest College MD, 1998, Wake Forest Univ. School of Medicine	Internal Medicine University of Rochester		Senior Instructor Medicine University of Rochester
Pietropaoli, Anthony P	M White	BA, 1986, College of the Holy Cross MD, 1990, SUNY Upstate College of Medicine	Internal Medicine University of Pittsburgh	Pulmonary & Critical Care Medicine University of Rochester	Asst. Professor of Medicine, Pulmonary & Critical Care Unit, University of Rochester
Pope, Charlene*	F White	BSN, 1974, University of Maryland MPH, CNM, 1978, Johns Hopkins Univ. PhD, 2001, Univ. of Rochester	Midwifery Internship, Booth Maternity Center, Philadelphia, PA	Social and Behavioral Medicine Comm. & Prev. Medicine	Assistant Professor, University of South Carolina, College of Nursing
Popelka, Sandro*	M White	DDS, 2000 Free University of Berlin, Germany	Eastman Dental Center University of Rochester	Fellow, Eastman Dental University of Rochester	Fellow, Eastman Dental University of Rochester
Puri, Savita	F Asian	MD, 1968, All India Institute of Medical Sciences			Ass't Professor Radiology University of Rochester
Quinn, Jill	F White	BA, 1975, Alfred University MS, 1979, University of Rochester PhD, 2003, University of Rochester			Fellow, Geriatrics & Gerontology University of Rochester
Rand, Cynthia M*	F White	BA, Hamilton College MS, Worcester Polytechnic Inst. MD, SUNY Stony Brook	Penn State Hershey Med Ctr.	Fellow, Pediatrics University of Rochester	Fellow, General Academic Pediatrics University of Rochester
Rashid, Megan R	F White	BA, McGill University Washington Univ School of Medicine	Pediatrics University of Rochester	Fellow, Pediatric Nephrology University of Rochester	Fellow, Preventive Cardiology University of Rochester
Ren, Yan Fang*	M Asian	DDS, 1984, Beijing Medical Univ	Eastman Dental Center University of Rochester	Fellow, Eastman School of Dentistry University of Rochester	Assistant Professor Eastman School of Dentistry University of Rochester
Ritchlin, Christopher	M White	MD, 1982 Albany Medical College BA, 1976 University of Rochester	Internal Medicine Mt. Sinai Hospital, NY		Associate Professor Rheumatology/Immunology University of Rochester
Robinson, Arvin*	M White	AB, 1960, University of Pennsylvania MD, 1964, Medical College of Virginia	Radiology Duke University	Fellow, Pediatric Radiology Duke University	Professor Dept. of Radiology University of Rochester
Roberts, Timothy*	M White	MD, 1995 University of Oklahoma BS, UC Davis	Pediatrics UCLA at San Diego	Adolescent Medicine University of Rochester	NAVY Pediatrician
Rueckmann, Erik	M White	BS, 1994, SUNY Geneseo MD, 2002, Upstate Medical University	Emergency Medicine University of Rochester		Emergency Medicine University of Rochester
Ryan, Julie	F White	BS, 1997, University of Chicago PhD, 2005, University of N Carolina at Chapel Hill			Research Ass't Professor University of Rochester
Salloum, Rabih	M White	BS, 1984, American University of Beirut MD, 1988, American University of Beirut			Medical Director, Nutrition University of Rochester
Schmit, Jacquie	F White	MD, 2002, University of Rochester BS, 1996 University of South Dakota	Emergency Medicine University of Rochester	Emergency Medicine University of Rochester	Deceased
Shah, Manish N	M Asian	MD, University of Rochester BA, University of Chicago	Ohio State University	Robert Wood Johnson Clinical Program, University of Chicago	Assistant Professor, Emergency Medicine University of Rochester
Shear, Sephanya	F White	BS, 1989, University of Vermont MS, 1992, Emory University MD, 2002, University of Washington	Surgery University of Washington		Reproductive Epidemiology University of Rochester
Shrivastava, Rakesh	M Asian	MD, 1997, Institute of Medical Sciences	Medicine Rush University		Clinical Sr. Inst. Of Medicine University of Rochester
Shyu, Chandler	M Asian	BS, 1998, University of California BA, 1998, University of California MD, 2002, University of Rochester	Radiology University of Rochester	R25 Trainee University of Rochester Radiology	Post Doc Fellow Radiology, University of Rochester
Sigrest, Ted	M White	BA, 1973, Mississippi State University BS, 1981, University of Mississippi		Fellow, Pediatrics University of Rochester	Fellow, General Academic Pediatrics University of Rochester
Sinkin, Robert A*	M White	BA, 1967, Colgate University MD, 1980, Univ of Rochester	Pediatrics Oakland, CA	Fellow, Neonatology University of Rochester	Medical Director, NICU, Pediatrics University of Rochester
Smith, Heidi	F White	BSN, 1995, University of Rochester MD, 2001, Yale University		Pediatrics University of Rochester	Instructor Emerg. Medicine University of Rochester
Smith, Claudine*	F African American	BS, 1986, Fairleigh Dickinson University MD, 1991, Ross University School of Medicine	Family Practice SUNY Buffalo		Clinical Instr, Family Medicine Montefiore Medical Group
Stahlhut, Rick	M White	BA, 1978, University of Indianapolis MD, 1982, Indiana University MS, 1986, Harvard School of Public Health	Preventive Medicine University of Rochester		Resident, Preventive Medicine University of Rochester

Table G5C10.
Prior Training and Current Positions of Rochester Clinical Research Curriculum Participants (continued)

STUDENT NAME	MINORITY STATUS	PREVIOUS INSTITUTIONS and DEGREES	RESIDENCY TRAINING	FELLOWSHIP TRAINING	PRESENT POSITION
Steider, Anne	F White	BS, 1990, Valparaiso University MA, 1994, University of Dayton PhD, 2001, Gallaudet University		Preventive Cardiology University of Rochester	Senior Clinical Instructor University of Rochester
Stevens, Timothy P*	M White	ScB, Biology, Brown University, 1983 MD, University of Rochester, 1987	Pediatrics University of Rochester	Fellow, Neonatology University of Rochester	Assistant Professor, Pediatrics University of Rochester
Syed, Labib H*	M Asian White	BA, University of Western Ontario MD, UNIBE MD, Case Western Reserve University	Robert Packer Hospital General Surgery, 2000-2001 University of Rochester		Post Doc Fellow Radiology, University of Rochester
Tabak, Carolyn J*	F White	BS, University of Pennsylvania MD, Case Western Reserve University	Franklin Square Hosp. Ctr. University of Rochester	Preventive Cardiology Fellow University of Rochester	Fellow, Peds & Preventive Cardiology
Talens, Teresa	F White	BA, 2004, University of Rochester			MPH Graduate Student University of Rochester
Tanski, Suzanne	F White	MD, 1998 University of Connecticut, AB 1992 Vassar College	Pediatric University of Rochester	General Pediatrics University of Rochester	General Pediatrics University of Rochester
Thingvoll, Erik	M White	BS, 1997, University of Rochester MD, 2001, University of Rochester		Neonatology University of Rochester	Fellow, Neonatology University of Rochester
Thomas-Taylor, Danielle M	F African American	BS, SUNY Geneseo MD, Mt. Sinai School of Medicine	Pediatrics University of Rochester	Fellow, General Academic Pediatrics	Fellow, General Academic Pediatrics
Vargas, Roberto L	M Hispanic	Pre-Med, Univ Puerto Rico Doctor in Medicine, Univ Puerto Rico	Pathology University of Rochester	Fellow, Radiology University of Rochester	Resident in Pathology
Vyas, Anant*	M Asian	MBBS, 2000 Sardar Patel University, India	Internal Medicine Rochester General Hospital Rochester, NY	Fellow, Preventive Cardiology Heart Research University of Rochester	Fellow, Preventive Cardiology Heart Research University of Rochester
Wagmiller, Jennifer	F White	MD, 2000 University of Rochester BA, 1992 The Catholic University of America	Columbia Presbyterian New York NY	Fellow, Health Services Research University of Rochester	Fellow, Health Services Research University of Rochester
Watson, David F*	M White	BS, Wofford College DMD, Med Univ South Carolina	Eastman Dental Center University of Rochester	Eastman Dental Center University of Rochester	Fellow, Eastman Dental Center University of Rochester
Weiss, Oren I*	M White	BSc, 1990, Hebrew Univ Jerusalem DMD, 1993, Hebrew Univ Jerusalem	Eastman Dental Center University of Rochester	Eastman Dental Center University of Rochester	Assistant Professor Eastman Dental Center University of Rochester
Wilson, Matthew	M African American	BS, Northeastern University MS, Columbia University MD, University of Rochester	Family Medicine University of Rochester	Fellow, Preventive Cardiology University of Rochester	Resident, Family Medicine University of Rochester
Wing, Richard	M White	BA, 1991, Tufts University A.M., 1993, Harvard University MD, 2000, UMDNJ-Newark	Internal Medicine, University of Rochester		Senior Instructor, Medicine University of Rochester
Wittman, Brenda*	F White	BA, 1995, Emory University MD, 1999, University of Rochester	Pediatrics University of Rochester	Fellow, Pediatric Hematology, University of Rochester	Fellow, Pediatrics University of Rochester
Wu, Justine	F Asian	BS, 1997, Trenton State College MD, 2000, New Jersey Medical School		Reproductive Health University of Rochester	Clinical Inst. Family Medicine University of Rochester
Yawman, Daniel*	M White	BA, Univ of Notre Dame MD, SUNY Buffalo	Pediatrics University of Rochester	Fellow, Pediatrics University of Rochester	Fellow, Pediatrics University of Rochester
Yussman, Susan*	F White	MD, 1997 University of Louisville BA, 1993 Washington University, St. Louis	Pediatrics Oregon Health Sciences Univ. Portland Oregon	Adolescent Medicine Fellow University of Rochester	Adolescent Medicine Faculty Threshold Center for Youth Rochester, NY
Zareba, Grazyna*	F White	PhD., 1989 Poland MS, 1980 Poland	Dermatology University of Rochester	Fellow, Toxicology University of Rochester	Research Assistant Professor University of Rochester
Zottola, Paul*	M White	DDS, 1998 University of Pennsylvania BA, 1994 Colgate, Rochester, NY	Periodonotology Eastman Dental Center University of Rochester	Periodonotology Eastman Dental Center University of Rochester	Practice in Periodonotlogy University of Rochester

Table G5C11: Individual K-Awards at the University of Rochester

No.	Sponsor	Award Number	Title	Principle Investigator	Begin Date	GCRC Support	RCRC Scholar	Written in PM438
1	HRSA	K01 HP00030	Geriatric Academic Career Award	Heppard, Brian L	9/30/2002			yes
2	NIMH	K01 MH64718	Impact of Depression and Function on Healthcare Use and Cost	Friedman, Bruce	2/1/2003			yes
3	NIMH	K01 MH068491	Risk and Protective Mechanisms in Child Maltreatment	Kim, Jungmeen E	7/1/2003			
4	NIMH	K01 MH66317	A Prospective Study of Suicide Prevention in the USAF	Knox, Kerry L	7/1/2003			yes
5	NIA	K01 AG022072	Preparation for Future Care in Older Adults	Sorensen, Silvia	7/1/2003			
6	NIA	K01 AG20980	Economic and Policy Analysis in Geriatric Disease	Noyes, Ekaterina Ivanovna	9/1/2003		yes	yes
7	HRSA	K01 HP0074	Geriatric Academic Career Award	Clark, Nancy S	9/30/2003			
8	NHLBI	K01 HL080938	Bcr and PPAR gamma as Targets for Transplant Arteriopathy	Alexis,Jeffrey D	8/1/2005			
9	HRSA	K01 HP00170	Geriatric Academic Career Award	Nelson,Dallas L	9/30/2005			
10	NIGMS	K08 GM36303	The Role of GDF-15 in Organ Injury	Koniaris, Leonidas George	9/1/2001			
11	NIAID	K08 AI51154	Impact of Efavirenz Resistance Mutations on HIV-1	Koval, Christine E	3/1/2003	yes		
12	NHLBI	K08 HL04492	TGFB and Gene Therapy in Silica Induced Lung Fibrosis	Sime, Patricia Janet	4/1/2003			
13	NIAID	K08 AI055888	Antigen-independent CD8 T cell-induced Hepatitis	Pierce, Robert H	7/1/2003			
14	NINDS	K08 NS046633	The role of Hypoxia Inducible Factor-1 alpha in stroke	Rempe,David A	7/15/2003			
15	NIDDK	K08 DK64381	Roles of PTH/PTHrP Receptors in Osteoblastic Cells	Calvi, Laura	8/1/2003			
16	NIAMS	K08 AR48303	B cell functional and signaling abnormalities in SLE	Anolik, Jennifer Howitt	9/1/2003			
17	NHLBI	K08 HL67746	uPA Receptor Signaling and Cell Migration	Davies, Mark Glynn	9/1/2003	yes		
18	NIAID	K08 AI062978	Yeast Aspartyl Proteases in Cell Wall Integrity	Krysan,Damian J	8/15/2005			
19	NEI	K08 EY016742	Muller Cell Domains in the Retina	DiLoreto,David A	9/1/2005			
20	NIDDK	K08 DK069346	Basolateral Principal Cell K + Channels	Gray, Daniel A	9/30/2005			
21	NIA	K23 AG020647	Attention and Memory Influences on Navigation in AD	Mapstone, Mark Edward	2/15/2003	yes		
22	NINDS	K23 NS43091	Epidermal Innervation as an Outcome Measure	Herrmann, David N	5/1/2003	yes		
23	NHLBI	K23 HL070930	Cardiovascular Risk 50 Years After Thymic Irradiation	Adams,M Jacob	7/1/2003	yes	yes	yes
24	NIMH	K23 MH64476	Postpartum Depression in a Pediatric Clinic	Chaudron, Linda H	7/1/2003			yes
25	NINDS	K23 NS41952	Epidemiology of Traumatic Brain Injury	Bazarian, Jeffrey J	9/1/2003	yes	yes	yes
26	NIAAA	K23 AA00318	Alcohol Dependence and Suicide	Conner, Kenneth R	9/1/2003		yes	yes
27	NCI	K23 CA102216	Monoclonal Antibody Therapy for Follicular Lymphoma	Friedberg,Jonathan W	9/1/2003			
28	NINDS	K23 NS02184	Mood Fluctuations in Parksinson's Disease	Richard, Irene Hegeman	9/1/2003	yes		
29	NIMH	K23 MH64528	Treating Depressed Women with Sexual Abuse Histories	Talbot, Nancy L	9/1/2003			yes
30	NICHD	K23 HD043881	Long-term Treatment of Polycystic Ovary Syndrome	Hoeger, Kathleen M	12/1/2003	yes	yes	yes
31	NIMH	K23 MH064517	Emergency Linkage to Outpatient Psychiatric Care	Currier, Glenn	12/3/2003			
32	NIA	K23 AG19545	Function, Quality of Life and Nursing Home Use in PACE	Friedman, Susan	2/1/2004	yes		
33	NICHD	K23 HD046541	Attentional Dyxfunction in Children with Phenylketonuria	Arnold, Georgianne	6/7/2004	yes	yes	yes
34	NEI	K23 EY015525	Outcome Measures in Idiopathic Intracranial Hypertension	Friedman, Deborah	8/1/2004		yes	yes
35	NHLBI	K23 HL080068	Neurocognitive Function in Children with Hypertension	Lande, Marc	9/10/2004	yes	yes	yes
36	NHLBI	K23 HL080077	Estrogen and the Pathophysiology and Outcomes of Sepsis	Pietropaoli,Anthony P	4/15/2005	yes	yes	yes
37	NIDCD	K23 DC006229	Bilirubin-induced Auditory Neuropathy in Preterms	Amin,Sanjiv	9/15/2005			
38	NEI	K23 EY016700	Adaptive optics imaging in genetic macular disease	Chung,Millicent M	9/30/2005			yes
39	NIA	K23 AG023552	Perception and Reading in Aging and Alzheimer's Disease	Riggs,Garrett Hughes	9/30/2005			
40	NIAMS	K24 AR48143	Integrative Pathophysiology of Myotonic Dystrophy	Thornton, Charles A	5/1/2003	yes		
41	NINDS	K24 NS42098	Neurology Outcomes Research: Clinical Trials/Training	Holloway, Robert G	9/1/2003			
42	NINDS	K24 NS048323	Cerebrovascular Disease in Sickle Cell Anemia	Lerner, Norma	4/1/2004		yes	yes
43	NIMH	K24 MH71509	Late-Life Depression Outcomes in the Medically Ill	Lyness,Jeffrey M	4/1/2005			

Note: PM438, Practical Skills in Grantwriting, was developed with support from the Rochester Clinical Research Curriculum award (K30).

Table G5C12: Research Training Programs at the University of Rochester

No.	Sponsor	Award Number	Title	PI	Project Period	Trainees pre/post/shrt-trm	Annual Direct Costs
1	NICHD	K12 HD01332-06	Rochester Women's Reproductive Health Career Center*	Woods, J.	7/26/99 - 3/31/10	0/3	359,203
2	NHLBI	K30 RR022680-02	Clinical Research Curriculum	Pearson, T.	6/01/99 - 5/31/10	0/58	277,778
3	NCI	R25 CA089396-05	Radiology Cancer Research Training Curriculum*	Pearson, T.	7/29/01 - 6/30/06	0/6	176,163
5	NCI	R25 CA102618-02	Cancer Control Research Training Curriculum (R25T)*	Morrow, G.	7/1/04 - 6/30/09	0/6	499,672
6	NIMH	R25 MH068564-02	Suicide Research and Prevention MHREG	Caine, E.	7/3/03 - 6/30/08		228,109
7	NIEHS	T32 ES007026-28	Training in Environmental Toxicology	Ballatori, N.	7/1/78 - 6/30/08	15/3	715,188
8	NHLBI	T32 HL07949-05	Cardiovascular Research Training	Berk, B.	7/1/00 – 6/30/06	3/4	301,069
9	NIDA	T32 DA07232-20	Pharmacology of Drug Abuse	Bidlack, J.	9/1/96 - 6/30/06	3/2	227,770
10	NIMH	T32 MH018911-17	NIMH Institutional NRSA*	Caine, E.	9/30/92 - 6/30/08	0/5	273,158
11	NIMH	T32 MH20061-05	Postdoctoral Training in Suicide Prevention Research*	Conwell, Y.	9/17/01 – 7/31/06	0/6	304,664
12	NIAID	T32 AI049815-05	Training for HIV Replication and Pathogensis	Dewhurst, S.	7/1/01 – 6/30/06	4/0	161,584
13	NINDS	T32 NS07489-06	Interdepartmental Neuroscience Training	Federoff, H.	9/30/00 – 6/30/10	6/0	279,964
14	NHLBI	T32 HL66988-05	Multidisciplinary Training in Pulmonary Research	Frampton, M.	9/1/01 – 8/31/06	4/4	404,846
15	NHLBI	T32 HL07152-30	Graduate Training in Hematology Research	Francis, C.	7/1/75 - 6/30/06	0/4	214,054
16	NIMH	T32 MH065181-03	Multidisciplinary Training in Developmental Neuroscience	Freeman, R.	7/1/03 - 6/30/08	2/0	84,007
17	AHCPR	T32 HS00044-15	NRSA Training Grant (Health Services Research)*	Friedman, B	7/1/91 - 6/30/08	5/0	213,860
18	NIAID	T32 AI007464-11	Training in Pediatric Infectious Diseases	Gigliotti, F.	9/1/95 - 8/31/10	0/2	105,435
19	NINDS	T32 NS007338-16	Experimental Therapeutics in Neurological Disease*	Griggs, R.	7/1/90 - 6/30/10	0/4	218,494
20	NIA	T32 AG020493-01A2	Research Training in Geriatrics and Gerontology*	Hall, William	5/1/05 - 4/30/10	0/4	272,949
21	NIAID	T32 AI007362-15	Molecular Pathogenesis of Bacteria and Viruses	Iglewski, B.	9/30/90 - 8/31/06	6/0	243,191
22	NINR	T32 NR007109-05	Interventions with High-Risk Children and Youth	Kitzman, H.	7/1/01 – 4/30/06	4/2	257,702
23	NEI	T32 EY07125-16	Training in Visual Science	Knill, D.	9/30/00 - 9/29/10	6/1	349,882
24	NIAID	T32 AI007285-19	Pre- and Postdoctoral Training Program in Immunology	Lord, E.	9/30/86 - 6/30/07	8/1	379,811
25	NIMH	T32 MH073452-01	Postdoctoral Training in Geriatric Psychiatry Research*	Lyness, J.	8/1/05 - 7/31/10	0/3	183,828
26	NIGMS	T32 GM068411-01A1	Training in Cellular, Biochemical and Molecular Sciences	Maquat, L.	7/1/05 - 6/30/10	2/0	87,814
27	NCI	T32 CA009363-24	Cancer Center Training - Experimental Therapy Models	McCance, D.	7/1/80 – 6/30/07	0/6	281,142
28	NIDR	T32 DE007202-15	Oral Cellular and Molecular Biology and Training Grant	Melvin, J.	8/1/90 – 7/31/07	5/3/10	541,906
29	NIMH	T32 MH19942-09	Research Training in Learning, Development and Biology	Newport, E.	7/1/97 - 6/30/07	4/2	252,378
30	NIGMS	T32 GM007356-30	Medical Scientist Training*	O'Banion, M.K.	11/1/76 - 6/30/09	11/0	500,302
31	NINDS	T32 NS051152-01	Training Grant in Neuroinflammation and Glial Cell Biology	O'Banion, M.K.	7/1/05 - 6/30/10	2/2	171,991
32	NIEHS	T32 ES007271-12	Training in Environmental Health Sciences Biostatistics	Oakes, D.	7/1/92 - 6/30/09	2/1	134,978
33	NHLBI	T32 HL007937-06	Research Training in Preventive Cardiology*	Pearson, T.	8/1/00 – 7/31/10	1/6	390,562
34	NIAMS	T32 AR007472-17	Training Program in Dermatological Research	Pentland, A.	7/1/87 - 4/30/09	2/2	201,558
35	NIDR	T32 DE007165-20	Training Program in Oral Infectious Diseases	Quivey, R.	7/1/85 – 6/30/06	4/4	385,915
36	NIAID	T32 AI007169-23	Training Program in Viral Diseases, Vaccines and Biodefense	Reichman, R.	7/1/79 – 8/31/08	3/5	399,917
37	HRSA	T73 MC00029-11	Interdisciplinary Leadership Education in Neurodevelopmental and Related Disorders	Sulkes, S.	7/1/94 – 6/30/06	1/4	432,556
38	NIDCD	T32 DC00035-12	Research Training in the Language Sciences	Tanenhaus, M.	7/1/99 – 6/30/09	5/3	345,903

* Indicates that trainees in the given program have participated in the Rochester Clinical Research Curriculum, supported by the institution's K30 award.

Table G5D1: Training Experience of Highlighted Mentors, Prior 10 Years

Mentor	Cluster	# of Trainees		# Continuing in Training		# Completed, in Academia	
		Pre-Doc	Post-Doc	Pre-Doc	Post-Doc	Pre-Doc	Post-Doc
Bazarian, Jeffrey	Traumatic Brain Injury		14		3		11
Billings, Ron	Oral Infectious Disease and Clinical Trials		14		4		
Conwell, Yeates	Center for the Study and Prevention of Suicide	1	17		10		4
Dewhurst, Stephen	Antiviral Immune Responses	18	12	8	1	8	8
Fiscella, Kevin	Healthcare Disparities	2	9		3	2	6
Fisher, Richard	Hematologic Malignancies	1	12		1	1	9
Fisher, Susan	Cancer Control and Prevention	17	33	8	16	3	8
Frampton, Mark	Ultrafine Particles and Nanobiology	1	7		2	1	2
Frisina, Robert	Presbycusis	21	8	6	6	12	1
Gerich, John	Metabolic Syndromes		7		2		5
Griggs, Robert	Neurodegenerative Diseases		2				2
Gross, Robert	Mitochondrial Research	2	1			2	
Iglewski, Barbara	Respiratory Infections	5	7	2	2	1	4
Mosmann, Tim	Autoimmunity	8	16	3	8	2	5
Moss, Arthur	Cardiovascular Clinical Trials	8	15		1		
Moxley, Richard	Neuromuscular Diseases		2		1		
O'Keefe, Regis	Bone Biology	12	11	6	2	6	6
Paige, Gary	Sensory Integration and Plasticity	4	2	3		1	2
Pearson, Thomas	Preventive Cardiology		21		11		6
Pentland, Alice	Healthcare Communication/Telemedicine		6				6
Reichman, Richard	Vaccine Development and Testing	2	5			1	1
Rosier, Randy	Arthritis	1	3		1	1	2
Shoulson, Ira	Clinical Trials in Neurology		11		1		8
Szilagyi, Peter	Childhood Asthma Prevention	4	15			2	12
Taubman, Mark	Vascular Biology	5	16	2	2	3	13
Topham, David	Liver Biology and Hepatitis	4	2	4	1		1
Treanor, John	Antiviral Therapy		8		2		1
Wu, Hulin	Biomedical Informatics		10		2		5
Yoon, Geun-Young	Biomedical Optics in Ophthalmology	3	3	3			3
Yu, Yan	Biomedical Imaging	1	6	1			4

Table G5D2: Relevant Research Support for Highlighted Mentors

Grant Title	*Role*	*Sponsor*	*Award #*	*Type of Research*
Mentor: Bazarian, Jeffrey				
Epidemiology of Traumatic Brain Injury	PI	NINDS	K23 NS41952	Bench to Bedside
Mentor: Billings, Ron				
A longitudinal study of lead exposure and dental caries	Co-I	NIH	R01DE013950	Clinical
A collaborative intervention study with the EDC Division of Pediatric Dentistry and the URSMD Pediatrics Department to reduce or eliminate early childhood caries in high risk children	PI	NYSDOH		Clinical
Surveillance of oral health of Monroe County School Children	PI	MCDOH		Clinical
Improving Clinical Outcomes for Early Childhood Caries	Co-I	NIH	R21DE016280	Clinical
Rochester Collaborative to Reduce Oral Health Disparities	PI	NIH	R21DE15004	Clinical
Enhancing Oral Healthcare to Underserved Children	Co-I	HRSA	D30 HP20029	Clinical
Follow-up Study of Early Childhood Caries (ECC)	Co-I	NIH	R03DE12959	Clinical
Mentor: Conwell, Yates				
Postdoctoral Training in Suicide Prevention Research	PI	NIMH	T32MH20061	Training
The Developing Center on Public Health and Population Interventions for the Prevention of Suicide	Co-I	NIMH	P20 MH071897	Clinical
China Collaborative Suicide Research Training Program	Co-I	FIC	D43 TW007273	Training
Geriatric Mental Health Academic Award (GMHAA)	PI	NIMH	K07 MH00748	Clinical
Suicide Prevention: Research and Research Training	PI	NIMH	K24 MH01759	Clinical
Attempted Suicide in Late Life Major Depression	PI	NIMH	R01 MH51201	Clinical
Suicide in Later Life: A Psychological Autopsy Study	PI	NIMH	R01 MH54682	Clinical
UR-NIMH Clinical Research Center for the Psychopathology of the Elderly	Co-I	NIMH	P50 MH40380	Clinical
Robert Wood Johnson Foundation: Depression in Primary Care - Testing a consumer directed care model	PI	RWJF		Clinical
Elder Suicide Prevention in the Aging Services Network	PI	AFSP		Clinical
Senior Health and Research Alliance	PI	NIMH	R24 MH071604	Clinical
Mentor: Dewhurst, Stephen				
Targeted Neuroprotection for HIV-1 Associated Dementia	Co-I	NIH	PO1 MH064570	Bench to Bedside
Mentor: Fiscella, Kevin				
Randomized trial of mifepristone for fibroids	PI	NICHD	R01 HD 042578	Clinical
RCT of Primary Care-based Patient Navigation-Activation	PI	NCI	U01 CA116924	Clinical
The impact of HMOs on disparities	PI	AHRQ	R01 HS10910	Clinical
Do reporting biases mitigate cost estimates	PI	AHRQ	R01 HS0 13173	Clinical
Using Census Data to Monitor Care to Vulnerable Groups	PI	AHRQ	R01 HS 109295	Clinical
Health Habits in Pregnancy	PI	CDC	TS237-12/12	Clinical
Mentor: Fisher, Richard				
Phase II Study of IL-2/LAK in Metastatic Cancer	PI	NCI	NCI-CA 32102-06	Bench to Bedside
Clinical Trials of Activated Leukocytes	PI	NCI	NO1-CM-73704	Clinical
Biology and Treatment of AIDS Lymphomas	PI	NCI	R01-CA 55509-01	Bench to Bedside
Mentor: Fisher, Susan				
A Comprehensive Investigation of Viral-Induced Lymphoma	PI	NCI	RO1 CA121180	Bench to Bedside
School-based Asthma Therapy: Stage 2 Effectiveness Study	Co-I	NHLBI	RO1 HL079954	Bedside to Community
Technology-assisted Smoking in the Dominican Republic	Co-I	FIC	RO1 TW005945	Bedside to Community
Radiology Cancer Research Training Curriculum	Co-I	NCI	R25 CA08936	Clinical
Randomized Control Trial of Mifepristone for Fibroids	Co-I	NICHD	RO1 HD042578	Clinical
Treatment Response Markers in Advanced Laryngeal Cancer	Co-I	NCI	RO1 CA83087	Clinical
Planning Grant for Research to Prevent or Reduce Oral Health Disparities	Co-I	NIDCR	R21 DE15004	Clinical
Predicting Response to Therapy and Early Detection of Recurrent Oral Cancer	Co-I	NCI	RO1 DE13346	Clinical
Defining Antigenic Targets of Autoimmune Sensorineural Hearing Loss	Co-I	NIDCD	RO1 DC03686	Bench to Bedside
Screening behaviors of breast cancer survirors	Co-I	IDPH		Bedside to Community
Chromosome 18 Tumor Suppressor Genes in Oral Cancer	Co-I	NIDR	RO1 DE12477	Bench to Bedside
Screening behaviors after familial breast cancer mortality	PI	NCI	RO3 CA83378	Bedside to Community
Impact study - Preservation of the larynx in the treatment of advanced laryngeal cancer	Co-I	VA	CSP #268	Bedside to Community
Minority social networks as recruitment strategies	Co-I	NCI		Bedside to Community
Human papillomavirus type 16 antibodies and cervical dysplasia: A case-control study	PI	IDPH		Bedside to Community
Laboratory Testing in Pre-eclampsia	Co-I	AHCPR		Clinical
Biology and treatment of AIDS lymphoma	Co-I	NCI	RO1 CA55509	Clinical
Retrospective cohort study of stomach and large bowel cancer after gastric surgery	PI	VA	HSR&D: 88.161	Clinical
Mentor: Frampton, Mark				
Ultrafine particle-induced oxidative stress	PI	NIH	RO1 ES11853	Clinical
Cardiovascular effects of ultrafine particle exposure in humans	PI	NIH	RO1 ES013394	Clinical
Ultrafine particle characterization, health effects and pathophysiological mechanisms	Co-PI	EPA	RD83241501	Clinical
Clinical Studies of Exposure to Ultrafine Particles	Co-PI	EPRI	WO6235	Clinical
Ultrafine Particles and Cardiac Responses: Evaluation in a Cardiac Rehabilitation Center	Co-PI	NYSERDA		Clinical

Table G5D2: Relevant Research Support for Highlighted Mentors (continued)

Grant Title	*Role*	*Sponsor*	*Award #*	*Type of Research*
Mentor: Frisina, Robert				
Aging Auditory System: Presbycusis and Its Neural Bases	Co-I	NIA	P01 AG09524	Basic & Clinical
Center for Navigation and Communication Sciences	Co-I	NIDCD	P30 DC05409	Clinical
Targeted Analysis of Candidate Genes for Age-Related Hearing Loss – Presbycusis	PI	Am. Hearing Res. Fnd.		Clinical
Mentor: Gerich, John				
Alpha and Beta Cell Function in Normal and Diabetic Man	PI	NIDDK	R01 DK020411	Bench to Bedside
General Clinical Research Center	Co-I	NCRR	M01 RR000044	Bench to Bedside & Clinical
Role of the Kidney in Glucose Homeostasis in Normal and Diabetic Humans	PI	NCRR	M01RR000044-37S10	Bench to Bedside
Human kidney in gluconeogenesis and protein metabolism	PI	NCRR	M01RR000044-41066	Bench to Bedside
Mentor: Griggs, Robert				
Controlled Trial of Dichlorphenamide in Periodic Paralysis.	PI	FDA	FR-R-000821	Clinical
Dichlorphenamide vs Acetazolamide for Periodic Paralysis	PI	NINDS	R01 NS045686	Clinical
Mechanism of Corticosteroid Benefit in Duchenne Dystrophy	PI	Muscular Dystrophy Assoc		Clinical
Molecular Characterization of Late-Onset Distal Myopathy	PI	Muscular Dystrophy Assoc		Bench to Bedside
Muscle Protein Synthesis in Neuromuscular Disease	PI	NINDS	R01 NS22099	Clinical
Natural History of Facioscapulohumeral Muscular Dystrophy	PI	NYS/Ed.	M020114	Clinical
Nervous System Channelopathies: Pathogenesis & Treatment	PI	NCRR	U54 RR019482	Clinical
Pathogenesis & Treatment of the Periodic Paralyses	PI	NINDS	R13 NS050966	Clinical
Mentor: Gross, Robert				
Chemotherapy Agents and the Inhibition of Neuronal Birthing in the Brain: The Cause of 'Chemo Brain?'	PI	Army	BC021198	Bench to Bedside
Clinical Experience and Use of Sabril in Patients with Partial Seizures	Site PI	Marion-Merrel Dow		clinical
Pregabalin In-Patient Monotherapy Trial	Site PI	Pfizer		clinical
Keppra in Primary Generalized Epilepsy	Site PI	UCBPharma		clinical
An assessment of Behavioral Changes Associated with Lamotrigine and Levetiracetam in Patients with Epilepsy	Site PI	GSK	N/A	clinical
Mentor: Iglewski, Barbara				
Regulation of Pseudomonas aeruginosa Proteases	PI	NIH	R37 33713-09	Bedside to Community
Differential Gene Expression in Pseudomas aeruginosa	PI	CFF	IGLEWS03FG00	Bedside to Community
Azithromycin Sensitivity of Pseudomonas aeruginosa	PI	CFF	IGLEWS03FG1	Bedside to Community
Mentor: Mosmann, Tim				
Immune Mechanisms of Human Papillomavirus	PI	NIAID	P01 AI048198	Bench to Bedside
Anti-Human Papillomavirus T Cell Effector Responses	PI	NIAID	P01 AI048198-04003	Bench to Bedside
Differentiation and Function, Precursor and Effector T Cells	PI	NIAID	R01 AI048604	Bench to Bedside
Bi-Directional Interactions Between Immunity and Pregnancy	PI	NIAID	R01 AI051869	Bench to Bedside
RSV Specific Response in Viral Elimination and Disease	PI	NICHD	R21 HD043964	Bench to Bedside
Human Immunology Center at the University of Rochester	PI	NIAID	R24 AI054953	Bench to Bedside
Mentor: Moss, Arthur				
Long QT Syndrome: Population	PI	NIH	R01HL33843	Clinical
Long QT Syndrome: Genetic Studies	PI	NIH	R01HL51618	Clinical
Long QT Syndrome: Emotional Triggers of Cardiac Events	PI	NIH	R01HL68764	Clinical
Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy	PI	Guidant		Clinical
THROMBO	PI	NIH	R01HL48259	Clinical
Mentor: Moxley, Richard				
Anabolic Actions of Insulin in Neuromuscular Disease	PI	NIAMS	R01 AR38894	Clinical
Growth Hormone Therapy in Myotonic Dystrophy	PI	Muscular Dystrophy Assoc.		Clinical
Efficacy and Safety of Deflazacort versus Prednisone and Placebo in the Treatment of Duchenne/Becker Muscular Dystrophy	PI	Nordic Merrell-Dow		Clinical
Phenotype-Genotype and Insulin Resistance in Myotonic Dystrophy	PI	Muscular Dystrophy Assoc.		Clinical
Myotonic Dystrophy: Muscle Wasting & Altered Metabolism	PI	NIAMS	R01 AR44069A	Clinical
Mexiletine Treatment of Myotonic Dystrophy	PI	FDA		Clinical
National Registry for Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members	PI	NIAMS	HHSN2640052274C	Clinical
Muscular Dystrophy Cooperative Research Center	PI	NINDS	U54 NS48843	Clinical
Muscular Dystrophy Cooperative Research Center Supplement	PI	Muscular Dystrophy Assoc.		Clinical
Mentor: O'Keefe, Regis				
Proto-oncogene expression and the regulation of chondrocyte metabolism	PI	OREF		Bench to Bedside
Wilmot Cancer Research Fellowship	PI	JP Wilmot Foundation		Bench to Bedside
Identification and characterization of an operant anti-inflammatory mechanism for the control of wear debris osteolysis	PI	OREF		Bench to Bedside
Wear debris osteolysis: New strategies for prevention	PI	NIAMS	R29 AR44220	Bench to Bedside
Autocrine and ionic regulation of chondrocyte phenotype	Co-I	NIAMS	R01 AR40325	Bench to Bedside
Growth factors and epiphyseal chondrocyte maturation	PI	NIAMS	R01 AR38945	Bench to Bedside
Gene therapy for prosthetic loosening	PI	NIAMS	R01 AR46545	Bench to Bedside
Acetabular bone loss following prosthetic hip arthroplasty	Co-I	NIAMS	R01 AR48149	Clinical
Cellular and Molecular Effects of Lead on Chondrogenesis and Cartilage Differentiation	PI	NIEHS	P01 ES11854	Bench to Bedside
Cyclooxygenases and bone repair	PI	NIAMS	R01 AR48681	Bench to Bedside
Prostaglandin Signaling in Wear Debris–Induced Osteolysis	PI	NIAMS	R01 AR46545	Bench to Bedside

Table G5D2: Relevant Research Support for Highlighted Mentors (continued)

Grant Title	*Role*	*Sponsor*	*Award #*	*Type of Research*
Mentor: Paige, Gary				
Sensorimotor Integration in Spatial Orientation	PI	NIA	RO1 AG16319	Clinical
Plasticity in the Vestibuloocular Reflexes and Perception	Co-I	NIDCD	RO1 DC04153	Clinical
Resource for the Study of Neural Models of Behavior	Co-I	NCRR	RO1 RR09283	Clinical
Center for Navigation and Communication Science	PI	NIDCD	P30 DC05409	Clinical
Sensory-Motor/Adaptive Mechanisms in Equilibrium Control	PI	NIA	RO1 AG06442	Clinical
Falls and Hip Fractures in the Elderly	Co-I	NIA	PO1 AG06815	Clinical
Resource for the Study of Neural Models of Behavior	Co-I	NCRR	P41 RR06853	Clinical
Aging of Vestibular and Visual Control of Eye Movement	PI	NIA	P60 AG10463	Clinical
Function and Placticity in Canal-Otolith Interactions	PI	NIDCD	RO1 DC01935	Clinical
Otolith Processing in the Linear VOR and Motion Perception	Co-I	NIDCD	RO3 DC03365	Clinical
Sensori-Motor Integration and Adaptation in Spatial Localization	Co-PI	HFSP	RG-0174/1998-B	Clinical
Function and Plasticity in Canal-Otolith Interactions	PI	NIDCD	RO1 DC01935	Clinical
Influences of Fixation and Gravity on the Linear VOR	PI	NASA	NCA2-618	Clinical
Mentor: Pearson, Thomas A.				
Genesis of Atherosclerotic Lesions .	PI	NHLBI		
Precursors of Premature Disease and Death	PI	NIA		
Cardiovascular Disease in Black and White Physicians	PI	NHLBI		
Rural Lipid Resource Center	PI	NHLBI		
Improving animal Resources at The Mary Imogene Bassett Hospital	PI	NCRR		
The Role of Lp(a) in Coronary Heart Disease in Blacks vs. Whites	PI	NHLBI		
Dietary Effects on Lipoproteins and Thrombogenic Activity	PI	NHLBI		
Development and Evaluation of the Bassett Telemedicine Network	PI	HRSA		
Biosocial Influences on Postpartum Weight Retention.	PI	NICHD		
The Rochester Prevention Research Center	PI	CDC	U48 DP000031	
Cardiovascular Health Intervention Research and Translation Network	PI	CDC	U48 DP000031-02S1	
Mentor: Pentland, Alice				
PGE2 Receptor Function in Skin	PI	NIH	RO1 CA117821	Bench to Bedside
Cyclooxygenase and PGE2 Receptor Function in Skin Cancer	PI	NIH	RO1 AR46828	Bench to Beside
Regulation and Function on CPLA2 in UV Injury	PI	NIH	RO1 AR40574	Bench to Bedside
Center for Future Health	Co-PI	Keck		Bench to Bedside
Mentor: Reichman, Richard				
Adult AIDS clinical trial unit (AACTU)	PI	NIAID	U01 AI027658	Bench to Bedside
Mentor: Rosier, Randy				
Growth plate radiation response: mechanism and therapy	PI	NCI	R01 CA71603	Bedside to Community
Activation of chondrocyte maturation in osteoarthritis	PI	NIA	R01 AR45700-01	Bench to Bedside
Lead toxicity in the skeleton and its role in osteoporosis	PI	NIEHS	P01 ES011854 (sup)	Bedside to Community
Mentor: Shoulson, Ira				
Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP)	PI	NINDS	R01 NS24778	Clinical
DATATOP Extension Protocol (DATE)	PI	Somerset Pharmaceuticals		Clinical
Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism and Changeover (DATX)	PI	NINDS	R01 NS24778	Clinical
Earlier vs. Later Levodopa in Parkinson's Disease (ELLDOPA)	Co-I	NINDS	R01 NS34796	Clinical
Investigation of Tolerability in a Randomized Trial of OPC-14117 in Huntington's Disease (INTRO-HD)	PI	Otsuka America Pharmaceutical Inc		Clinical
Open Label Deprenyl in DATATOP Extension Protocol (MISSED-DATE)	PI	Somerset Pharmaceuticals		Clinical
Deprenyl/Tocopherol Antioxidateive Therapy of Parkinsonism: Preliminary Endpoint Protocol (PEP)	PI	NINDS	R01 NS24778	Clinical
Preliminary Endpoint Protocol Changeover for Deprenyl and Tocopherol Antioxidative Therapy (PEPX)	PI	NINDS	R01 NS24778	Clinical
Prospective Huntington's At Risk Observation Study (PHAROS)	PI	NHGRI	R01 HG02449	Clinical
Mentor: Szilagyi, Peter				
Surveillance for New Vaccines (plus supplementary grants)	PI	CDC	U01 IP000017	Bench to Bedside &
Rochester Center for Adolescent Immunization Research	PI	CDC	U01 IP000040	Clinical
Evaluation of the State Children's Health Insurance Program (SCHIP)	PI	HRSA	U01 HS10450	Clinical
School-based Asthma Therapy- Stage 2 Effectiveness Study	Co-PI	NHLBI	R01 HL079954	Clinical
Healthcare Financing for Children with Special Needs	PI	MCHB	H17 MC00235	Clinical
Mentor: Taubman, Mark				
Growth related genes in vascular smooth muscle	PI	NHLBI	R01 HL043302	Basic
A Novel Form of Tissue Factor and Cardiovascular Disease	PI	NHLBI	R01 HL073364	Basic
Regulation of mRNA stability in vascular smooth muscle	PI	NHLBI	R01 HL077669	Basic
Mentor: Topham, David				
Evaluation of Control Measures Against Diseases Other than AIDS	Co-I	NIAID	NO1 AI25460	Clinical
Rochester Center for Immunity Modeling for Biodefense	Co-I	NIAID	N01 AI050020	Clinical
A Model System for the Study of Human B-cell Tolerance	Co-I	NIAID	RO1 AI49660	Bench to Bedside
Role of cycloxygenase-2 for optimal humoral responses to vaccination	Co-I	NIAID	R21 AI071064	Bench to Bedside
Mentor: Treanor, John				
Evaluation of Control Measures Against Diseases Other than AIDS	PI	NIAID	NO1 AI25460	Clinical
Modeling Immunity for Biodefense	Co-I	NIAID	NO1 AI 500020	Bench to Bedside
Biodefense of Immunocompromised Populations	Co-I	NIAID	NO1 AI 50029	Bedside to Community
General Clinical Research Center	PI	NCRR	M01 RR000044	Clinical & Bench to Bedside

Table G5D2: Relevant Research Support for Highlighted Mentors (continued)

Grant Title	*Role*	*Sponsor*	*Award #*	*Type of Research*
Mentor: Wu, Hulin				
Models and Inferential Tools for HIV-1 Dynamics in Vivo	PI	NIH	R29 AI43220	Bench to Bedside
Modeling Cellular Kinetics in Treated HIV Patients	PI	NIH	RO1 AI45356	Bench to Bedside
Nonparametrical Modeling of Long-Term HIV/Cell Dynamics	PI	NIH	RO1 AI52765	Bench to Bedside
AIDS Clinical Trial Modeling and Simulations	PI	NIH	RO1 AI055290	Bench to Bedside
Center for Biodefense Immune Modeling	PI	NIH	NO1 AI50020	Bench to Bedside
Mentor: Yoon, Geun-Young				
Customized Contact Lenses	PI	NEI	R01 EY014999	Clinical
Effect of corneal wound healing on ocular optics after laser refractive surgery	Co-I	NEI	R01 EY15836	Bench to Bedside
Stereoscopic vision	Co-I	NEI	R01 EY012851	Bench to Bedside
Characterization of Tear Dynamics	Co-I	NEI	R03 EY016420	Clinical
Effect of dynamic movements of customized contact lens on visual performance	PI	NYSTAR		Clinical
Vision improvement with customized contact lenses	PI	NYSTAR		Clinical
Correction of the eye's aberration using phase plate	PI	NYSTAR		Clinical
Further development of wavefront sensing in an awake-behaving cat model for refractive surgical applications	PI	NYSTAR		Clinical
Impact of tear film dynamics on optical quality in dry eye patients	PI	Rochester Eye Bank		Clinical
Improvement of outcome of laser refractive surgery (Vision Alliance Research Funding)	co-PI	Bausch & Lomb		Clinical
Development of wavefront sensing technology (Unristricted Research Funding)	PI	Bausch & Lomb		Clinical
Mentor: Yu, Yan				
Robot-Assisted Platform for Intratumoral Delivery	PI	NIH	R01 CA091763	Bench to Bedside
Orthogonal compound ultrasound for cancer detection and therapies	PI	NIH	R21 A102236	Bench to Bedside
Sono-Contrast Induced Functional Imaging and Spectroscopy	PI	NIH	R33 CA107860	Bench to Bedside

Table G5D3: Research Interests of Highlighted Mentors

Mentor: Bazarian, Jeffrey
Dr. Bazarian's research interests focus on the epidemiology and primary prevention of Mild Traumatic Brain Injury (Concussion), and novel diagnostic mechanisms such as serum markers (S-100B, Cleaved tau) and neuroimaging (CT scan, Diffusion Tensor Imaging). Long term research goals include establishing diffusion tensor imaging as research gold standard for axonal injury after mild traumatic brain injury, and discovering and validating new surrogate serum markers of
Mentor: Billings, Ron
Dr. Billings' work revolves around dental caries epidemiology, especially early childhood caries and oral health disparities, and especially in underrepresented minorities.
Mentor: Conwell, Yates
Dr. Conwell is Co-PI of the NIMH-funded Developing Center for Public Health and Population Interventions for the Prevention of Suicide (PNP-Center), and co-director of the UR Center for the Study and Prevention of Suicide (UR/CSPS). This multi-disciplinary group has three principal objectives: 1) to define risk and protective factors for suicidal behavior in vulnerable populations; 2) to design and test preventive interventions; and 3) to support the education of junior investigators in the rigorous conduct of suicide research. Dr. Conwell's particular focus is on suicidal behaviors in older
Mentor: Dewhurst, Stephen
Dr. Dewhurst's research interests include viral vectors and vaccine development for HIV/AIDS; mechanisms of neuronal apoptosis in HIV/AIDS; and salivary gland gene therapy studies.
Mentor: Fiscella, Kevin
Dr Fiscella's research has focused on addressing racial and ethnic disparities in health and health care. He has directed a number of large research projects that involve translational research. Examples include examining the use of HEDIS measures to monitor care to minority populations, using Patient Navigators to address disparities in cancer-related care, and evaluation of mifepristone for symptomatic fibroids.
Mentor: Fisher, Richard
Dr. Fisher is well known as an expert in biological research and the treatment of lymphoma. He has led national and international studies on Hodgkin's Disease and Non-Hodgkin's lymphoma.
Mentor: Fisher, Susan
Dr. Susan Fisher's major area of independent research has been in the field of oncology with a particular interest in virally-induced malignancies. She has conducted large epidemiologic investigations of gastric, cervical and breast cancer and post-transplant lymphomas. She has published multiple papers on the role of SV40 in cancer, and her current research interests focus on SV40 as an etiologic factor in lymphoma; HPV and sunlight as cofactors in skin cancer; and molecular indicators of prostate cancer risk.
Mentor: Frampton, Mark
Dr. Frampton's research focuses on the human health effects of exposure to gaseous and particulate air pollution. His laboratory is examining the mechanisms for effects of particle exposure on vascular endothelial function, and cardiovascular function, in both healthy and susceptible subjects.
Mentor: Frisina, Robert
Dr. Frisina's research program focuses on important areas of enquiry regarding presbycusis. His group has made noteworthy advances in the neuroscientific understanding of the etiologies of presbycusis. They are now pursuing a set of synergistically-related human and animal experiments attacking issues regarding functional aspects of the neural and molecular bases underlying age-related auditory declines.
Mentor: Gerich, John
Dr. Gerich's current NIH-supported research deals with glucose counterregulatory mechanisms, the roles of beta cell dysfunction and insulin resistance in the pathogenesis of type 2 diabetes, and the regulation of glucose metabolism. The research employs isotopic techniques to measure glucose production, gluconeogenesis, glycolysis, glucose oxidation, limb-organ balance measurements, indirect calorimetry, and glucose clamp experiments.
Mentor: Griggs, Robert
Dr. Griggs' research interests revolve around the pathogenesis and treatment of nervous system channelopathies, especially rare diseases such as Anderson Tawil syndrome, the nondystrophic myotonias caused by sodium and chloride channels mutations, and the episodic ataxias EA1 and EA2.
Mentor: Gross, Robert
Dr. Gross participates in epilepsy treatment trials, both industry- and investigator-initiated. These encompass the assessment for safety and efficacy novel potential anti-seizure drugs; the assessment of adverse effects or interactions of anti-seizure drugs; and novel contexts for the use of anti-seizure drugs. Other studies involve the effect of chemotherapy agents on neuronal birthing in the brain; this effect, to reduce the rate of neuronal birthing, may allow the development of an animal model of the cognitive disorder seen in humans undergoing chemotherapy, known as 'chemo brain.'
Mentor: Iglewski, Barbara
Research in the Iglewski laboratory focuses on the pathogenesis of the opportunistic pathogen Pseudomonas aeruginosa. Using both genetic and molecular techniques, the lab identifies genes which regulate the production of virulence factors and those that control biofilm development and antibiotic resistance. Whole genome profiling is done with both Affymetrix as well as glass slide microarrays. In vitro studies are complemented with in vivo experiments. Specifically the lab determines if a given bacterial gene or genes are expressed in the lungs of patients with cystic fibrosis who are colonized with P. aeruginosa. Gene expression in vivo is correlated with the phenotype and genotype of the bacteria isolated from the patients lungs and with clinical status and antibiotic therapy.
Mentor: Mosmann, Tim
Dr. Mosmann's research involves immune system regulation by T cell subsets and their cytokines, particularly the Th1 and Th2 subsets of CD4+ T cells and naïve, uncommitted CD4 T cells. His lab has developed two new assays - a multicolor Elispot assay to detect the simultaneous expression of two or more cytokines by individual human or mouse T cells; and a cytotoxicity assay that can detect individual cytotoxic cells.

Table G5D3: Research Interests of Highlighted Mentors (continued)

Mentor: Moss, Arthur

Dr. Moss' research is related to the geneotype-phenotype aspects of the inherited Long QT Syndrome (LQTS). Research into this disorder began 25 years ago with the establishment of the NIH-supported International Long QT Syndrome Registry. Major translational findings from this ongoing research include a fundamental understanding of the contribution of specific ion channels to myocyte action potential and cardiac electrophysiology, appreciation that the clinical electrocardiographic pattern in LQTS is related to distinctive mutations in ion-channel potassium and sodium genes, understanding that triggering of cardiac events in this disorder is uniquely related to specific mutant genotypes, documentation that effective pharmacologic and device-related therapy is influenced by the underlying genetic ion-channel mutation, and more recently, that the risk for fatal cardiac events in subjects with LQTS is related to the magnitude of biophysical functional disorder (reduced ion-channel current) as measured by in vitro cellular expression

Mentor: Moxley, Richard

Dr. Moxley's research interests include the pathomechanism and treatment of myotonic muscular dystrophy types 1 & 2 and Duchenne muscular dystrophy, development of reliable measures to assess burden of disease in patients and family members affected by myotonic dystrophy, Duchenne muscular dystrophy, and facioscapulohumeral muscular dystrophy, development of better end-point measures to assess myotonia, muscle weakness, brain symptoms, endocrine function, sleep disturbance, respiratory and cardiac function in myotonic dystrophy, establishing reliable and validated patient reported outcome measures for pain, fatigue, and functional limitations in myotonic dystrophy and facioscapulohumeral muscular dystrophy, and establishing standards of care for patients with myotonic dystrophy and Duchenne muscular

Mentor: O'Keefe, Regis

Dr. O'Keefe's research interests include the role of cyclooxygenase in cartilage and bone repair, and the molecular basis of osteolysis.

Mentor: Paige, Gary

The overall goal of Dr. Paige's research is to understand how the brain integrates sensory input from the outside world (vision and audition) with the internal senses (vestibular and somatosensory) to achieve accurate spatial perceptions, and how they coordinate behaviors (eye, head and postural movements) that allow us to orient towards and interact with external objexts as well as navigate through our complex and cluttered environment. An equally important aspect is how plastic neural mechanisms are utilized to register errors and in turn adaptively adjust performance in order to maintain proper spatial calibration across sensory modalities and the behaviors they influence. Finally, an important concern is the neural degeneration that accompanies natural aging as well as pathology, and the functional ramifications within sensory, cognitive, and motor systems underlying spatial orientation.

Mentor: Pearson, Thomas A.

Dr. Pearson's research interests are in clinical atherosclerosis research studies of the epidemiology and prevention of atherosclerotic cardiovascular disease. He directed an experimental pathology laboratory until 1991, developing an animal model of atherosclerosis. He has been involved with a number of studies of disease mechanisms, including Principal Investigator of NHLBI-funded studies of the role of lipoprotein(a) in coronary disease in Blacks vs. Whites (The Harlem-Bassett Study). Dr. Pearson has performed a number of epidemiologic studies. He directed the Johns Hopkins Precursors Study, a long term, NHLBI/NCI/NIA funded prospective study of medical students dating back to 1947; and was Principal Investigator of the Meharry-Hopkins Study which followed a cohort of African American physicians in parallel to the Precursors Cohort. He has been the principal and collaborating investigator of a number of single and multicenter clinical trials, especially with dietary factors such as coffee, chocolate, and fatty acids, and those testing cholesterol-

Mentor: Pentland, Alice

Research in the Pentland Lab addresses the role of cyclooxygenases and prostaglandin receptors in epidermal function and carcinogenesis. The role of these lipid mediators in the induction of squamous cell carcinoma of the skin is being studied in the context of ultraviolet light injury.

Mentor: Reichman, Richard

Dr. Reichman's research interests focus on human papillomavirus and human immunodeficiency virus infections. He has conducted studies of HPV infections utilizing recombinant DNA produced virus-like particles (VLPs), animal models, and patients enrolled in clinical trials to investigate pathogenesis, efficacy of antiviral drugs, and human immune responses to HPV. Recently initiated studies focus on the interactions between AIDS and HPV infection by carefully following cervical disease in women with coincident human immunodeficiency virus (HIV) infection. Also, ongoing studies examine mechanisms of HIV resistance to antiretroviral drugs using HIV isolates obtained from patients. Techniques utilized include tissue culture and nucleic acid sequencing.

Mentor: Rosier, Randy

Dr. Rosier's research program involves investigation of the regulation of endochondral ossification, the formation of bone through mineralization of cartilage. This process is essential to bone formation and development in children, and is a fundamental element of fracture healing. Cartilage mineralization also occurs pathologically in degenerative arthritis and in heterotopic bone formation after surgery or trauma ma. Endochondral ossification is under control of systemic hormones such as parathyroid hormone, vitamin D, and growth hormone, as well as regulatory molecules synthesized by chondrocytes which have autocrine or paracrine effects. The complex interactions of these growth factors regulate the orderly sequence of biochemical events associated with chondrocyte proliferation, hypertrophy, and matrix mineralization.

Mentor: Shoulson, Ira

Dr. Shoulson's research has focused on the experimental therapeutics of neurodegenerative disorders, including Parkinson's disease and Huntington's disease. His investigative approach has been more integrative than reductionist, requiring multi- and inter- disciplinary collaborations, the creation of innovative academic milieus for cooperative research, and importantly the creation of new knowledge applicable to the human good and clinical practice. This integrative approach has been reflected in Dr. Shoulson's creation of the Parkinson Study Group and Huntington Study Group, independent multi-center academic research consortia in North America, as well as the American Society for Experimental Neurotherapeutics (ASENT), a non-profit organization devoted to forging collaborative research between

Table G5D3: Research Interests of Highlighted Mentors (continued)

Mentor: Szilagyi, Peter

Dr. Szilagyi is a health services researcher with nearly 20 years of experience in studying methods to improve the organization, financing and delivery of healthcare to vulnerable children and their families. He has conducted research on improving immunization delivery, studying new vaccines, studying the delivery of health insurance for uninsured children, and investigating asthma care.

Mentor: Taubman, Mark

Dr. Taubman's laboratory is focused on the role of vascular smooth muscle cells (SMC) in regulating inflammation and thrombosis in the arterial wall. There are three major areas of investigation: 1) the regulation of tissue factor expression in SMC culture and the regulation of tissue factor expression and activity in the injured vessel wall and in animal models of atherosclerosis; 2) examination of MCP-1 regulation in cell culture and in animal models of arterial disease; and 3) studies to elucidate the function of the EGLN3/SM20 gene using muscle cell cultures and an EGLN3 knockout mouse.

Mentor: Topham, David

Dr. Topham has over 10 years of experience in viral immunology and numerous publications on the CD4 and CD8 T cell responses to influenza and parainfluenza virus infections. The lab is NIH funded to investigate the CD8 T cell immune response and memory to influenza infection in mice, and human immune responses to experimental vaccines. Completed and ongoing studies include a study human response to vaccinia (smallpox vaccine), experimental vaccines for malaria (AMA-1), and H5 influenza. Dr. Topham is also a member of the University of Rochester Center for Immune Modeling for Biodefense (URCIMB), an NIH-funded contract to develop mathematical models of the immune responses to influenza virus infection in animal models and humans. The Topham lab has systems and techniques in place to study CD4 and CD8 T cell responses to influenza both quantitatively and qualitatively in both mouse and human systems. As such the Topham lab forms a robust interface between the development and testing of experimental vaccines and

Mentor: Treanor, John

Dr. Treanor's research interests are focused primarily on clinical trials of novel vaccines and other control measures for human infectious diseases, such as antiviral agents and passively administered antibody. Most of the work of our group is directed toward evaluation of novel vaccine approaches for potential pandemic influenza viruses, we also perform studies of novel approaches to conventional influenza vaccines and antivirals, particularly neuraminidase inhibitors. The Vaccine and Treatment Evaluation Unit also performs clinical studies of vaccines for smallpox, anthrax, malaria, genital herpes, papillomavirus, and pertussis, and pneumococcal disease, working in collaboration with investigators in pediatrics, microbiology and immunology, and the Center for Vaccine Biology.

Mentor: Wu, Hulin

Dr. Wu's research interests include clinical trial modeling and simulations, modeling HIV RNA/cellular dynamics, modeling AIDS epidemics, AIDS clinical trials, modeling immunity to viral infection, pharmacokinetics and pharmacodynamics(PK/PD) studies, biomedical informatics, longitudinal data analysis, nonparametric regression methods and mixed-effects models. His research areas reflect the biometric/quantitative methods in translational and

Mentor: Yoon, Geun-Young

It has long been known that the human eye suffers from the optical defect called the wavefront aberration. The aberrations that are not corrected by conventional ophthalmic lenses are especially severe in patients with keratoconus (abnormal cone shape cornea), corneal transplant or central visual field loss. Accurate measurement and correction of the aberration could result in substantial improvements in vision. In Dr. Yoon's laboratory, advanced diagnostic and therapeutic methods using various optical technologies have been developed and applied to better understand patients' problems and to improve their visual performance. The lab's innovative and translational research efforts to achieve these goals include development of a robust wavefront sensor which measures the large amounts of the ocular aberration, customized ophthalmic lenses to correct the aberration, biomechanical and optical response of the cornea to laser refractive surgery, optical measurement of tear dynamics to investigate dry eye symptoms, development of an intraocular imaging system for presbyopic correction, vision improvement in eyes with age-related macular degeneration.

Mentor: Yu, Yan

Dr. Yu's specialty is medical and atomic physics, and the effectiveness of new treatment-delivery systems such as prostate brachytherapy. Yu's current research focuses on developing a robotic platform to treat localized cancers and better ultrasound and imaging techniques for detection and verification of cancer.

Table G5E1. Biomedical Informatics Resources - Systems

Location	Systems	Service/Function
Clinical Trials Coordinating Center	• eRT clinical trial system • clinical trial database	• clinical trial data management • case report form management • clinical trial reporting • user training
Dept. of Comm. & Prev. Medicine	• health service research database	• health service research data management • reporting
Division of Biomedical Modeling and Informatics	• MATLAB • SAS • S-PLUS • immunology research database • Protégé-2000 knowledge acquisition tool • Guideline Interchange Format process model • Guideline Execution Engine • GESDOR ontology mapping tool (Guideline Exec. by Semantic Decomp. of Representation)	• mathematical/statistical modeling • computer simulation • immunology research data management • biomedical knowledge modeling/management • clinical decision support
Division of Medical Informatics	• AllScripts TouchWorks electronic medical record • Clinical Data Repository/Clinical Data Warehouse • patient sign out system • surgical forms tracking system • results notifier system • medical imaging database • web-based patient profile system • faculty database	• clinical information service • clinical data management o medication o laboratory o problem o allergy o immunization • administrative data management
General Clinical Research Center	• general clinical research database • clinical trial protocol system • online GCRC application system	• general clinical research data management • case report form management • protocol-specific software training • reporting
Heart Research Follow-up Program	• cardiovascular research database • cardiovascular clinical trial system	• cardiovascular research data management • cardiovascular clinical trial facilitation
Miner Library	• literature databases • e-journals • e-books • clinical evidence databases • drug information databases • online biomedical reference information systems	• online information resources • website management
Office for Human Subject Protection	• online IRB application and database system	• research administration and regulation
U. Rochester	• multi-node clustered computing system	• parallel processing computing service

Table G5E2. Biomedical Informatics Resources - Standards

Categories	Standards	Service/Function
controlled medical terminologies	• Systematized Nomenclature of Medicine – Clinical Terms • ICD-9-Clinical Modification • Current Procedural Terminology, 4th Revision	• clinical data encoding • administrative data encoding
clinical data interchange	• Health Level Seven 2.5	• clinical data exchange
clinical data reference information model	• Health Level Seven Reference Information Model	• clinical data reference information
clinical document model	• Health Level Seven Clinical Document Architecture	• clinical document model
biomedical process model (proposed)	• Guideline Interchange Format	• biomedical process representation o practice guideline o clinical trial o critical pathways