Fall 2010

Philanthropy is a 'critical' part of cancer geneticist's successes *page 4*

Training grants help promising scientists launch their careers *page 5*

Researchers ask why some smokers are more likely to get cancer *page 6*

New cancer and heart research building will foster collaboration *page 7*

Masonic Cancer Center News

A publication for those who support cancer research, education, and care at the University of Minnesota

Individualizing medicine

Physicians and scientists seek to improve treatment outcomes by incorporating genetics into cancer care

A leading-edge breast cancer clinical trial starting in September at the University of Minnesota is designed to test new targeted therapies—and it has researchers and patients alike excited about the possibilities.

Researchers at the Masonic Cancer Center are especially excited by the study's potential to improve outcomes for women with early-stage breast cancer in a short timeframe. Called I-SPY2, the trial will compare the effectiveness of several potential new breast cancer medications in a single clinical trial and almost immediately evaluate whether they're working.

A typical clinical trial examines one drug at a time and often involves five years of enrolling subjects and collecting data—and then another five years to analyze the treatment's effectiveness, says Masonic Cancer Center oncologist Tufia Haddad, M.D.

But this trial is designed to move much faster.

"The testing is going to be done right up front, in real time, in women with advanced but potentially curable breast cancer," says Haddad, who directs the University's part of the 17-site clinical trial. "We'll be able to monitor the tumor response to treatment and determine drug effectiveness within six months."

The study also involves genetic analyses of breast tumor tissue, which will help physician-researchers determine which drug is most beneficial for each patient.

continued on page 2

Photo by Richard Anderson

Oncologist Tufia Haddad, M.D., says real-time MRI monitoring and data analysis through the I-SPY2 clinical trial will help to determine which new drugs are most beneficial for breast cancer patients.

University of Minnesota
Driven to Discover℠

Individualizing medicine continued from cover

"Ultimately, the goal is to identify targets from the tissue—whether it's genes, proteins, or patterns in the tumor—that predict whether or not this drug will work in this particular tumor for this particular woman," Haddad says.

Eventually, she says, the idea is that doctors will be able to tell breast cancer patients up front which drug is most likely to give them the best results.

Different people, different treatments

This tailoring of treatments, often referred to as "personalized" medicine, grew out of the observation that patients with the same type of tumor responded differently to one standard treatment. Cancer researchers are discovering that each tumor is genetically different, even within the same type of cancer, suggesting that treatments should also differ.

"One person's pancreatic tumor may be very different than another person's pancreatic tumor," says the Masonic Cancer Center's Brian Van Ness, Ph.D. "Some people's tumors are very aggressive, and some people's tumors are not. Some people's tumors respond to therapy, and some people's tumors do not."

But why? Likely, there are genetic variations in the tumor that will affect the way it behaves and responds to treatments, says Van Ness, head of the Institute of Human Genetics's Division of Medical Genomics. Environmental factors also play a role, he says.

A pioneer in a pioneering study

Gail Hudson was the first patient to enroll in the I-SPY1 clinical trial.

June 9, 2009, is a day Gail Hudson remembers clearly. It's the day she was diagnosed with breast cancer.

Almost immediately following that diagnosis, Hudson started researching her treatment options. She found that the National Cancer Institute (NCI) recommends centers that emphasize investigator-initiated, research-based clinical care—and that the Masonic Cancer Center, University of Minnesota, is one of two NCI-designated Comprehensive Cancer Centers in the state.

"It was pretty clear to me what I wanted to do," says Hudson, a 52-year-old Minneapolis resident and wife, mother, and producer at KSTP TV. "I just thought it was important to be in a place where they were doing cutting-edge research."

At the University, she learned about the first phase of the I-SPY clinical trial, which involved receiving the standard treatment regimen as well as genetic analysis of her breast tissue and some extra MRI monitoring. The idea of extra monitoring comforted her, and she enrolled, becoming the first participant in the I-SPY1 trial.

By the time of her lumpectomy last November, the chemotherapy had nearly melted away Hudson's tumor. Only two small spots of precancerous cells remained and were removed during surgery.

Today Hudson is "almost" back to her normal life, although she still feels more fatigued than she did before her cancer treatment. And because she has dense breast tissue—a risk factor for breast cancer—she'll continue to receive an annual MRI in addition to her annual mammogram.

"I really feel strongly about trying to help other people, and it was an honor to be a part of the study," Hudson says.

That means that different types of breast tumors, for example, will need different cocktails of drugs to treat them, says David Largaespada, Ph.D., who leads the Masonic Cancer Center's Genetic Mechanisms of Cancer Research Program.

"It's just something that we've had to face—the complexity of cancer," he says. "That complexity doesn't mean we should give up—it just means that this is why it has taken a long time and why it's hard."

But Largaespada says researchers are seeing signs of progress as new therapies show dramatic successes in subgroups of patients. Now they just need to find out *why* so they can help target the treatments to patients who will benefit most.

Partnering for progress

That's exactly what the I-SPY2 breast cancer study aims to accomplish.

Women who participate in the study will receive the current standard of care, chemotherapy and surgery—widely considered the best breast cancer treatment regimen available, Haddad says—and could be randomly selected to receive one of four investigational drugs on top of that.

Breast tumor tissue samples taken before and after treatment will be analyzed as scientists look for patterns in groups of women who had the most positive results. Once these patterns are determined and new drugs are matched with these positive outcomes, the next woman who joins the trial and has that specific genetic pattern will be assigned that specific drug. This "adaptive" design is new to breast cancer clinical trials.

Masonic Cancer Center director Douglas Yee, M.D., leads the national committee in charge of selecting drugs for the trial.

Effective drugs that add to standard chemotherapy will "graduate" for testing in larger clinical trials. Drugs that do not help to improve outcomes will be dropped.

Photo by Scott Streble

Our genetic backgrounds and environment influence whether we develop cancer and how our bodies react to medications, says scientist Brian Van Ness, Ph.D.

Initially, four drugs will be evaluated in the I-SPY2 study, but Yee says there are many promising new drugs on deck to take their place as others "graduate" or are dropped.

The collaborative network is a great example of how working together can help bring new treatments to patients in need faster, Yee says.

"No single institution has all the areas of expertise necessary to complete this type of clinical trial," he says. "Everybody is very committed to making this thing happen. We all hope that this trial will be faster, smarter, and better in bringing new discoveries to breast cancer treatment."

Learn more about personalized medicine at the University

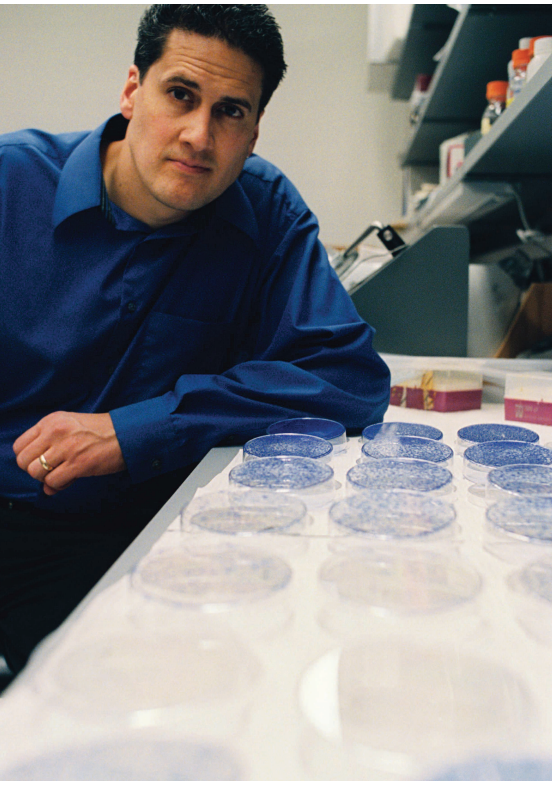
The fall issue of the *Medical Bulletin*, the Medical School's magazine, includes an article featuring more examples of how Masonic Cancer Center researchers are using genetics to personalize cancer care. Read it online beginning in late October at **www.mmf.umn.edu/mb.**

Cancer genetics research moves forward faster with philanthropic support

A tool called "Sleeping Beauty" is helping Masonic Cancer Center geneticist David Largaespada, Ph.D., and his lab team find more and more genes linked to cancer.

But Largaespada believes the real fairy-tale ending will come later, when cancer is considered a largely solved problem.

Photo by Richard Anderson



David Largaespada, Ph.D., and his lab team have identified more than 100 genes linked to cancer.

The Sleeping Beauty tool is essentially a piece of DNA that researchers can make "jump" from one section to another in the chromosomes of cells. This helps the scientists discover which genes and gene pathways are related to cancer development.

Working with genetically modified mice that model human cancers, Largaespada and his team have identified dozens of new cancer genes with Sleeping Beauty's aid. His lab has reported finding 77 genes tied to colorectal cancer—only seven of which were known previously—and 17 genes tied to liver cancer.

"Now we have a lot of unpublished data on new cancer genes for the [gastrointestinal] tract and liver [and] also for brain tumors, sarcomas, and several other types of cancer," Largaespada says. "It has really exploded in the lab."

Funding from the Margaret Harvey Schering Trust for Cancer Research is behind many of Largaespada's successes. The Schering Trust has been a source of support for his lab since 2006, and most recently it committed another $500,000 to his work. The trust also has funded an endowed chair in cancer genetics that Largaespada has held since the chair was created.

When Largaespada and his colleagues first developed this Sleeping Beauty method for finding cancer genes, they earned a five-year, $1.25 million research project grant from the National Institutes of Health (NIH).

But in Largaespada's mind, that was just the beginning.

"I wanted to expand the technology so I could show that it would work for other types of cancer besides our initial report, which was on sarcoma and T cell leukemia," he says. "And I also knew that I wanted to do it fast. The Schering Trust allowed us to get some pilot data showing that the Sleeping Beauty method worked for other types of cancer."

In fact, that pilot data has earned his lab two additional research project grants from the NIH to study gastrointestinal and liver cancers as well as a new grant from the National Brain Tumor Society.

The Margaret Harvey Schering Trust for Cancer Research was created by the late philanthropists Friedrich Schering and Margaret Harvey Schering, who believed in supporting basic science cancer research to help answer questions about why cancer occurs and how to cure it, according to trustee Mark Gaasedelen.

Largaespada says the trust's ongoing support is critical to taking his work to the next level. Now he's connecting the genetics of tumors with clinically relevant traits such as whether a cancer spreads, how it responds to treatment, and whether it recurs.

"These are the things that the clinicians really care about, and all of those things are probably controlled by the genetics of the tumor cell," he says.

Gaasedelen believes that funding Largaespada's team's research is a "perfect match" with the Scherings' intentions.

"It's got to be very, very difficult and very, very frustrating at times, but these guys are driven to find answers," he says. "I feel confident that the money is being well spent."

Training grants help promising scientists jump-start their careers

As a third-year graduate student in cancer biology at the University of Minnesota, Mariangellys Rodriguez set her sights on a short-term goal. She'd heard about the Cancer Biology Training Grant, a means to acquire two to three years of research funding, and she realized that getting the grant would be an important step toward her future.

"I applied as soon as the application was available," she says.

Supported by the National Cancer Institute (NCI), the grant is now in its 35th year at the University and supports a wide array of laboratory-based research areas, including cancer genetics, tumor biology and progression, immunology, and therapeutics.

And while earning one of these prestigious grants is an honor for graduate students and postdoctoral fellows, the grants showcase an institution as well.

"The [National Institutes of Health (NIH), of which the NCI is a part] awards training grants to institutions that have made a commitment to creating a strong training program, with resources, infrastructure, faculty, and excellent trainees," says Yoji Shimizu, Ph.D., who has directed the cancer biology training program for the last 10 years.

The Cancer Biology Training Grant selection committee handpicks recipients each year, carefully considering applicants' grades, quality of courses, letters of recommendation, and proposed scientific research. The committee also seeks qualities of excellence: "intelligence, motivation, independence, initiative, productivity"—in short, "evidence that these young people have the requisite skills to be the next faculty members and leaders in cancer research," Shimizu says.

Rodriguez, for instance, works in the lab of breast cancer researcher David Potter, M.D., Ph.D., studying how a particular enzyme present in most breast cancers may induce dietary fatty acids, like omega-3 in fish oil, to cause certain breast cancer cells to multiply. The training grant has enabled her to conduct expensive tests that otherwise would have been difficult to include in her research plan. She also has attended a national cancer research conference using the grant money.

Just as significantly, Rodriguez says, being part of the program furthered her professional development. Through their mentors in the Masonic Cancer Center, grant recipients are exposed to new topics in cancer research and get public speaking experience through seminars and journal clubs. Rodriguez especially found useful the informal "roundtable," in which grantees discussed their work to help one another "troubleshoot an experiment that wasn't working, or find an answer to a question that wasn't apparent," she says.

Rodriguez now has finished the training program and landed much-sought-after fellowship funding from the NIH.

"[The program] documents the ability of a young scientist to compete for funding," Shimizu says. "Ultimately, that's what they'll need to do to be successful in their careers."

And for Rodriguez, the future looks bright.

—Kate Ledger

After completing a portion of her research through a Cancer Biology Training Grant at the University, scientist Mariangellys Rodriguez landed a sought-after fellowship through the National Institutes of Health.

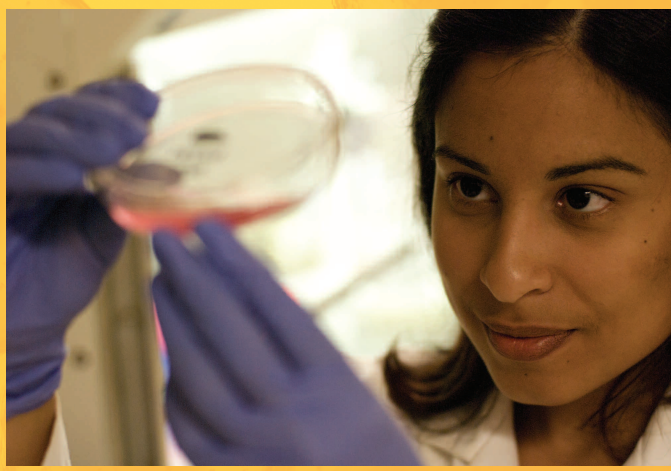


Photo by Richard Anderson

Team investigates why smokers in certain ethnic groups are more likely to get lung cancer than others

Stephen Hecht, Ph.D.

Tobacco researchers at the Masonic Cancer Center led by Stephen Hecht, Ph.D., will conduct a five-year study on why African Americans and Native Hawaiians are more susceptible to getting lung cancer from cigarette smoking than other ethnic groups.

This study—a collaborative effort of the University of Minnesota, University of Southern California, and the University of Hawaii—is funded with a new $10.7 million program project research grant (see box) from the National Cancer Institute.

A previous study showed that African Americans who smoked fewer than 10 or between 10 and 20 cigarettes per day were 2.5 to almost 5 times more likely to develop lung cancer than Japanese Americans and Latinos who smoked the same amount. They were about twice as likely to get lung cancer as Caucasians who smoked the same amount.

The study further found that while about 30 percent of African Americans and 27 percent of whites currently smoke cigarettes, about 8 percent of African American cigarette smokers smoke more than 25 cigarettes per day compared with 28 percent of white smokers who smoke more than a pack a day. This indicates that although African Americans are less likely than whites to be heavy smokers, they have a higher risk of getting smoking-related lung cancer.

Native Hawaiians' risk of smoking-related lung cancer for was found to be similar to that of African Americans.

"Those findings imply that African American and Native Hawaiian smokers metabolize nicotine and tobacco carcinogens differently than whites, Japanese Americans, and Latinos," Hecht says. "Our new research study will aim to find out why this appears to be the case."

What is a program project research grant?

Program project grants from major federal funding agencies such as the National Cancer Institute support large, multiproject research efforts and are awarded only to elite investigative teams studying pressing health issues.

This type of grant usually involves several independent investigators who share knowledge and core resources. It requires project leaders to work together closely toward a common goal, recognizing that the whole is greater than the sum of its parts.

Leave a legacy for future generations

Your annual gifts to the Minnesota Medical Foundation at the University of Minnesota make a real difference for people suffering from cancer and those who have survived it.

You can continue to make annual gifts after your lifetime, as well, by including the Minnesota Medical Foundation in your estate plans. The income generated from your endowed gift will allow you continue to help advance world-class medical research, education, and care at the University.

For example, if you're making an annual gift of $500 to cancer-related research, education, or outreach today, an endowed gift of $10,500 in your estate plan would provide the same amount of support every year after your lifetime in perpetuity.

For sample bequest language or to speak to a gift planning officer, contact the Minnesota Medical Foundation's Office of Gift Planning at 612-625-1440 or 800-922-1663, or find more information at ***www.mmf.umn.edu/giftplanning****.*

University, Mayo formalize partnership with Swedish research powerhouse Karolinska Institute

Under the mantle of the Minnesota Partnership for Biotechnology and Medical Genomics, the University of Minnesota and Mayo Clinic in June committed to a formal research relationship with the Karolinska Institute of Stockholm, Sweden.

Karolinska is the top-rated medical research university in Europe. The partnership aims to accelerate and build on the existing relationships among the three institutions.

Perhaps due to Minnesota's Scandinavian heritage, the state's research universities have more than 30 years of relationships, partnerships, exchanges, and joint projects with Karolinska that have resulted in publications, research grants, and discoveries aimed at improving the health of people worldwide.

At the start, research collaborations will focus on regenerative medicine, bio-omics (which includes genomics, proteomics, and metabolomics), and immunity—all emerging areas of biomedical science.

Other plans include establishing fellowships for promising young investigators, as they will become tomorrow's global leaders in biomedical research, to support exchanges in targeted research areas.

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New cancer and heart research building will foster collaboration

As University of Minnesota leaders continue to refine the design plans for a new Cancer and Cardiovascular Research Complex in the institution's burgeoning Biomedical Discovery District, investigators are eager to take advantage of the building's many benefits.

The new facility is expected to house 24 lead cancer researchers plus their staffs. Among those researchers is David Largaespada, Ph.D., who oversees the Masonic Cancer Center's Genetic Mechanisms of Cancer Research Program.

Largaespada uses mouse models of human cancers in his work. He envisions a "mouse hospital" where his team can conduct preclinical studies of potential treatments to help determine which therapies might be beneficial for patients.

"The therapies that will work are going to be complex," Largaespada says.

And that's why the new research building is so important, he adds. Not only will it have a large attached vivarium for housing mice and easy access to the University's world-leading Center for Magnetic Resonance Research, but it will also offer him and his colleagues in chemistry, genetics, and mouse modeling a space to work together seamlessly.

This kind of interconnectedness fosters research productivity, allowing scientists to move basic science breakthroughs to the clinic faster.

"I think it will be a really good neighborhood for this kind of work," Largaespada says.

Designed to be the centerpiece of the Biomedical Discovery District, the Cancer and Cardiovascular Research Complex will include advanced laboratory, instrumentation, and support facilities for cancer and heart research. Construction is scheduled to begin on this 280,000-square-foot building next spring.

To learn how you can support cancer research in the new facility, please contact Catherine McGlinch at 612-626-5456 or c.mcglinch@mmf.umn.edu.

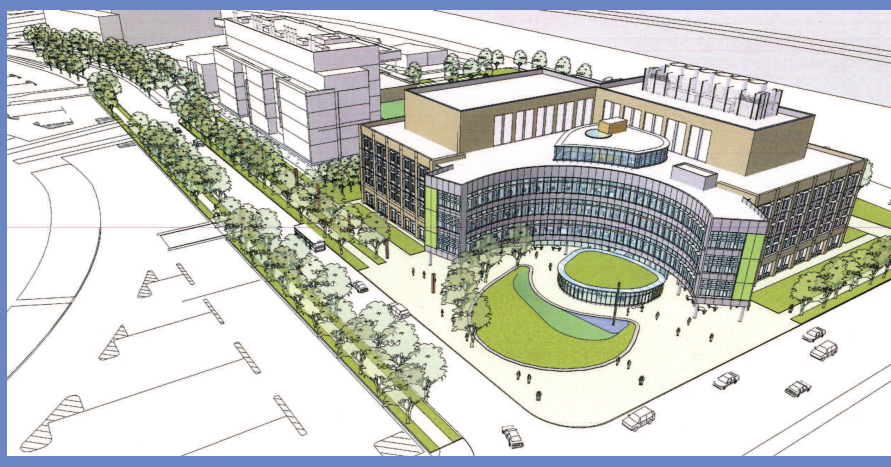

Image courtesy of Architectural Alliance

University of Minnesota

Minnesota Medical Foundation
McNamara Alumni Center
200 Oak Street SE, Suite 300
Minneapolis, MN 55455-2030

Selwyn Vickers, M.D.

Coveted SPORE grant makes the University a leading site for pancreatic cancer research and care

The University of Minnesota has been awarded jointly with the University of Alabama at Birmingham (UAB) Comprehensive Cancer Center one of the National Cancer Institute's most coveted cancer research grants.

The five-year, $11.5 million Specialized Program of Research Excellence (SPORE) grant aims to give the two cancer centers the means to achieve breakthrough research discoveries to better understand, diagnose, and treat pancreatic cancer, a deadly disease with a poor prognosis.

The SPORE program is designed to promote interdisciplinary research and move basic science findings from the laboratory to clinical settings. Its ultimate goal is to reduce cancer incidence and mortality as well as improve survival and patients' quality of life.

Two research projects are assigned to the University and will be conducted by Masonic Cancer Center scientists. One is focused on identifying and targeting pathways of pancreatic cancer progression and metastasis, while the other is focused on developing an oncolytic adenovirus to attack pancreatic tumor stem cells.

"This SPORE grant is an honor and a testament to the high-level cancer research capabilities at the University of Minnesota, its Masonic Cancer Center, and UAB," says Selwyn Vickers, M.D., the grant's coprincipal investigator and associate director of the Masonic Cancer Center's Translational Research program. "Most importantly, this [grant] further assures patients and their families that when they come to the University of Minnesota for treatment of pancreatic cancer, they're coming to one of the best places in the whole United States."

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Nicole Endres, *Editor*
Lisa Haines, juju, *Design*

For more information, please contact:
Catherine McGlinch
Director of Development
612-626-5456 (direct)
800-922-1663 (toll free)
c.mcglinch@mmf.umn.edu

www.mmf.umn.edu
www.cancer.umn.edu

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