Healthier, longer, stronger

Masonic Cancer Center researchers are fueling the fight against heart disease after breast cancer treatment

Scientists have understood for many years that heart disease can be an unwelcome side effect of even the most successful breast cancer treatments. Some chemotherapy drugs—including anthracyclines, considered a cornerstone of breast cancer treatment—and some targeted therapies put patients at risk for heart problems. Those who receive radiation to the left breast—closer to the heart—may have an increased risk for heart damage, as well.

But today at the Masonic Cancer Center, University of Minnesota doctors are exploring innovative ways to detect, treat, and sometimes even predict and prevent heart problems before they develop.

“When we treat women for breast cancer, we’re not just treating that disease but looking at how we can keep the rest of you healthy as well,” explains Anne Blaes, M.D., a University hematologist/oncologist who specializes in breast cancer and heads the U’s Cancer Survivor Program. “And now, with women often surviving for many years after breast cancer treatment, it’s so important to fully understand how heart continued on page 2

Photo by Brady Willette

Chetan Shenoy, M.B.B.S., aims to show how cardiovascular magnetic resonance imaging could be used to predict which cancer patients are most at risk for developing heart problems.
disease can affect patients not just during treatment but years down the road.”

University doctors who employ today’s leading-edge treatments for breast cancer patients are also hard at work with their laboratory research colleagues developing tomorrow’s breakthrough therapies. As they learn more about how and why heart disease—now the leading cause of noncancer death among breast cancer survivors—affects their patients, they are zeroing in on more effective tools to fight back.

One such project involves the use of cardiovascular magnetic resonance imaging (CMR), a relatively new imaging technique that can detect structural heart disease even in patients who show no symptoms and who have had more conventional screening tests come back clean.

“While CMR is used widely for evaluation of some cardiac diseases, it’s still not widely used for evaluation and monitoring of cancer patients,” says cardiologist Chetan Shenoy, M.B.B.S., an assistant professor in the Department of Medicine.

Through Shenoy’s work, that may soon change. In a research program currently under way at the Masonic Cancer Center, Shenoy is working to demonstrate that by using CMR to evaluate heart health before patients begin cancer treatment, doctors may be able to predict which patients are most at risk for developing heart problems.

“Currently, we don’t have a good way of predicting who will develop cardiotoxicity,” Shenoy says, “and unless patients have preexisting heart conditions, they’re all treated the same way. But with CMR, we can detect even ‘silent’ heart problems, so we can identify higher-risk patients. Then, we can think about alternative cancer treatment options, prescribe preventive cardiac medications, and monitor them more closely to detect heart problems sooner rather than later.”

Getting that sort of jump on the detection of cardiotoxicity, Shenoy believes, could result in not just fewer patients developing heart problems but also improved cancer outcomes and lower health care costs.

A pioneering partnership

Three years ago, the U opened one of the first cardio-oncology clinics in the Midwest so that cardiologists and oncologists could more effectively work hand-in-hand to minimize heart problems in cancer patients. The clinics—located on the U campus in Minneapolis, as well as in Burnsville and Edina—provide specialized care for both current cancer patients and long-term survivors.

“I see patients in remission who were treated with chemotherapy or radiation 10 to 15 years ago who have developed heart problems, many of whom were unaware that they were at additional risk for heart disease when they received cancer therapy,” says Suma Konety,
M.D., M.S., head of the Cardio-Oncology Clinic and an assistant professor of cardiology. “I also frequently see patients who develop cardiac problems during cancer treatment.”

In addition to her practice, Konety also conducts research aimed at improving cardiac outcomes for breast cancer patients. She established a cardiac-cancer registry to provide researchers with extensive data on patients with those dual diagnoses; such registries have been shown to help doctors improve patient outcomes. She also collects blood samples from patients who have a decrease in heart function during cancer treatment to watch for genetic markers that might be contributing to heart problems. If such markers are identified, she says, doctors might ultimately be able to perform a blood test before starting chemotherapy to determine if patients are at risk for developing cardiotoxicity and start medications to prevent that disease process or modify their cancer treatments accordingly.

Like Konety and Shenoy, Blaes focuses much of her research on cardiac complications of chemotherapy. She is currently looking at the impact of aromatase inhibitors—anti-estrogen therapy used to treat breast cancer—on overall vascular health.

Additionally, Blaes and Konety are working together on improving breast MRI, which provides digital 3-D imaging of breast tissue that is superior to traditional mammography. They are now exploring innovative ways to capture both breast and heart images in one setting, which would allow doctors to diagnose and treat potential heart problems more quickly.

An ounce of prevention

With close to 3 million breast cancer survivors living in the United States, U doctors have also developed ongoing education programs to keep survivors informed about their health and, ultimately, prevent problems whenever possible.

“At our annual Cancer Survivorship Conference,” says Blaes, “we now include a special breakout session on heart health.” (The next conference will be held on April 23, 2016, and is free and open to all cancer survivors, no matter where they received treatment.)

Meanwhile, she notes, breast cancer survivors should do whatever else they can to optimize their heart health: don’t smoke, maintain healthy a weight and cholesterol level, and get 150 minutes of exercise every week.

Blaes and her colleagues prefer the “ounce of prevention” approach to cardiotoxicity.

“While most research efforts at other institutions are directed at the early detection of cardiotoxicity, our research here is focused upstream on primary prevention,” adds Shenoy, “and that has the potential for huge impact in the field.”
There’s something inside Reuben Harris, Ph.D., that compels him to push harder, to find answers that others say can’t be found.

“I definitely don’t like taking no for an answer,” laughs Harris, a University of Minnesota professor of biochemistry, molecular biology, and biophysics; Masonic Cancer Center member; and newly minted Howard Hughes Medical Institute (HHMI) Investigator. “I guess there’s a drive inside that propels me in a way that it might not for others.”

Indeed. In just the middle of his career, Harris is on a serious roll. When two years ago he published results of his research in the prominent journal *Nature* that showed he and his team had discovered that a particular enzyme in the body fuels cancer, the world took note. Scientists around the globe are, Harris says, “joining the fray, big time.”

Why? Because Harris’ discovery has transformed the way scientists think about mutations that drive cancer. Previously, mutations were considered to be random events we can’t control; through Harris’ work we now know that many cancer mutations have a cause that comes from inside the body—versus from sun, or smoking cigarettes—and Harris knows what it is.

“Since we published that paper,” Harris says, “we’ve gone on to discover that this enzyme (called APOBEC3B) causes mutations in approximately half of all cancers. This is a tremendous therapeutic opportunity because enzymes can be controlled, so ... once we figure out how to control it, we may be able to stop cancers from evolving and thereby make them more treatable.”

As he says, it’s easier to dam a river if you work near the headwaters.

An elite circle

When he becomes an HHMI Investigator—his five-year term begins in September—Harris will join an elite circle of scientists. Just ask Tucker LeBien, Ph.D., vice dean for research at the Medical School and associate vice president for research at the Academic Health Center, what Harris’ achievement means to the University.
“Reuben’s award is far and away the most significant recognition of any faculty member working in biomedical research in recent memory,” LeBien says. “It trumps everything.”

LeBien also weighs in on just why Harris’ research is so exciting: “Much of cancer research is about treating existing cancer, but Reuben asks, ‘Why does the cancer occur in the first place?’ Understanding the origins of cancer will lead us to create prevention strategies we haven’t even thought of yet.”

The distinguished board of Nobel laureates and National Academy of Science members who reviewed nearly 1,000 applications on behalf of the HHMI—the largest private benefactor of medical research in the world—agreed that Harris’ work stood out. The rigorous application process, which takes months and culminates in an in-person interview, winnows the field until a small number—this year just 26—are chosen.

Becoming an HHMI Investigator is a major prize for a scientist because the award doesn’t fund a particular research project; essentially, it funds scientific creativity, something Harris has in spades. While the HHMI defines its Investigators as “thought leaders,” LeBien calls Harris “a kind of intellectual catalyst who stimulates and inspires others to think outside the box in their own research, and that’s the kind of thinking that yields big progress.”

The HHMI award includes an impressive package of support for Harris, including his salary, an annual scientific budget, equipment, and more for five years. After that time, his funding may or may not be renewed, depending on the progress of his work.

“They fund you at a high level, give you experimental freedom, and then expect high-impact research that moves the field forward by leaps,” says Harris.

While the HHMI award dwarfs most other grants, Harris is quick to voice his gratitude to smaller organizations like the local Randy Shaver Cancer Research and Community Fund and the Minnesota Ovarian Cancer Alliance (MOCA), which helped him get to this point.

“It is truly gratifying when our early support leads to important discoveries in the treatment of cancer,” says MOCA’s executive director, Kathleen Gavin. “We’re proud to support [him] and hopeful that this new funding will accelerate the pace of Dr. Harris’ brilliant work.”

“Minnesota should take great pride that we have such amazing scientists right here, and we’re very proud to support Reuben’s work,” adds Roseann Giovanatto-Shaver, executive director of the Shaver fund. “The future looks very bright when you meet people like Reuben.”

**The next five years**

As he enters this next phase of his career, Harris has his eye on two big goals: continuing to recruit and train the most talented, driven people to work in his lab, and zeroing in on ways to control APOBEC3B. He puts a little more grit in it, saying he and his team will “wield mutations like a double-edged sword to kill cancer and viruses.

“The freedom to swing for the fence is what I’ve been looking for my whole career,” Harris adds. “This HHMI award has given me and my team the green light to delve into a lot of high-risk research, and I’m going to use every ounce of that support to keep finding answers to big questions.”

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Partnering for faster progress

*Masonic Cancer Center researchers collaborate with biopharmaceutical company to speed up development of natural killer cell therapies*

The University of Minnesota has found a new research partner in the clinical-stage biopharmaceutical company Fate Therapeutics, Inc. The company develops programmed cell therapies to treat life-threatening diseases and will work with Masonic Cancer Center scientists Jeffrey Miller, M.D., and Dan Kaufman, M.D., Ph.D., to further develop their research on natural killer (NK) cell-based cancer immunotherapies.

The collaboration will focus on two therapeutic programs that aim to exploit NK cells’ inherent ability to detect and destroy cancerous cells while leaving normal cells unharmed—potentially without the side effects associated with high-dose chemotherapy or radiation.

“The University of Minnesota has pioneered the basic research and clinical investigation of NK–cell–based therapeutics, and we look forward to collaborating with their expert team in the development of NK–cell–based immunotherapies that may provide distinct advantages in transforming the treatment of cancer,” says Fate Therapeutics president and CEO Christian Weyer, M.D., M.A.S.

While Masonic Cancer Center scientists have shown that NK cells can effectively and safely kill cancer cells, making enough of them to become a viable therapeutic option has been a challenge. Fate Therapeutics plans to use its cell programming approach and proprietary induced pluripotent stem cell technology to develop “off-the-shelf” NK-cell–based cancer therapeutics—sparing the time and expense of having to isolate these cells from donors.

Much of Miller’s and Kaufman’s work leading up to this agreement was supported by the Masonic Cancer Center’s Cancer Experimental Therapeutics Initiative and funded in large part by Minnesota Masonic Charities.

“None of this would have been possible without financial support from many sources, including substantial philanthropic funding,” says Douglas Yee, M.D., director of the Masonic Cancer Center. “Our mission is to advance patient care by developing new cancer treatment strategies based on robust scientific evidence. Drs. Miller and Kaufman worked tirelessly to provide both laboratory and early-stage clinical investigation demonstrating the great potential for this NK cell immunotherapy.”

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In recognition of ‘breakthrough potential’

The Masonic Cancer Center’s Jeffrey Miller, M.D., has been awarded the National Cancer Institute’s prestigious Outstanding Investigator Award.

Miller, who holds the Roger L. and Lynn C. Headrick Chair in Cancer Therapeutics, is internationally known for his work on developing natural killer cell immunotherapies to treat a range of cancers, from acute leukemia to solid tumors.

The Outstanding Investigator Award is given to scientists who have exceptional records of productivity in cancer research and comes with up to $600,000 per year for seven years to provide funding stability for their work. This long-term support is meant to allow investigators the freedom to embark on projects of unusual potential; opportunities to pursue high-risk, high-reward research; and more time to develop new techniques.
Alex Vo was a freshman at the University of Minnesota in 2010 when he heard about the Cancer and Health Disparities Summer Internship. It’s designed to offer undergraduates like him a rare opportunity to work with world-class scientists.

“We started this program in 2009 to create an infrastructure that would help kids from underserved communities succeed academically and encourage them to choose careers in health-related professions,” explains Masonic Cancer Center member Kola Okuyemi, M.D., M.P.H., who cofounded the program with colleague Christopher Pennell, Ph.D.

They hit a home run with Vo, a first-generation college student who is now in his second year of medical school at the U.

During his internship, Vo worked on Okuyemi’s Power to Quit program, a smoking-cessation effort directed at people experiencing homelessness. Vo developed methods for locating the highly transient study participants.

“It really opened my eyes, not just to homeless people, who are so marginalized in our society, but to health disparities and what we can do to eliminate them,” Vo says.

Vo also credits the experience with guiding him toward a career in primary care: “I never saw a doctor of Asian descent while I was growing up, and I think people feel that when you see somebody who looks like you, who’s had some of your same experiences, you’re going to be more comfortable talking with them.”

Okuyemi reports that, six years after starting the philanthropy-funded internship program, the majority of early participants are pursuing graduate or medical degrees.

“To solve our health care problems, we need people from all communities, because talent is universal, but opportunity is not,” says Okuyemi, who also directs the U Medical School’s Program in Health Disparities Research. “We need to make opportunity universal, too.”

Make a gift to support the Cancer and Health Disparities Summer Internship program at give.umn.edu/giveto/marysumpmann.

Remembering Julie Ross, Ph.D.

The Masonic Cancer Center lost a dedicated scientist, trusted colleague, and caring mentor on June 19 with the death of Julie Ross, Ph.D.

A leader in molecular epidemiology, Ross focused on infant leukemias, myeloid leukemias, and the role of mitochondrial DNA in transplant outcomes. She was internationally recognized for her work.

Ross was a career-long University faculty member. In 2012 she was named the inaugural recipient of the Suzanne Holmes Hodder Chair in Cancer Research through Children’s Cancer Research Fund.

Memorials may be directed to the Masonic Cancer Center Digestive/Gastrointestinal Research Fund at give.umn.edu/giveto/ross.
Thursday, September 3, is Innovations in Cancer Prevention and Care Day at the Minnesota State Fair.

Protect your family’s skin all day with free SPF 30 sunscreen from Vanicream, safe for everyone from birth on up. It’s available every day of the fair in dispensers at each information booth, thanks to a partnership of Vanicream, the Masonic Cancer Center, and the Minnesota State Fair.

And stop by the University of Minnesota building (located on Dan Patch Avenue between Cooper Street and Underwood Street) to talk to experts from the Masonic Cancer Center and University of Minnesota Cancer Care.

Test your knowledge with our cancer quiz, discover exciting cancer research efforts under way in our own backyard, and learn how to stay healthy before, during, and after a cancer diagnosis. Stay for a presentation by one of our experts or approach them with questions on your own.

Find more information at www.mnstatefair.org/fun/new or by downloading the free app UofM@theFair.