Switching gears

Longtime HIV researcher makes a breakthrough cancer discovery

“Mutant variants of human cells”: the phrase conjures up images of a bad sci-fi movie. But Reuben Harris, Ph.D., has been studying cell mutations for more than 20 years, and his recent finding is more akin to an Oscar-winning blockbuster.

So remarkable is his work that the prestigious journal *Nature*—widely considered the journal of note for scientists—in February published his discovery that a protein that occurs naturally in the body appears to be a driver for more than half of breast cancers he studied. This breakthrough could lead to new diagnostic tools and, potentially, new treatments for breast cancer.

Harris’s finding has its roots in HIV research. His team has been exploring the role that seven proteins known as APOBEC3s play in the body’s fight against HIV infection.

“My lab studies mechanisms of mutation,” explains Harris, a member of the Masonic Cancer Center, University of Minnesota. “Specifically, we’ve been looking at mechanisms that impact the evolution of HIV, which is like a chameleon hiding in the genomes of our bodies, mutating rapidly to resist treatment.”

In the course of that work, Harris—also an associate professor of biochemistry, molecular biology, and biophysics at the University—had an epiphany. What, he wondered, were those seven proteins? continued on page 2
up to in “normal” cells not infected with HIV? And what part might they play in diseases like cancer?

In research supported by the National Institutes of Health, students in his lab invented highly sensitive tests that allowed them to measure the expression levels of each one of these genes specifically.

“That was really key because these seven proteins are closely related to one another,” Harris says, “and they were very difficult to detect and measure.”

With this new measuring ability in hand, and with seed grant support from the University’s Clinical and Translational Science Institute, the team compared the APOBEC3 proteins in both breast cancer cells and healthy cells from the same person and found an anomaly: one of the seven—APOBEC3B—was turned on in many of the breast cancers studied, yet it was virtually undetectable in normal breast tissue.

“Additional experiments showed that this protein was mutating the genome of the cancer cells,” Harris says. “And without mutation, there is no cancer. So this protein, we postulate, may be a key driver of cancer.”

In other words, what Harris’s team discovered is a new source of mutation.

“We know sun causes mutation,” Harris says. “We know certain chemicals cause mutations. But for the first time, we’ve identified an enzyme in our own bodies that causes a large number of mutations. How do we protect against an in-built source of mutation? You can’t slather on sunscreen to protect against this.”

Harris’s discovery, made in collaboration with Masonic Cancer Center director Douglas Yee, M.D., and colleague Natalia Tretyakova, Ph.D., could have a profound impact on physicians’ ability to diagnose some breast cancers: Take a tissue sample, and if this protein is overexpressed in the sample, there’s a strong likelihood that it’s cancerous.

“A next step would be to find the APOBEC3B ‘sunscreen,’” says Harris. “Find out what slows down or stops this enzyme.”

Researchers already know that it can be done. Harris’s lab has identified compounds that can slow down the activity of related APOBEC3 enzymes, and he speculates that this can also be done for APOBEC3B.

But can it be done in a human body with an active metabolism? That, he says, is yet to be determined.

Harris isn’t taking time to bask in the glow of his Nature publication. He and his colleagues have more work to do.

“Once something like this comes out, hundreds of other researchers will take notice, which helps move things along a lot faster,” Harris says. “And for everybody out there with APOBEC3B-positive breast cancer, a community effort will be crucial for translating this discovery into real clinical benefits.”
Pat Rudolph had never pegged herself as the meditation type. Yet here she was in a weekly, two-hour mindfulness meditation course with a dozen strangers.

“I’ve never laid still for 20 minutes in my life,” Rudolph thought when she enrolled in a Masonic Cancer Center study looking at the potential of mindfulness-based therapy to ease stress and anxiety in cancer survivors. “And I’m usually uncomfortable in a group. I was the biggest skeptic in the class.”

The study, led by oncologist and Masonic Cancer Center member Anne Blaes, M.D., aims to determine whether mindfulness meditation, combined with reflection and peer support, can quantifiably improve health for patients in the first few months after treatment.

“Patients who’ve gone through cancer treatment have more chronic conditions, more depression and anxiety, more general medical problems,” explains Blaes, an Eastern Star Scholar and Building Interdisciplinary Research Careers in Women’s Health Scholar. “Finishing chemo and radiation, they go through this whole new phase. We tell them, ‘Congratulations, you’re done! Come back in three months!’ And there’s a real letdown in terms of anxiety, depression, fear of the unknown.”

For many patients, it’s the first time the diagnosis is truly sinking in, Blaes adds—just as the support network is evaporating.

The anxiety and depression patients face can be intense, even crippling, and often the last thing they want is more medicine, she says. “They come in and ask, ‘What can I do? I don’t want another pill.’”

So Blaes is measuring whether, and to what extent, mindfulness meditation techniques affect depression, anxiety, sleep quality, sexual function, and immune response. It’s part of her ongoing effort to explore the promise of complementary medicine to enhance the healing process for cancer survivors.

The study is supported largely by the Hourglass Fund, founded by cancer survivor and motivational speaker Ruth Bachman to advance research in integrative cancer care.

Study participants attend eight weekly, two-hour classes in which they learn mindfulness meditation techniques, practice at home daily, and complete reading and reflection assignments. The course also includes a full-day retreat.

Not long into the course, Rudolph, a breast cancer survivor, began feeling noticeably more relaxed.

“I could sleep better at night,” she says. “This calms you enough to get the rest you really need; you rest more deeply.”

Moreover, the peer support proved invaluable, Rudolph says, and the group still meets regularly. The exercises Rudolph learned also have been “hugely effective” for helping to treat her lymphedema, a common after-effect of breast cancer surgery that causes fluid buildup in the body.

And Rudolph, the skeptic, continues to use the meditation techniques. That’s the intent behind the course, and if the study bears fruit, Blaes hopes to advocate for more widespread, accessible use of mindfulness meditation courses for cancer survivors.

“Survivors know the limitations of Western medicine. I [often] send patients to health psychologists, but I’m not there—and the psychologist isn’t there—when they wake up at 2 in the morning. They need tools they can use at home.”
A match made in India

Anesthesiologist and Bangalore, India, native Kumar Belani, M.D., has become a matchmaker, cultivating relationships between scientists at the University of Minnesota and in India.

Partnering with University hematologist-oncologist Daniel Weisdorf, M.D., Belani helped to initiate a flourishing research and clinical care partnership between the University’s world-renowned blood and marrow transplantation (BMT) program, which Weisdorf directs, and Manipal Hospital in Bangalore. When the project began in 2006, it focused on educational and training opportunities but has since evolved to also include scientific collaborations aimed at improving tissue matching for BMT patients of Indian descent.

The collaboration started when Belani arranged for a group of University physicians to visit Manipal Hospital.

“It’s one of the flagship hospitals in India,” he says.

“They had one weakness—they didn’t do bone marrow transplants.”

Following that visit, physicians and nurses from Manipal Hospital came to the University to observe its acclaimed BMT practice firsthand. These exchanges, along with regular teleconferences with Weisdorf, helped Manipal Hospital develop its own transplant protocols. Today the hospital has completed more than 75 transplants using the University’s program as a model.

Through working with his Indian colleagues, Weisdorf discovered that there are limited data about HLA haplotype tissue, which is central to finding the right tissue-type match for BMTs, for people of South Asian descent. The lack of information makes it difficult to find a non-family marrow donor match.

So today Weisdorf is studying tissue matching with 12 medical centers in India and the U.S. National Bone Marrow Donor Program in hopes of using the research findings to develop a model for a BMT donor registry in India.

Across the street, across the state, across the country, and across the world, members of the Masonic Cancer Center are helping people live healthier lives. Not only does the impact of our research stretch across borders and oceans, but some of our leaders are working directly with leaders in other countries to accomplish a myriad of goals—to share knowledge, to exchange ideas, and even to help meet basic needs. Here are three examples of this work.
Different paths to good outcomes

The first time Linda Carson, M.D., visited Baruch Padeh Medical Center in Poriya, Israel, she found a “very barebones” setup.

The hospital environment was a reflection of the region in general, says Carson, who is head of the University’s Department of Obstetrics, Gynecology, and Women’s Health. “People live much more simply,” she says.

And that simplicity crosses over to care delivery, too. While many clinics and hospitals in the United States invest heavily in providing comfortable surroundings for patients, the Poriya hospital didn’t. It didn’t even have air-conditioning, Carson notes.

But she found that her colleagues in Israel still produced good outcomes for patients. “When you’re providing good care, the setting doesn’t matter so much,” she says.

On their first trip to Poriya in 2005, Carson and a few other Minnesota faculty members helped their new colleagues set up an outpatient chemotherapy infusion clinic and trained its doctors and nurses. The clinic is still the only one of its kind in the region, she says.

The Minnesota contingent also found a great collaborator in Ilan Atlas, M.D., a gynecologic oncologist at Baruch Padeh Medical Center. Every six weeks the Minnesota and Poriya groups present cases to each other via teleconference. Atlas also talks to University medical students and residents about what it’s like to struggle with the high costs of medical care, stressing “the importance of getting real value out of what we’re doing,” Carson says.

And Atlas, who plays guitar for patients getting chemotherapy at his hospital, also has taught his new colleagues about the stress-reducing effects music during treatment—an idea that Carson thinks is worth pursuing back at the University.

Putting basic health care supplies within reach

The first time pediatric blood and marrow transplant physician Troy Lund, M.D., Ph.D., visited Uganda, he discovered a surprising number of well-funded labs and research initiatives dedicated to infectious diseases like HIV, AIDS, and malaria. But he also saw a severe lack of resources for some of the most significant causes of childhood mortality there: pneumonia, diarrhea, and dehydration.

So Lund created the Medicine for Sick Children Foundation, an independent program that provides medical education, clinical care, and advocacy for suffering children. Since the organization’s inception, Lund and others have supplied antibiotics, first aid supplies, and pharmaceutical therapies for kids in Uganda through a “medicine cabinet kit” program.

These kits provide first aid supplies like those one would find in medicine cabinets in American homes, and they are delivered or shipped to orphanages across Uganda. Partners in Africa teach the orphanage mothers how to properly use the supplies and follow up on and systematically track the orphans’ health conditions.

Today Lund’s efforts are yielding results: About 250 children aged 6 months to 16 years regularly benefit from his kits.

“There are too many foundations that leave ‘stuff’ in Africa and have no follow-up to what they have done,” Lund says. “If our efforts aren’t making a measurable impact in preventing childhood mortality, we’ll shift our focus to ensure the foundation does indeed serve its intended purpose—that is to reduce childhood morbidity in the developing world.”
With philanthropy, research team targets a biological drug for treating leukemia

Michael Verneris, M.D., senses an urgent need every time he looks into the faces of his young patients who have acute lymphoblastic leukemia at the Journey Clinic at University of Minnesota Amplatz Children’s Hospital.

“The need to develop new treatments, less toxic and more effective than chemotherapy, is huge,” he says, “and I feel that sense of urgency every week when I sit next to a patient and have to explain that the options are slim.”

Fortunately, the flip side of Verneris’s work in the clinic is laboratory research, and he’s currently elbow-deep in a project that could one day lead to just the sort of new treatment he and his patients yearn for. The innovative research, led in tandem by Masonic Cancer Center members Verneris and Daniel Vallera, Ph.D., focuses on a bioengineered molecule that has the ability to hitch two of the body’s cells together: one, the cancer cell, and the other, a natural killer (NK) cell.

“Basically, we’re developing a biological drug that uses the body’s immune system to recruit NK cells to kill the leukemia cells,” explains Vallera, who has been at the forefront of this type of research since 2001, when he retooled his lab to genetically engineer targeted biological drugs, or drugs that are created from human genes.

Vallera’s lab has concentrated on making the drug, which is a vehicle for introducing that molecule into the body, while Verneris’s team does the testing. So far, the results are promising.

“It looks great in the test tube,” says Verneris. Now supported by a $100,000 grant from St. Baldrick’s Foundation, Vallera and Verneris will move next to testing the drug in mice and then, if all goes well, in humans.

“Private donations have become more and more important,” Vallera says, “because it’s difficult to get government funding for work like ours that focuses on drug development.”

What the research team has achieved so far with relatively small amounts of money is significant—and that, Verneris believes, is a testament to the Masonic Cancer Center and its intended purpose.

“What we’re able to do here is sit in a room with a bunch of really smart people and say, ‘what if?’ or ‘how can we?’” Verneris says. “That’s how this research began, with one of those discussions. There’s amazing synergy between the scientists here, and that’s the great strength of this Masonic Cancer Center.”

Groundbreaking cancer researcher John Ohlfest, Ph.D., died on January 21 of malignant melanoma. He was 35 years old.

Ohlfest, the first recipient of the Hedberg Family/Children’s Cancer Research Fund Endowed Chair in Brain Tumor Research, gained renown for using both gene therapy and novel immunotherapies to coax a patient’s own immune system into attacking cancer cells. His work with brain tumors in dogs also gained national prominence.

“In the field of medicine, John was a star,” says his supervisor John Wagner, M.D., scientific director of clinical research in the University’s Stem Cell Institute. “He had only one goal in mind—total cure. What John could have accomplished over a long career we will never know—but even now, he continues to inspire us to continue our quest of finding cures for previously incurable diseases.”
University team and leading-edge technologies help Minnetrista woman beat breast cancer—twice

When Kathy Heins was diagnosed with breast cancer at age 32, she chose to stay positive. “Hey, I’m not going to die from this,” she told her friends and family.

After she was treated at the Masonic Cancer Clinic at the University of Minnesota, the disease gradually faded into the background of her life.

Eight years later, Heins returned to the University for a routine visit with her new doctor, Douglas Yee, M.D., director of the Masonic Cancer Center. Yee recommended a new magnetic resonance imaging technology to screen Heins for any signs of a new cancer. The scan revealed another tiny new breast cancer—so small it could not be detected by a mammogram.

As a mother of two young children, Heins felt an even stronger resolve to overcome breast cancer this time. Now cancer-free, she appreciates Yee’s close attention and her chance to benefit from the latest research advances through the Masonic Cancer Center. Improved therapy, early detection, and swift action saved her life—twice.

IRA charitable giving opportunity extended for 2013

Thanks to recent legislation, you can again benefit from a popular tax-advantaged giving option.

Make a gift of up to $100,000 directly from your IRA to the University of Minnesota Foundation (UMF) to support the Masonic Cancer Center, University of Minnesota before December 31, 2013, and you can avoid paying federal income tax on the amount of your gift.

These rules apply to IRA charitable rollovers in 2013:

- Only IRAs are eligible (other types of retirement accounts are not).
- You must be age 70 1/2 or older at the time you make your gift.
- Your gift must come directly from the IRA custodian to UMF.
- You can give up to $100,000 from your IRA to one or more qualified charities in 2013 (and if your spouse has a separate IRA, you can each give up to $100,000).
- Your gift must be outright; it cannot be used to fund a charitable gift annuity or charitable remainder trust.

While you will not be able to claim a charitable deduction for your IRA rollover gift, you also won’t owe federal income tax on any amount up to $100,000 that you distribute to a qualified charity.

To learn more about supporting the Masonic Cancer Center through the IRA charitable rollover option or through another type of planned gift, contact Jay Kautt at 612-626-0510 or jkautt@umn.edu.

Upcoming events

Saturday, April 6
8th Annual Cancer Survivorship Conference
McNamara Alumni Center
University of Minnesota
This annual conference focuses on questions and issues survivors and their families may face after cancer treatment or stem cell transplantation. To register for this free event, visit z.umn.edu/mccevents or call 612-624-2620.

Wednesday, April 17
2013 John H. Kersey, M.D., Lectureship
2-650 Moos Tower
University of Minnesota
Open to the public, this event will feature Melvyn F. Greaves, Ph.D., professor of cell biology at the Institute of Cancer Research in London. He will present “A Darwinian eye-view of cancer.” For more information, call Sharon at 612-624-1913.
The Masonic Cancer Center, University of Minnesota lost one of its most prominent and influential physician-scientists March 10 with the sudden death of John Kersey, M.D. He was 74 years old.

A native Minnesotan and a graduate of the University of Minnesota Medical School, Kersey dedicated his life to developing new treatments for childhood cancer. He founded both the University’s blood and marrow transplant program and what’s now known as the Masonic Cancer Center, which became a National Cancer Institute–designated Comprehensive Cancer Center under his watch in 1998.

Kersey also led the team that performed the world’s first successful bone marrow transplant for malignant lymphoma in 1975. That patient is alive and well today.

“John was the driving force that helped the University of Minnesota become internationally recognized for excellence in cancer treatment and research,” says Aaron Friedman, M.D., dean of the Medical School and the University’s vice president of health sciences. “His enthusiasm for his work was contagious, and his passion for bringing people together to solve problems changed the way cancer research is conducted.”

And while his research successes were plentiful, colleagues say that Kersey’s generosity as a friend and collaborator set him apart.

“The world has been positively changed by John’s scientific, educational, and clinical contributions,” says Douglas Yee, M.D., who succeeded Kersey as director of the Masonic Cancer Center in 2007. “John provided mentorship and guidance to researchers around the world who will now carry on his legacy.”

To make a gift to the John H. Kersey Chair in Cancer Research in his memory, visit www.give.umn.edu/giveto/kerseychair.