University of Minnesota

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Masonic Cancer Center News

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

Helpful, not harmful?

U researchers employ viruses to safely and effectively kill cancer cells

We all know that viruses cause illness, from the not-so-serious common cold to the potentially deadly influenza, AIDS, and measles. So it seems counterintuitive that scientists would turn to viruses in their search for cancer treatments, right?

"When we think about viruses, we think disease," says Masato Yamamoto, M.D., Ph.D., a professor in the Department of Surgery and member of the Masonic Cancer Center, University of Minnesota. "But by wisely using viruses, we can design therapies that target cancer cells."

It's not a new idea. Scientists have been exploring the use of "oncolytic viruses," as they're called, for decades. But recently, astonishing successes have prompted hyperbolic headlines such as *Time* magazine's May 2014 headline proclaiming "Measles vaccine cures woman of cancer." And suddenly, the world's spotlight is on oncolytic viruses as the next great hope for cancer treatment.

Working with adenovirus (common cold virus), measles, vesicular stomatitis virus (VSV), and others, a strong cadre of Masonic Cancer Center investigators is at the forefront of this exciting research.

In Yamamoto's lab, the main focus is using the adenovirus to deliver a knockout punch to pancreatic cancer cells.

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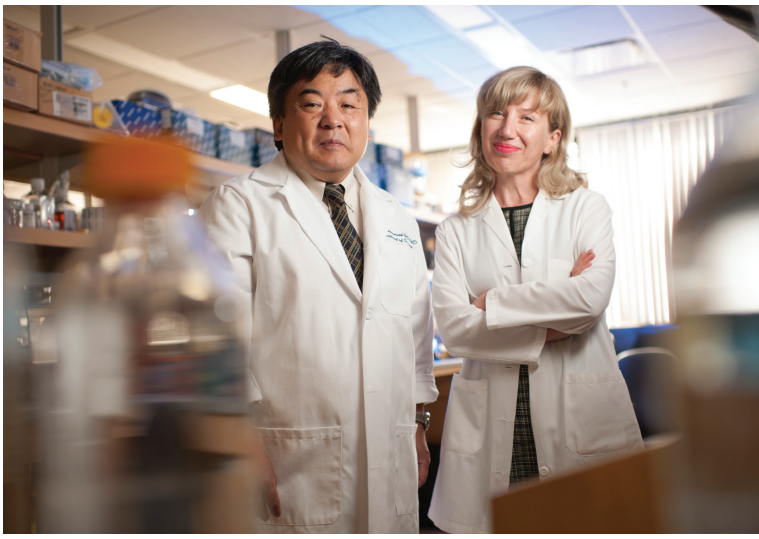
Photo by Scott Streble



Masato Yamamoto, M.D., Ph.D., and Julia Davydova, M.D., Ph.D., are pitting modified versions of the common cold virus against cancer.

Helpful, not harmful? *(continued from cover)*

Julia Davydova, M.D., Ph.D., an assistant professor of surgery who works with Yamamoto, explains how it works: "This is a gene therapy approach, meaning we design special viruses that can deliver a piece of DNA to kill tumors. We use the adenovirus as our [tumor-destroying] agent because it can express the gene of interest at high concentrations specifically in tumor tissues while eliminating cancer cells as a part of viral replication. Besides, adenovirus' replication machinery has been carefully scrutinized and established, it doesn't integrate into the genome, it doesn't cause mutations, and, since it's a common cold virus, it's not associated with any severe disease."

Photos by Scott Streble

Masonic Cancer Center scientists have genetically modified different versions of the common cold virus to target and destroy different types of cancer cells, such as pancreatic, prostate, esophageal, gastric, lung, and head and neck cancers.

That's a brief explanation for a process that takes years, in which scientists work to create and then clone powerful, specialized versions of the adenovirus that can home in on cancer cells and destroy them.

Recent trials in the lab show it works. When mice with malignant pancreatic tumors were given a single intravenous injection of the specially engineered adenovirus, four out of 10 tumors disappeared completely—something Yamamoto calls "an amazingly good result."

Targeting mesothelioma

Over the past seven years, Robert Kratzke, M.D., Masonic Cancer Center member and associate professor of hematology, oncology, and transplantation, has zeroed in on using viruses—primarily measles and VSV—to treat lung cancer and mesothelioma.

What he's found is remarkable: when the measles virus is injected into a mouse model of mesothelioma, the virus infects the cancer cells, causing them to break apart. It also releases a protein that triggers the body's immune response against other cancer cells—a very effective one-two punch.

"At first glance, it sounds dangerous, using measles as a treatment for cancer," Kratzke says, "but the strain of measles virus we use is identical to the strain used to vaccinate children. We just give a higher dose."

Now in a Phase I clinical trial run in partnership with the Mayo Clinic, the oncolytic measles virus is being injected directly into the chest cavities of people who have mesothelioma.

"We've seen one tumor shrink 40 percent in just a matter of weeks," reports Kratzke, "and we're at the lowest dose. We're excited to see what happens at higher doses."

Since he has already shown that the measles virus can cure mesothelioma in mice, Kratzke is optimistic about this new clinical trial, which will be open for several more years.

Likewise, use of VSV is showing great promise for treating cancer. A virus that primarily

infects livestock, VSV has been shown to be effective in the lab against brain tumors. It's now being used in a Mayo Clinic clinical trial in Arizona for people who have liver cancer, and Kratzke is working on developing it for use against lung cancer and mesothelioma.

"It's proven pretty effective in shrinking tumors in mice," says Kratzke, "and we're hopeful that, because of work already done in Mayo's liver cancer trial, we'll be able to move the VSV oncolytic virus forward much faster."

Challenges remain

When Kratzke says "much faster," he's using science-speak to describe a process that's inherently and frustratingly slow.

Davydova elaborates. "Our ability to create exciting new viruses greatly outshines our ability to test them in the clinic," she says. "Each time we modify the virus, it's considered to be a new drug, so it has to go through the painstaking process of approval. It can take six or seven years, or even longer, to go from cloning the virus in the lab to bringing it into the Phase I clinical trial."

Given infinite resources, the teams could push ahead much faster, Kratzke says. "Producing enough virus to treat patients is quite expensive, and we're dealing with new viruses that no companies are marketing yet, and insurance companies don't pay for the treatment. So we rely on grants and philanthropy to keep moving forward."

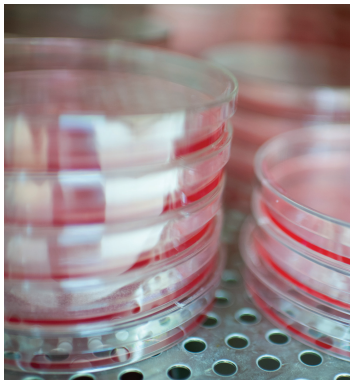
Optimism is growing

Challenges not withstanding, scientists are buoyed by increasing evidence that oncolytic viruses are, indeed, effective weapons against various types of cancer.

"We've had such great achievements with the new generation of adenoviruses," says Davydova. "The data are very exciting."

Kratzke agrees. "When you see raw data that show a four-fold improvement in mice that receive the oncolytic virus versus the control group that gets a simple saline injection, that's exciting," he says. "So now we work on fine-tuning the delivery, the dosages, and the timing of the dosages."

"I see great promise in this," adds Yamamoto, who hopes to open a clinical trial for people who have pancreatic cancer soon. "Our cancer center is very strong and is committed to enhancing work in this area. With that support, I believe we can design really effective treatments for devastating cancers."



To learn more or to support this research, contact Cathy Spicola at 612-625-5192 or cspicola@umn.edu.

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You can set up your monthly contribution online safely and securely. Visit **giving.umn.edu/monthlygifts** to get started or to learn more.

Ask the expert:

When kidney cancer can be so deadly, why don't we hear much about it?

Christopher Weight, M.D., a urologic surgeon and an assistant professor with the U's Institute for Prostate and Urologic Cancers, explains.

First of all, how common is kidney cancer?

CW: *There are about 60,000 kidney cancer cases a year. It's one of the top 10 most common types of cancer and one of the most lethal. Part of the reason for its lethality is the lack of symptoms. Because there are few symptoms, it can often grow, unchecked, and even metastasize without causing any pain. If it has spread outside of the kidney at diagnosis, we have a low chance of curing it.*

Why doesn't kidney cancer get the attention or funding that, for example, prostate cancer or breast cancer get?

CW: *Breast and prostate cancers are more common than kidney cancer. Advocates for these two cancers have been active for the past 20 to 30 years trying to influence lawmakers and raise money. We have a lot of catching up to do with kidney cancer.*

What is the University of Minnesota doing to combat kidney cancer?

CW: *We're looking at kidney cancer outcomes using large national databases such as SEER and Medicare. These look at big trends in patients. One particular interest we have is trying to understand the benefits of removal of the tumor and a thin rim of normal kidney versus removal of the full kidney.*

Also, [Masonic Cancer Center member] Tom Griffith, Ph.D., has done some exciting research in the lab that's yielding promising results. We know that the immune system plays a large role in kidney cancer. Our research shows that mice with kidney cancer had a very encouraging response to a new medication that induces cell death while stimulating the immune system. We're hoping to do a trial in people to see if we can observe the same sort of response.

How would funding benefit research?

CW: *Funding would help us complete a clinical trial with the medication we are developing here at the University. Trials are expensive and require a lot of resources. Since government funding is scarce for kidney cancer right now, we really depend on philanthropy. Gifts also could help lead toward funding a trial in kidney cancer screening with small ultrasound probes, which could help diagnose tumors when they are smaller and more likely to be cured.*

Masonic Cancer Center names new associate director of administration

After a national search, Seanne Falconer, M.B.A., has been appointed associate director of administration for the Masonic Cancer Center, University of Minnesota. She has most recently served as director of Harvard Catalyst Clinical Research Program Operations, a program of the Harvard Clinical and Translational Science Center. She earned her M.B.A. from the Yale School of Management and holds a certificate in professional fundraising from Boston University.

Falconer succeeds Mary Sumpmann, R.N., who retired in June. In honor of Sumpmann's 22 years of service to the Masonic Cancer Center, where she had worked since its inception, a scholarship fund to support undergraduate student cancer research opportunities has been established in her name. Make a gift at **giving.umn.edu/giveto/marysumpmann.**

Staying strong

U docs help a young woman find solutions during cancer treatment and beyond

Courtesy of University of Minnesota Health

Leah Arnold is ever grateful to the care team that aided her long road to recovery after non-Hodgkin lymphoma.

In 2002, Leah Arnold was a newly married college graduate preparing to take the Medical College Admissions Test when she noticed a lump on her neck. Doctors told her it was related to stress, but over the next several months, the lump in her neck grew, and she began having trouble breathing and swallowing.

A tumor stretching from her neck to her heart was discovered. Arnold was diagnosed with non-Hodgkin lymphoma.

Arnold immediately began chemotherapy and radiation, but it did not stop new tumors from forming in her kidney, liver, and lungs. She needed a bone marrow transplant, and she was referred to University of Minnesota Medical Center, where Masonic Cancer Center member and hematologist/oncologist Linda Burns, M.D., and team took charge of her care. Tests revealed that Arnold's younger brother, Justin, was a perfect match, and she received a transplant of his stem cells in July 2003.

"I was basically out of it for the next 80 days," says Arnold. "My father and father-in-law were both retired, so they became my caregivers in order that my husband could continue to work."

Arnold faced some rough spots in her recovery. Following the transplant, she dealt with graft-versus-host disease, infection, scleroderma, and fractures, including a broken rib from rolling over in bed.

"My doctors just kept searching for solutions," she says. "They never gave up. I had an amazing transplant team."

That group's hard work has allowed her to move forward with her life. In 2011, Arnold received her forensic science certificate, and she now works for the Minnesota Bureau of Criminal Apprehension. Plus, today she's off all of her posttransplant immunosuppressant medications.

Arnold is continually grateful for the medical staff that surrounded her. And she has a special reason for staying strong now.

"My dad was diagnosed with lymphoma almost exactly a year after my transplant, and he did not make it," she says. "We drew strength from each other. Now, I want to live for him. I am here for a reason."

Making the match

Finding a good match between a bone marrow transplant patient and his or her donor is critical for minimizing complications.

Matches are made based on human leukocyte antigens (HLAs), proteins found on most cells in the body that tell the immune system which cells belong to the body and which don't.

The transplant community has stringent HLA matching requirements to ensure the best outcomes: An adult marrow donor must match at least six of the eight main HLA markers doctors review to qualify matches, though today most would only use a seven-of-eight match.

Using the power of math to fight cancer

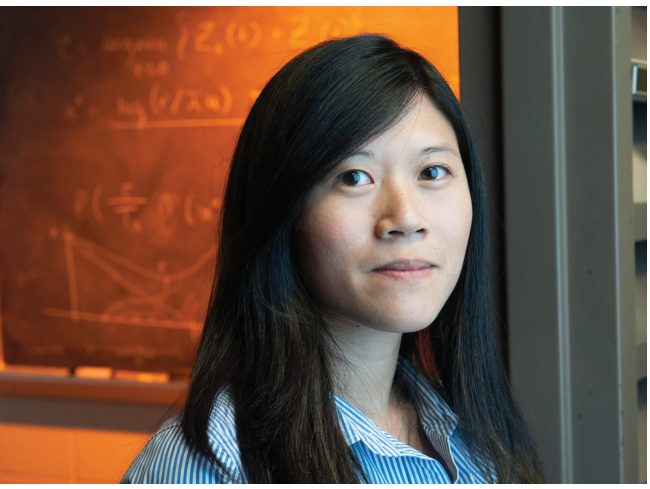


Photo by Scott Streble

Outside of clinic walls, Jasmine Foo, Ph.D., applies probability theory to create models that predict how cancers will grow, or at what point cancers become resistant to treatment.

Imagine a person newly diagnosed with cancer, overwhelmed and scared, facing treatment for the first time, placing her trust in the physician who seems to hold all the answers.

What she doesn't see is the phalanx of scientists who stand, invisibly, behind that physician. And what might amaze this new patient is that her therapy may have been fine-tuned not by oncologists but by mathematicians like Jasmine Foo, Ph.D.

Foo works in the School of Mathematics at the University of Minnesota, but her focus is on cancer—specifically, applying probability theory (the study of randomness) to create models that predict how cancers will grow, or at what point cancers become resistant to treatment. She's deep in the trenches of that work now, since she was named a McKnight Land-Grant Assistant Professor for 2013–2015, an honor that comes with both research dollars and a one-year leave to focus solely on research.

One of her primary interests is designing optimal treatment strategies that can overcome resistance to therapy, essentially foiling cancer cells' nasty ability to dodge and weave around cancer drugs.

"Drug resistance is a primary reason for cancer treatment failure," explains Foo, "but what if we dosed differently? If we changed the strategy of delivering the drugs, could we get better results?"

The answer appears to be yes. Working with researchers and clinicians, Foo developed a mathematical model that significantly improved treatment for non-small-cell lung cancer; following validation of the model in the lab, the protocol is currently being evaluated through a clinical trial in New York.

Foo, a Masonic Cancer Center member, also uses her considerable math skills to study how cancer cells arise out of healthy tissue, looking at distinct differences in how cancers evolve in various parts of the body. She's also interested in quantifying genetic diversity of cells within a single tumor, which can give the treatment team insight into how or when to best attack tumors at various stages.

Her models can also help develop guidelines for surgeons who are removing tumors, since mathematicians have learned that the size and geometry of the premalignant tissue field around tumors can vary greatly from cancer to cancer.

While it takes a long time to go from the beginnings of a math model to clinical application, it takes even longer for new drugs to reach the marketplace. So math modeling has become a critical tool for wringing the most good out of available treatments, while researchers keep working on the next blockbuster drugs.

"We're not designing completely new treatments," Foo says, "but improving upon existing therapies. It's great to be part of such a growing field, and it's so rewarding. I'm very optimistic that math modeling will improve the quality of treatment for cancer patients."

More mothers smoke during pregnancy than previously thought, says U study

New research from the Masonic Cancer Center has shown evidence of more mothers smoking while pregnant than reported on their children's birth certificates.

The research, led by Anne Joseph, M.D., M.P.H., used a newly developed testing method that allows investigators to look at small blood samples while maintaining accurate results. The test was developed at the University of Minnesota by Sharon Murphy, Ph.D.

The researchers used the new technique to test newborns' dried blood spots for cotinine, which is created by the body after exposure to nicotine. Twelve percent of the dried blood spots' results indicated that the mother had smoked within the last several days before giving birth. Forty-one percent of those mothers had not reported themselves as smokers.

"Prenatal exposure to tobacco smoke has been connected to both short- and long-term effects on babies, including lower birth weights, birth defects, asthma, and neurobehavioral problems," says Logan Spector, Ph.D., lead author of the paper, which was published online in the journal *Pediatrics*. "These effects also don't consider other potential lifetime risks, such as cancer."

The current process of recording mothers' smoking habits relies on information documented on birth certificates. This information can be imprecise, as some mothers may feel guilty about their habits. The new testing method is a more objective way to determine smoking rates among pregnant women.

Tribute to a leader

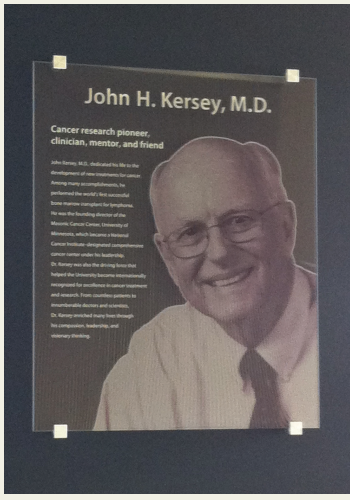
Masonic Cancer Center leaders unveiled a permanent tribute to the center's founding director, John Kersey, M.D., in the U's Cancer and Cardiovascular Research Building on May 13. The display is prominently featured in the lobby of the building, which is open to the public—a rarity for research facilities.

Kersey, a native Minnesotan, had served on the University of Minnesota faculty since 1971. He stepped down as director of the Masonic Cancer Center in 2007 after 15 years in that role but remained a dedicated research scientist at the institution until his sudden death on March 10, 2013, at age 74.

The text on the commemorative glass panel reads as follows:

Cancer research pioneer, clinician, mentor, and friend

John Kersey, M.D., dedicated his life to the development of new treatments for cancer. Among many accomplishments, he performed the world's first successful bone marrow transplant for lymphoma. He was the founding director of the Masonic Cancer Center, University of Minnesota, which became a National Cancer Institute–designated comprehensive cancer center under his leadership. Dr. Kersey was also the driving force that helped the University become internationally recognized for excellence in cancer treatment and research. From countless patients to innumerable doctors and scientists, Dr. Kersey enriched many lives through his compassion, leadership, and visionary thinking.



Make a gift to the John H. Kersey Chair in Cancer Research at ***give.umn.edu/giveto/kerseychair.***

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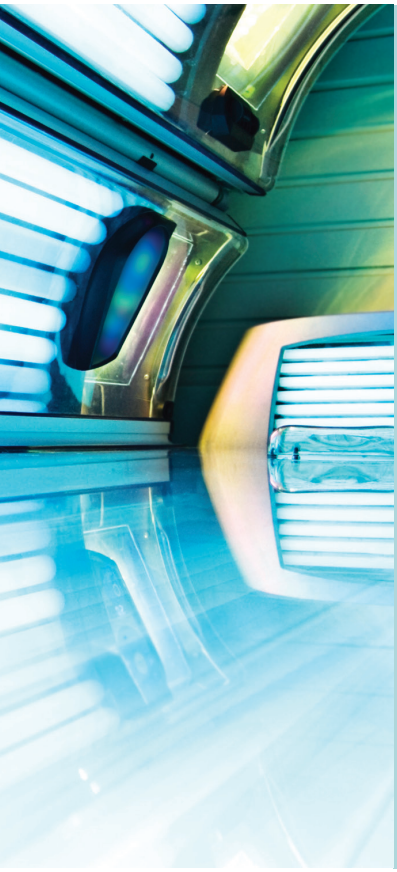

New law bans minors from tanning beds

Whether before prom or a vacation, teenagers have often used tanning beds to get a sun-kissed look before big events in their lives. But on August 1, Minnesotans under 18 years old were forced to rethink their tanning habits.

Gov. Mark Dayton in May signed a bill into law that prohibits minors from using indoor tanning beds, making Minnesota the eighth state to pass such a law.

The research that led to this policy change was driven by DeAnn Lazovich, Ph.D., an epidemiologist and coleader of the Masonic Cancer Center's Prevention and Etiology program. She provided critical testimony during the legislative session about her research that has overwhelmingly linked indoor tanning to melanoma, one of the deadliest forms of skin cancer.

People who tanned indoors were 74 percent more likely to develop melanoma than those who had never tanned indoors, according to Lazovich's studies. The more times a person tanned indoors, the higher the risk.

The legislation was proposed in 2013 and passed in 2014, a timeline much faster than Lazovich expected. "I was amazed because I was told by the American Cancer Society that these things could take years to pass," she says.

Prior to the legislation, Minnesota law required all those under age 16 to have parental permission to use indoor tanning beds, but salons weren't always enforcing the rule. Now Lazovich hopes banning indoor tanning for all minors will make it easier to enforce.

"It's definitely a good start," Lazovich says.

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