

Dialogue

2014 Volume I

James P. Wilmot Cancer Center | University of Rochester Medicine

Special Edition:
Cancer Research at Wilmot



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MEDICINE

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CANCER CENTER

Celebrating Science at Wilmot

“Why me?” is a question that crosses the minds of many people who cope with cancer.

Science offers tremendous perspective, because the truth is that cancer is an unfortunate

price for us living on earth. It's a complex disease of the cells, and having billions of cells leaves us vulnerable to molecular and genetic errors far beyond our control.

Science also provides great optimism – and in this special edition of *Dialogue* we're thrilled to share stories about how our world-class researchers are changing and improving patient care at the Wilmot Cancer Center.

You'll get a sense of the breadth and depth of our bench. For example, at one end of the spectrum, we investigate the link between our DNA and the response to treatment, how cancer spreads, and how to interrupt and stop metastasis. We study the use of genomic fingerprints to clarify a diagnosis or make treatment decisions,

and whether some FDA-approved drugs can be repurposed, skirting the long and expensive drug-discovery process. At the survivorship end of the spectrum, we are fortunate to have a renowned group with special interests in geriatrics, exercise to improve quality of life, and the toxicities of treatment.

With approximately 100 cancer investigators at the University of Rochester, we recently created four large research teams:

- **Hallmarks of Cancer** (biology)
- **Blood Cancers**
- **Solid Tumors**
- **Cancer Control & Survivorship**

The reorganization has truly been an exercise in team-building. Our initial action – to take inventory and discuss our

research portfolio – resulted in several new and vibrant collaborations. A specialist in bone cancer, for instance, discovered a potential partnership with a kidney cancer specialist; brain and breast cancer researchers began working together more closely, and laboratory scientists saw the importance of involving clinicians earlier in their projects, to ensure an outcome that enhances patient care.

As we reviewed our portfolio we were also reminded that we have unique strengths in Rochester worth celebrating and exploiting. Above all, our approach to studying how cancer arises is distinguished by a focus on shared features among many cancers, as opposed to single mutations specific to only one cancer type.



Jonathan W. Friedberg, M.D., M.M.Sc.
Director, James P. Wilmot Cancer Center



Hartmut "Hucky" Land, Ph.D.
Director of Research & Co-Director, James P. Wilmot Cancer Center

On the Cover

Michael R. O'Dell, B.S., Research Assistant (left) and Aram Hezel, M.D., Associate Professor and Vice Chief of Hematology/Oncology

photo by Matt Wittmeyer

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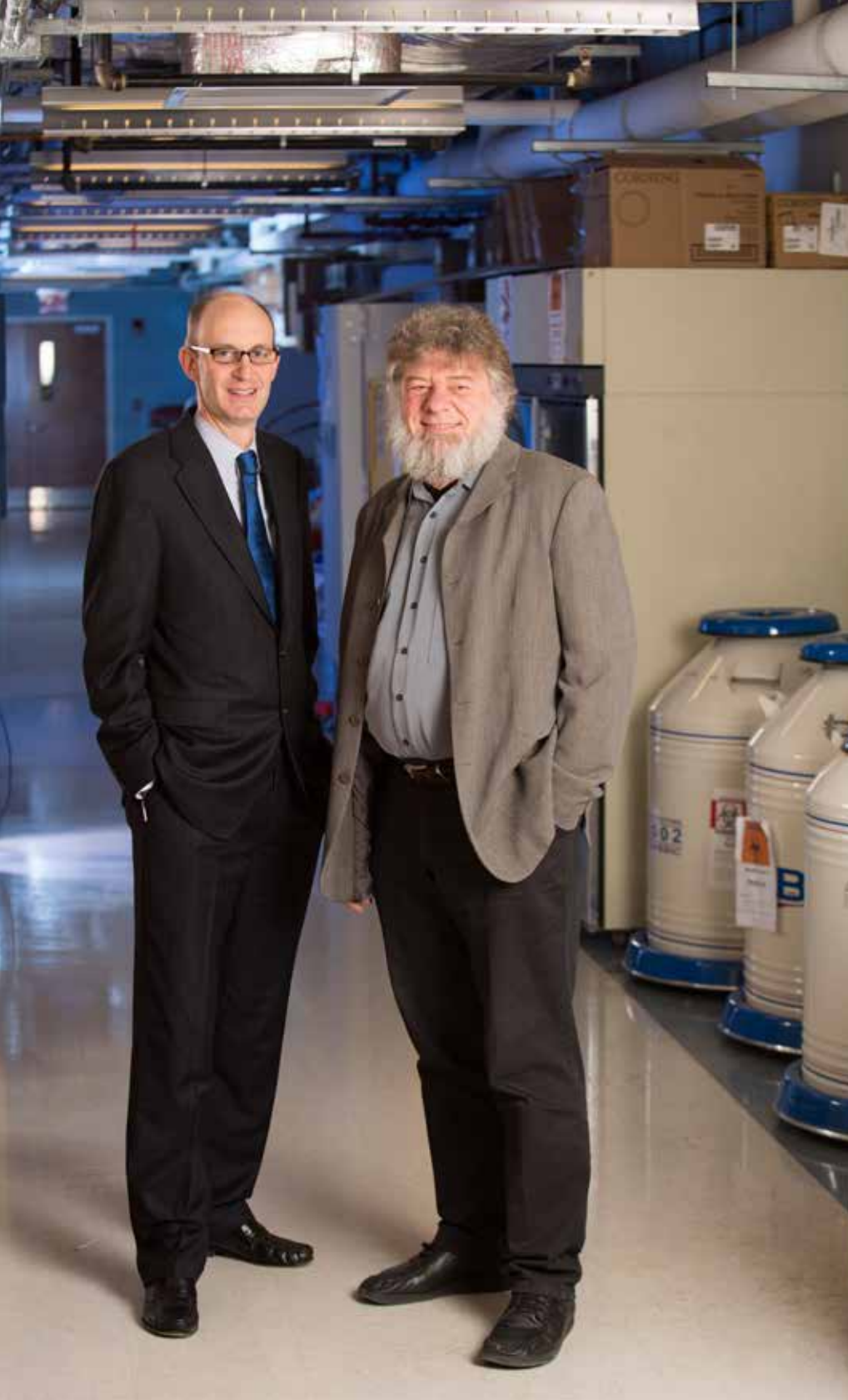
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This is an important difference to note – because with hundreds of subtypes of cancer, it's very hard to investigate and attack each mutation with the same fury. The single-mutation approach also leaves many patients out of luck, when a new targeted treatment eradicates the disease in only one group. By pinpointing fundamental shared properties common to many cancers, our goal is to broaden the impact of research by developing therapies that are relevant to many more patients.

We're also celebrating a commitment to what has become known as "precision medicine." A buzzword in cancer research these days, precision medicine takes advantage of technology and an explosion in genomics data to resolve a difficult diagnosis, or predict the

course of the disease. However, collecting and knowing how to appropriately use the data to benefit patients requires tools, teamwork, and expertise – something that makes us unique in the region.

In this publication we're proud to showcase our rich history of collaboration among seasoned investigators, rising junior faculty, and hard-working, ambitious students, who all recognize that long gone are the days when one research lab could do it all. With support from the generous community of Rochester, we have fantastic opportunities on the horizon. Both of us are strongly committed to building upon this outstanding foundation with additional recruitments within our strategic focus areas.

**Jonathan W. Friedberg,
M.D., M.M.Sc.**

Hartmut "Hucky" Land, Ph.D.

“ In Rochester we’re committed to the science that will lead the way to the next generation of targeted cancer treatments and ultimately personalized cancer medicine. ” –Hartmut (Hucky) Land, Ph.D.



Wilmot Cancer Center Research: **Hallmarks of Cancer**

Connections between research labs and people in the community are fairly rare, but we're trying to change that. Why? Outside voices offer perspective, and push scientists to work quicker, smarter.

A recent encounter between Hartmut "Hucky" Land, the leader of our cancer research enterprise, and a friend who had been treated for cancer, reveals why these interactions can be so powerful: "Without research," the friend assured Land, "I would be dead today."

In fact, many people are reaping the life-saving benefits of targeted cancer therapies and other newer treatments with fewer side effects that have come down the pike in the last couple of decades. The problem, however, is that targeted drugs are highly specific and apply only to a limited number of cancers and, thus, a limited number of people.

Our goal—and the essence of our research program for the future—is to maintain the triumphs of targeted therapy while also broadening them, so that the next generation of personalized treatments reaches more people.

As the name suggests, currently available targeted drugs pinpoint specific mutated proteins in certain cancers. Conversely, our approach is to study entire gene networks that control the activity of many cancers.

As mediators, these gene networks are the underlying mechanism essential to the cancer cell's ability to survive, evade, grow, and metastasize. We believe that successful disruption of this wider network – a.k.a. the hallmarks of cancer – is the best route to stopping the disease.

Rochester scientists have already identified ample networks of potent mediators, and now we're trying to uniquely answer the question: How can we use the hallmarks of cancer to find new interventions?

Teams from across the campus are working tangentially on this question, including experts in biomedical genetics, optics, RNA biology, immunology, pathology, and medicine, to name a few.

New technology also permits us to mine and manage vast data—both homegrown information and shared, globally accessible databases—as we push into the future on this interesting path.

Wilmot scientists, for example, are using modern technology to study secondary properties of FDA-approved drugs like antibiotics to find out if they could be useful to treat lymphoma, brain cancer, and other malignancies. And in some cases scientists can match a cancer patient's genetic information to existing treatments for other cancers, offering fresh options.

When you've been touched by cancer, science can seem to unfold much too slowly. But each incremental step exposes new and unexpected possibilities that change the way we think, live, and make treatment decisions.

Thanks to research, many patients indeed have advantages that didn't exist 20 years ago—or even a few months ago in some cases. Our vision is to understand the hallmarks of cancer, so that no one is left out in the next stage.

COMMON CANCER TARGETS TEAM, from left to right: **Alison Frontier, Ph.D., Associate Professor; Mark Noble, Ph.D., Professor; Jianwen Que, B.Med., Ph.D., Assistant Professor; Lei Xu, Ph.D., Assistant Professor; Helene McMurray, Ph.D., Assistant Professor; Hartmut (Hucky) Land, Ph.D., Director of Research and Co-Director of the Wilmot Cancer Center; Joshua Munger, Ph.D., Associate Professor; Jiyong Zhao, Ph.D., Associate Professor; Aram Hezel, M.D., Associate Professor, Vice Chief, Division of Hematology and Oncology**



Cancer-Proof Creatures

Lynne E. Maquat, Ph.D.,

J. Lowell Orbison Endowed Chair and Professor, Department of Biochemistry and Biophysics, and Director of the Center for RNA Biology

Lynne Maquat has received one of the highest honors possible in research—election to the National Academy of Sciences. She was rewarded for her exceptional work in RNA biology, in which she investigates cellular pathways and clues to the molecular basis of human disease. She is considered the uncontested pioneer on the subject.

Many chemotherapy drugs (for example, doxorubicin, marketed as Doxil) work by damaging our DNA, and in doing so cause the death of rapidly dividing cancer cells. Her lab investigates a specific RNA quality-control pathway that forces cell death when cells are damaged. By studying this process of cell suicide, her team is gaining insight into why and how cancer patients respond to treatment.

The ultimate goal is to define molecular targets for new cancer treatments with lower adverse side effects.

The homely naked mole rat recently climbed to the big leagues of scientific visibility. In *Nature*, an international journal that publishes groundbreaking research, the husband-and-wife biology team of **Vera Gorbunova, Ph.D.**, and **Andrei Seluanov, Ph.D.**, reported that the rodent's tissues are rich with high molecular weight hyaluronan (HMW-HA)—a substance that affords cancer resistance. The team also identified the gene responsible for the overproduction of HMW-HA.

Hyaluronan aids in healing and keeps tissues supple. Currently it's used as an anti-wrinkle agent or to relieve

knee arthritis. The next step is to find out if HMW-HA could induce an anti-cancer response in the human body.

In addition, Gorbunova and Seluanov reported more details on why the subterranean creatures almost never get cancer as they age. In the *Proceedings of the National Academy of Sciences* the team suggests that the secret to mole rats' longevity is having virtually perfect proteins, a result of high-functioning ribosomes—the site within cells where proteins are created. Proteins with no abnormalities allow cells to age gracefully, proving that beauty is not just skin deep.





Developing new cancer drugs is an expensive process, taking an average of 14 years and yielding a high rate of failure, according to the National Institutes of Health. With renewed urgency, our “shots on goal” initiative is a strategy designed to bypass the bottlenecks and accelerate the pace of drug discovery.

Instead of starting from scratch, our scientists scout the Food and Drug Administration’s library of hundreds of approved cancer therapeutics and find ways to repurpose them. The FDA already has studied the drugs for safety and effectiveness, and yet many of these drugs have additional properties that, if investigated and applied properly, could be used to treat other diseases.

For example, **Mark Noble, Ph.D.**, who spearheads the project, is investigating the widely used breast cancer drug, tamoxifen, as a treatment for brain and other cancers; his lab also has discovered 20 possible compounds that might block the side effects of tamoxifen that produce mental foggiess in some people.

Jiyong Zhao, Ph.D., is studying whether doxycycline, a frequently prescribed antibiotic, could be used as a therapy for some B-cell lymphomas; and **Allison Frontier, Ph.D.**, has discovered 60 new drug derivatives that work on a well-known cancer-causing cellular pathway.

“Shots on goal” is in its infancy, but we’re inspired because, as sports fans know, you can’t score unless you take a shot on goal.

George Edelman Jr. has felt the effects of cancer in his life for more than 35 years—first with the loss of a close family friend, and then his wife. His mission was clear. With the development of the Edelman-Gardner Cancer Research Foundation in 1984, he set out to raise \$1 million to advance cancer research at the Wilmot Cancer Center.


Over nearly 20 years, the Hilton, N.Y.-based foundation generously raised and gifted \$600,000 to purchase equipment, provide grants, award fellowships and support research projects at the Cancer Center. From golf, bowling and euchre tournaments, to motorcycle and bicycle rides, book sales and bottle drives, Edelman and team rallied family, friends and community members to generate funds.

Then, in 2002, the Edelman-Gardner Foundation made its first \$250,000 pledge to the Cancer Center, providing \$50,000 for five years to fund “seed grant” projects. Scientists were able to start or continue cancer research projects, using the early data to pursue additional funds from government agencies or other foundations. This investment in research at the Cancer Center turned into \$7.6 million in additional funding to further the research mission in Rochester.

One of the seed grants from Edelman-Garner was awarded to Cancer Center Director of Research, **Hucky Land, Ph.D.**, and **Aram Hezel, M.D.**, gastrointestinal oncologist, to further study a new

potential target in pancreatic cancer that Land identified as part of his research into the common vulnerabilities of cancer cells. Hezel will build upon Land’s laboratory findings to determine whether the new target is effective in treating pancreatic cancer.

In 2013, Edelman-Gardner committed an additional \$250,000 for seed grant funding through 2017, exceeding the \$1 million goal that Edelman set out to achieve in 1984—a true gift to the Wilmot Cancer Center and regional community.

A photograph of two elderly men, George Eldelman Jr. and George Kaufman, sitting on a couch in front of a large window. George Eldelman Jr. is on the left, wearing a green sweater with a yellow collar and brown pants. George Kaufman is on the right, wearing a light green shirt and a dark argyle vest. Both men are smiling at the camera. The background shows a bright window with some greenery visible outside.

**George Eldelman Jr. (left) and
George Kaufman, members of
the Edelman-Gardner Foundation**

**“ The question that’s asked every day in our labs: ‘How can these findings be useful for the clinic?’
Our work isn’t just for intellectual gratification. It’s all about developing new treatment approaches.”**
– Steven H. Bernstein, M.D.



Wilmot Cancer Center Research: **Blood Cancers**

Whether it's an ugly mass growing on a vital organ or tumors concealed deep in the bone marrow, our most primitive cells are the culprits giving rise to cancer.

Wilmot blood cancer researchers study the way in which many hidden cancers crop up—often without warning—from what are known as hematopoietic stem cells, the precursors to red and white blood cells and platelets.

Blood cells perform critical jobs, such as transporting oxygen or fighting infection. A healthy bone marrow continually stimulates production of blood cells, pumping out approximately 500 billion a day.

When this elaborate system malfunctions, it can spit out a wide spectrum of blood cancers. With 20 different forms of leukemia and lymphoma, for example, diseases vary from slow-growing and curable to aggressive and lethal.

Our team is on a mission to make inroads across the spectrum.

Due to our longstanding research strength in blood-borne malignancies, we've attracted a critical mass of nationally respected experts. Our scientists focus on four major aspects: the cancer stem cells that drive leukemia; harnessing the immune system to fight lymphoma; the bone marrow microenvironment, i.e., the vessels, tissues and cells that send the wrong growth signals to blood cells; and new drug trials based on promising preclinical data.

Perhaps what sets us apart the most is our successful study of the microenvironment—the neighborhood in which cancer blooms. By learning how to properly manipulate the bone marrow microenvironment, for example, we hope to reverse the effects of aging on the blood system.

Discoveries from our leukemia team about the growth of leukemia stem cells are also guiding the next level of investigation in labs across the country. Because relapse is such a problem with this disease, their primary interest is to examine leukemic stem cells during treatment to see what changes lead to a recurrence. We're also analyzing the genes of hundreds of patients, in hopes of identifying more targets for drugs.

The lymphoma team also challenges the status quo by raising questions about fundamental biology and suggesting new ways to manage the disease. Why do cancer cells escape the robust activity of healthy immune cells, which are usually pretty good at wiping out villains? Can we reprogram cancer cells to become tumor fighters?

Another priority is translational research, which has a more immediate impact on patients. The Cancer Center's preclinical investigation into a new class of drugs called oral tyrosine kinase inhibitors for chronic lymphocytic leukemia (CLL) progressed to a phase 2 clinical trial. And now we're leading the nation in enrollment of patients, many of whom had few options left. In fact, more than 300 people with various blood cancers are taking part in dozens of studies at Wilmot.

Strong laboratory data that inform physicians and lead to treatment is what research is all about. For Cancer Center patients, it's also about gaining access to the latest information and the newest therapies—as knowledge learned in the lab is applied in the clinic.

LEUKEMIA TEAM, from left to right: **Frank Akwaa, M.D.**, Instructor in Medicine; **Jane Liesveld, M.D.**, Professor, Clinical Director of Leukemia/Blood and Marrow Transplant Program; **Mike Becker, M.D.**, Associate Professor, Director of Adult Leukemia Service/Blood and Marrow Transplant Program; **Laura Calvi, M.D.**, Professor, Co-Director of the Multidisciplinary Neuroendocrinology Clinic; **Craig Mullen, M.D., Ph.D.**, Professor; **Sophia Balderman, M.D.**, Instructor in Medicine; **Jason Mendler, M.D., Ph.D.**, Assistant Professor; **Jessica Shand, M.D.**, Assistant Professor



Steven H. Bernstein, M.D.

In the 35 years since Francis Ashley was diagnosed with chronic lymphocytic leukemia (CLL), so much has happened in his world.

He retired from the Albright-Knox Art Gallery in Buffalo, where he was a financial officer. He watched his children grow, marry, and produce five grandchildren, and then five great-grandchildren. Many of the younger ones visit him and his wife, Donna, on weekends at their Stafford, N.Y. home. He

saw his mother celebrate her 100th birthday.

At age 78, Ashley's own longevity perhaps can be attributed to some good genes. But he believes that research and clinical care at Wilmot deserve credit, too.

He made it through a very grave period in 1997 when the disease flared. He endured aggressive chemotherapy and relied on the judgment of

Wilmot nurses and oncologists to pull him through. Later, when **Paul Barr, M.D.**, joined the Wilmot team, Ashley became a patient of Barr's and began exploring clinical studies.

Barr and other scientists had conducted preclinical testing of a drug combination – from a class of agents known as oral tyrosine kinase inhibitors – that will likely change how we treat CLL. As a result of the successful preclinical

research, Barr is leading the Cancer Center's participation in a national study of two experimental drugs in this class, Idelalisib and GS 9973.

Ashley said he feels terrific since he began taking Idelalisib and GS 9973.

"At our age and with this type of cancer – it's like we've been revived," said Ashley, whose wife accompanied him to a recent follow-up appointment at Wilmot.

"At this point, you go for it. We have a lot of faith in Dr. Barr and in the fact that research brings about more options with the passage of time."

When his great-grandchildren aren't filling the house with fun and love, he's content reading historical fiction and mysteries, and enjoying quieter days.

"Recently I've felt the best I have in years," Ashley added. "It's a blessing."

Steven H. Bernstein, M.D., professor and co-director, Lymphoma Biology Program

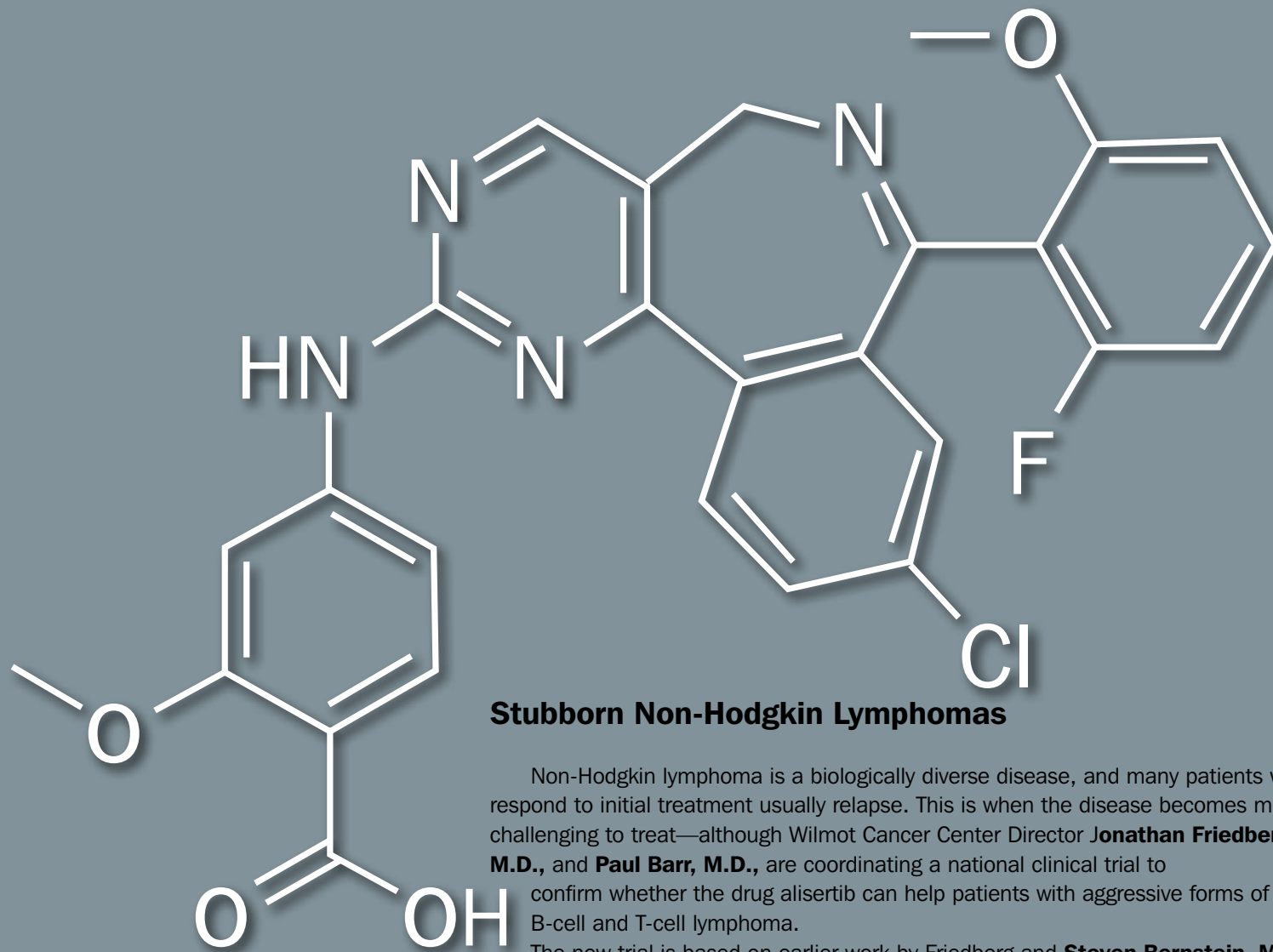
Steve Bernstein knows that you cannot understand a disease of the lymph system without investigating its critical link to the immune system. His lab, therefore, is learning how to reprogram a patient's own immune cells to fight back against lymphoma and other blood cancers.

He's also looking at how cancer cells evade the normal, robust activity of the immune system and how this plays a role in tumor growth. A key question: Can we reprogram the immune cells in tumors to become cancer fighters?

In 2010, Bernstein was named to the National Medical and Scientific Advisory Board for the Leukemia & Lymphoma Society, and in 2012 he was named to the advisory board of the Lymphoma Research Foundation. These organizations are the largest with a dedication to blood cancer research, education and patient services.



Paul M. Barr, M.D., director of the Clinical Trials Office at Wilmot, and his patient, **Francis Ashley**, of Stafford, N.Y.



Stubborn Non-Hodgkin Lymphomas

Non-Hodgkin lymphoma is a biologically diverse disease, and many patients who respond to initial treatment usually relapse. This is when the disease becomes more challenging to treat—although Wilmot Cancer Center Director **Jonathan Friedberg, M.D.**, and **Paul Barr, M.D.**, are coordinating a national clinical trial to confirm whether the drug alisertib can help patients with aggressive forms of B-cell and T-cell lymphoma.

The new trial is based on earlier work by Friedberg and **Steven Bernstein, M.D.** They reported results of a phase 2 clinical study in the *Journal of Clinical Oncology*, which is widely read by clinicians and scientists, showing that lymphoma patients tolerate alisertib and may respond to the drug's anti-cancer activity.

Among a sample of 48 patients, 27 percent saw their disease stabilize significantly; researchers also confirmed that alisertib works by targeting a specific protein, Aurora A, which is overproduced in active and aggressive lymphomas. The new data is particularly important for T-cell patients, who have fewer treatment options.

Other studies are testing alisertib in combination with other therapies for additional subtypes of lymphoma, and for the treatment of colon and breast cancer, and other solid tumors.

Alisertib (MLN8237) Chemical Structure
Source: selleckchem.com

As we age and our blood system becomes less efficient, often we cannot generate enough mature red blood cells in the bone marrow. Too few red cells can cause aplastic anemia, heart failure, bleeding disorders and a weakened immune system.

Michael Becker, M.D., and **Laura Calvi, M.D.**, are collaborating to reverse damage to the blood-production cycle. In one project, they hypothesize that the naturally occurring substance prostaglandin₂ (PGE₂), used as a treatment for stomach ulcers and for softening the cervix to induce labor, also speeds replenishing of blood cells in the bone marrow.

Cancer patients who require stem-cell transplants are vulnerable to infection during the first six weeks afterward; Becker and Calvi are focused on finding a way to intervene with PGE₂ during this critical window. The University has filed patents covering their methods, and the preclinical research has been published in top medical journals.

In a second project, their labs are studying whether parathyroid hormone (PTH), a treatment used to enhance bone healing in osteoporosis, might also be applied to the bone marrow to stimulate blood-cell production.

Becker and Calvi's approach is unique in the world of blood cancer researchers. They target the bone marrow microenvironment, or the diverse groups of cells that surround bone and blood-producing cells, and send growth signals to spur production. It's a new strategy, sorely needed, to solve a problem with few good options for patients.



**Laura M. Calvi, M.D., Professor
and Co-director, Multidisciplinary
Neuroendocrinology Clinic.**

“ Team science is the future. You cannot go forward successfully without well-intentioned collaboration. We’re dedicated to pushing each other by bringing outside perspectives to individual projects, and finding synergy that sparks new partnerships for each tumor type.” – John Krolewski, M.D., Ph.D.



Wilmot Cancer Center Research: **Solid Tumors**

With 45 investigators from 11 departments, the Wilmot Cancer Center's solid-tumor research team is diverse, deep and energized.

They recognize that collaboration is critical. The physicians on the team see what patients need, and bring that sense of urgency. The scientists, steeped in the complexity of cancer, ground physicians with the realities of biology and genomics. Together they're forming coalitions, defining new initiatives and understanding each other in new ways.

The goal is to locate common threads relevant to many cancers, and to reach across the aisle to apply specific knowledge from one area to another. Our primary focus will be on genitourinary cancers (prostate, bladder, kidney and testicular, for example), gastrointestinal cancers (pancreas, liver, colon, esophageal), breast cancer and brain cancer.

Several new interactions already are taking shape. For example, prostate cancer investigators are working with geriatric oncologists to better understand the link between anti-androgen therapy and muscle loss in older men. Breast cancer researchers are working with those who study the brain to examine key signaling events in a molecular pathway that seem to initiate both breast and brain tumors. Researchers on the GI team discovered important similarities between liver and pancreatic cancer, and are using the data to better understand each type.

Other multidisciplinary partnerships are emerging.

Pathologists and surgeons are exploring how to employ specific tumor features and gene expression patterns to arrive at the most personal, accurate diagnosis and prognosis possible. Biomedical engineers, optics and imaging experts are developing new ways to track cancer metastasis and patient response to treatment. And scientists who study hormones such as estrogen and androgen are applying their knowledge to several hormone-related diseases.

A major effort also is underway to speed the pace of drug discovery. Our investigators are combing databases of FDA-approved compounds to find new applications for existing medications. Preclinical studies suggest, for example, that a malaria drug stops the growth of primary liver cancer cells; and tamoxifen, which is widely used to treat breast cancer with few side effects, also might have efficacy for brain cancer. Exciting research is also occurring in lung cancer, bone cancer, melanoma, and head and neck cancers.

Big problems require big teams—and we're sparking many new multidisciplinary connections to improve the way we care for patients.

GU CANCER TEAM, from left to right: **Deepak Sahasrabudhe, M.B.B.S., Professor; Chunkit Fung, M.D., Assistant Professor; Chawnshang Chang, Ph.D., Professor; Elizabeth Guancial, M.D., Assistant Professor; John Krolewski, M.D., Ph.D., Professor; Ron Wood, Ph.D., Research Associate Professor; ShuYuan Yeh, Ph.D., Professor; Yuhchayau Chen, M.D., Ph.D., Professor, Chair of the Department of Radiation Oncology**



Ryan Dawes, third-year graduate student in the Brown lab.

Edward Brown III, Ph.D., Associate Professor, Biomedical Engineering, Neurobiology & Anatomy

Tracking breast cancer and the way it spreads to other organs is the chief concern of biomedical engineer Ed Brown. He uses an impressive tool—a multi-photon laser microscope—that allows scientists to see high-resolution images deep inside living tissue. In fact, Brown is one of the first to apply this technology to cancer.

Using optics, his lab investigates the matter between tumor cells and how it affects metastasis. One goal is to understand how likely a person's tumor will spread, to prevent overtreatment or under-treatment of patients; another is to manipulate

molecules to change or stop the course of metastasis.

His lab has other important projects as well. Researchers study the link between stress exposure and stress hormones to cancer progression, while others investigate how brain activity and its modulation by antidepressants affect brain metastasis.

Brown is a Pew scholar and a National Institutes of Health New Innovator, two of the most prestigious awards available to young scientists. He collaborates with his wife, **Ania Majewska, Ph.D.**, an expert in brain synapses.

Cancer cells that spread from the breast to the brain.

Steel Lillies

Sarcoma, a cancer that manifests in the bone or soft tissue in the body, rarely effects adults—accounting for only about one percent of all adult cancers. Tiffany Lill wanted to raise awareness and funding for research of this little-known cancer, so she founded STEEL Lillies in January 2012 while undergoing treatment for the disease.

Sadly, the Rochester native and mother of two young children lost her courageous battle with sarcoma in April 2012 at 39 years old. STEEL Lillies has lived on as a legacy for Tiffany—spearheaded by Jim Lill, Tiffany's husband, and Steve and Diane Bayer, Tiffany's parents. The organization has hosted two 5K run/walk events and one gala event since June 2012, raising more than \$135,000 toward their pledge of \$250,000 commitment to the Wilmot Cancer Center to support sarcoma research.


In the fall of 2012, the Department of Orthopaedics at the URMW joined forces with STEEL Lillies to match every dollar raised by the organization up to \$250,000. This jump-started efforts to determine how the money would be allocated. Quickly, it was determined that the funds would be best used to recruit a talented physician that was also interested in sarcoma research to join the Wilmot Cancer Center team.

One year later, **Emily Carmody Soni, M.D.**, left MedStar Washington Cancer Institute at Georgetown University to join the URMW. For Dr. Carmody Soni, this was a homecoming. Born and raised in Rochester, N.Y., she earned her medical degree from the URMW. Her research at the Wilmot Cancer Center will focus on finding novel ways to treat bone and soft tissue sarcoma.

As other sarcoma patients continue to confront the disease, STEEL Lillies hopes that research at Wilmot will improve outcomes.



STEEL Lillies, Jim Lill
(standing), **Tiffany's**
husband, with Tiffany's
parents Diane and Steve
Bayer, and Emily Soni, M.D.
(seated, center)



Michael R. O'Dell, B.S.,
Research Assistant (left)
and **Aram Hezel, M.D.,**
Associate Professor and Vice Chief
of Hematology/Oncology

Mystery, Liver Cancer & Mice

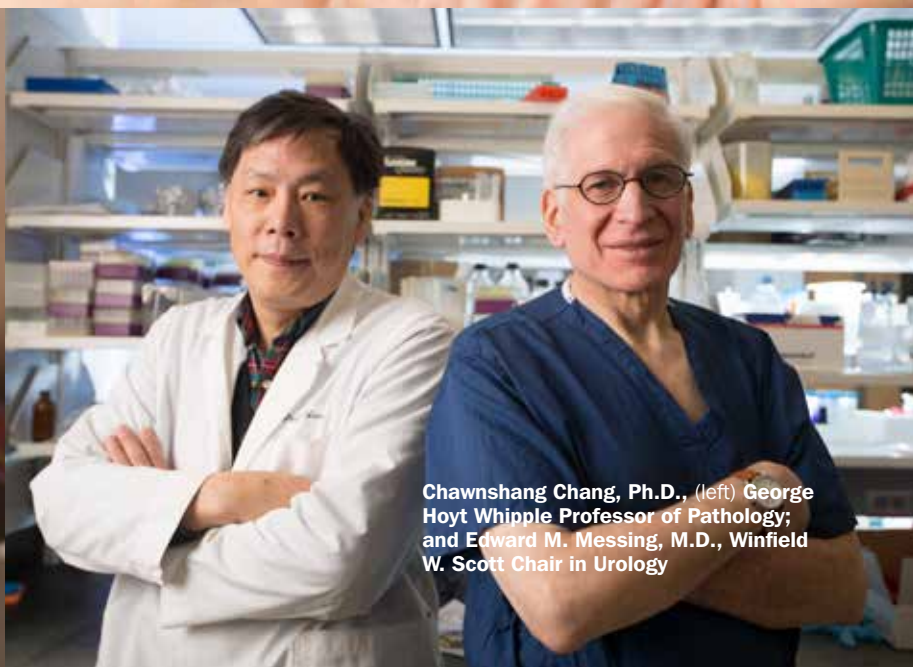
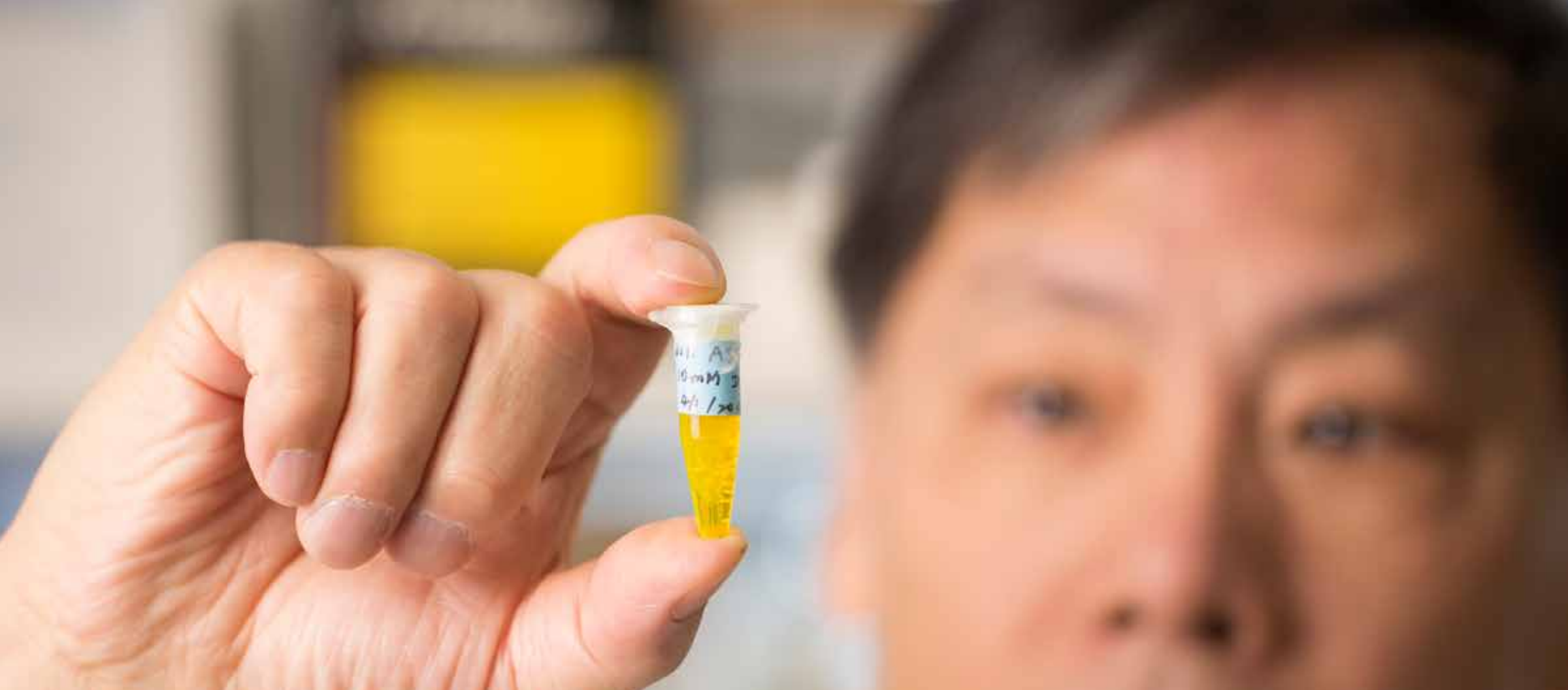
Intrahepatic Cholangiocarcinoma (IHCC) is a type of liver cancer that's eluded scientists for years.

Because it arises in the bile ducts and tends to be very aggressive, it has been difficult to understand what early, biological steps lead to full-blown malignancy.

Aram Hezel, M.D., and his team have invented the first genetically engineered mouse model of IHCC, allowing them to search for these clues. Using the model, they study the gene mutations involved in this

rare cancer, and can test dozens of existing treatments in a short time span, accelerating the discovery process. Initial findings, for example, show that chloroquine—a drug commonly used to treat malaria—is effective against IHCC in the mouse model.

Cancer Research, the oldest and most frequently cited cancer journal in the world, published Hezel's work. The high-impact study provides a first glimpse at the genetic underpinning of the disease.



Chawnshang Chang, Ph.D., (left) George Hoyt Whipple Professor of Pathology; and Edward M. Messing, M.D., Winfield W. Scott Chair in Urology

Prostate cancer is the most common malignancy among men in the world, and it's been in the headlines lately due to concerns about PSA testing and overtreatment. As the debate roared on, Edward M. Messing, M.D., chair of Urology and Wilmot Cancer Center investigator, published important new data showing that despite the tradeoffs of PSA testing, it's still worth doing. In fact, eliminating the test entirely would likely result in rising numbers of men with metastatic cancer at diagnosis.

Less talked about is an aggressive type of prostate cancer (CRPC) that is resistant to androgen-deprivation therapy and other aggressive treatments.

Defeating CRPC is the mission of Chawnshang Chang, Ph.D., who, along with Messing, leads a team of urology scientists at the George Whipple Laboratory for Cancer Research.

Chang's laboratory discovered an experimental compound known as ASC-J9, a derivative of the spice ginger and chemically modified. Excitement arises from the fact that Chang's drug degrades the androgen receptor, the protein molecule responsible for fueling the growth of prostate tumors. This is a completely new approach to stopping the growth-promoting action of androgen.

“ We’ve always believed in focusing on the human side of the disease. What has evolved from that foundation is a number of powerful interventions that begin with diagnosis and continue post-treatment to help patients maintain an optimal quality of life during their cancer experience. ” – Gary Morrow, Ph.D.



Wilmot Cancer Center Research: **Cancer Control & Survivorship**

The number of cancer survivors is expected to reach 18 million by 2022—an inspiring statistic if there ever was one.

The growing ranks, however, point to an urgent need for more research aimed at helping people cope with the physical and psychological effects of not only the disease itself, but its treatments and what to expect as the years pass.

Recently we launched a new clinical survivorship program. Unique to the Rochester region, it offers patients a nurse navigator to aid in the recovery process by answering questions about surveillance and providing appropriate resources on how to stay healthy.

This new aspect of patient care stems from a strong tradition of successful research in survivorship.

Our scientists are national leaders in the study of treatment toxicities, side effects, and overall health as patients strive to move past cancer. Also included in our research portfolio is the management of sleep disorders, nausea and other persistent side effects; protecting survivors from radiation-induced tissue damage and the risks of second cancers; and post-treatment memory loss and other cognitive problems.

For most of the past 40 years we've focused on side effects and symptom-management research, referring to the latter as “cancer control.” We have one of the oldest and highly regarded programs in this field in the country, continuously funded since 1983.

Going forward, however, we're guided by a national priority to expand the agenda of survivorship science. An important future initiative is to prevent and lessen the health problems that patients develop months or years after chemotherapy, radiation and targeted therapy—known as the late effects of treatment—and to calculate who is likely to benefit the most from treatment without being harmed. Risk estimates and prediction models, a cornerstone of personalized medicine, will become the norm as we study genetic factors, age, inflammation and other biological markers that influence outcomes.

Another priority is to study wellness. Exercise, a plant-based diet, smoking cessation and certain alternative medicine interventions are believed to help survivors live better, not just longer. Because patients are interested in these topics, we're committed to investigating whether healthy living keeps cancer at bay and promotes healing.

Already we can lay claim to the country's largest study of the benefits of yoga for breast cancer survivors. Our PEAK Lab (Physical Exercise Activity Kinesiology Clinical Research Core) provides graded exercise stress testing, pulse oximetry, balance testing and other services to patients, and supports clinical trials in survivorship.

Keeping the body physically strong is essential. But as we know, the psychological toll also commands attention.

We're discovering how best to empower teens and young adults with coping mechanisms. We're helping older adults and their families learn to rationally discuss treatment options in a way that aligns with their values and wishes. We're working with health care professionals so they can meet the unique needs of their patients who are people living with cancer. Our studies carry out a powerful agenda to improve the experience during every step of the journey at Wilmot.

CANCER CONTROL & SURVIVORSHIP TEAM, from left to right: **Luke Peppone, Ph.D., Assistant Professor; Karen Mustian, Ph.D., Associate Professor; Gary Morrow, Ph.D., Professor; Joe Roscoe, Ph.D., Research Associate Professor; Michelle Janelins, Ph.D., Assistant Professor; Mohamedtaki Tejani, M.D., Assistant Professor**

Unwelcome but Essential Questions

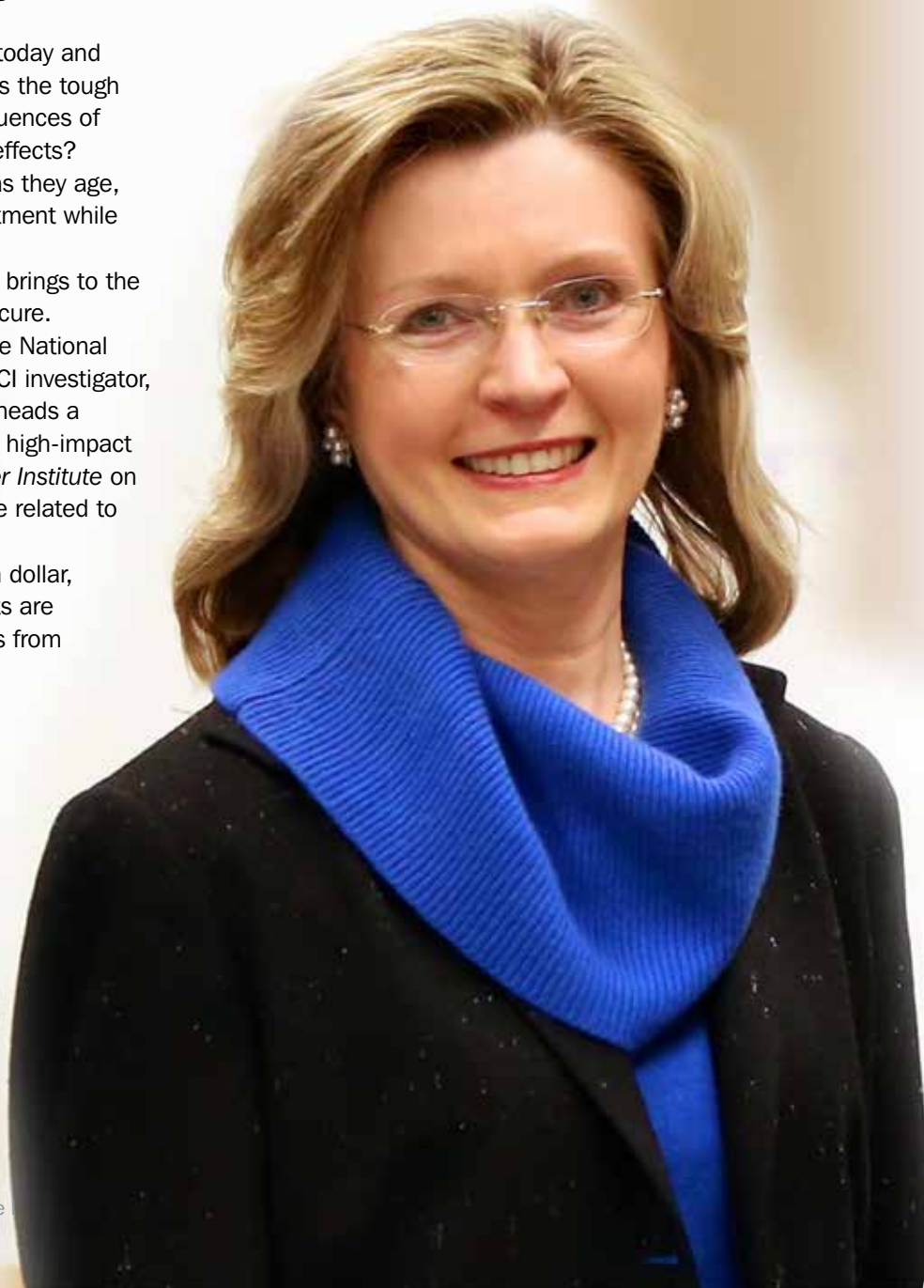
After surviving cancer, most people don't like to think about the downside to treatment—especially the chance that chemotherapy or radiation might cause a second malignancy.

But for a growing number of survivors today and in the future, it's crucial that someone asks the tough questions. What are the long-term consequences of therapy? Who is most at risk for late side effects? What is the best way to manage patients as they age, particularly when the patient received treatment while very young?

This is what **Lois Travis, M.D., Sc.D.**, brings to the table: a dedication to lessen the cost of a cure.

Survivorship research is a priority at the National Cancer Institute, and Travis, as a former NCI investigator, is an international leader in the field. She heads a national scientific committee that issued a high-impact report in the *Journal of the National Cancer Institute* on second cancers and cardiovascular disease related to treatment.

She's also spearheading a multimillion dollar, multi-center study to identify which patients are genetically more susceptible to side effects from cisplatin-based chemotherapy. Millions of people are counting on her team to find concrete ways to prevent serious health problems among survivors.



Here's a bit of irony: Age is the single most important risk factor for cancer. And yet we lack a national consensus on the most appropriate way to treat older cancer patients or follow them through their survivorship years, partly because this group traditionally has been excluded from clinical studies.

By launching the Specialized Oncology Care and Research for the Elderly (SOCARE) clinic at the Wilmot Cancer Center, **Supriya Mohile, M.D., M.S.**, and her team are committed to changing this situation.

It's a hot research field with many important implications for patients. Mohile was awarded a \$2 million grant, for example, to study whether measuring a person's physiological age rather than chronological age is better when considering chemotherapy. Recently she published an important study linking falls and functional impairment with chemo-induced peripheral neuropathy.

We've all known people who are younger or older than their years. Isn't it important to look beyond age when considering treatment options?

Despite a fast-growing older population, specialized research into geriatric oncology is in its infancy. In Mohile, we have a pioneer. She is one of only a handful of scientists nationwide leading this effort. She's plugged into the network that expects to provide oncology thought leaders with the tools, training and hard data to help them in their clinics every day.



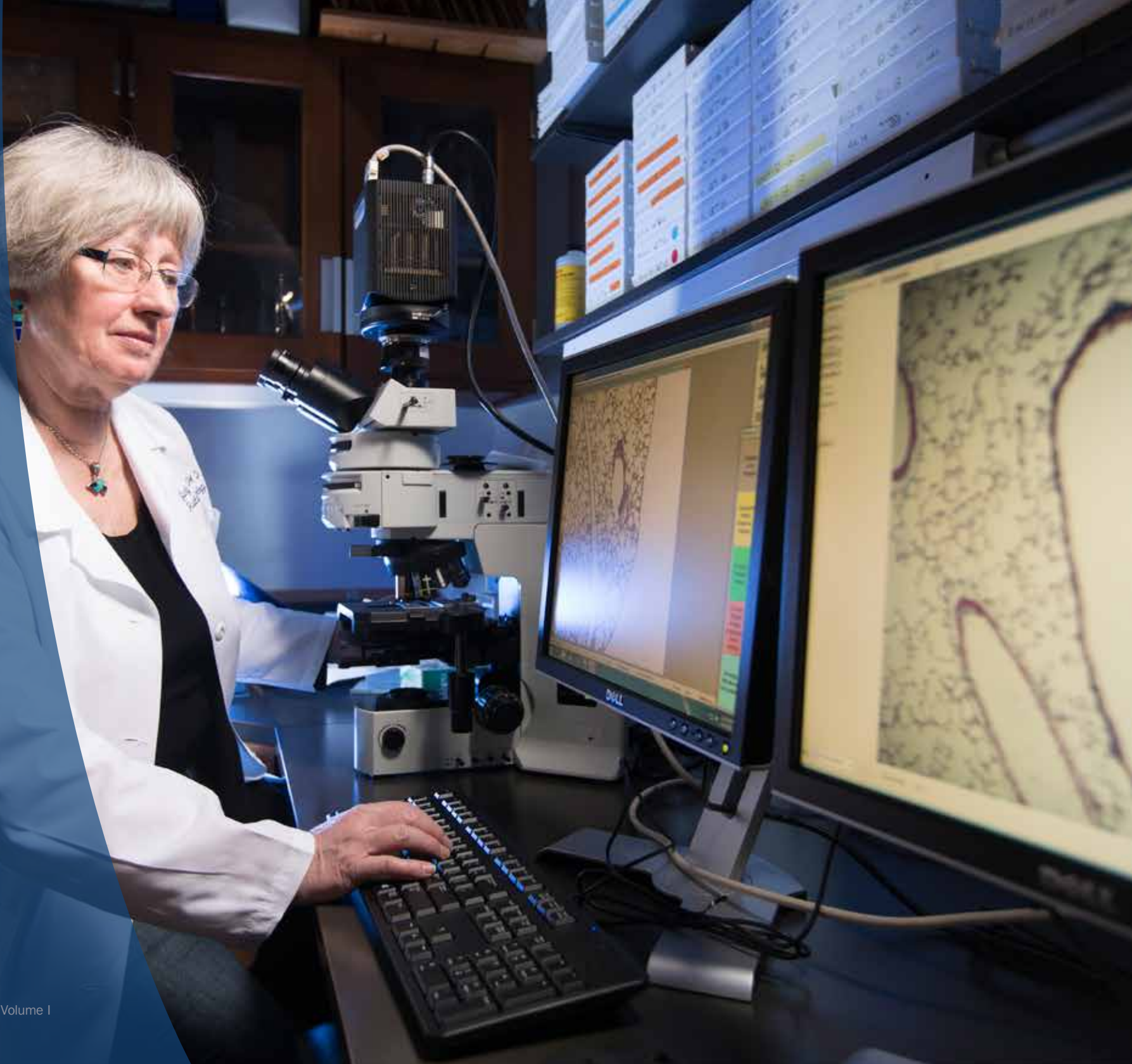
**Supriya G. Mohile, M.D. in the
Wilmot Cancer Center atrium**

**Jacqueline P. Williams, Ph.D.,
FASTRO**, Professor of
Environmental Medicine &
Radiation Oncology

Despite our best efforts to target only the tumor during radiation therapy, nearby normal tissue can suffer some degree of damage. This is Jacky Williams' bailiwick—the study of the way radiation impacts surrounding structures in the body, such as the brain, lungs, and skin. The risks to patients vary widely, from itchy, tight skin near the radiotherapy site to life-threatening fibrosis in the aftermath of lung cancer treatment.

Williams is looking for ways to predict which people are more likely to suffer harm from radiation. One possible clue: inflammation. Are people with high baseline inflammatory biomarkers in more danger? Or is it the patients who seem to develop severe inflammation during treatment?

A native of Cardiff, Wales, who was educated in London, Williams influences her field worldwide through top leadership positions in four important organizations: The American Society for Radiation Oncology, the Radiation Research Society, the National Council on Radiological Protection & Measurements, and the International Association of Radiation Research.



A savvy health-care consumer, Karen Ashbaugh believes in combining the best medical practices with the best wellness strategies.

Knowing that some people question the value of things like dietary supplements and acupuncture, she's hopeful that science will sort out the problems and answer doubts.

To be proactive, the 62-year-old Fairport, N.Y. resident and four-year breast cancer survivor volunteered to participate in a clinical research study for curcumin, the natural ingredient that gives curry

and turmeric its bold yellow hue, for the prevention of skin infection and damage from radiation therapy.

"I was anxious to take part in a study that looked promising but needed more scientific backing," Ashbaugh said, recalling her participation in 2010. "With my interest in integrative medicine, I wanted to know if this approach could complement the standard of care. I thought it was a brilliant idea."

She swallowed 12 curcumin capsules daily during her treatments. And although

none of the study participants knew if they were taking curcumin or a placebo pill, Ashbaugh noticed that her skin reactions seemed very mild compared to what she had expected. Afterward she found out she had been taking the powerful antioxidant and anti-inflammatory, and this group, in fact, had fewer skin problems.

The experience left Ashbaugh "intrigued and engaged" in cancer research, she said. The IBM sales executive also volunteers at the Breast Cancer Coalition of Rochester, where she serves on the research grant

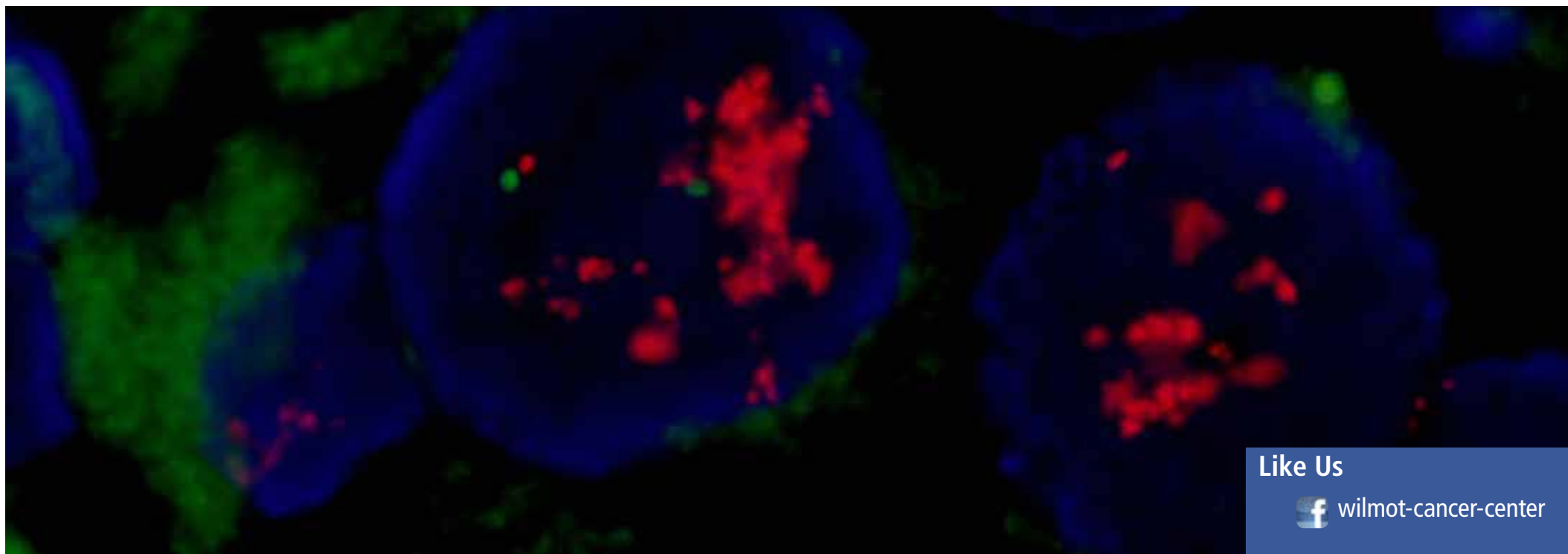
review committee. One of recipients of a BCCR grant is graduate student **Ryan Dawes**, who is studying the role of stress in the progression of breast cancer. Ashbaugh got her first glimpse of bench science when she and the other BCCR members toured the Wilmot lab where Dawes is conducting his experimental work.



Karen Ashbaugh
of Fairport, N.Y.

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