University of Minnesota

Spring 2017

# Masonic Cancer Center News

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

## Predicting cancer's next move

*With a physics-based research approach, Masonic Cancer Center scientists are looking for clues to stop the most unstoppable cancers*

What is a "physical sciences approach" to cancer? At the University of Minnesota, it represents a new frontier in the way researchers look at cancer and how it spreads—and how it could result in new, personalized therapies for even the toughest-to-treat cancers like brain and pancreatic cancers.

"There's been a real lack of application of the physical sciences to oncology research in the past, such as trying to understand how cells work by using engineering concepts like math modeling and instrumentation," says Masonic Cancer Center member David Odde, Ph.D., a professor in the U's Department of Biomedical Engineering. "But now that's changing."

In a big way. The National Cancer Institute (NCI) recently awarded an $8.2 million Physical Sciences Oncology Center grant to the University to develop a "cell migration simulator"—just the sort of innovation Odde talks about. The grant welcomes the U into an elite network of 10 institutions around the country that are working on this physics-based approach to cancer research.

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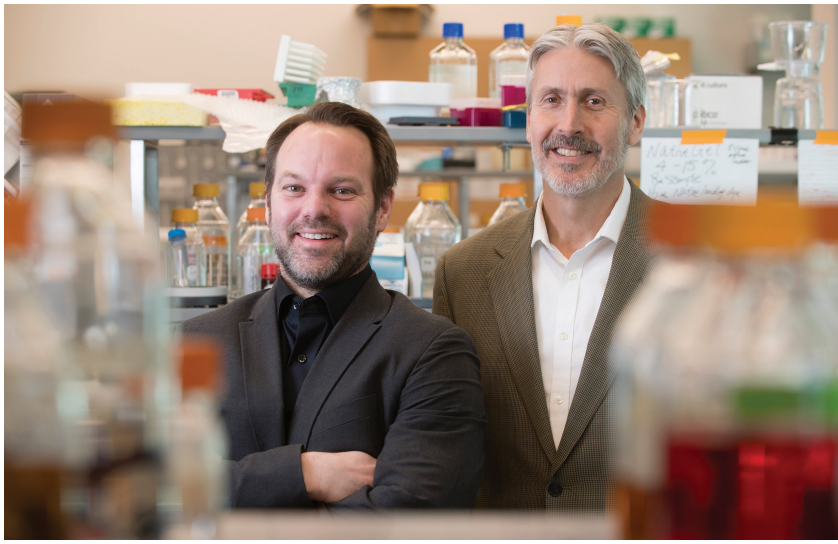
*Photo by Scott Streble*



*Paolo Provenzano, Ph.D., and David Odde, Ph.D., are using engineering concepts to predict how cancer cells will spread in the body, starting with brain and pancreatic cancers.*

# Predicting cancer's next move *(continued from cover)*

Cell movement is of paramount interest, particularly in cancers where cell migration—metastasis—is a major concern, such as brain and pancreatic cancers. How do cells move themselves forward? What makes them move faster or slower? Can we predict their movement? And, ultimately, can we stop them or slow them down?


*Image courtesy of Ben Bangasser, Ph.D., and David Odde, Ph.D.*

*A brain tumor cell generates traction forces on an engineered surface. The color corresponds to the level of mechanical force that the cell exerts locally, with red indicating higher force.*

Looking at cancer cells as tiny machines, Odde uses the cell migration simulator, which is a computer model, to predict how they will move. And, with somewhat tempered optimism, he is very pleased with the results so far.

"Our 1.0 version of the simulator made powerful predictions that we tested and found to be true," says Odde. "Next we want to take patient-derived cells and see if we can predict, using our simulator, how they'll progress."

As he conducts his research, Odde expects to continually modify and improve his simulator so he can keep studying new cells, maybe even on a patient-by-patient basis.

"It's like a flight simulator," he says. "One day you want to fly a Cessna, the next day you want to fly a fighter jet. It's the same simulator, but the details are different."

Ultimately, by understanding cell migration patterns, Odde hopes to unlock the secret to suppressing the movement. That could stop cancer from progressing into more deadly stages and instead turn the cancer into a low-grade, localized disease for which we already have powerful treatment tools such as surgery and radiation, he says.

## Inside out, outside in

The U's new Center for Modeling Tumor Cell Migration Mechanics, created by the NCI grant, formalizes work begun years ago by Odde and others, work that lacked the financial support this grant now gives them.

In the new center, the work breaks down into two projects: one, led by Odde, looks at cancer cells from the inside out, while the other, led by Paolo Provenzano, Ph.D., an assistant professor in the Department of Biomedical Engineering, looks at those cells from the outside in.

"Paolo's studying the environment the cancer cells live within," explains Odde, "while I'm focused on the guts of the cell."

Odde and David Largaespada, Ph.D., the associate director for basic sciences at the Masonic Cancer Center and holder of the Hedberg Family/Children's Cancer Research Fund Chair in Brain Tumor Research, colead the U's team. They work closely with partners at the Cleveland Clinic, who provide critical insight and perspective on clinical applications.

## Understanding the environment

Provenzano, with a background in mechanical engineering, applied math, and experimental mechanics, became interested in applying his unique skills to the cancer field almost 15 years ago.

"At that time," he says, "if I were hosting a national conference for people who were using physical science to understand cancer, I probably could have held it in my house. There weren't many people who saw this as important to the research."

But in the past seven years or so, says Provenzano, scientists have come to understand that the small spaces surrounding a cancer cell are profoundly important. Learning more about the cell environment helps researchers not only understand how

the cells move through it, but also why that environment produces barriers to treatments like chemotherapy.

Once he's armed with answers, Provenzano hopes to be able to re-engineer those environments to eliminate the barriers to treatment and effectively kill the cancer cells.

## Endgame

The primary goal of all of this work, of course, is getting new treatments into the clinic where they can help patients. Through work with the cell migration simulator, Odde, Largaespada, Provenzano, and colleagues hope that they'll be integrating their findings into clinical practice within the next five years.

To that end, they're already asking patients if they're willing to donate, in the course of their regular treatment at U-affiliated cancer clinics, tissue samples that can be analyzed using the simulator.

"There are some big ideas here," says Odde. "We don't have new treatments yet, but ... maybe we hit a home run. I'm pretty optimistic that this kind of modeling will have a big impact, and from that, we'll keep building."


Novel ideas in research can stall out or even fail to get off the ground because scientists don't have the funding to pursue them. That's why private gifts in the form of smaller seed grants can have such a huge return on investment.

Paolo Provenzano, Ph.D., for instance, received philanthropic support as a Masonic Scholar and from the Randy Shaver Cancer Research and Community Fund that helped him develop the ideas that underlie this new Physical Sciences Oncology Center grant and generate preliminary results that were crucial components of the grant proposal.

Funding David Odde, Ph.D., received from Children's Cancer Research Fund and a Masonic Cancer Center grant helped him develop essential preliminary data and also provided bridge support that enabled his work to advance during gaps in the grant process.

"Investigators really need to have this kind of funding available when they're trying to do something new, because new ideas don't always fit into existing federal funding programs," Odde says. "[Philanthropy] really encourages and enables innovation."

# Treatment, precisely

*A national, multipronged clinical study matches cancer patients with investigational treatments designed to attack their specific tumors*

*Photo by Brian Carnell*

What if doctors could treat every cancer patient with a therapy designed specifically for his or her unique genetic makeup? Researchers at the Masonic Cancer Center are now enrolling patients in a clinical trial designed to do just that.

Called NCI-MATCH (National Cancer Institute–Molecular Analysis for Therapy Choice), this national study began with 12 "arms," with each arm evaluating a drug previously shown to be effective against a specific cancer-related abnormality. Since the study opened last year, that number has grown to 24 arms; new ones will be added as new drugs are added.

**Are you a match for the NCI-MATCH trial?**

*Want to know if you're a candidate for this study? Call Belinda Nestor at the Masonic Cancer Center's Clinical Trials Office at 612-626-4274.*

"It's part of our ongoing precision medicine program," explains Masonic Cancer Center member and gynecologic oncologist Melissa Geller, M.D., M.S., "and it's an exciting trial because there are multiple promising therapies here. The first question, though, is 'does your tumor match?'"

To find out, the first step is taking a biopsy of a patient's tumor. The sample is sent to a centralized testing site that identifies the tumor's genomic profile. If the tumor does contain a specific mutation covered in the MATCH trial, the patient is enrolled and treated with the investigational therapy.

*Gynecologic oncologist Melissa Geller, M.D., M.S., says the nationwide NCI-MATCH trial fits perfectly into the U's precision medicine program—tailoring treatment for each individual patient's cancer.*

"But even if their tumor does not match initially," Geller says, "they may be eligible for a future substudy. Also, the NCI and the MATCH trial keep track of these mutations, so as new arms are added, we may be able to go back and enroll people based on earlier results."

Emil Lou, M.D., Ph.D., a gastrointestinal oncologist and Masonic Cancer Center member, coleads the trial at the University with colleague Bruce Peterson, M.D. Lou likens it to a search for the right key.

"Each tumor is composed of a unique set of identifiers," he says. "The question that this trial investigates is, do we already have a drug that works for that genomic profile, like a key for a specific lock?"

Because the study focuses on matching therapies to specific mutations, versus the location of the cancer in the body, patients with a broad range of tumors are being tested. Lou explains that the same mutation found in one person's lung cancer, for instance, may be found in another's colon cancer.

"The field of oncology is undergoing a fundamental shift that's had a tremendous effect on how we treat complex cancers," says Lou. "This NCI-led trial illustrates that approach. It's a very promising time for patients, and we're moving full-speed ahead with this and other similar trials here at the University of Minnesota."

Photo courtesy of Stephanie Oeding

# 'How lucky'

***A little girl with a rare blood cancer receives a lifesaving bone marrow transplant—and a second chance at a full life—from her big brother***

*Four-year-old Ava Oeding is energetic and healthy, thanks to a bone marrow transplant at University of Minnesota Masonic Children's Hospital. Her big brother, T.J., bravely provided the bone marrow that saved her life.*

It was the worst possible news: little Ava Oeding, who'd had suspicious bumps on her face and a series of nagging fevers for over a year, was diagnosed with the very rare juvenile myelomonocytic leukemia (JMML) when she was just 2 years old.

"It was such a scary time," recalls Ava's mom, Stephanie Oeding. "I don't think we realized then just how lucky we were to be at the U."

Two years later, with her vibrant daughter bouncing around their home in Becker, Minnesota, Stephanie Oeding looks back on the process and marvels at how many people at University of Minnesota Masonic Children's Hospital worked together to help Ava back to health. They first met pediatric hematologist/oncologist Lucie Turcotte, M.D., but they ultimately worked with scores of nurses, doctors, and other staff at the hospital and its Journey Clinic.

Margaret MacMillan, M.D., M.Sc., Ava's pediatric blood and marrow transplant specialist, confirms just how rare JMML is. "It's found in only about 1 in 1.6 million children under the age of 5. We only see one or two cases of JMML here each year."

The only potential cure for JMML is a bone marrow transplant, MacMillan says, which requires a compatible donor. Luckily, Ava's big brother, T.J., who was 5 when she was diagnosed, was a match.

In January 2015, Ava and Stephanie moved into the bone marrow transplant unit at U of M Masonic Children's Hospital, leaving dad Andy and T.J. at home. Ava had chemotherapy treatments for about a week, and then the Oedings had two kids in the hospital when T.J. was admitted for transplant day.

Twenty-one days later, when Ava's blood test first showed signs of healthy white blood cells, it was cause for celebration. And now, two years later, MacMillan believes that Ava's chance of relapse is quite small and that the energetic little girl is on the road to becoming a "healthy, fabulous young lady."

"I truly don't know how they do it every day," says Stephanie Oeding of the extended care team who helped Ava before, during, and after her 41-day hospital stay. "They treated Ava like their own child. We thank the Lord we had these amazing people to help us."

For MacMillan, the quest to keep improving the standard of care for children like Ava is never-ending.

"These little kids do not have time on their side. We can't just wait for the next breakthrough to come along," she says. "We're constantly focused on research, on developing new clinical trials and improving the standard of care for every single child who comes through our doors."

# HELP FROM THE PET STORE

## Researcher looks to 'dirty' mice for better models of adult humans' immune systems

Researchers have long noted disparities between the functioning of the human immune system and that of laboratory mice. Could it be because, unlike us, the mice live in antiseptic cages, shielded from exposure to infectious organisms?

A landmark University of Minnesota–led study lends credence to that idea. It has found that immune cells of lab mice bear relatively little resemblance to those of adult humans. Instead, they resemble the immature immune cells of newborn babies, who also have been sheltered from the unhygienic real world.

*Photo by Brian Carnell*

*David Masopust, Ph.D., was named to the inaugural class of Howard Hughes Medical Institute Faculty Scholars for his immune cell function research.*

The researchers reasoned that intimacy with "dirty" pet store–raised cage companions could transfer microbes to the sheltered lab mice and give their immune systems the challenge they needed to develop to maturity. Sure enough, after 52 days of cohousing, the lab mice's immune systems matured to a state much more like that of adult humans, says Masonic Cancer Center member and study coauthor David Masopust, Ph.D.

While not discounting any previous investigations using lab mice, Masopust and his colleagues make the case that studying cohoused mice "could provide a relevant tool for modeling immunological events in free-living organisms, including humans." The work was published in the journal *Nature*.

This type of innovative thinking has earned Masopust a place in the inaugural class of Howard Hughes Medical Institute (HHMI) Faculty Scholars. The Faculty Scholars program—led by the HHMI, Simons Foundation, and Bill and Melinda Gates Foundation—targets early career researchers and provides flexible funding resources to allow them to take chances and follow interesting and creative research leads. Eighty-four scholars were selected for the honor out of more than 1,400 applicants.

"This recognition of Dave's work puts him in a class with some of the most elite investigators in the nation," says Tucker LeBien, Ph.D., associate vice president for research in the U's Academic Health Center. "His fundamental research on immune cell function has changed the field in incredible ways, and this program will only provide more opportunity for discovery."

This new knowledge about "dirty" mice doesn't necessarily mean that research done with lab mice should be thrown out, Masopust cautions.

"Clean mouse research is good, but dirty mouse research adds something," says Masopust, who is also an associate professor in the Medical School's Department of Microbiology and Immunology, "and we hypothesize that there are many cases where dirty mice will be more predictive [of human responses]."

## *HPV antibodies linked to improved survival rates after head and neck cancer*

*Photo by Stephen Garret*

*Heather Nelson, Ph.D., M.P.H.*

Human papillomavirus (HPV) is a viral infection with a well-known connection to cervical cancer. Now, new research from the Masonic Cancer Center indicates that people with HPV-fighting antibodies in their systems are more likely to survive for at least five years after treatment for head and neck cancers.

The outcome was indicated irrespective of the anatomic location of a patient's tumor and personal history of tobacco and alcohol consumption, says lead author Heather Nelson, Ph.D., M.P.H.

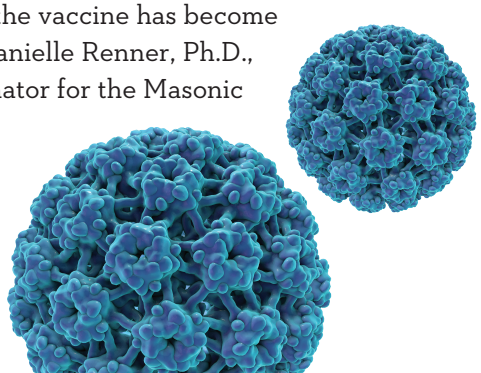
In ongoing clinical trials, doctors are evaluating whether people who have HPV-associated cancers can be treated less aggressively—and whether they experience fewer negative side effects—than people who have non-HPV-associated cancers.

Nelson and her colleagues are designing studies to evaluate whether other viruses elicit a similar immune response that affects outcomes as well. Minnesota Masonic Charities, the National Cancer Institute, and the National Institute of Environmental Health Sciences funded the work.

This study emphasizes the importance of the relatively new HPV vaccine. "With the vaccine coming on the market, we will now see a downward trend of these cancers even happening," Nelson says.

That's why the Masonic Cancer Center is working with community agencies, such as the American Cancer Society and the Minnesota Cancer Alliance, on efforts to educate the public about the vaccine's benefits.

"With all the research that's coming forward, the idea of advocating for the vaccine has become a priority," says Danielle Renner, Ph.D., education coordinator for the Masonic Cancer Center.



# Silver lining

Even during treatment for Stage IV colon cancer, Danna Mezin was surprisingly energetic. The former UnitedHealthcare executive and her husband, Dick Koats, created the Mezin-Koats Colon Cancer Research Fund at the Masonic Cancer Center and poured themselves into advancing research on treatments for the disease that would eventually claim Mezin's life.

After she passed away in March 2015, Mezin's family and friends continued to raise money for research in her honor. And UnitedHealthcare's Medicare and Retirement unit launched a "Save a Life" campaign to encourage call center staff to schedule preventive screenings for its members.

Mezin and her story inspired thousands. We'll let the numbers do the talking.

**1,505 gifts totaling $399,727.71**
to the Mezin-Koats Colon Cancer Research Fund since its inception in April 2014 through December 2016

**3 colon cancer research projects**
funded so far at the Masonic Cancer Center

**7,890 colonoscopies scheduled and 78,110 at-home colon cancer test kits delivered**
through the "Save a Life" campaign since it began in May 2015 through December 2016

**179 estimated lives saved so far**
by these colon cancer screenings through the "Save a Life" campaign

University of Minnesota

**University of Minnesota Foundation**
McNamara Alumni Center
200 Oak Street SE, Suite 500
Minneapolis, MN 55455-2010



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# Join the movement

Grab a bike and join our quest to defeat cancer. Chainbreaker is a cycling event and celebration supporting the Masonic Cancer Center and lifesaving cancer research across the University of Minnesota.

Chainbreaker participants can choose a ride that matches their skill level, including one-day rides of 25, 50, or 100 miles and a two-day ride of 180 miles. The cycling and entertainment experience is August 11, 12, and 13.

Get geared up and ready to ride!

**Register to ride at chainbreakerride.org.**

CHAINBREAKER

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Nicole Endres, *Editor*
Carolyn Bernhardt, Barbara Knox, and Deane Morrison, *Writers*
Lisa Haines, juju, *Design*

To find out how your gift can make a difference, please contact:
Sharon Kunau
612-624-1913
skunau@umn.edu

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