



Welcome to the Member Retreat & Advisory Board Meeting July 11, 2016

Overview

Steve Dewhurst, PhD
CFAR PI

Overview

Progress report

- Evaluation Presentation
- Faculty Highlights

Scientific Working Groups

- Current SWG's
- Future SWG's

Cores

- Current Cores
- Other Activities Supported by Cores

Future Plans

- Future Directions
- Survey Results

CFAR Evaluation

Ann Dozier, PhD

July 2016

Process

Semi-structured interviews

Interviewees based on list provided (N=26)

- Executive Committee Members
- Recipients (current/recent) of pilot/micro grant funding
- Interviewed: Executive Committee: 9
Investigators: 5

Interview: Role in/with CFAR
What is working well
What could be improved
New areas to consider

Overall Comments

“very helpful to have this system around you”

- “Fantastic”
- “Tremendous resource”
- “The structure itself brings people together but it is more than the structure it is the people”
- Viewed as responsive/nimble
- “Generally all are interested in helping each other and helping bring up the next generation of investigators and getting more people into HIV research”
- Positive response to suggestions and ideas even if they a bit “crazy”
- balance low and high risk projects
- “Intellectually generous”
- Raised institutional identity – useful internally and externally

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Funding Programs

“ I never thought I would be doing research in HIV”

- Made a key difference in writing preliminary data for submission of proposals to external funders
 - for some coupled this with funding from other sources (e.g. department)
 - pilots described as a ‘jumpstart’ ;
 - microgrants viewed positively
 - Also an example of how something that was being done at another site was adapted here;
- Review processes well run; it is fair and based on merit
- Recipients subsequently submitted applications for external funding based on results generated by pilot
 - Do not have as many applications as would like to have
 - Outreach required (“cold calls”)

Funding Programs

“personal mentoring is the glue that will hold things together”

- Mentorship component required in the pilot proposal
 - Meetings with mentors have been more on individual basis vs. As a mentor team
 - Mentors viewed as available, providing high quality mentorship and prompt response to requests
 - Integration of CFAR mentor with existing mentor teams - challenging
- Facilitated contact with mentors for those in early careers and who are new to the field;
 - “provides an opportunity to ask questions that you might not want to ask of your senior mentor”

Junior Faculty Mentoring

“... not just me alone in my department...”

- New initiative
 - engage with junior investigators
 - consistently viewed as a positive development
 - described as “very translational”
- “so now I have a group of people, not just me alone in my department; at a similar stage, we are from all different areas of HIV”
- Need assistance with publications including what journals to submit to, how to prioritize;
 - a publication syndicate was suggested as one mechanism to review each other’s papers
- Also noted, mentoring mechanism with people from all the cores that meets every couple of months it is about specific individuals and how best to do mentoring in CFAR
 - there may be inconsistency across the mentors which may be a reflection of how mentoring is viewed at the institutional level

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Grant Review Service

“knowledgeable people who can say no, no, no, you are thinking about that totally wrong”

- Process has improved
 - getting better feedback
 - those involved with the review
 - seem more involved
 - putting more effort into providing feedback
 - however..... not well utilized

SWGs

“bringing different disciplines together
results in better science”

- “Working across disciplines makes it harder to collaborate because they use different tools, techniques, different way of thinking”
- SWGs sunsetted after five years need to find new focal areas that have critical mass of investigators and scientific rigor
 - HIV Trauma
 - Cure
 - Photonics
 - RNA
 - Niche populations
 - mHealth
 - Mental health
 - With sunsetting “momentum that we have built up, gets lost”
- We are a smaller research university; “that kind of makes it difficult to lump everyone under a sufficient nexus to build a substantial brand”

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Cores

“Junior investigators are more receptive than senior investigators”

- Role of the core leadership in active outreach seen as critical
 - “Need to look to other approaches rather than emails to get the information out about our services”
 - Outreach to departments is seen as key
- Access to clinical/patient populations through the CTU viewed as valuable especially to those who had not done this before
- Discounts provided for CFAR users
- Provide access to needed instrumentation
- Cores involvement with proposals under development for extramural funding seemed variable or inconsistent

Cores

- May be mismatch of demand and funded effort
 - Problem when demand for services is low and/or when funded individual is not significantly invested
 - “....so do not contribute significantly to the science or think about the science and might not be involved early in the project”
- Question raised as to how much do the leaders feel like they own their cores
 - How much time do they have or are they willing to invest
 - Some cores have a clear identify
 - Cores need to be investigator driven
 - Are they adequately innovative
- Variable views on how much the cores know how to use or refer to each other

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Investigator Issues

“people need to better understand how their research could be applied to HIV AIDS”

- Use of existing investigators
 - Are some maxed out
 - people are tied up with their own work
 - “we have a good set of core investigators, but we can only do so much”
- Lack of a pipeline of young investigators and clinical investigators
 - have we tapped out those already in the institution who might to do HIV related work
 - “people need to better understand how their research could be applied to HIV AIDS; who how the tools/ techniques they use could be used in HIV - Has been done sporadically but could be continuous”

Investigator Issues

“junior investigators given money to look at HIV, tipped the scales to have them look at HIV”

- Resources are geared for junior investigators
 - “more senior investigators don’t necessarily need them”
 - “CFAR has an obligation to support pilots and junior investigators but not necessarily to support senior investigators unless they have funding or have the blessing of the CFAR leadership”
- Needs of more established investigators may be different
 - “don’t need to go after every pilot; how to prioritize what to go after”

Research Collaborations

CTSI sponsored survey (Summer 2015)

- 26 CFAR investigators responded
 - 277 collaborations
 - 83 within CFAR
 - representing 49 different investigators
- 79 investigators named CFAR investigators as collaborators
 - representing 180 collaborations with 54 CFAR investigators
 - representing 23 different departments

Areas to consider

- Mental health and HIV viewed as another opportunity; function of lack of people
- Working in some of the HIV areas is referred to as “niche” - studying particular methods or organs that could be studied in the context of HIV;
 - “It is happening but it’s not organized under any structural entity and some examples were vascular, bone, kidney, microbiome”
- What are the other opportunities to take advantage of the ACTG-CFAR relationship
- Collaborations with Buffalo may be under-tapped resource

Areas to consider

- Is there a potential missed opportunity related to mhealth and social science related research
 - “Have enough of a core to bring things to scale; cannot contribute to each other’s work as they are tied up in their own”
- Comment regarding collaborations with the data science institute and need for greater infrastructure
 - opportunities to bring in masters and PhD level students
- Molecular level work was also mentioned that there is only one person doing HIV related and is tapped out

Questions/Issues

- Role for CFAR with non-Junior faculty
- Additional strategies to use to increase applications for pilot funding
- More effective engagement with investigators developing extramural funding proposals (Core consultation; grant review)
- What innovations are needed in the Cores?
- Can we further mine the existing collaborators?
- Question was raised about chasing the funding that pays the bills vs. what may be motivating to the scientist
 - meaningful or substantial science may not align with what is needed to get funding (or re-funded)
- UR is small research university
 - With changing landscape of HIV funding, how does this impact recruitment of new HIV investigators

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Highlighted Faculty

Steve Dewhurst, PhD

Juilee Thakar, PhD

Assistant Professor
Microbiology & Immunology
Biostatistics and Computational Biology

Juilee Thakar, PhD

Background: PhD in Bioinformatics at U Wurzburg (2006); Post-doc in Systems Immunology at Penn State (2010-'13); Research scientist at Yale (2010-2013); joined UR faculty in Nov 2013

Research focus: study of complex systems relevant to infectious disease dynamics and molecular pathogenesis

History/Timeline of CFAR Services utilized

- Became CFAR member in November 2015 and attended CFAR meeting in November 2015.
- Mentoring from Drs. M Keefer, Steve Dewhurst, Sanjay Maggirwar and Giovanni Schifitto have facilitated new collaborations and development of projects in the fields of HIV research
- Dr. Maggirwar has provided critics on grants
- CFAR Junior faculty mentoring group has facilitated collaborations and career development
- CFAR funding to attend CFAR annual meeting in Seattle
- CFAR pilot funding to investigate gene regulatory networks associated with atherosclerosis in people living with HIV

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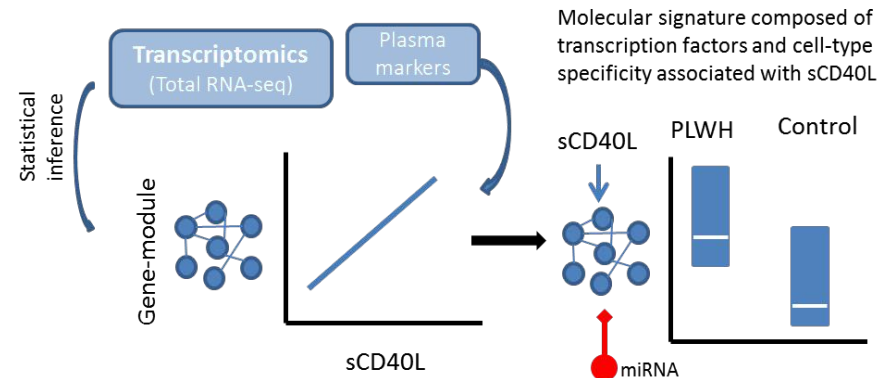
Impact: CFAR support has been instrumental in developing new collaborations in the field of HIV research

- HVTN Initiatives Program (HIP) award, June 2016: “Assessing impact of vaccine regimen on vaccine-induced antibody durability” (\$74k); collaboration with Kelly Seaton, PhD at Duke Vaccine Center
- CFAR facilitated HVTN collaboration with Erica Andersen-Nissen, Lamar Fleming and Julie McElarth to investigate transcriptional changes in PBMCs upon HIV vaccination on pre-vaccination day and days 1, 3 and 7
- CFAR facilitated interactions with Drs. Sanjay Maggirwar and Giovanni Schifitto has led to investigation of atherosclerosis in people living with HIV, (one manuscript in preparation and CFAR pilot 2016)
- CFAR facilitated interactions with Dr. Ronald Swanstrom to initiate cross-CFAR data integration and analysis has led to initial discussions to plan a cross-CFAR workshop.
- Data analysis for CFAR-CTU investigators (James Kobie and Krupa Shah) as a member of core E

Current projects/funding

CFAR funded (awarded June 2016) project:

“Serology-based systems modeling to improve treatment for atherosclerosis in people living with HIV” (\$50k).

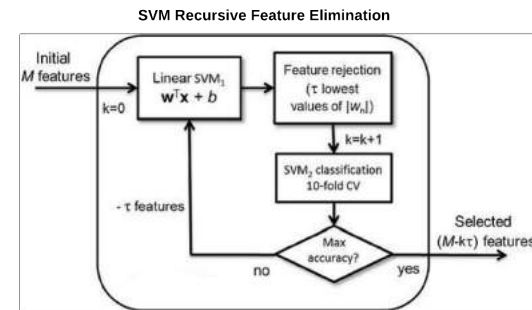


Data analysis as a part of core E

In collaboration with James Kobie we identified 10 features out of features that can classify IDUs from healthy subjects

Future projects/funding

- Organize a workshop for training CFAR member in omics analysis and cross-CFAR data integration
- Continued investigation of a) atherosclerosis in people living with HIV and b) HIV vaccine research
- Continued mentoring from M Keefer, Steve Dewhurst, Sanjay Maggirwar and Giovanni Schifitto



Jian Zhu, PhD

Assistant Professor
Microbiology & Immunology

Background

Host machineries regulating HIV transcription and latency

Host target based development of anti-HIV "cure" reagents

Ultrasensitive approaches to determine HIV viral reservoirs and loads

CFAR Services

Mentoring (grant reviewing)

Networking (internal and external)

Human sample access (blood, lymph node)

Impact

Funding competition

Peer reviewing (journals and study sections)

Current projects/funding

R21 (Zhu) "Cooperation of BRD4 and Tat Associated Proteins in HIV"

R01 (Zhu) "Investigation of Latency Promoting Genes (LPGs) in HIV Oral Reservoir Cells"

R01 (Zhu) "Role of FACT Proteins in Regulating HIV Transcription and Latency"

R01 (Kielkopf) "Structural Control of Human Co-factors for Retroviral Gene Expression"

Future projects/funding

HIV persistence in the context of drug abuse (Phipps, Kobie, Thakar)

Detection of HIV reservoir cells and viral RNAs (Berger, Miller)

Other information

Meeting with other junior investigators (Kobie, Senn, Elliott)

Encouraging the use of new technologies (Maggirwar, Kobie)

LaRon E. Nelson, PhD, RN, FNP

Assistant Professor &
Dean's Endowed Fellow in Health Disparities
School of Nursing

Background

- **Practice:** public health nurse and local public health leadership
- **Research Interests:** health and social disparities, care coordination, PrEP implementation science, mHealth, symptom management

History/Timeline of CFAR Service Use

2014 – present	Associate Director of International Research
2014 – present	Mentoring: Keefer - HVTN; McMahon: PrEP research
2015 – present	Pilot study of smartphone based intervention

Impact: Mentoring and Networking Impact

Gretchen Birbeck – HIV/AIDS research in sub-Saharan Africa

Giovanni Schiffito – Stigma, stress and neurology

Brent Johnson – Statistical modeling of HIV testing for MSM

Current projects/funding

1. R21 - Exploring Stigmas and Delays in HIV Diagnosis, Linkage, and Retention in Care for MSM 
2. URM C Pilot - Feasibility of Mobile App for HIV symptom monitoring, clinical follow-up and peer support for HIV positive MSM 
3. HVTN 704/HPTN 085 – AMP Study 
4. OHTN Research Chair in HIV Program Science with African, Caribbean and Black Communities 

Future projects/funding

- R01 – Implementation of multi-level intervention to facilitate ARV use for PrEP and HIV treatment among MSM 

Gretchen L. Birbeck, MD MPH DTMH

Rykenboer Professor of Neurology

Center for Human Experimental Therapeutics
Public Health Sciences

Background

- Clinician--primary training in adult Neurology
 - Post docs: Health Services Research, Epidemiology, Pediatric Epilepsy, Tropical Medicine
- Clinical research focusses on common neurologic conditions in resource-limited tropical settings (sub-Saharan Africa)

History/Timeline of CFAR Services utilized (arrived July 2013)

- Microgrants x 2—to facilitate analysis of cerebral malaria imaging data and get samples to US for deep sequencing
- Collaborations with Peds Neuro-HIV expertise
- Opportunities for expanding capacity in qualitative research

Impact (of these CFAR Services on career) Examples might include things like mentoring, networking, grant reviews, assistance with grant applications, providing funds to obtain data used to submit NIH grant applications, connections to faculty you are now collaborating with and any current CFAR funding

- CHASE R01 (Cohort of HIV-Associated Seizures and Epilepsy) Study
- Recruit of child neurologist who will be central to the long-term success of above project—also extends my collaborations into Bostwana
- Nascent research program developing on differential effects of cerebral malaria in children with HIV
- Collaborating with Zambian Social Scientists on qualitative study of the “Tap Gap”—to Fogarty/NINDS in Jan ‘17

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Current Scientific Working Groups

Steve Dewhurst, PhD

Scientific Working Groups

Current Scientific Working Groups

- CNS Reservoirs of Infection and Aging
- HIV RNA Biology



CNS Reservoirs of Infection and Aging Scientific Working Group

Harris A Gelbard, MD, PhD - Director
Giovanni Schifitto, MD - Associate Director

Outline

- Aims of the CNS Reservoirs and Aging SWG
- Working Group Members
- Progress on Aims

Neuro SWG Aims

- **Aim 1:** to bring together and support investigators from diverse backgrounds including physics, optics & chemistry plus neurologists and gerontologists... with the goal of developing new indices that measure the impact of HAND on the CNS during activities of daily living (ADLs).
- **Aim 2:** to further support investigators from these disciplines to understand pathogenetic mechanisms of HIV-1 and drugs of abuse that affect neurovascular function and communication with microglia and synaptic elements....with the goal of translating findings from Aim 1 to preclinical models of HAND neuropathogenesis.

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Neuro SWG Aims

- **Aim 3:** to support a drug development program for a new chemical entity that effectively inhibits a key neuropathogenetic enzyme, mixed lineage kinase type 3 (MLK3), and has a favorable CNS profile...with the goal of achieving investigational new drug (IND) status & initiating a Phase 1 trial.
- **Aim 4:** Provide mentoring for investigators with preclinical and clinical interests focused on HAND and adjunctive therapeutics.

SWG Members

Handy Gelbard, Center for Neural Dev. & Disease

Giovanni Schifitto, Neurology

Steve Dewhurst, Microbiology & Immunology

Michael Elliott, Center for Vaccine Biology & Immunology

Todd Kraus[†], Chemistry

Brad Nilsson[†], Chemistry (*new 2014/2015*)

Sanjay Maggirwar, Microbiology & Immunology

Qing Ma, University of Buffalo

Krupa Shah, Medicine (Geriatrics)

Vankee Lin, Nursing (Neuroscience)

Gretchen Birbeck, Neurology (*new 2014/2015*)

Michael Potchen, Imaging Sciences (*new 2014/2015*)

David Bearden, Child Neurology (*new 2016*)

Aim 1

- New collaboration with Vankee Lin, a neuroscientist in the school of Nursing. Developing cognitive training interventions to improve clinical outcomes in HIV infected individuals with cognitive impairment.
- Collaboration with Drs. John Joska, Eric Decloedt from the University of Cape Town. Planning concept proposal to NIMH for a clinical trial of NNRTI based vs. PI based trial to assess impact on CNS injury via Neuroimaging and CSF biomarkers in individuals with HIV-associate cognitive impairment.

Aim 2

- Collaboration with Todd Krauss and Gelbard labs to develop super-resolution imaging methods (fPALM/STORM) using synthesized quantum dots for synaptic anprotein changes in HAND (TURA funded, R21/RO1 planned)
- Comparison of genetic methods for switchable XFP expression vs. quantum dot technology for nanoscale imaging of subcellular organelles; 1st manuscript by fall 2016

Aim 3

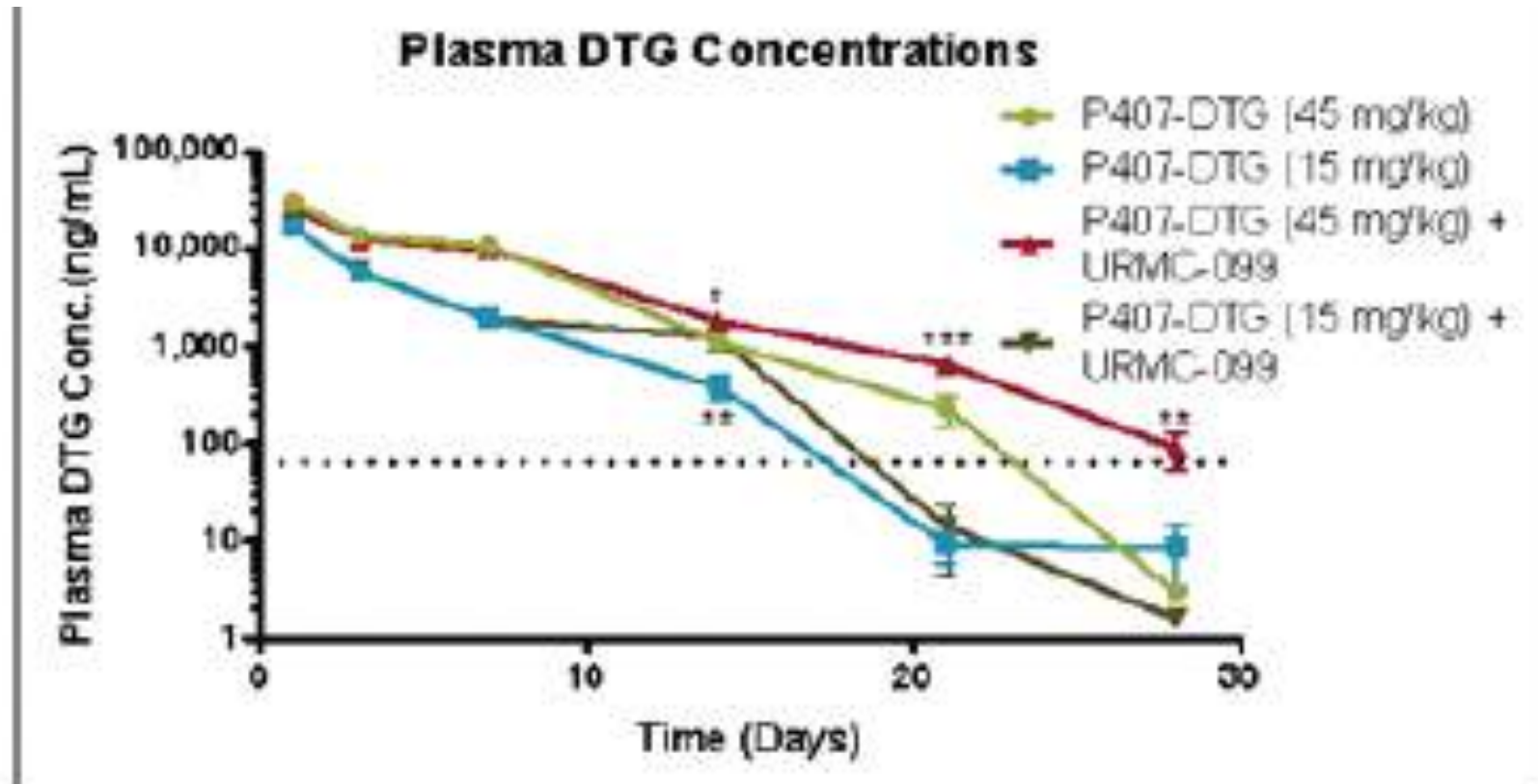
URMC-099 as: (1) novel therapeutic for HAND; (2) adjuvant for nanoformulated cART (eradication):

- Advance URMC-099 through safety and preclinical studies to IND filing for HAND through Wavodyne Therapeutics, Inc (incorporated 02/15; national/international patents granted 2014, 2015, 2016).
- Nanoformulated cART with URMC-099 for eradication (RO1 funded; 2 new RO1s for 08-09/16 for formulation strategies); URMC-099 now with new nanoformulation strategy to create co-crystals with ARVs; licenses to GSK under discussion

URMC-099 milestones:

- The Mixed Lineage Kinase-3 Inhibitor URMC-099 Improves Therapeutic Outcomes for Long-Acting Antiretroviral Therapy. **Nanomedicine**. 2016 Jan;12(1):109-22. *featured article selected for cover of January 2016*
- Efficacy demonstrated in *in vivo* models of **post-operative cognitive dysfunction** (POCD) – R21/R33 IGNITE grant with Duke University Medical Center pending review; **multiple sclerosis** (experimental autoimmune encephalomyelitis) – Harrington Discovery Project pending review; **congestive heart failure/ischemia reperfusion injury** (RO1 to Cincinnati Children's Hospital funded); **non-alcoholic steatohepatitis** (NASH) – Gilead/career development award to Mayo pending; *in vitro* models of **Alzheimer's disease** (AD) – **J. Neuroinflammation** (*in press*)
- ~50% preclinical safety and toxicology pharmacology studies for IND completed through WavoDyne Therapeutics, Inc.

URMC-099 eradication data with dolutegravir:



**After 28d exposure, [DTG @45mg/kg]
is increased 2log by URMC-099**

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Aim 4: Mentoring

- David Bearden (Birbeck, Gelbard) – Asst. Prof. (new hire from CHOP)
- Krupa Shah (Dewhurst) – Asst. Prof. (K23 on frailty & aging; developing R21 on frailty, aging & immune functioning w. Juilee Thakar)
- Michelle Kiebala (Maggirwar) – RAP (R03)
- Jennifer Urban (Nilsson, Kraus and Gelbard) – Predoc (UR TG)
- Jennetta Hammond (Gelbard) – Postdoc (F32); K award planned for fall 2016
- Qing Ma (Morse, Schifitto) – UB, Junior Faculty (K08 award); planned investigation of URM-099
- Charles Venuto (Morse, Schifitto) – CHET (K23) HIV-HCV interaction and the CNS

Plans for Upcoming Year

- Continue IND-enabling/nanoformulation (i.e. long-acting) studies with URM-099
- Submission of new RO1 to evaluate the dynamic relation of measurable neuronal and glia CSF biomarkers and imaging outcomes to assess evolution of CNS injury
- Biomarkers (ICAM-5) for CNS disease in children with HIV-1 and seizures from CHASE cohort
- Nanoscale (fPALM/STORM) studies of virus trafficking in CNS cells

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CFAR: HIV RNA Biology Scientific Working Group

David Mathews, MD, PhD - Director
Ben Miller, PhD - Associate Director

HIV RNA Biology SWG

- Encourage investigators in RNA Biology to study HIV.
- Provide scientific direction to those at the interface of HIV and RNA Biology.
- Mentor young investigators and investigators new to HIV.

RNA SWG Aims

- **Aim 1:** To provide leadership and scientific direction.
 - i. directly targeting HIV RNA structures
 - ii. preventing HIV-1 recombination (and thus its ability to develop drug resistance)
 - iii. reactivating latent viral reservoirs.
- **Aim 2:** To build collaborations in strategic focus areas.
- **Aim 3:** To provide mentoring and support for new investigators
- **Aim 4:** To facilitate programmatic integration.
Provide support for pilot projects and access to key services and tools.

SWG Members

David Mathews, Biochemistry & Biophysics

Ben Miller, Dermatology

Bob Bambara, Microbiology & Immunology

Scott Butler, Microbiology & Immunology

Paul Dunman, Microbiology & Immunology

Dimitri Ermolenko, Biochemistry & Biophysics

Clara Kielkopf, Biochemistry & Biophysics

Dorota Piekna, Microbiology & Immunology

Gaurav Sharma[†], Electrical & Computer Engineering

Harold Smith, Biochemistry & Biophysics

Doug Turner[†], Chemistry

Joseph Wedekind, Biochemistry & Biophysics

Accomplishments

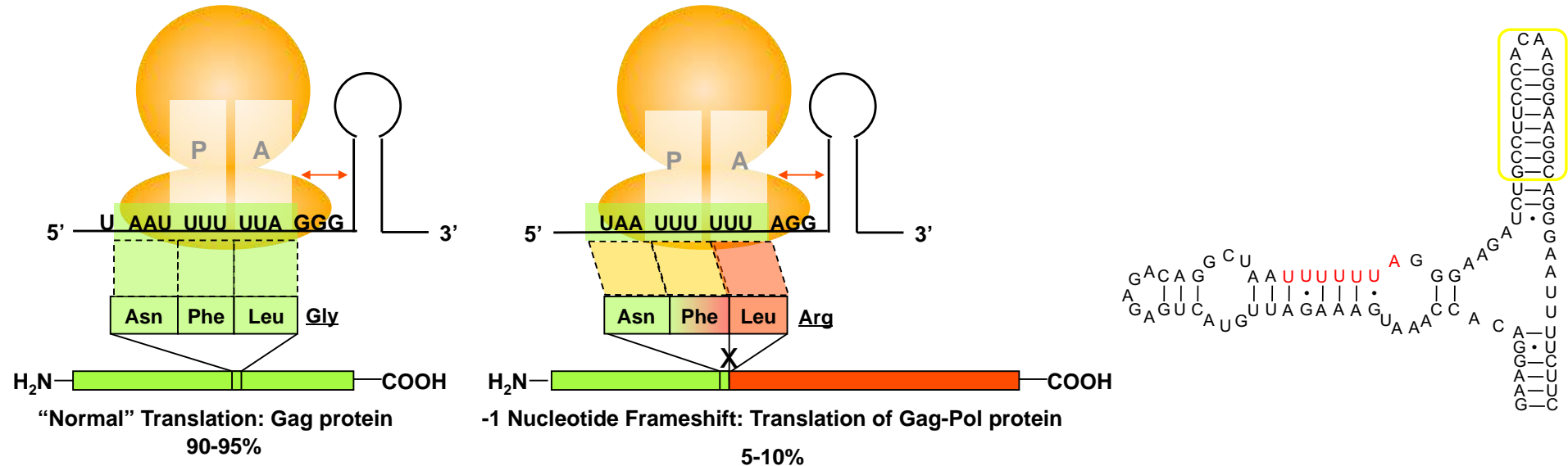
- **Funding:** 3 new R01s funded (Jian Zhu, Clara Kielkopf).
- **Community:** Two monthly RNA clubs with HIV talks from Ermolenko lab, Miller lab, and Wedekind lab.
- **Mentoring:** Dmitri Ermolenko, Dorota Piekna, and Jian Zhu.
- **Pilot Award:** To Joseph Wedekind for “Structural Analysis of a Novel Protein Interaction Targeting HIV-1 TAR RNA.”

Plans for Upcoming Year

- Use two of the monthly “RNA club” meetings for HIV-related RNA research.
- Continue to encourage new research interests in HIV with mentoring.

HIV RNA Biology SWG

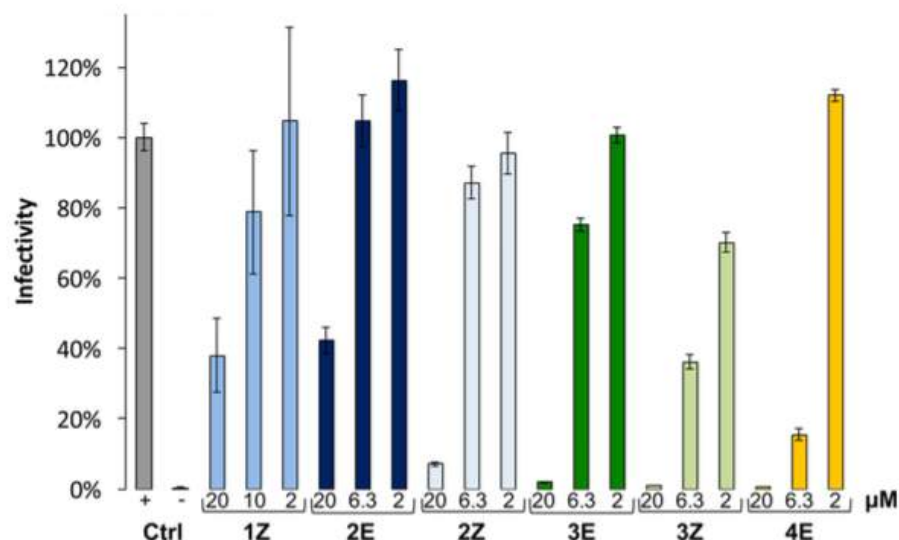
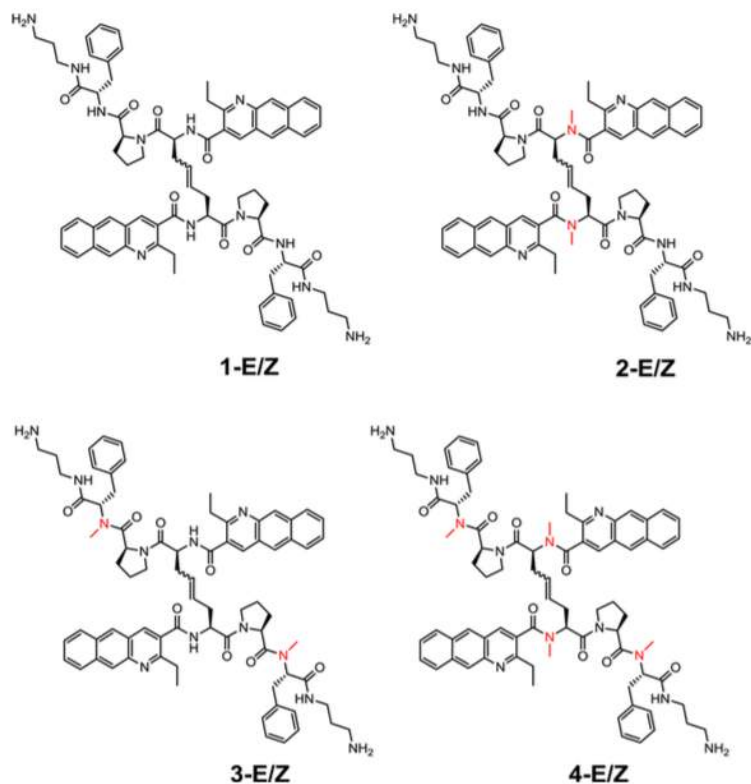
Example of relevant science: altering Gag-Pol frameshifting



5 R01 GM100788 "RNA targeted small molecules: connecting binding kinetics to sequence selectivity" (Miller, Benjamin); initial data generated in a D-CFAR pilot

HIV RNA Biology SWG

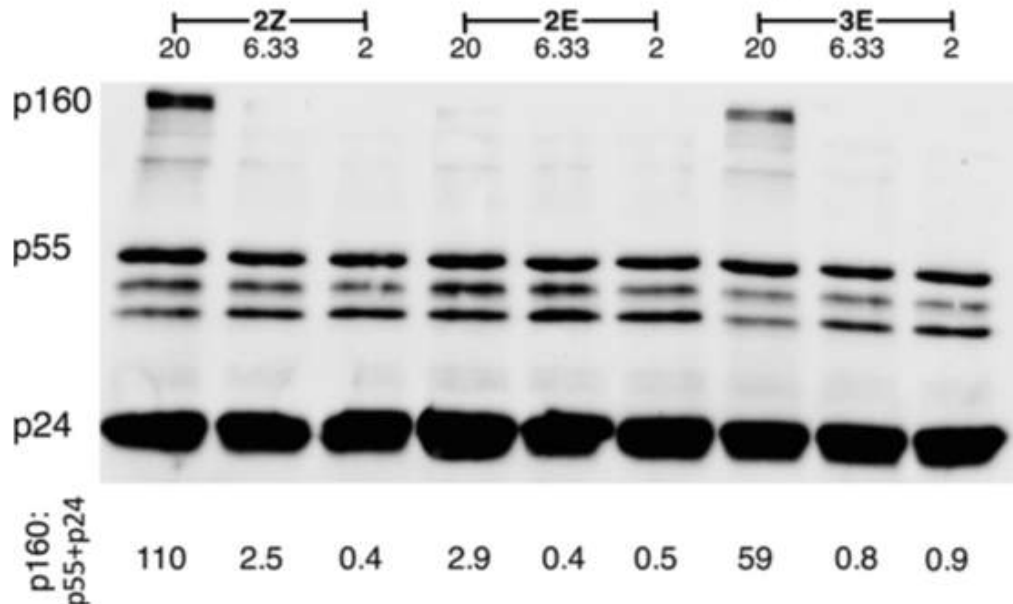
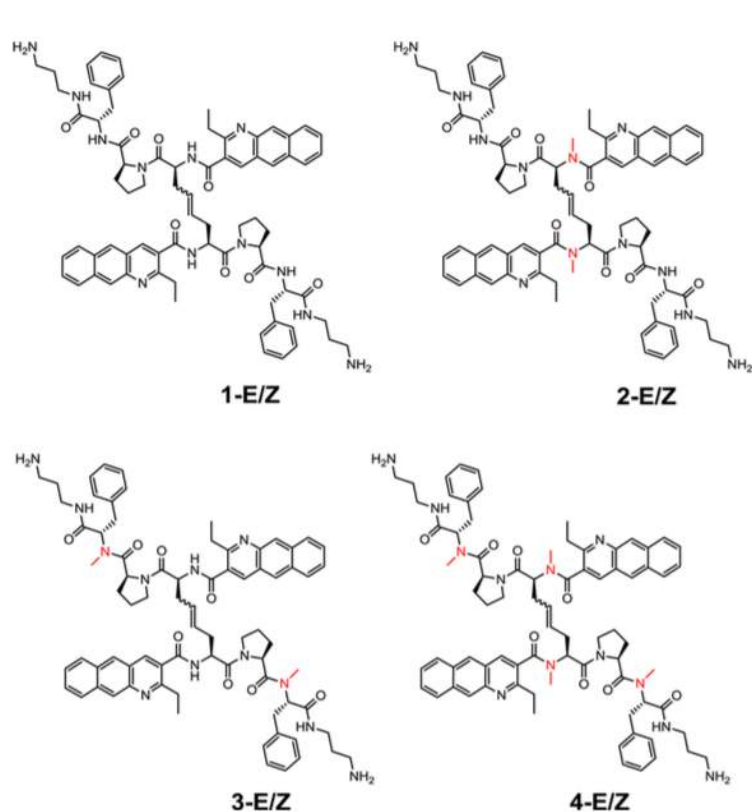
Example of relevant science: altering Gag-Pol frameshifting



Nanomolar-affinity HIV-1 FSS RNA-targeted compounds are able to inhibit pseudotyped HIV in a dose-dependent manner (Hilimire, et al. *ACS Chem Biol.* **2016**, 11, 88-94.)

HIV RNA Biology SWG

Example of relevant science: altering Gag-Pol frameshifting



*Pseudotyped virus produced in the presence of FSS RNA-targeting compounds shows altered Gag-Pol ratios (Hilimire, et al. ACS Chem Biol. **2016**, 11, 88-94.)*

Unpublished data: compounds inhibit “live” HIV.

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Future Scientific Working Groups

Steve Dewhurst, PhD

Scientific Working Groups

Potential Future Scientific Working groups

- HIV Associated Cardiovascular and Cerebrovascular Disease
- Stress, Trauma and Vulnerable Populations
- HIV Cure

Suggested selection criteria for new SWG's:

- At least 3 NIH funded PIs with R01 or equivalent funding
- At least 10 total faculty (so we have critical mass)
- Clearly defined opportunities for expanding funding by at least 50-100% over 3-5 years, and also doing exciting/impactful science

HIV-Associated Cardiovascular and Cerebrovascular Disease

Giovanni Schifitto, MD
Sanjay Maggirwar, PhD

HIV-Associated Cardiovascular and Cerebrovascular Disease

The SWG addresses HIV-associated end-organ diseases and specifically three areas of interest:

- Acute stroke
- Cerebral small vessel disease (CBVD)
- Cardiac dysfunction/Left ventricular diastolic dysfunction

Stroke

Table 4 Association between HIV infection and ischemic stroke^a **Sico et al. Neurol 2015**
Veteran Aging Study: N= 76,835

	HR ^b (95% CI)	p Value
HIV infection	1.17 (1.01-1.36)	0.04
Age ^c	1.86 (1.72-2.01)	<0.01
Race/ethnicity ^d		
African American	1.33 (1.14-1.54)	<0.01
Hispanic	1.18 (0.91-1.53)	0.22
Other	0.96 (0.68-1.36)	0.83
Hypertension ^e		
Treated	1.76 (1.41-2.2)	<0.01
Untreated	2.41 (2.08-2.8)	<0.01
Diabetes	1.58 (1.36-1.83)	<0.01

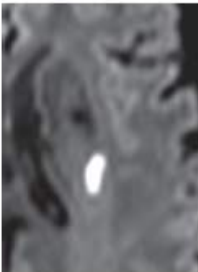

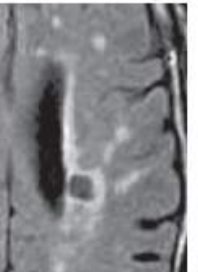

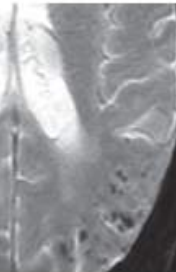


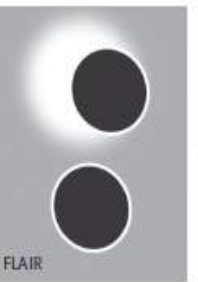


Table 5 Association of HIV-specific biomarkers and ischemic stroke

HIV status	Stroke risk, HR (95% CI) ^a	p Value
Model 1		
HIV –	1 (referent)	
HIV +; CD4 ≥500	0.99 (0.78-1.25)	0.91
HIV +; CD4 200-499	1.06 (0.86-1.32)	0.57
HIV +; CD4 <200	1.66 (1.30-2.12)	<0.01
Model 2		
HIV –	1 (referent)	
HIV +; HIV-1 RNA <500	0.97 (0.80-1.19)	0.78
HIV +; HIV-1 RNA ≥500	1.36 (1.15-1.63)	<0.01
Model 3		
HIV –	1 (referent)	
HIV +; HIV-1 RNA <500; on HAART	0.89 (0.7-1.12)	0.3
HIV +; HIV-1 RNA ≥500; on HAART	1.38 (1.07-1.80)	0.02
HIV +; not on HAART	1.30 (1.09-1.56)	<0.01

Cerebral Small Vessel Disease

Cerebral small vessel disease present in >70% of postmortem brains examined in HIV+ subjects (Soontornniyomkij et al., AIDS 2014)

Hawaii Aging with HIV Cohort Study found white matter hyperintensity in 48% of the subjects that had a MRI study (McMurtray et al., J Stroke Cerebrovasc Dis 2008)

	Recent small subcortical infarct	White matter hyperintensity	Lacune	Perivascular space	Cerebral microbleed
Example image					
Schematic					
Usual diameter	≤20 mm	Variable	3–15 mm	≤2 mm	≤10 mm
Comment	Best identified on DWI	Located in white matter	Usually have hyperintense rim	Most linear without hyperintense rim	Detected on GRE seq. round or ovoid, blooming
DWI	↑	↔	↔/(↓)	↔	↔
FLAIR	↑	↑	↓	↓	↔
T2	↑	↑	↑	↑	↔
T1	↓	↔/(↓)	↓	↓	↔
T2*-weighted GRE	↔	↑	↔ (↓ if haemorrhage)	↔	↓↓
↑ Increased signal ↓ Decreased signal ↔ Iso-intense signal					

Wardlaw et al. Lancet Neurol 2013; 12: 822–38

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Cardiac Dysfunction

Inflammation, ARVs, Co-infections



Endothelium, myeloid cells, smoking



CENTRAL ILLUSTRATION Identified Scientific Gaps in HIV-Related CAD and Recommended Research Approaches

EPIDEMIOLOGY	PATHOPHYSIOLOGY	PREVENTION AND TREATMENT
Scientific Gaps <ul style="list-style-type: none"> Incidence and prevalence of coronary artery disease (CAD) in patients with HIV Interplay of HIV, inflammation, antiretroviral therapy (ART), coinfections, and traditional risk factors on development of CAD Impact of sex and race on clinical outcomes 	Scientific Gaps <ul style="list-style-type: none"> Mechanisms of the interplay of HIV, inflammation, ART, coinfections, and traditional risk factors in development and progression of CAD Molecular pathways underlying chronic inflammation in HIV Impact of microbial translocation, viral reactivation, replication, and production on lipid metabolism, endothelial function, immune senescence, and thrombosis Synergistic effects of smoking on mechanisms underlying HIV-related CAD Mechanisms of HIV-related coagulation and platelet abnormalities, and thrombosis Novel targets for therapy in HIV-related CAD Need for better animal and molecular models Characterization of atherosclerotic plaque in HIV patients 	Scientific Gaps <ul style="list-style-type: none"> Potential differences in the prevention and treatment of HIV-related CAD Efficacy and effectiveness of evidence-based CV therapies in HIV patients Novel therapies to address unique pathophysiology of HIV-related CAD
Recommended Approaches to Gaps <ul style="list-style-type: none"> Consolidate current knowledge through reviews and meta-analyses Utilize current HIV and cardiovascular (CV) studies to examine questions about HIV-related CAD Add and adjudicate CV events (CAD, venous thrombosis, pulmonary embolism) in HIV cohort studies to detect general trends by leveraging cohorts with large numbers of HIV patients Enrich CV cohort studies with HIV patients to allow for detailed assessment of CAD rates and the relative contributions of traditional and HIV-specific risk factors on the development of CAD Examine long-term outcomes and determinants of outcomes following CV events Conduct studies evaluating HIV-related CV disease in women and minorities, and address health disparities 	Recommended Approaches to Gaps <ul style="list-style-type: none"> Combine pre-clinical development of resources with hypothesis-generating research Develop more robust animal models to explore the relationship between HIV-related inflammation and atherosclerosis Pursue mechanistic studies evaluating the role of inflammation, microbial translocation, and immune activation in HIV-related CAD 	Recommended Approaches to Gaps <ul style="list-style-type: none"> Add CV outcomes to HIV trials to understand the effects of HIV interventions on CAD Increase enrollment of HIV patients into CV trials Collaborate with HIV trial networks early during protocol development to address CV questions Conduct pilot trials of interventions addressing novel risk factors in HIV-related CAD, which could be further tested in larger studies that include HIV and non-HIV populations Develop best practices to incorporate HIV testing into clinical trials Leverage existing CV databases, claims data, and electronic health records to evaluate patterns of care in the prevention, diagnosis, and treatment of HIV-related CAD, post-event outcomes, and implementation of evidence-based CV therapies in the HIV population

Shah, M.R. et al. J Am Coll Cardiol. 2015; 65(7):738-44.

HIV = human immunodeficiency virus.

SWG Members Funded Research in CVD/CBVD

Giovanni Schifitto:

- cART Accelerates Vascular Aging in HIV Infected Subjects - 5R01HL123346

Sanjay Maggirwar:

- Role of Tetherin In HIV-Associated Thrombosis – 5R01HL128155
- Inflammatory Mechanisms Associated With HIV-1 Dementia – 4R01NS054578
- Platelet-Mediated Neuroinflammatory Response to HIV – 2R01NS066801

SWG Funded Research in CVD/ CBVD

Minsoo Kim:

- Inflammatory Cues Regulating Effector T Cell Recruitment – 5P01AI102851

Marc Halterman:

- Targeting Phosphatase Regulated Cleavage Of HIF-1-Alpha In Ischemic Brain Injury - 5R01NS076617-05
- Mechanisms Of Lung-Dependent Neutrophil Priming in Global Cerebral Ischemia-Reperfusion Injury - 5R01NS092455-02

Craig Morrell:

- Novel Platelet Functions For IN T-Cell Helper Cell Responses - 5R01HL124018-02

Additional Members of the SWG

Charles Lowenstein, MD; Cardiology

Bradford Berk, MD, PhD; Cardiology

George Schwartz, MD; Nephrology

Richard Phipps, PhD; Environmental Medicine

Marvin Doyley PhD; Electrical Engineering

Gretchen Birbeck MD; Neurology

David Bearden MD; Pediatric Neurology

Curtis Benesch MD; Neurology

Bogachan Sahin; Neurology

Future Plans of CVD/CBVD SWG

- Apply expertise in myeloid cell biology by the SWG in the context of HIV-associated CVD/CBVD
- Connect with available cohorts to explore CVD/CBVD biomarkers
- Establish new prospective cohorts to address specific mechanisms
- Design new intervention to treat HIV-associated CVD/CBVD

Future Plans of CVD/CBVD SWG

Stroke:

- Use the ACTG Longitudinal Linked randomized Trial (ALLRT) cohort to investigate predictors of stroke
- Investigate epidemiology and risk factors for stroke in children in Zambia
- Collaboration with ACTG network to implement future trials for the prevention of stroke

Future Plans of CVD/CBVD SWG

CSVD:

- Establish a CSVD cohort; resubmit RO1 9/2016 on role of platelets-monocytes complexes in CSVD
- Develop new technologies to assess vascular reactivity and microcirculation- Collaborations with Electrical Engineering, Eye institute, General Electric

Cardiac dysfunction/Left ventricular diastolic dysfunction:

- Increased myocardial fibrosis is an underlying factor leading to cardiac dysfunction. Novel sensitive approaches to measure cardiac elastography would help pathogenesis studies as well as clinical intervention
- We have expertise in elastography that would facilitate MRI and US based investigations

Stress, Trauma, and Vulnerable Populations

Theresa E. Senn, PhD

Stress, Trauma, and Vulnerable Populations: Significance

- Stress and trauma affect behavior and biology in ways that increase risk for HIV and negatively impact health of individuals infected with HIV.
- Groups at high risk of HIV infection report high rates of exposure to stress and trauma.
- Individuals infected with HIV also report high rates of trauma.

Stress, Trauma, and Vulnerable Populations: Mission

- SWG Mission: To understand and ameliorate the negative HIV-related consequences of stress and trauma in vulnerable populations.

Stress, Trauma, and Vulnerable Populations: Recent Pilot RFA

Applications should address how stress and trauma affect biological, behavioral, and structural factors to:

- affect PrEP uptake and adherence
- impact health-related outcomes for individuals infected with HIV
- impede access, linkage, and retention in HIV care
- affect HIV prevention interventions
- influence HIV-related health disparities

Stress, Trauma, and Vulnerable Populations: Current CFAR Funding

Current Funding (R01/equivalent): Vulnerable Populations

1. PrEP implementation with US HIV-serodiscordant couples: Couples PrEP demo project (R01; PI: J. McMahon, School of Nursing)
2. HIV Vaccine Trials Network (HVTN) site; AIDS Clinical Trials Group (ACTG) site (site PI: M. Keefer, Department of Medicine)

Stress, Trauma, and Vulnerable Populations: Current CFAR Funding

Other funding (not R01)

1. Supporting Health in Drug Treatment Court for Women with HIV/Hep C (K23)
2. Exploring Stigmas & HIV Diagnosis Delay, Linkage & Retention for MSM in Ghana (R21)
3. Dev. of a Novel HIV Risk Reduction Intervention for Abused Women (R34)
4. The Impact of Trauma on Mucosal Immunity (2014 CFAR Pilot Award)
5. An mHealth Application to Promote Community Engagement & HIV Testing Among Chinese MSM” (2015 CFAR Pilot Award)
6. Sexually Oriented Engagements with Multiple Networked Technologies by Young Black Men Who Have Sex with Men (2015 CFAR Pilot Award)
7. Feasibility and Acceptability of using a Mobile Application for HIV Symptom Monitoring, Clinical Follow Up, and Peer Support among HIV Infected MSM in Ghana, West Africa (2015 CFAR School of Nursing/School of Medicine Award)

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Stress, Trauma, and Vulnerable Populations: Plans to increase R01 funding

1. Develop current K23, R34, and R21 into R01s
2. Recruit non-CFAR investigators with R01 funding into the SWG

Stress, Trauma, and Vulnerable Populations: Non-CFAR Funding

R01 Funding from non-CFAR Affiliated Faculty

1. Prevention of Depression in Maltreated and Non-maltreated Adolescents (R01; S. Toth, Dept. of Psychology and Mt. Hope Family Center)
2. Neural Basis of Reward-Based Choice (R01) and Repeated Cocaine Exposure and Striatal Contributions to Cognitive Control (R01; B. Hayden, Brain and Cognitive Sciences)
3. Cognitive Training to Protect Immune Systems of Older Caregivers (R01) and Managing Sleep Systems and Modifying Mechanisms of Traumatic Stress (R01; K. Heffner, School of Nursing)

Stress, Trauma, and Vulnerable Populations: Potential Members

CFAR members with NIH/CFAR funding in stress, trauma, and vulnerable populations	J. Kobie; T. Senn; D. Morse; L. Nelson
CFAR members with NIH/CFAR funding in vulnerable populations	J. McMahon; V. Silenzio; M. Wharton; E. Brockenbrough;
Non-CFAR members with NIH R01 funding in stress, trauma, and vulnerable populations	J. Fudge; N. Talbot; R. Pollard; T. O'Connor; J. Moynihan; K. Heffner; B. Chapman; S. Toth; J. Manly; F. Rogosch
CFAR members researching stress, trauma, and vulnerable populations, but no NIH funding in this area	C. Cerulli; N. Trabold; R. Bossarte; C. Nichols-Hadeed; K. Knox; M. Scharf; E. Poleshuck; K. Fiscella; C. Seplacki; A. Alio; A. Braksmajer; M. Urban
CFAR and non-CFAR members involved in brain neuroimaging	G. Schiffito; B. Hayden; J. Foxe

Stress, Trauma, and Vulnerable Populations: Relevant NIH Funding Opportunities

<u>Development and Testing of Novel Interventions to Improve HIV Prevention, Care, and Program Implementation (R34)</u>	Interventions that incorporate a syndemic approach to HIV prevention with consideration of conditions such as <u>intimate partner violence, childhood sexual abuse, stigma, or discrimination</u>
<u>Targeted Basic Behavioral and Social Science and Intervention Development for HIV Prevention and Care (R01)</u>	Studies that consider an integrated approach to prevention and care for subjects with co-morbidities, with a special emphasis on <u>those that experience violence/abuse</u>
<u>Advancing Structural Level Interventions Through Enhanced Understanding of Social Determinants in HIV Prevention and Care (R01)</u>	Interventions that address the negative influence of <u>social violence</u> on HIV prevention, care and treatment outcomes; How do <u>stigma/discrimination</u> associated with HIV interact with stigma/discrimination associated with race, gender and/or sexual orientation?
<u>Strengthening Adherence to Antiretroviral-Based HIV Treatment and Prevention (R01)</u>	Studies to develop and test approaches for improving ART adherence and outcomes by addressing upstream social/structural determinants (e.g., <u>HIV stigma</u>)
<u>Substance Use and Abuse, Risky Decision Making and HIV/AIDS (R01)</u>	Do gene x environment (e.g., drug or alcohol use, <u>trauma</u>) interactions predict the propensity of individuals to engage in HIV-risk behaviors?

Stress, Trauma, and Vulnerable Populations: Potential Research Areas

High Priority Topic	What SWG Could Address
implementation research for retention, engagement, and adherence	<ul style="list-style-type: none"> • how stressors impact adherence; how to improve adherence • provider-level interventions
HIV-associated comorbidities and complications	<ul style="list-style-type: none"> • interaction of stressors and HIV on inflammation • impact of stressors on non-infectious comorbid conditions (e.g., cardiovascular disease, diabetes) • how early life stress interacts with HIV to lead to neurocognitive disorders
reduce health disparities in HIV incidence and outcomes	<ul style="list-style-type: none"> • intervention research to address the needs of vulnerable groups disproportionately burdened by HIV and by trauma
developing and testing promising vaccines	<ul style="list-style-type: none"> • how stressors affect the protective immune response/vaccine response

Stress, Trauma, and Vulnerable Populations: Related Meetings

- 2013 Interagency Federal Working Group Report: Addressing the Intersection of HIV/AIDS, Violence against Women and Girls, & Gender–Related Health Disparities
- 2015 Greentree Conference: Violence Against Women & HIV
- 2016 White House meeting on HIV Stigma
- Annual International Conference on Stigma

Stress, Trauma and Vulnerable Populations: Goals

Aims	Year 1 Goals
To provide leadership & scientific direction	Identify 3 important research areas
To build basic & behavioral science collaborations	Pubs joint-authored by behavioral and basic scientists Grants jointly submitted by behavioral and basic scientists
To build collaborations with non-CFAR faculty	Non-CFAR faculty join the SWG
To provide mentoring/funding for new investigators	Provide grant advisement and individual mentoring Pilot grant related to the SWG
To build collaborations with community stakeholders	Create a community advisory board
To foster scholarly productivity	Increase no. publications authored by SWG faculty Increase no. NIH grants submitted by SWG faculty

HIV Cure

Ben Miller, PhD

HIV Cure

HIV Cure: The HIV Cure SWG focuses on new basic research and translational approaches to curing HIV, and demonstrating that a cure has taken place. Focus areas include (but are not limited to) identifying mechanisms of viral latency and re-activation, novel biomarkers, therapeutic strategies, and novel diagnostic tools including integrated photonic sensors.

HIV Cure: Why this SWG?

- UR has particular strengths in interdisciplinary research bridging physics/engineering/optics with biology/medicine
- There is a growing strength in “big data” / data sciences, along with genomics
- CFAR members are active in national photonics initiatives

**Wegmans Hall:
Goergen Institute
Of Data Sciences**



HIV Cure: Potential Members

- **Handy Gelbard** (HIV and aging; CNS effects of HIV)
- **Ben Miller** (Novel therapeutic targets and multiplex diagnostics)
- **Jian Zhu** (Transcription and Latency)
- **Dorota Piekna** (Latency)
- **Dmitri Ermolenko** (Mechanisms of translation and novel therapeutic targets)

HIV Cure: Current funding

- **5 R01 DE025447 “Investigation of latency promoting genes (LPGS) in HIV oral reservoir cells” (Zhu, Jian)**
- **1 R01 GM117838 “Role of FACT proteins in regulating HIV transcription and latency” (Zhu, Jian)**
- **5 R01 MH104147 “Novel kinase and nanoformulated protease inhibitors for eradication of CNS HIV-1” (Gelbard, Harris)**
- **5 R01 GM100788 “RNA targeted small molecules: connecting binding kinetics to sequence selectivity” (Miller, Benjamin)**

HIV Cure: Current funding

- **4 R01 GM099719 “Structural dynamics of translation” (Ermolenko, Dmitri)**
- **5 R21 AI116180 “Cooperation of BRD4 and TAT associated proteins in HIV transcription and latency” (Zhu, Jian)**
- **DoD, State, and Corporate consortium: “AIM Photonics”**

(Provides a framework for translating discoveries in diagnostics, disease biomarkers, etc.)

HIV Cure: Congruence with Trans-NIH Plan for HIV-Related Research

From the Plan: "High-priority research opportunities focused on research towards a cure include:

- Understanding viral and host mechanisms – including differential tissue and cellular distribution – that direct HIV persistence, latency, and reservoir formation
- Developing and testing novel interventions, including therapeutic vaccines and next generation monoclonal antibodies and derivatives, to control or eliminate latent and/or persistent reservoirs of HIV in the presence of effective ART.
- Identifying and validating novel biomarkers, assays, and imaging techniques to advance research toward a cure.
- **Members of the HIV Cure SWG are engaged in research in all three of these areas**

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HIV Cure: Applicable RFAs

- RFA-AI-16-028: Understanding HIV Rebound (P01)
- RFA-AI-16-038: Silencing of HIV-1 Proviruses (R61/R33)
- RFA-MH-17-101: Novel strategies for targeting HIV-CNS reservoirs without reactivation (R01)
- RFA-MH-17-100: Novel strategies for targeting HIV-CNS reservoirs without reactivation (R21)
- RFA-AI-16-024: Identification of small molecules for sustained-release anti-HIV products (R01)
- RFA-AI-16-012: Pilot clinical trials to eliminate the latent HIV reservoir (U01)

HIV Cure: Future Plans

- Bimonthly meetings of core faculty to build community
- One World AIDS Day keynote speaker focused on Cure in 2016 (Paul Wender, Stanford)
- Spring CFAR-wide Cure Mixer to drive new collaborations

CFAR Cores

Mike Keefer, MD

CFAR Cores

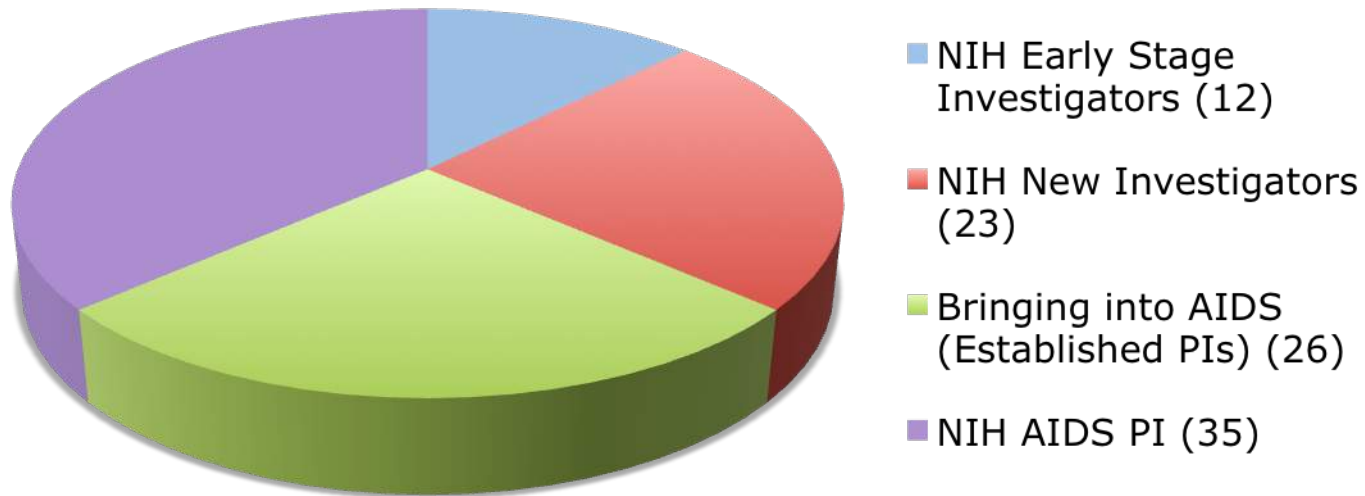
Services organized within five cores:

- Administrative Core
- Developmental Core
- Clinical and Translational Sciences Core
- Basic Science Core
- Biostatistics, Bioinformatics and Computational Biology Core

Administrative Core

Mike Keefer, MD

CFAR Membership 2016



2016 Faculty total: 96 (increase from 94 last year)
(11 new to CFAR and 9 left UR)

Increase from 16 to 19 CFAR members without any NIH funding₉₉

UR CFAR Mission

To provide leadership, services & infrastructure to:

- Establish multidisciplinary collaborations that achieve high-impact discoveries
- Support early career development of young HIV/AIDS investigators
- Establish a distinctive scientific identity, placing the UR at the forefront of HIV/AIDS research

Administrative Core

Financial Support

Scientific Program of Excellence (Institutional Recognition)

- HIV/AIDS research now one of our strategic Programs of Research Excellence within the SMD 5 year Research Strategic Plan

Partnership With School of Nursing

- \$50K matching pilot funds each year

Deans Support (Financial)

Administrative Core

Financial Support

Recognition as an Institutional Priority

- Dean agreed to fund 2 new pilot programs of \$50k each from institutional funds for the next 5 years.
- SMD Pilot award: Dr. Martin Zand funded for "Patient Journey and Network Analysis of HIV Patient Retention and Outcomes"

Synergy from Dean Support

- Joint pilot award RFA with SMD and School of Nursing
 - Dr. LaRon Nelson and Dr. Amina Alio funded for "Feasibility and Acceptability of using a Mobile Application for HIV Symptom Monitoring, Clinical Follow Up and Peer Support among HIV Infected MSM in Ghana, West Africa"

Administrative Core

Recent Changes

Change in Leadership Faculty:

- Core B - Developmental Core
 - Ben Miller, PhD – Core Director
 - James Kobie, PhD – Co-Associate Core Director
 - Teri Senn, PhD – Co-Associate Core Director
- Core C -Clinical and Translational Sciences Core
 - Michael Keefer, MD - Co-Director
- Core E - Biostatistics, Bioinformatics and Computational Biology Core
 - Rob Strawderman, ScD – Core Director
 - Brent Johnson, PhD – Associate Core Director

International Programs & Collaborations

LaRon E. Nelson, PhD, RN, FNP

International Programs: Landscape & History (Core A)

Current Landscape (selected):

Vince Silenzio (China)

CFAR Pilot Focus: An mHealth Application to Promote Community Engagement & HIV Testing

Tinashe Mudzviti (Zimbabwe)

CFAR Supplement - Evaluate Long-term In-Utero Tenofovir

Gretchen Birbeck (Malawi, Zambia)

CFAR Microgrant Focus: Examining HIV viral diversity among Zambian adults using HIV deep sequencing at Scripps Research Institute

International Programs: Landscape & History (Core A)

Technical Assistance and Support (selected):

Giovanni Schiffito (Canada)

- R01- *Effects of cART long term exposure on neuronal function and brain microstructure in HIV infected individuals ART naïve starting cART*

LaRon E. Nelson/Amina Alio (Ghana)

- UR SMD/SON – *Feasibility and acceptability of using a mobile application for HIV symptoms monitoring, clinical follow-up and peer support for HIV infected MSM in Ghana*

Amina Alio (Niger), LaRon Nelson (Ghana), Omar Ndoeye (Senegal)

- CFAR Proposal - *Understanding HIV prevention needs and acceptable strategies for prevention and care of Muslim MSM in West Africa region*

International Programs: Landscape & History (Core A)

Recently Completed (selected):

Gretchen Birbeck - Malawi, Zambia

CFAR Microgrant Focus: Cerebral Imaging

- **Contributed to R01 - Cohort of HIV-Associated Seizures and Epilepsy in Zambia (CHASE): scale up and expansion informed by R21 findings**

Amina Alio – South Africa

CFAR - Pilot Effect of Religion on Behavior

- **Using results as preliminary studies section of NIH R-level research application planned for January 2017 submission**

International Programs: Opportunities

- Facilitate more research focused in West Africa to leverage presence of multiple UR projects in the region
- Pursue collaborative cross-border HIV/AIDS research opportunities with communities and with HIV/AIDS institutions in Greater Toronto
 - Implementation science, including PrEP
 - Vaccine research and other studies
- Faith Inter-CFAR Working Group
- Leverage Fulbright African Scholars

Administrative Core

Future Plans for next 12 months

Plans

- Recruitment of ACTG CRS Leader
- Continue to engage CFAR investigators in projects aligning with the ACTG and HVTN research priorities
- Strengthen linkages with New York State 'End the Epidemic 2020' initiative
- Explore partnering with Rochester's Photonics R&D hub

Administrative Core

Future Plans for Reapplication

Plans

- Establish 2 new 'Scientific Working Groups'
- Leverage institutional investment in Data Science and establish an identity for the CFAR in Data Science/Health
- Further develop partnership with Deaf and Hard of Hearing community to establish an identity with this marginalized community

Administrative Core

Key Contacts:

Steve Dewhurst, Core Director

Michael Keefer, Associate Core Director

LaRon Nelson, Assoc. Dir. International Research

Laura Enders, Program Administrator

Contact Laura Enders for more information

<https://www.urmc.rochester.edu/center-for-aids-research.aspx>

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Developmental Core

Ben Miller, PhD

Developmental Core *Mission*

- Stimulate new research by funding pilot awards
- Provide comprehensive, structured mentoring support for the early career development of young faculty, and a grant pre-review service to enhance extramural grant applications.
- Create an outstanding intellectual and scientific environment for HIV/AIDS research
- Support new faculty recruitment

Developmental Core

Stimulating New Research

Pilot Awards (\$20,000-40,000 DC)

- Young faculty members
- Innovative studies with potential for high impact
- Multidisciplinary collaborations
- Particularly encouraged for new SWGs

NIH Supplement Funding (\$100,000)

- Funding for a broad range of projects to address key gaps in understanding of HIV/AIDS
- Support early stage investigators or well established investigators in non-HIV fields

Microgrants (\$2,500)

- To advance research objectives on existing NIH-funded research activity, or generation of preliminary data for planned applications

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Developmental Core *Services*

CFAR Pilot/Supplement Proposal Critical Review

- Internal application review
 - Opportunity to discuss with members of review committee, with goal of revising and improving proposal

Mentoring

- Multidisciplinary mentoring from a diverse mentorship team
- Cross-departmental: Scientific/Technical and/or Career development

Grant Review Service

- Increase competitiveness of extramural proposals (new investigators, established investigators new to HIV/AIDS)
 - Proposal Shaping Phase
 - Proposal Refinement Phase
 - Responding to Review Committee Critiques

Developmental Core

Recent Grant Award Successes

Pilot Awards

2015 Pilots:

- **Joe Wedekind** – “Structural Analysis of a Novel Protein Interaction Targeting HIV-1 TAR RNA” (\$50K)
- **Crag Morrell, Sanjay Maggirwar and Charles Lowenstein** - “Platelet derived Beta-2 (β 2M) Microglobulin Accelerates HIV-Associated Neuroinflammation and Injury” (\$100K)
- **Juilee Thakar** - “Serology based systems modeling to improve treatment for atherosclerosis in people living with HIV” (\$50K)

2016 Pilots: pending

Developmental Core

Recent Grant Award Successes

Microgrants

2015 Microgrants:

- **Sherry Spinelli** – “The Role of Exosomes in Thrombotic Risk in HIV: Effects of ART and tobacco smoke”

2016 Microgrants:

- **Gretchen Birbeck** – “Examining HIV viral diversity among Zambian adults using HIV deep sequencing at Scripps Research Institute”
- **Vir Singh** – “Identification of the long noncoding RNAs (lncRNAs) required for establishment and maintenance of HIV latency”
- **Tim Mosmann** – “Exploratory Analysis of Existing T cell Response Data from HVTN 105 Using SWIFT: Scalable Weighted Iterative Flow-clustering Technique”
- **Joe Wedekind** – “Purchase of replacement 500 W electrophoresis power supply” to support Pilot

Developmental Core

Recent Grant Award Successes

CFAR Supplements, Related Awards

2015: Supplement:

- Matthew DeLisa (Cornell) in “TACA-specific antibodies for Comparing Glycan Biomarkers in HIV Comorbidities” in topic area: Glycomics in HIV Co-Morbidities (\$100k)

2016: Supplement:

- Elizabeth Asiago Reddy (SUNY Upstate) in “Discrete Choice Experiments for PrEP Uptake in Young Men Who have Sex With Men” in topic area: Advancing PrEP Delivery (\$147k)

Developmental Core

Recent Grant Award Successes

Other Extramural Awards

The awards below reflect extensive CFAR mentoring support, grant review assistance and assistance from Core C in developing the human subjects research components of these awards

- 2015: **Jian Zhu** (second new R01 award (September)) “Role of FACT Proteins In Regulating HIV Transcription and Latency”
- 2015: **Gretchen Birbeck** (R01) “Cohort of HIV-Associated Seizures And Epilepsy In Zambia (CHASE): Scale Up And Expansion Informed By R21 Findings”
- 2016: **John Cullen and Kate Cerulli** – “Exploring the Use of an eScreen Tool to Meet the Needs of Potential HVTN Study Participants” HVTN Initiatives Program (HIP)
- 2016: **Juilee Thakar** and Kelly Seaton – “Assessing Impact of Vaccine Regimen on Vaccine Induced Antibody Durability” HVTN Initiatives Program (HIP)

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Developmental Core

Facilitating Faculty Recruitment

Recent Hires of HIV/AIDS Researchers new to UR

- **Felix Yarovsky:** Assoc Prof - joined June 2015 (from UT Southwestern)

Researchers New to HIV/AIDS

- **Craig Morrell, DVM, PhD:** Associate Professor (cardiology)
- **Charles Lowenstein, MD:** Professor (cardiology)
- **Martin Zand, MD, PhD:** Professor (nephrology)
- **Vankee Lin, PhD:** Assistant Professor (nursing)

Planned future Recruits

- Commitment to 1-2 new faculty in Infectious Diseases for CTU renewal, leadership
- School of Nursing Post-Doc/Transitional Post-Doc in HIV

Developmental Core

2015-2016 activities

CFAR Mentoring: Offers structured mentoring support for the professional development of young investigators.

- *Recognizing mentee targets and pairing them with appropriate mentors for meeting on regular basis – initial mentor and mentee pool contains 24 and 43 members respectively.*

Examples of mentee-mentor (primary) pairs identified

LaRon Nelson: *Jim McMahon*

James Kobie: *Mike Keefer*

Danielle Benoit: *Handy Gelbard*

Tinashe Mudzviti: *Gene Morse*

Dmitri Ermolenko: *Ben Miller*

Krupa Shah: *Steve Dewhurst*

Jian Zhu: *Ben Miller*

Xing Qiu: *Giovanni Schifitto*

Developmental Core

2015-2016 activities

CFAR Mentoring: *Mentee Targets and Prioritization*

- Identification of new mentees, including new hires
- Assessment of faculty needs
- Prioritization followed this general order
 - (1) Junior faculty who are current or recent recipients of CFAR pilots/supplements
 - (2) Junior faculty working in HIV/AIDS and related disciplines
 - (3) Those interested in transitioning to HIV/AIDS and related research
 - (4) Established investigators transitioning to HIV/AIDS
 - (5) Postdocs in or transitioning to HIV/AIDS research
 - (6) Established investigators in HIV/AIDS field

Junior Faculty are defined as Tenure Track Assistant Professors, and Early Stage Investigators (Research Assistant and Associate Professors)

Developmental Core

2015 – 2016 activities

CFAR Mentoring: Grant Review Services

- **Step One: Proposal shaping phase.** Draft specific aims will be orally presented and discussed with customized ad hoc review panel chosen from CFAR mentor pool.
- **Step Two: Proposal 'refinement' phase.** Full proposal draft will be reviewed by the same panel to provide comments using NIH review format.
- **Step Three: Resubmission phase.** Review of critiques and discussion of strategy for moving forward

2015-2016 grant review users to date:

- Krupa Shah and Vankee Lin (R01)
- Vir Singh (R21)
- Giovanni Schifitto and Sanjay Maggirwar (R01)
- John Cullen and Kate Cerulli (Pilot)
- Juilee Thakar (Pilot)
- Dmitri Ermolenko (R01 renewal)
- Dorota Piekna-Przbylskaya (Pilot)

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Developmental Core

2015 – 2016 activities

CFAR Mentoring: *Peer Mentoring Group*

- **A Peer Mentoring Group has been established.** Comprised of untenured faculty, this group will discuss the issues they encounter regarding their career development as well as provide feedback for continuous improvement of CFAR mentoring and programmatic activities
- **Leadership** of the Peer Mentoring Group is provided by James Kobie and Teri Senn

Developmental Core

Jr. Faculty Peer Mentoring (Teri Senn, SON and James Kobie SMD)

- Synergize with other UR Jr. faculty resources
 - Led peer mentoring discussion at the UR Jr. Faculty Biomedical Research Association
 - Needs and Use Survey (Fall '15)
 - Peer Mentoring Mission Defining / Feedback Roundtable (Fall '15)
 - Mini-Research Symposium (March '16)
 - 13 Jr. faculty attended and presented
 - Rising Star Roundtable Breakfast w/ Jason Farley (JHU) (April '16)
 - 10 Jr. faculty attended, career development focused discussions
 - Unofficial CFAR Jr. Faculty Happy Hour (April '16)

Developmental Core

Jr. Faculty Peer Mentoring Planned Activities:

- Initiate Publication Syndicates (SON and SMD)
- dedicated bi-weekly hour to writing and feedback
- Skill building event (Fall '16)
 - Networking/Branding, Talking across the aisle (basic/behavioral) or
 - NIH K award workshop
- Needs and Use Survey (Fall '16)
- Rising Star Roundtable Series (~2 per year)
 - recently tenured and/or R01 funded external seminar speakers

Developmental Core

2015 – 2016 activities

CFAR Mentoring: *Assessment*

- Assessment of the increased participation of the faculty in the program
- Assessment of increased quality of grant applications as judged by their funding
- Assessment of benefits to the mentees and mentors – publications, visibility and development of academic leadership
- Assessment of participation in current and evolving SWGs

Developmental Core

Statistics and Summary of Usage

Usage Statistics

- 31 Mentor – Mentee pairs established for junior faculty
- 8 senior faculty peer mentor teams established
- Junior faculty peer mentor group established and active
- CFAR grant review service employed for 4 R21/R01 applications and 3 pilots
- Model has been taken up by other groups at U of R (Department of Microbiology & Immunology)

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Developmental Core

Future Plans for next 12 months (Selected)

Extend mentoring program

- CFAR grant review service will continue to grow
- Provide opportunities for participation in grant training workshops
- Ensure that mentors and mentees are interacting frequently

Work collaboratively with others in faculty hiring (CTU and School of Nursing)

Structure pilot RFPs to facilitate new SWG development

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Developmental Core

Future Plans for Reapplication

Leverage Institutional priorities and interagency opportunities / public-private partnerships

- Institute for Data Sciences
- AIM Photonics

Developmental Core

Key Contacts:

Benjamin Miller, Co-Director

Steve Dewhurst, Co-Director

James Kobie, Co-Associate Director

Teri Senn, Co-Associate Director

Laura Enders, Program Administrator

Website

<http://www.urmc.rochester.edu/cfar/services-cores/developmental.cfm>

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Clinical and Translational Sciences Core (CTSC)

Co-Directors:
Michael Keefer, MD
James McMahon, PhD

CTSC Mission

To provide key services to UR investigators to promote collaborative clinical and translational research in areas that impact upon the spread, treatment and control of HIV/AIDS.

CTSC Core Services

Regulatory Support

- Preparation of clinical protocols, consent forms, procedures, data safety and monitoring plans
 - IRB protocol development and submission
 - Preparation of annual IRB reports
 - Assistance with internal IRB audits
 - Study close-out procedures

Research Design Consultation and Review

- Consult on project aims, study design, sampling, recruitment
- Grant and manuscript review

CTSC Core Services

Study Coordination and Operational Services

- Hands-on assistance in setting up and maintaining best practices
 - Preparation of manuals and training procedures
 - Tailored to needs of investigator/project

Customized Access to Patients/Samples

- Access to HIV-infected patients or persons at high risk for HIV
- Biological specimens with pre-specified clinical characteristics

Facilitate Recruitment and Outreach – Custom Cohorts

Identify and establish collaborations with:

- Community-based HIV/AIDS organizations; CABs
- Other organizations that could aid in implementation of clinical research

CTSC Core Services

Integration with Other Institutional Resources

Identify, leverage, and integrate institutional resources that encourage/enhance clinical and translational research:

- Integrate resources from other CFAR Cores
- Identify and integrate resources from within URMC
- Identify and facilitate expert consultations or collaborations
- Facilitate access to national CFAR resources (e.g. repositories, networks)

CTSC Core Services

CFAR Member CTSC Users:

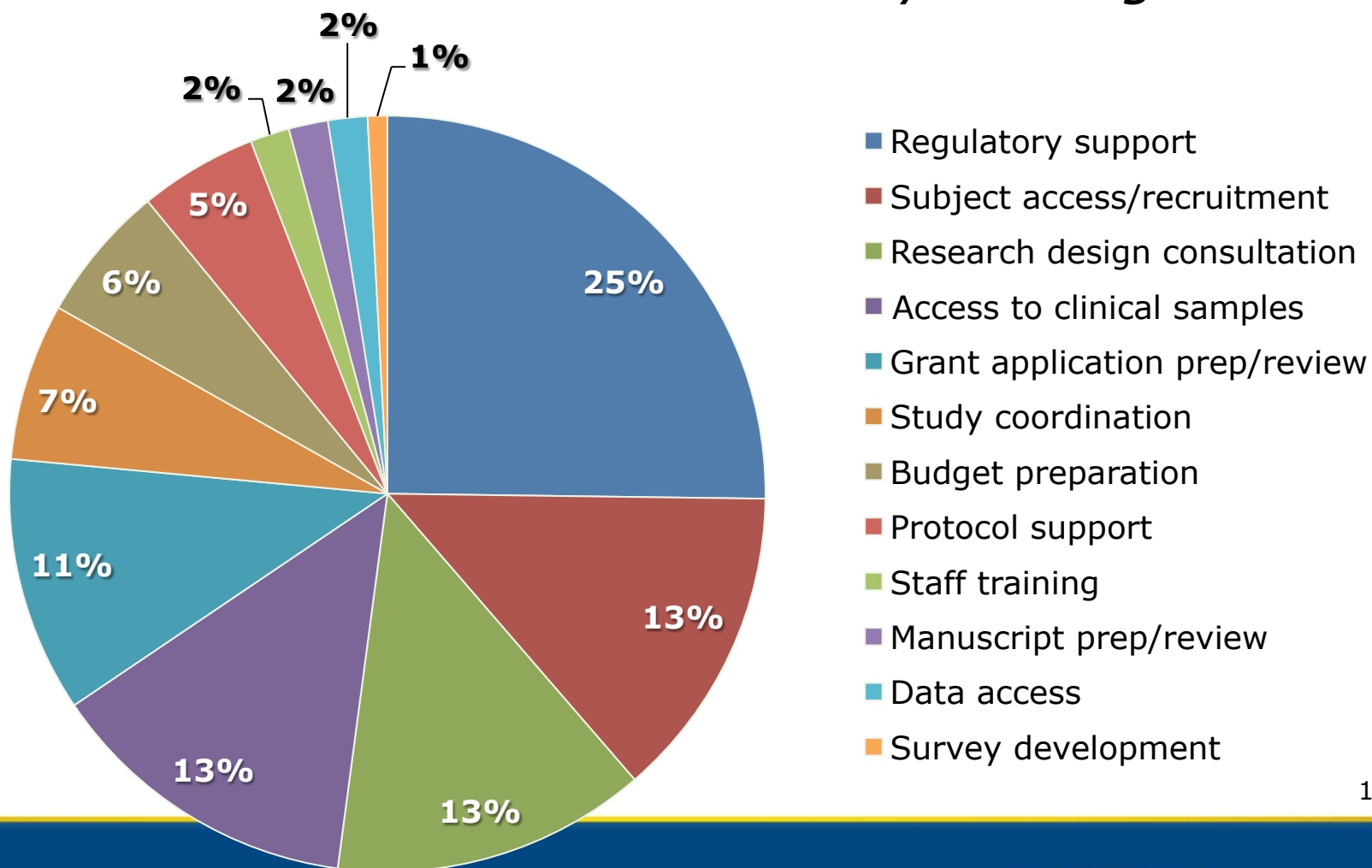
CFAR Investigators Supported: 25

Projects Supported: 35

- 12 CFAR Pilots/Microgrants
- 3 CFAR Supplement Grants
- 20 NIH-funded Grants
 - 9 R01s

CTSC Core

Statistics and Summary of Usage



CTSC Core

Selected 2015-2016 Activities

CTSC “Mixer” Fall 2015

- CTSC Mixer event October 13, 2015:
 - Guest speaker Dr. Sarit Golub, City University of New York
 - Attended by 43 CFAR and allied researchers, clinicians and community service professionals
 - Goals:
 - Increase awareness of UR-CFAR locally and regionally among HIV-related community organizations (e.g., Anthony Jordan health center participated as recruitment site)
 - Facilitate inter-professional collaborations (e.g., Dr. Elizabeth Reddy from Syracuse, SUNY Upstate, formed collaboration with Drs. Senn and McMahon)

CTSC Core

Selected 2015-2016 Activities

New Pilot Funding for CTSC Members: Joint School of Nursing (SON)/School of Medicine and Dentistry (SMD) Program of Excellence HIV/AIDS Pilot Grants

- Next RFA fall 2016
- Annual \$50,000 contribution each from SON and SMD
- Must be dual SON/SMD PIs
- Intended to facilitate multidisciplinary translational HIV/AIDS research (e.g., nursing, medicine, clinical, behavioral)
- 2015 Award - Dr. LaRon Nelson and Dr. Amina Alio funded for "Feasibility and Acceptability of using a Mobile Application for HIV Symptom Monitoring, Clinical Follow Up and Peer Support among HIV Infected MSM in Ghana, West Africa"

CTSC Core

Future Plans Next 12 months

- Improve proactive outreach to CFAR investigators and providers (e.g., better outreach through departments)
- Better consolidation of resources for subject recruitment
- Improve manuscript development assistance from pilot projects
- Increase awareness of grant preparation and review service
- Better coordination with Core E to involve statistical consultation earlier in the proposal development process
- Develop innovative strategies to promote HIV-related research among those in adjacent fields
- Innovative ideas to increase applications for pilot funding
- Develop clinical/behavioral SWG (Trauma, Stress & HIV)

CTSC Future Events

- Monroe County Partnering to End the Epidemic (MCPeTE)(Keefer)
- World AIDS Day

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CTSC Core

Future Plans for Reapplication

- Maintain integration of clinical, behavioral and translational research within a single core (synergy, increased inter-professional collaborations, innovation)
- Expand role in providing scientific direction and leadership in Clinical Trials Unit and End of AIDS initiative in New York State
- Foster regional collaborations (Western NYS region: Buffalo, Syracuse, Finger Lakes)
- Further develop and expand inter-CFAR working groups: newly established Faith Initiative Working Group (Keefer, Nelson, Alio); develop new WG on Nursing, Allied Health Professions and HIV (w/ Johns Hopkins: Farley, McMahon)

CTSC Core

Key Administration:

Mike Keefer, Co-Director

James McMahon, Co-Director

Laura Enders, Program Administrator

Catherine Bunce, Study Coordinator/RN

Emily Cosimano, Study Coordinator/RN

Website

<http://www.urmc.rochester.edu/center-for-aids-research/services-cores/clinical-sciences.aspx>

Basic Science Core

Sanjay B. Maggirwar, PhD - Director
James Kobie, PhD - Associate Director

Basic Science Core

Mission

- Enhancing basic and laboratory-based HIV/AIDS research by broadening research capabilities and promoting collaboration
 - ✓ Access to cutting-edge instrumentation & technologies
 - ✓ Support, education and training to enable efficient use of resources
 - ✓ Foster new developments in HIV/AIDS and HIV-related research

Basic Science Core

Current Services

Customized Protein Production

- Produces, purifies and characterizes biologically active macromolecules (e.g. HIV-1 Env oligomers, HIV Tat protein)

Structural Biology Facility

- Access to biophysical instrumentation (e.g. BIAcore T100, AXS X8 Prospector X-ray source and Mosquito robot)
- Access to FPLC resource (AKTA Pure Chromatography System) for purification of proteins, peptides and nucleic acids

Advanced Flow Cytometry

- Amnis ImageStreamX – hybrid fluorescent microscope/flow cytometer
- CyTOF – hybrid atomic mass spectroscopy/flow cytometer

Illumina HiSeq2500 & MiSeq Sequencers

Basic Science Core

Newly Initiated Services

- **High Throughput Screening Capacity:** Low cost access to: (i) Envision high throughput plate reader, a Janus dual-arm liquid handling robot, and a Flexdrop plate filler; (ii) Genome-wide siRNA library and knockdown service
- **Thermo Scientific Qexactive Plus:** Mass spectrometer that permits analysis of protein post-translational modification, proteomics profiling
- **Malvern NanoSight NS300 instrument:** Measures microparticles (platelets), nanoparticles
- **Gnotobiotic Mouse Facility:** Enable microbiome studies using germ-free mice

Basic Science Core

Education and Support

Training

- Seminars
- Posters and formal training sessions
- Visits by technical experts to individual faculty labs and supported Scientific Working Groups

Voucher Program

CFAR offers funding vouchers for direct application to instrumentation that best suits research needs.

Vouchers are competitively awarded and can provide up to \$4,000 in user fees.

Basic Science Core

Selected 2015-2016 Activities

Intra-CFAR Synergy Intensified

- Core D and CNS/Aging SWG supported the establishment of a new gnotobiotic mouse facility – yielding facility ownership for the next five years.
- Core D (with Core A and CNS/Aging SWG) coordinated efforts to purchase the NanoSight instrument that supports six HIV/AIDS research grants.

Core Services Enhanced

- Core D leveraged institutional funding towards purchase of (1) a BD Biosciences Accuri C6 and (2) a Nikon Ti-E Fluorescent Microscope to facilitate preliminary experiments at low cost and ease of use.

Contribution to New Scientific Breakthroughs in Cure Research

- Resources enabled Dr. Jian Zhu to study how HIV reservoirs are established. This resulted in one highly cited publication and two new R01 funding to JZ (R01 DE025447; R01 GM117838).

Basic Sciences Core

Future Plans for next 12 months

The Core plans to organize following complimentary activities:

- **Microbiome Round Table** to highlight Gnotobiotic Mouse Facility and its utility for HIV/AIDS research – Ken Cadwell of NYU will be an external speaker.
- **Pathways Discovery / HTS Mini Symposium** will be sponsored to highlight Pathway Discovery Resources, as well as to showcase HTS-related research at the UR – Sara Cherry from U Penn will be the keynote speaker.
- **Human Immune Activation Markers Monitoring Service.** We will assess the feasibility of a service that will assist behavioral, cardio/cerebral vascular, investigators in monitoring various serum analytes and blood immune cell types as part of their clinical research efforts.

Basic Science Core

Summary of Usage

Core D Users 2015-2016

NIH Funding Category		Number
NIH AIDS PI	1. NIH Independent Investigators (AIDS)	17
	2. NIH Independent Investigators (non-AIDS)	13
Bring into AIDS	3. NIH New Investigators	5
AIDS-research Pipeline	4. CFAR Users with no prior non-CFAR NIH funding	2
<u>TOTAL</u>		<u>37</u>

Basic Science Core

Key Contacts:

Sanjay Maggirwar, Core Director
James Kobie, Associate Core Director
Laura Enders, Program Administrator

Website

<http://www.urmc.rochester.edu/center-for-aids-research/services-cores/basic-sciences.aspx>

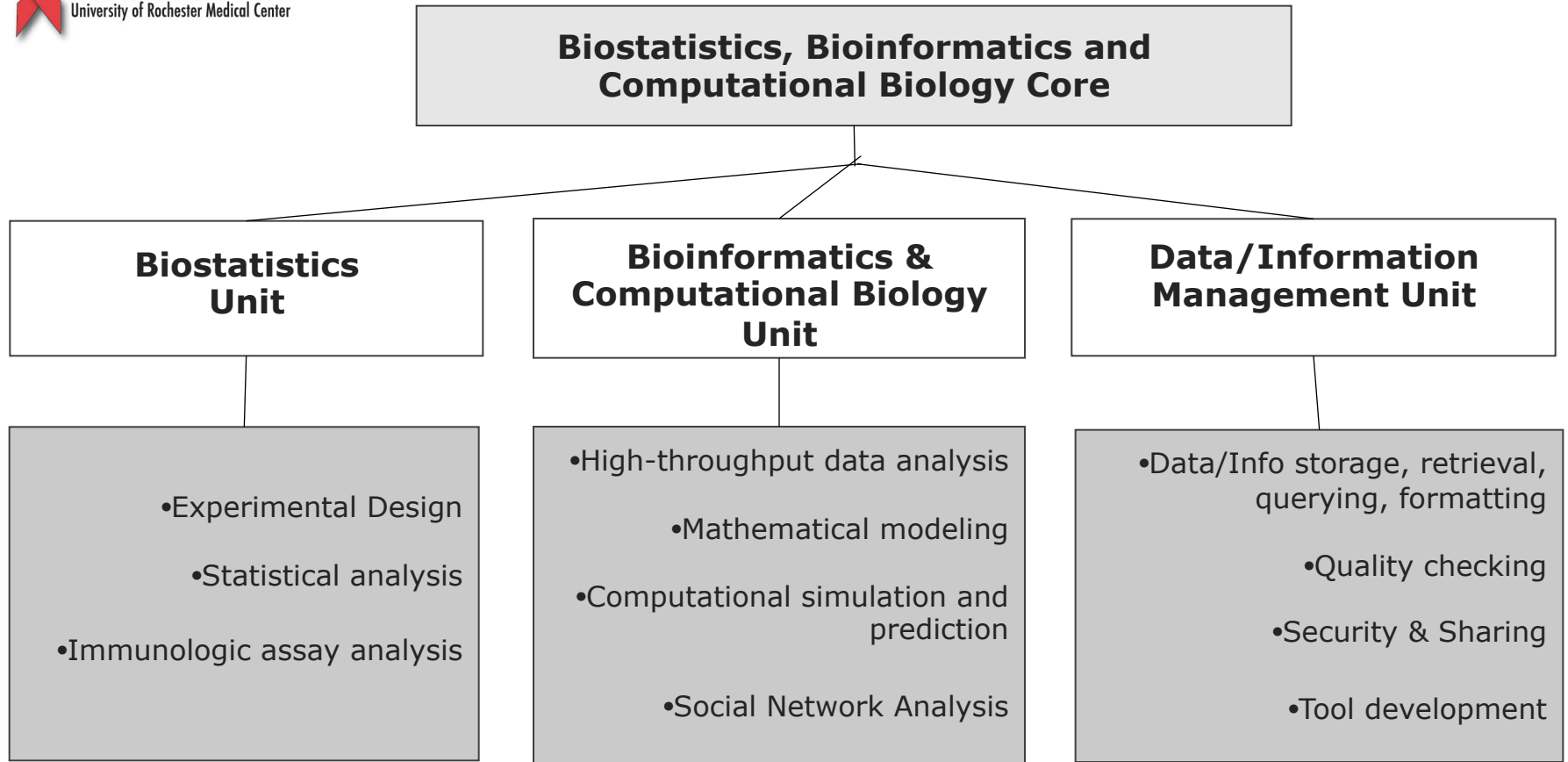
Biostatistics, Bioinformatics and Computational Biology Core

Brent Johnson, PhD

BBCB Core Mission

- To provide standard and novel statistical, bioinformatics and computational biology support to HIV/AIDS investigators
- Support HIV/AIDS investigators through:
 - Expertise in study design and data analysis
 - Co-author manuscripts and abstracts
 - Co-author grant applications
- Provide training
 - Seminars
 - Individual consultations

BBCB Core Overview



BBCB Services

- Assistance with grant applications
- Designing controlled experiments and observational studies, including sample size and power calculations
- Statistical analysis of experimental and observational data
- Lab, clinical and translational data management support
- Reproducibility, data sharing and dissemination to meet NIH requirements

BBCB Services (cont.)

- Education
 - HIV Dynamics Symposia in 2015
 - TBA Biostatistics Symposia in late 2016
- Training in basic tools and software
- Exemplify BBCB expertise in state-of-the-art tools for modern research problems in HIV/AIDS
- Facilitate connections with CIRC, Data Science Group, where appropriate
- Promote efficient use of Core E resources

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BBCB Core Service Policy

- Free services for:
 - CFAR pilot awards
 - Grant preparation (~10 hrs for junior PI, ~5 hrs for senior PI)
- Junior PIs may access more resources with approval from leadership
- Charge-back mechanism: \$180/hr and % effort support for grant proposals
- Co-I on grants, Co-authorship on manuscripts

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BBCB Core

Selected 2015-2016 Activities

Ongoing Collaborative Research

- Drs. Schifitto and Qiu on vascular aging and CNS injuries: 1 R01 renewal, 3 papers.
- Drs. Shah, Luque, Yang on hearing impairment, limited mobility in aging cohort: 3 papers

Successful Grant Application

- R34DA041240-01 (PI: Morse, Co-I: Yang)
- R01NS094037-01 (PI: Birbeck, Co-I: Johnson, Dewhurst), Cohort of HIV-Associated Seizures and Epilepsy in Zambia

Promotion of UR CFAR in Peer-reviewed Publications

- 4 methodology publications
- 12 collaborative publications

Administrative Personnel Changes 2015-2016

	2014-2015	2015-2016
Director	H. Wu	R. Strawderman
Assoc. Dir.	H. Miao	B. Johnson
Biostat. Unit Leader	X. Qiu	T. Wu
BCB Unit Leader	X. Qiu	X. Qiu
Data Core	J. Holden-Wiltse	J. Holden-Wiltse

BBCB Core

Changes in Expertise 2015-2016

Outgoing 2014-2015

- (H. Wu) Modeling HIV dynamics, computational immunology
- (H. Miao) Bioinformatics, High-throughput data analyses

Current expertise 2015-2016

- Clinical trials, survival & longitudinal data analysis (Strawderman, Johnson, Wu)
- Observational data analyses, causal inference (Johnson, Strawderman)
- Bioinformatics (Qiu, Wu)
- High-throughput, high-dimensional data analysis (Wu, Qiu)
- Computational immunology, network analysis (Thakar)
- Data core (Holden-Wiltse)

BBCB Core

Future Plans next 12 months

Continued Support for Junior Investigators

- Dr. Diane Morse (w/ Yang)
- Dr. James Kobie (w/ Wu, Holden-Wiltse, Thakar)
- Dr. Krupa Shah (w/ Qiu, Yang)

Bridging support for grant renewal

- Statistics data analysis support to fill the gap between the grant end and renewal

New Methodology Development

- New collaboration among Johnson, Strawderman, Senn for evaluating routine HIV testing from survey data
- New methods in epilepsy-HIV co-morbidity (Birbeck, Qiu, Johnson)

Education & Training

- Proposed BBCB symposia in Fall 2016

BBCB Core

Future Plans for Reapplication

- **Strengthen outreach to UR investigators**
 - Johnson connecting with SON faculty
 - Need to re-establish lab meetings in the medical center
- **Submit methodological grant applications**
 - Johnson to submit R01 in 9/2016
 - Thakar pilot into NIH Rxx submission

BBCB Core

Statistics and Summary of Usage

22 collaborative projects (1/1/2015 – 1/31/2016)

- 9 NIH or grant applications

16 co-authored papers in peer-reviewed journals

- 4 methodological
- 12 collaborative

3+ new projects post 2/1/2016

- incl. 2 new CFAR pilots

BBCB Core

Key Contacts:

Robert Strawderman ScD, Director
Brent Johnson, PhD, Associate Director

Website

<http://www.urmc.rochester.edu/center-for-aids-research/services-cores/biomathematical-modeling-biostatistics-bioinformat.aspx>

Community Activities

Mike Keefer, MD

CFAR Research Opportunities in Rochester

Opportunities

1. NIAID AIDS Clinical Trials Networks (ACTG and HVTN)
2. Collaboration with Monroe County Health Dept
3. Outreach to the African-American/Latino faith communities



NIH/NIAID HIV/AIDS Clinical Trials Networks Leadership

AIDS Clinical Trials Group (ACTG)

PI: Daniel R. Kuritzkes, M.D.; Brigham and Women's Hospital, Boston, MA

International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT)

PI: Sharon Nachman, MD; Johns Hopkins Hospital School of Medicine, Baltimore, MD

HIV Prevention Trials Network (HPTN)

PI: Wafaa El-Sadr, M.D., M.P.H., and Myron Cohen, M.D.; FHI 360, Durham, NC

HIV Vaccine Trials Network (HVTN)

PI: Lawrence Corey, M.D., Glenda Gray, M.B.B.Ch., and Scott Hammer, M.D.; The Fred Hutchinson Cancer Research Center, Seattle, WA

Microbicide Trials Network (MTN)

PI: Sharon L. Hillier, Ph.D., and Ian Michael McGowan, M.D., Ph.D.; Magee-Womens Research Institute and Foundation, Pittsburgh, PA



UR HIV/AIDS Clinical Trials Unit: Overview

Leadership (Multi-PI): Dr. Michael Keefer [Amneris Luque]

1. UR ACTG CRS: Site Leader- [TBD]

Key investigators- Giovanni Schifitto, MD; Gene Morse, Pharm D (UB); Andy Talal, MD (UB)

Jr investigators- Charles Venuto, PhD; Qin Ma, PhD (UB)

2. UR HVTN CRS: Site Leader- Dr. Michael Keefer

Key investigators- M Hay, MD; J Kobie, PhD

Junior investigators- L Nelson, PhD; A Alio PhD; J Thakar PhD; J Cullen, PhD

CTU-CFAR Synergy

Case Study: James Kobie, Ph.D.

Outcomes:

- Received a **CHAVI/HVTN Early Stage Investigator Award (2010-12)** with CFAR mentoring
- *Promoted to Assistant Professor in IDD at UR; provided independent start-up support (2012)*
- Joined HVTN CRS as a co-investigator (2012)
- Received an **HVTN Initiatives Program (HIP) award (2012-13)** with CFAR mentoring
- Member, HVTN Concept Working Group (2014)
- **Co-chair, HVTN protocol under development** (B cell lineage: B Haynes, Duke/CHAVI) (2014)
- Co-investigator, Mosmann HVTN Exploratory Study (pending, 2016)

- ***NIH R01 and R21, both directly related to the HVTN scientific agenda (2015)***
- *Co-chair, Office of AIDS Research Trans-NIH FY17 Extramural Planning Committee*
- *Associate Co-Director CFAR Core B (Developmental) – Jr. Faculty Peer Mentoring Group*
- *Associate Director Core D (Basic Science)*

CTU-CFAR Synergy

Case Study: Amina Alio, Ph.D.

Outcomes:

- Joined the HVTN CRS as a co-investigator (via a minority supplement in 2012-13)
- Took over co-leadership of CTU/HVTN 'Faith Initiative' CBPR projects (2012-present)
- Member, HANC Legacy Project Working Group (2012-present)
- Member, HVTN Social and Behavioral Working Group (2012-2015)
- Co-leader of the Research Committee of the newly established 'Inter-CFAR Faith Initiative Working Group' (2016)

CTU-CFAR Synergy

Case Study: LaRon E. Nelson, PhD, RN, FNP

Outcomes:

- 2015 - Became a **CTU/HVTN co-investigator (Site PI for HVTN 704/HPTN 085; 'Antibody-mediated protection' [AMP] phase IIB study)**
- 2015 - **Member, HVTN 704/HPTN 085 Protocol Team and Community Engagement Work Group**
- 2015 - Advocating for expansion of HPTN Black Caucus into HVTN
- 2015 - Member of the leadership team for the Faith Initiative Cross-CFAR Working Group
- 2016 - **Co-investigator on NIAID multi-site social/behavioral science supplement to AMP Study HVTN 704/HPTN085**
- 2016 – *Identified by White House/NIMH as global thought leader on HIV stigma research with MSM and invited to present research at White House meeting on stigma research*
- 2016 - *Awarded NIMH R21 Exploring Stigmas and Delays in HIV Diagnosis, Linkage and Retention among MSM in Ghana*
- 2016 - *Awarded 5-Year Ontario HIV Treatment Network Research Chair in HIV Program Science to lead PrEP implementation research with African, Black & Caribbean communities in Toronto*

CTU-CFAR Synergy

Case Study: Juilee Thakar, PhD

Outcomes:

- *Became CFAR member in November 2015*
- Became a **CTU/HVTN co-investigator** 2016 (attending HVTN full group meeting in May 2016)
- **HVTN Initiatives Program (HIP) award**, June 2016: “Assessing impact of vaccine regimen on vaccine-induced antibody durability” (\$74k); collaboration with Kelly Seaton, PhD at Duke Vaccine Center
- CFAR facilitated **HVTN collaboration** with Erica Andersen-Nissen, Lamar Fleming and Julie McElarth to investigate transcriptional changes in PBMCs upon HIV vaccination on pre-vaccination day and days 1, 3 and 7
- *CFAR facilitated interactions with Dr. Ronald Swanstrom to initiate cross-CFAR data integration and analysis has led to initial discussions to plan a cross-CFAR workshop.*
- Data analysis for CFAR-CTU investigators (James Kobie and Krupa Shah) as a member of core E

CTU-CFAR Synergy

Case Study: John Cullen, Ph.D.

Outcomes:

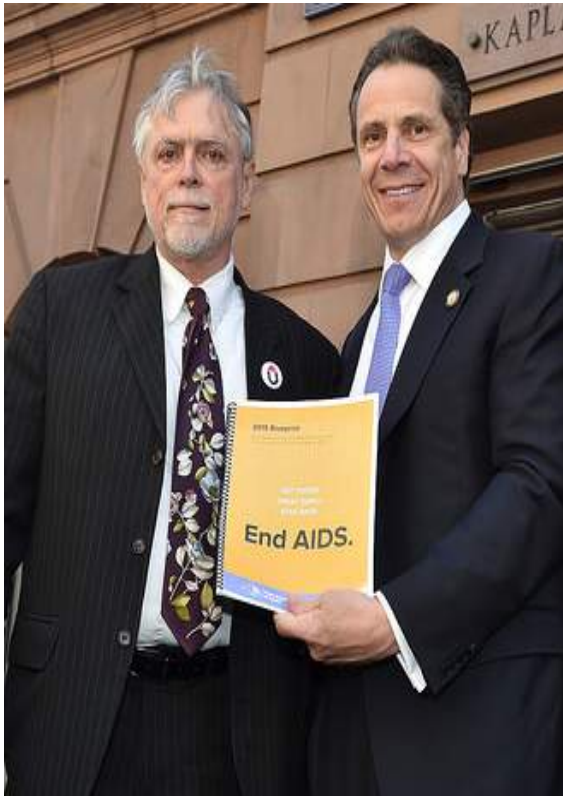
- *Joined the Susan B. Anthony Center (SBAC) in 2014 to work with vulnerable/at-risk populations*
- *Joined the CTU/HVTN team as a co-investigator 2015 (for HVTN 704/HPTN 085; ‘Antibody-mediated protection’ [AMP] phase IIB study)*
- **HVTN Initiatives Program (HIP) award, June 2016: “Exploring the use of an e-screen tool to meet the needs of potential HVTN study participants in AMP” (\$73k)**
- *Promoted to Assistant Director of UR Susan B. Anthony Center, July 2016*
- **Partnered with Psych research team to develop new recruitment method (text messaging) or HVTN 704/HPTN 085**

Collaboration with the Monroe County Health Department

New York State's 'End the Epidemic 2020' Initiative

April 29, 2015

We must add AIDS to the list of diseases conquered by our society, and today we are saying we can, we must and we will end this epidemic.
~Governor Cuomo



MEDICINE *of* THE HIGHEST ORDER





Monroe County Partnering to End the Epidemic (MCPEtE)

Mission:

To end the HIV/AIDS epidemic in Monroe County by 2020 through the development of county-wide partnerships of HIV clinical and non-clinical service providers, consumers and networks committed to specific objectives of the New York State 'End the Epidemic' (ETE) initiative.

Core Team: MCDPH, Jordan Health, Catholic Charities, Action for a Better Community, Trillium Health

Technical Advisor: NYSDOH AIDS Institute

MCPEtE Partners:

Clinical- UPMC affiliates (CFAR, HVTN CRS, SMH AIDS Center, National Center for Deaf Health Research, Women's Initiative Supporting Health), Huther-Doyle, Rochester Regional Health System, Unity Infectious Disease

Non-Clinical- Consumers, MCDPH, NYSDOH, Partners Advocating for Community Change (PACC), Black Leadership Commission on AIDS (BLCA)

Consumer Advisory Council:

Utilizing RATFA's (Rochester Area Task Force on AIDS) CAC.

MCPEtE Objectives

1. Increase the number of newly diagnosed/identified HIV+ patients in Monroe County by **20%** via existing testing programs, targeted care programs, ERs, Primary Care Providers and Urgent Care Centers
2. 100% of newly diagnosed will be linked to care within 3 business days
3. Increase patient retention in medical care from **88%** to **95%** among Monroe County providers.
4. Achieve patient re-engagement of 95% based on individuals who have fallen out of care (i.e., >6 months without an HIV medical visit or Viral Load).
5. Increase VL suppression rate from 83% to 95% across Monroe County Providers.
6. Increase linkage of high risk negative client to PrEP/PEP provider.

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Objectives (cont.)

7. Increase linkage to HIV prevention and treatment research among population groups with disparate rates of HIV infection and poor virologic control based on Monroe County HIV/STD epi data.

- Effort lead by LaRon Nelson and Catherine Bunce
- CFAR-sponsored MCPetE Symposium planned for Sept 30, 2016
 - MCPetE to identify top 3-4 barriers encountered to reaching goals
 - CFAR identify strategies to work on the barriers
 - Possible CFAR research contributions:
 - Martin Zand (big data)
 - Kate Cerulli/John Cullen (Promote Health)
 - Amina Alio (Faith community engagement)
 - Other

Outreach to the ‘Faith Community’ to engage heavily impacted communities in HIV prevention research

Rationale for engaging 'faith communities' via a FIWG

- Religious/spiritual belief systems have a major impact on individual/community actions that impact health
- Religious institutions hold a central place in communities that are disproportionately impacted by HIV/AIDS in the US (African-Americans, Latinos) and around the world
- **A strong evidence base for HIV/AIDS-related work in faith communities is needed to inform 'best-practices' and public health policies**

Inter-CFAR 'Faith Initiative' Working Group

Definition of 'Faith Community'- the predominant faith traditions (organized religion/spirituality) that provide the context to life in communities heavily impacted by HIV/AIDS around the world

Mission- bring together investigators to examine and conduct research to develop interventions in HIV/AIDS among high-risk and vulnerable populations, including women, MSM, LGBTQI, and sex workers, especially from minority groups in the US and from populations from sub-Saharan Africa

Ancillary Benefits

- Opportunity to establish/strengthen relationships (trust) between academic-based researchers and influential leaders in the African-American community
- Opportunity to increase diversity among CFAR investigator teams
- Opportunity to broaden HIV-related research within CFAR institutions (engage Departments of Sociology, Religion/Theology, Anthropology, etc)
- Opportunity to add value to the efforts of other existing Inter-CFAR Working Groups (Social/Behavioral Research Network, Continuum of Care, Incarceration, Women's, 'HIV in the South', etc)

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FIWG: Membership

CFAR Faculty/Researchers:

Amy Nunn MS, ScD (Tufts/Lifespan/Brown CFAR; Research Committee chair)

Amina Alio PhD (U Roch CFAR; co-chair of Research Committee)

LaRon Nelson PhD (U Roch CFAR)

Robert Miller PhD (U Roch CFAR/U Albany)

Pam Payne-Foster PhD (UAB CFAR/UA Tusc)

Robin Gaines-Lanzi PhD, MPH (UAB CFAR)

Paula Frew PhD (Emory CFAR)

John Blevins ThD (Emory CFAR/Rollins)

Mimi Kiser DMin, MPH (Emory CFAR/Rollins)

Billy Jeffries PhD (Emory CFAR/CDC)

Lauren Brinkley-Rubinstein PhD (UNC CFAR)

Sharon Parker PhD, MSW (UNC CFAR; NCA&T)

Jennifer Stewart PhD, RN (JHU CFAR)

Tonia Poteat PhD, MPH (JHU CFAR)

Yusuf Ransome MPH, DrPH (Harvard CFAR)

Organizational Liaisons/Community:

Michael Keefer MD (UR CFAR)

Cathy Bunce RN, MS (UR CFAR)

Rev Edwin Sanders (Nashville, TN)

David Haas MD (Tennessee CFAR)

Steve Wakefield (HVTN/HANC/U Wash CAB)

Stephaun Wallace (NCCC; HANC/U Wash CAB)

Gladys Thomas (NCCC; Penn CAB)

Kelly Ross-Davis (NCCC; UAB CAB)

Tony Walker (UAB CAB)

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Progress so far

Initial organizational meeting in conjunction with the Emory CFAR “HIV in the South” workshop in March 2016

- Developed a draft research agenda that fills gaps, aims to leverage opportunities for funding
- Follow-up meeting held with CFAR leadership/funders at HVTN meeting in DC in May 2016
 - Attended by NIAID (A Namkung, C Beaubien), NIMH (M Stirratt), NCI (B Read-Connole), Fogarty (J McDermott), OAR (S Carrington-Lawrence, B Mathieson)
- Forming ‘clusters’ that focus on different target groups
 - (e.g. MSM/trans; reducing stigma in mainstream African-American/Latino congregations; work in sub-Saharan Africa/traditional belief systems; etc.)₁₈₈

Next steps

- National Conference in Rochester (April 2017; via UR CFAR supplement) to assemble full membership for the first time
- Delineate areas of expertise and interests among members (website development; ‘Craigslist for collaborators’)
- Develop a Speaker’s Bureau to present on related topics at national/international meetings (CFAR Social & Behavioral Research Network annual meeting in Miami in October)
- Meet at CFAR Annual Meeting with NCCC leadership in Boston in November

Links With Industry

Mike Keefer, MD

Wavodyne Therapeutics



Handy Gelbard, MD, PhD

Background

- operating as a small biotech start-up in Rochester, led by a CEO (Jim New, PhD, MBA) with experience as a medicinal chemist, then global mergers and acquisitions for big pharma, Wavodyne is his 5th start-up since 2002.

History/ Timeline

- Incorporated in Delaware in 02/15, funded by private capital raise(s).
- Wavodyne has completed ~50% of IND-enabling studies on URM-099 through a non-U.S. CRO (Pharmaron)

Mission

- To advance URM-099 to the FDA as a first-in-class treatment for cognitive impairment

How fits with CFAR

- HAND is characterized by cognitive impairment

Current projects/products

- URM-099; genotoxicity studies ongoing

Future projects/products

- Continue IND-enabling studies
- Prepare for IND filing

Other info

- Continue academic work with UNMC to nanoformulate URM-099 with GSK integrase inhibitors

Adarza Biosystems



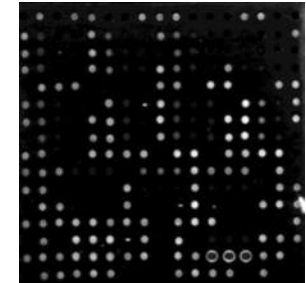
Ben Miller, PhD

Background

- Founded in 2008 based on label-free multiplex sensor technology (Arrayed Imaging Reflectometry) developed at U of R (12 patents licensed).

History/Timeline

- Completed first tranche of B-financing round in June
- Currently 20 full time employees
- Locations in Rochester (R&D) and St. Louis (Manufacturing)
- Board of directors includes David Smoller (past CSO, Sigma), Heiner Dreismann (past CEO, Roche Molecular), Andrew Jay (Managing partner, Siemens Venture); advisory board includes Dean Simcoe (VP, Siemens Healthcare); Rick Ryan (past VP, Millipore)



Mission

- *Deliver simple, sensitive, multiplex biodetection (protein, peptide, small molecule, etc.) products that provide more information per sample than currently possible*

How fits with CFAR

- Platform technology for developing new HIV-relevant research tools and diagnostics 195

Current projects/products: company internal

- Company focus: introduction of a 29-plex cytokine and inflammatory biomarker array in Q4 2016
- Will subsequently be extended to 100+ plex
- Projects underway in antigen arrays, drug screening, hybrid small molecule / protein detection

Current related projects at URMIC:

- Multiplex analysis of small molecule – RNA binding (HIV frameshift RNA)
- Antigen and antibody arrays for viral disease (major focus on influenza, but analogous arrays possible for HIV)
- Preliminary collaborative work with Tim Mosmann, Sally Quataert on HIV cure (biomarker arrays for identifying latent HIV infection)

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Presented by Mike Keefer, MD

Background

- NIH small business research grants (3) to develop diagnostics to detect and quantify cART/HAART patient latent HIV reservoirs
- Janet Huie (PI); Michael Keefer (UR PI); Emily Cosimano (AIDS Clinic); Christopher Lane (CTPL); Harris Gelbard (Consult); CFAR

History/Timeline

- 2015-2017 Grants; first samples collected/processed in early 2016
- NIH Phase II grant submission planned for 9/6/16

Mission

- Support HIV cure research

How fits with CFAR

- Cure SWG, RNA Biology SWG

Technology

- Quantitative autoligation detection reaction to detect multiply spliced HIV mRNA using fluorogenic probes

Current projects/products

- Latent HIV POC diagnostic for blood & oral samples
- Quantitative HIV RNA standard for latent HIV diagnostics

Future projects/products

- Phase II preclinical studies for latent HIV diagnostics (oral, blood)
- Phase II preclinical studies for latent HIV RNA standard

Other info

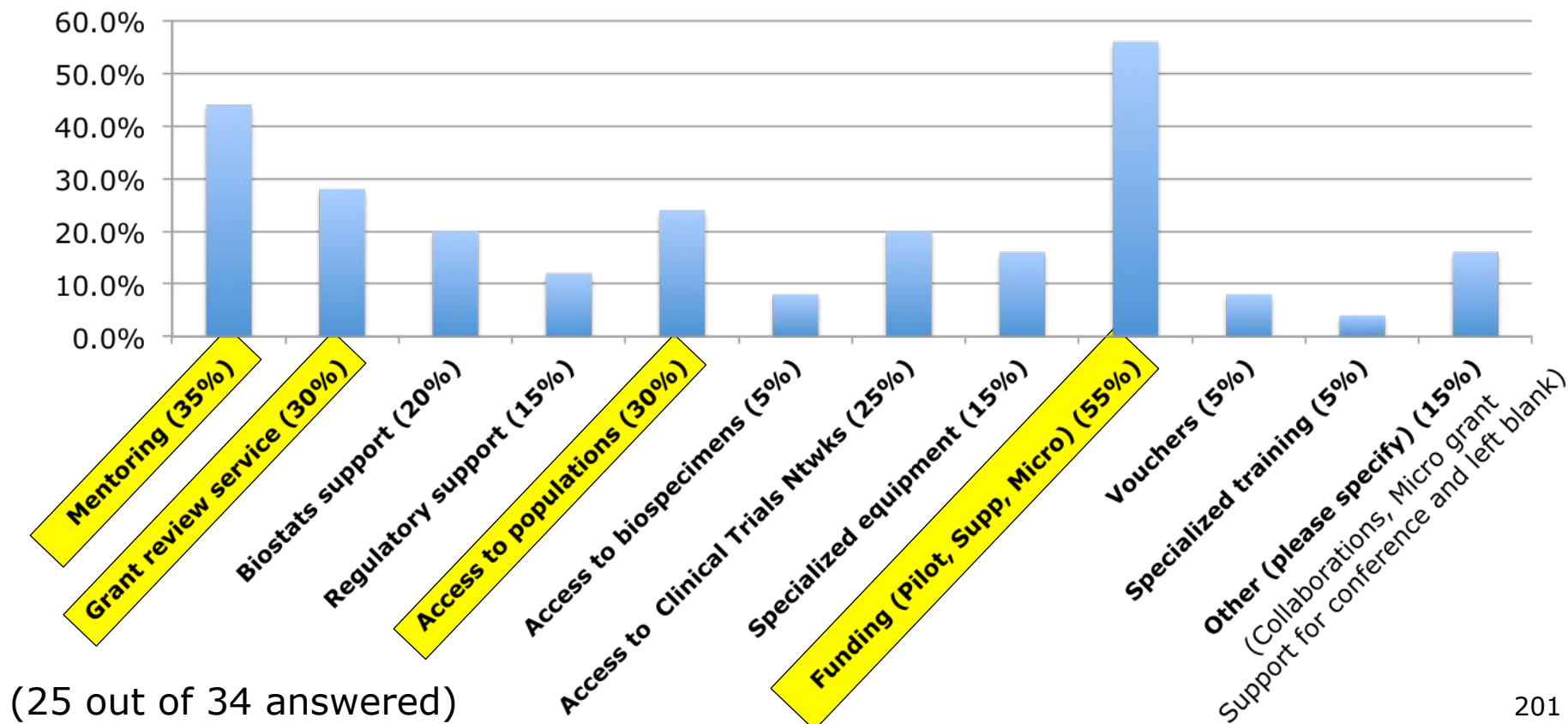
- Developing FACS application to isolate latent HIV+ cells

Selected Survey Results and Future Plans

Steve Dewhurst, PhD

Service Utilization

- 75.8% used at least one CFAR services within the last year



Topics of Interest for Events & Symposia

Topics identified for future events:

Drug Discovery (11), Vaccine Research (10), Behavioral Interventions (8), International Projects (7), PrEP (6), Use of Technology in interventions (3)

Topics for future areas of research (free text):

Cardiovascular (4), Stress, Trauma and Vulnerable Populations (4), Cure (4), Optics and Imaging (4), Microbiome (3), Co-morbidities/Co-infections (2)

53.1% interested in research outside of US

Countries of Interest for international work:

South Africa (3), Africa (4), Asia (2)

What support/resources would help you in international work?

Pilot grants that support collaborative projects with researchers outside US (3), **Specimen** Acquisition (2)

Pilot Program

Suggestions for Pilot program (free text):

- Rolling deadlines throughout the year (2)
- Longer lead time (2)
- Reduce/remove restrictions on eligibility (2)

Pilot Program

Ideas to attract largest number of high quality applications:

- **Improve outreach to faculty (57%),**
- **Strengthen mentoring and Junior Faculty peer mentoring (32%)**

Other suggestions:

- **Expand the scope of applications considered (2)**
- **Better support senior investigators (3)**

Grant Review Services

How do we more efficiently encourage use of grant Review Services?

- **Better Advertise (6)**

Career Development of Junior Faculty

What should CFAR do (do more of) to support the career development of Junior Faculty?

- **Grant writing and Grant Review/Discussion (6)**

Core C Usage

Have you used any of the following CFAR Core Services in the past year (through the Clinical and Translational Sciences Core)? If yes to any, please indicate how the service(s) can be improved.

Answer Options	Response Percent
Study Coordination/Enrollment/Regulatory Support	43.8%
Consultation on Design, Analysis, Implementation or Conduct of Studies Involving Human Subjects (including biological samples or existing data)	12.5%
Access to Patient Data or Samples	31.3%
Support with International Studies or Collaborations	6.3%
Study Recruitment and/or Community Outreach and Education	37.5%
Access to Hard-to-Reach Populations	25.0%
Grant application planning or preparation in relation to clinical projects or projects that utilize human subjects or specimens.	37.5%
Other Types of Services Not Listed (please list) Please also indicate here how any of the above services can be improved.	12.5%

Human Subjects

Do you currently use human subjects or human samples/specimens in your research?

- Yes (79%), No (21%)

If you don't currently use human subjects or human samples/specimens in your research, would you like to?

- Yes (12%), No (88%)

Human Subjects

- **Have you ever written a UR IRB (RSRB) protocol before?**
Yes (67%), No (33%)
- **Are you planning to write a UR IRB (RSRB) protocol in the near future?**
Yes (and I never written an RSRB protocol before) (9%)
Yes (and I have previously written an RSRB protocol) (52%)
No (39%)
- **If you are planning to write an RSRB protocol in the near future, would you like assistance in writing that RSRB protocol?**
Yes (and I never written an RSRB protocol before) (13%)
Yes (and I have previously written an RSRB protocol) (26%)
No (61%)

Core D Usage

Have you used any of the following CFAR Core Services in the past year (through the Basic Sciences Core)? If yes to any, please indicate how the service(s) can be improved.

Answer Options	Response Percent
Kintek RQF-3 Rapid Quench-Flow Instrument	7.7%
Illumina Hi-Seq 2500 or Mi-Seq Services	38.5%
Structural Biology Supported Assistance and Access to: BIAcore T100, Bruker AXS X8 Prospector X-ray source, Mosquito Robot	23.1%
Imaging and Mass Spectrometry: CyTOF or Amnis ImageStream GenX	38.5%
Customized Protein Production	7.7%
AKTA Pure Chromatography System	7.7%
High Throughput Screening Core	23.1%
Voucher Program (CFAR awarded funds for subsidizing the cost of tests or use of machines)	15.4%
Education or Training (training or education related to the use of specific scientific equipment)	0.0%
Other Types of Services Not Listed (please list) Please also indicate here how any of the above services can be improved.	23.1%

Core D Usage

Which of the following new Basic Science Core Resources would you potentially use?

- **NanoSight NS300 Instrument.** Allows high resolution characterization of extracellular nanoparticles of size 10-2000nm; can analyze protein aggregation, viscosity and zeta potential **(17%)**
- **Gnotobiotic Mouse Core Facility.** Provides germ-free mice that can be colonized with bacterial flora of interest, for microbiome-related studies **(10%)**
- **I would not use either one (73%)**

Core E Usage

Have you used any of the following CFAR Core Services in the past year (through the Biostatistics, Bioinformatics and Computational Biology Core)? If yes to any, please indicate how the service(s) can be improved.

Answer Options	Response Percent
Biostatistics support for Design and Analysis of HIV/AIDS-related Experiments, Clinical Studies, Prevention/Behavior Studies and Epidemiological and Translational Studies	100.0%
Mathematical Modeling Support to further HIV/AIDS-related Research and to Expand Existing Modeling Efforts to Investigate Dynamical Biological Processes	20.0%
Bioinformatics, Computational Biology and Biocomputing Tools and Algorithms (e.g., RNAseq/proteomics data processing and analysis, sequence analysis, gene regulatory network, signaling pathway, metabolic network, receptor/ligand binding)	20.0%
Translational Data Management and Informatics Services Including Development of Databases and Data Management Tools	10.0%
Other Services Not Listed (please list) Please also indicate here how any of the above services can be improved.	20.0%

Core E Usage

If yes to any, please indicate how the service(s) can be improved?

- Less expensive (2)

Core E Usage

If you do not use this Core, whom do you work with for your biostatistical and/or bioinformatics and/or data management and analysis needs?

Answer Options	Response Percent
Do it by yourself	44.0%
Work with other statisticians and bioinformaticians at UR	40.0%
Work with other statisticians and bioinformaticians outside UR	16.0%
I do not have biostatistical and/or bioinformatics and/or data management and analysis needs	16.0%
Other (please specify) (see below)	4.0%

Core E Usage

Please suggest at least one idea (more welcome) for NEW or IMPROVED services or support that would help advance your research.

- Outreach and training for investigators/users (2)

Future Plans

Future Plans

Plans for the Coming Year: Broad Needs

- **Faculty Recruitment.** Focus on ID Division in particular
 - need to fill ACTG leadership position
- **Start Writing the Renewal!** Define our narrative
 - ✓ intimate scale (mentoring)
 - ✓ uniquely collaborative environment with few silos
 - ✓ some local “jewels”/priorities that the CFAR must leverage.

Future Plans

Plans for the Coming Year: Defining our Identity (1)

- **SWGs.** Select 1-2 new SWGs (*HIV Associated Cardiovascular and Cerebrovascular Disease; HIV Cure*) - and align services, pilots to support these. Support a “Pre-SWG” in *Stress, Trauma and Vulnerable Populations*
- **CTU.** Very synergistic; CFAR provides scientific support & drives local research agenda; *national opportunities also.*
- **McPETE (Monroe County Partnering to End the Epidemic).** Local health initiative; UR CFAR can drive the scientific agenda; *should leverage this.*
- **National Role.** Inter-CFAR Faith Initiative Working Group.

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Future Plans

Plans for the Coming Year: Defining our Identity (2)

- **Data Science.** \$100M investment – computing, recruitment, MS programs (capstone projects).
- **PROMIS.** >2 million recorded patient encounters; data populates the EMR; implementation in AIDS Clinic and Trillium will create research opportunities.
- **Care Delivery & Implementation Science.** UR owns its hospitals & system is fully integrated under a single CEO/Dean. Creates great research opportunities.

Future Plans

Plans for the Coming Year: Defining our Identity (3)

- **AIM Photonics.** Unique asset with a mandate to produce new photonic devices. Creates opportunities re. late-stage development devices & detection, and is a point of connection to the Department of Defense and industry. *UR is the only clinical system (AHC) in the network; need to leverage this. Also need to continue to leverage UR Optics.*
- **National Center for Deaf Health Research.** Unique local asset; strong relationship w. Nat'l Technical Institute for the Deaf (NTID) at RIT. *Need to demonstrate some win(s) and define future strategy/niche.*

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