



Masonic Cancer Center News

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

Building on expertise

U scientists keep improving the use of natural killer cells against cancer

All humans, healthy or not, have cells called “natural killers” that help make up our immune systems. When cells become damaged, infected, or cancerous, NK cells recognize changes on those cells and kill them.

So, for people with cancer that continues to grow, why don't NK cells destroy the tumors?

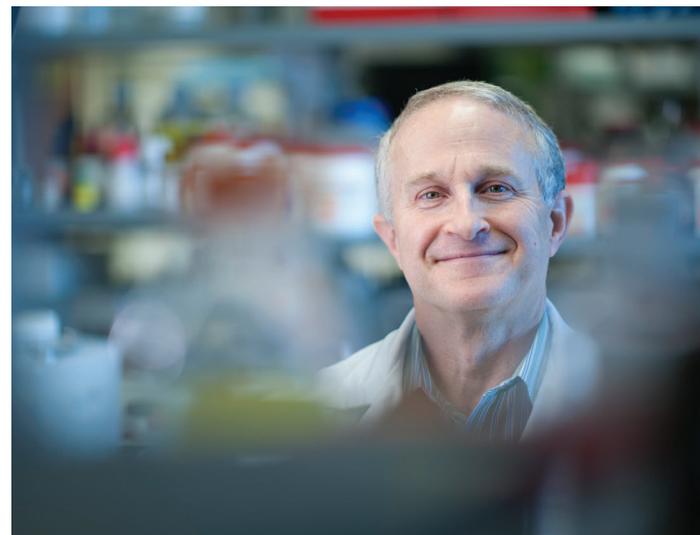
“When tumors start to grow, they suppress the immune system,” explains Jeffrey Miller, M.D., deputy director of the Masonic Cancer Center, University of Minnesota and director of its Cancer Experimental Therapeutics Initiative (CETI). “There’s no way to know how many times NK cells protect someone from cancer. We only know when they fail.”

Miller is just one of the scientists at the University studying NK cells and how best to use them in cancer therapies. In fact, the team is discovering ways NK cells can be activated and directed to seek and destroy tumor cells. It's exciting work because, well, it works.

“I started studying NK cells when I came to the U in 1991, exploring what capacity NK cells have to become cancer scavengers,” says Miller. “We’ve treated hundreds of patients in clinical trials since then and have definitely had success. But we know we can improve outcomes for patients.”

In one clinical trial, for instance, Miller
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Photo by Scott Strebbe



A research team led by Jeffrey Miller, M.D., builds on more than 20 years of experience to create better cancer therapies using natural killer cells.

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Songwriter's legacy lifts U bone cancer research up, up, up
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Building on expertise *(continued from cover)*

infused patients afflicted with resistant or relapsed acute myeloid leukemia (AML) with NK cells from a healthy donor and saw a 30 percent remission rate—definitely a positive outcome.

“What we know is that we can put stubborn cases of AML into remission,” says Sarah Cooley, M.D., a Masonic Cancer Center member and an assistant professor of hematology, oncology, and transplantation. “Now we’re trying to add different receptors to the NK cells to get a higher percentage of patients into remission.”

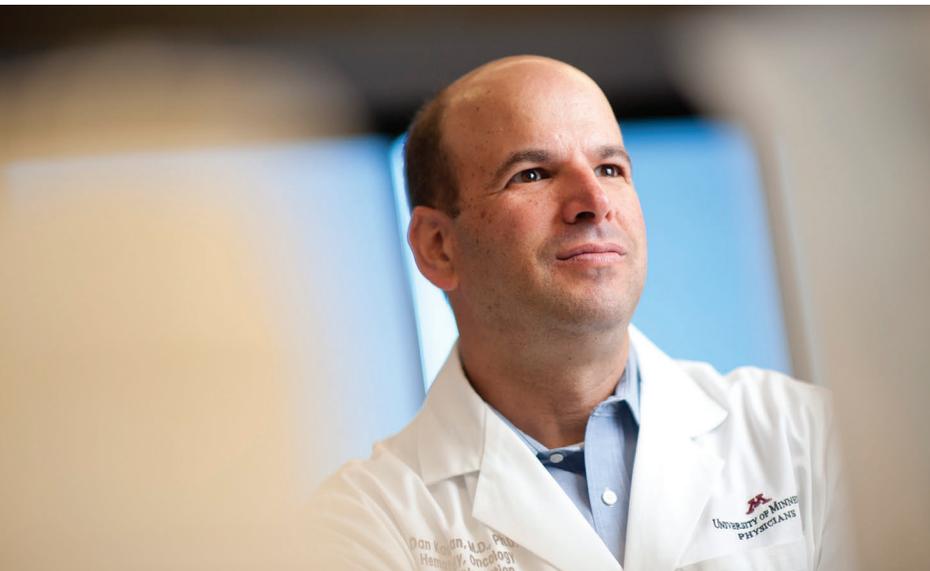


Sarah Cooley, M.D.

‘Team science’

Cooley is part of what Miller calls the “team science” approach: developing a critical mass of investigators focused on one area of research. Miller oversees 20-plus researchers, including University of Minnesota Medical School staff, laboratory workers, and postdoctoral fellows. To make sure everyone stays abreast of work going on in other labs, Miller holds regular meetings and presents clinical trial results to keep the lab team excited about what it’s doing.

Photo by Scott Strebler



Dan Kaufman, M.D., Ph.D., believes that by modifying natural killer cells, researchers could target and destroy more types of cancer.

“You have to build on your expertise to bring something meaningful to the cancer community,” explains Miller. “NK cell research is one of the Masonic Cancer Center’s specialties.”

Under that NK-cell research umbrella, the scientists investigate separate but related projects. Cooley focuses on two main areas: using donor NK cells, typically from a half-matched family member, and studying the roles of different receptors on NK cells. She is also part of a large grant from the National Cancer Institute that Miller oversees that examines the role of NK cells in transplants from unrelated donors.

In another nearby lab, Dan Kaufman, M.D., Ph.D., cultivates NK cells from human pluripotent stem cells. He recently developed a more efficient, cost-effective process for deriving NK cells from these stem cells, which could pave the way for a larger-scale production effort.

“Our ability to now produce large numbers of cytotoxic [cell-killing] NK cells could have far-reaching effects for future cancer therapies,” he says. “And it may also be possible to engineer the cells with antitumor and antiviral receptors to provide off-the-shelf products for cancer treatments. That’s the goal.”

Fine-tuning the formula

With each new discovery, the team develops a better understanding of how NK cells can be manipulated to attack and kill cancer cells; then they tinker with the formula and try again.

Miller and gynecologic surgeon Melissa Geller, M.D., M.S., are currently taking a new approach in a clinical trial for women who have ovarian cancer by infusing donor NK cells directly into the patients’ abdominal cavities instead of into the bloodstream as usual.

“We’re hoping we can improve the outcomes by putting NK cells into close proximity to the cancer,” Miller explains. “The goal for the study is to find the donor NK cells in the patient’s blood after seven or 14 days. If we can detect them in a blood test, we know the infused NK cells have expanded successfully.”

Like most clinical trials, the ovarian cancer study is expensive, so right now the team is starting with one infusion per patient. But if the results indicate that it’s a successful therapy for ovarian cancer, future plans may involve infusions every three months for the first year of treatment.

“These are the kinds of ideas we always have in the back of our minds,” says Miller. “We’re not there yet, but that could be the next step.”

Crossing the valley

Real advances in cancer treatment require not only the brightest thinkers but also the money to transform their ideas into reality—from start to finish.

Kaufman likens running a research laboratory to running a small business: “You’re always looking to raise capital.” He notes that the period between the successful conclusion of animal studies and the beginning of human clinical research is known among scientists as “the valley of death.”

“That’s the time when projects can stall, or even die,” he explains. “It’s very hard to get funding for that work.”

That’s the reason the Masonic Cancer Center created CETI in 2011. Headed by Miller and funded by Minnesota Masonic Charities and other philanthropists, CETI is designed to move the most promising lab research into clinical studies faster. Cooley, Geller, and Miller have all received support from CETI.

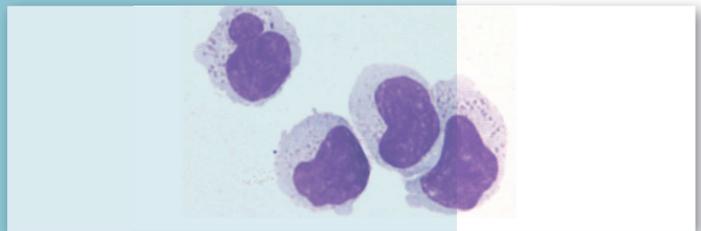
What’s the appeal of natural killer cells?

While cancer treatments like chemotherapy and radiation damage cells indiscriminately, natural killer (NK) cells target only cancerous cells, leaving normal cells unharmed.

NK cells can be collected from a donor’s blood, or they can be made in greater quantities from pluripotent stem cells. Physician-researchers also like that NK cell therapies don’t require as close of a genetic match between the recipient and donor as some other immunotherapies.

There’s also potential to manipulate them to target certain types of tumors. Today NK cells are good at killing blood cancers such as leukemia, says Dan Kaufman, M.D., Ph.D., but adding specific receptors to the cells could help them work better against solid tumors as well.

To find out how your support can help to advance NK cell research, contact Cathy Spicola at 612-625-5192 or cspicola@umn.edu.



“[Miller] has formalized our disparate group of researchers into a strong NK cell research team,” Cooley says. “He’s built a pipeline that helps us all go from preclinical testing to Phase I clinical trials, and he channels the funds where they’re needed most. And while we’re all at different places with our work, he keeps us working as a united team with a common goal: how can we use NK cells to cure cancer?”

Ask the expert:

Why are more women getting double mastectomies to treat breast cancer when it only affects one breast?



Todd Tuttle, M.D.

First of all, is it really true that more breast cancer patients are opting for double mastectomies?

Yes, multiple studies have shown that to be the case. We don't really know why. Some women may choose a double mastectomy followed by reconstruction surgery to ensure symmetry. But I think a lot of women do it because they believe it will improve their chances for long-term survival—and that concerns me.

A double mastectomy won't improve cancer survival rates?

Research has not shown a survival benefit with the second mastectomy. Most women's understanding of their cancer risk in the other breast is grossly exaggerated. For a woman with cancer in one breast, the 10-year risk of getting a cancer in the other breast is only about 4 to 5 percent. The greater risk is in having the cancer spread to the lungs, liver, or bones.

Angelina Jolie recently told the world about her double mastectomy, and she didn't have cancer. Does that make sense?

I actually like the Angelina Jolie story and hope it gets out even more, because she did it the right way. One of her doctors discovered a red flag in her family history—her mother had ovarian cancer at a young age. So Jolie underwent genetic counseling and testing and was found to carry the BRCA gene that is associated with a very high incidence of breast and ovarian cancer. Her decision to undergo prophylactic mastectomy was very reasonable. Women should talk with their doctors and get as much information as possible before making that decision.

Todd Tuttle, M.D., is a member of the Masonic Cancer Center and a surgical oncologist at the University of Minnesota Medical Center, Fairview.

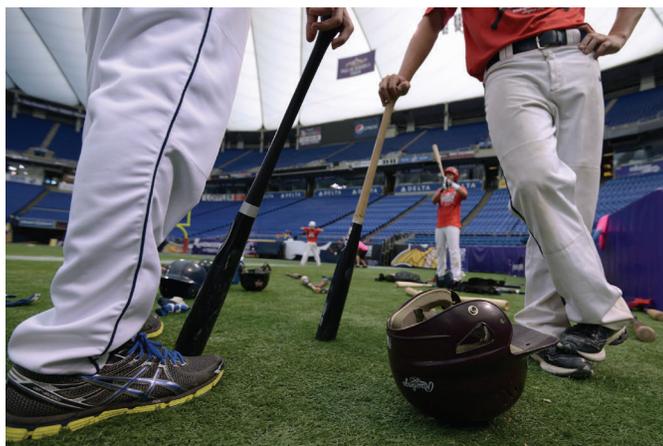


Photo by Jim Bovin

One for the home team

A group of 48 teens with the organization PHD Baseball (Pitching, Hitting, Defense) took their bats to cancer in August by attempting to play the world's longest baseball game while raising money for the Masonic Cancer Center, University of Minnesota. Players rotated in and out of 169 innings at the Hubert H. Humphrey Metrodome over the course of 40 hours, 15 minutes, and 26 seconds. Though the game likely will go down in the books as the fourth longest game in history, PHD Baseball still raised thousands of dollars for the Masonic Cancer Center.

University researchers keep searching for answers about why Iron Rangers have higher rates of mesothelioma

Does taconite dust lead to mesothelioma, a cancer of the lung's lining? This was the main question that the Minnesota State Legislature charged University of Minnesota researchers with answering through a \$4.9 million study called the Minnesota Taconite Workers Health Study nearly five years ago.

University researchers aim to determine whether exposure to particles in taconite dust released through mining in the Iron Range has caused the higher rates of mesothelioma identified there.

So far, they have found that for every year worked in the mines, a person's risk for mesothelioma increased about 3 percent. But there's more work to do, says lead researcher Jeffrey Mandel, M.D., M.P.H., of the School of Public Health.

"It's an important project for the University, the state of Minnesota, and the communities up north," says Mandel. "I knew it would be a complicated study to do, politically and scientifically, but this is a unique opportunity."

The results of a report published in April were shared at a meeting with Iron Range workers and their families. The relationship between taconite dust and mesothelioma was being called an "association" rather than a "cause."

"At this point in time, we're not suggesting a cause," Mandel says. "Workers are being told that the elevated rates of cancer seem to be related to the length of time that people worked in the industry."

The University team now has a good understanding of the exposures to taconite dust in the mines, Mandel says. Most cases of mesothelioma they're studying likely originated decades ago when the industry was new and fewer measures to protect workers' health were taken, he says.

Due to updated safety precautions, such as better ventilation and improved engineering systems to process the ore, researchers believe that miners today aren't more likely to develop cancer from their workplace than others.



Photo by Bergerson Photography

Exposure to dust from taconite operations today is generally within acceptable limits, researchers say. In fact, they found that air quality in communities surrounding taconite mines is cleaner in terms of particulates than the air in Minneapolis.

Nonetheless, the numbers of people who develop mesothelioma and other types of lung cancer on the Iron Range are still higher than what's expected in the general Minnesota population. Researchers are now conducting in-depth analyses to determine whether the taconite dust could be responsible for the heightened cancer rates.

"This is a time-consuming process, but we're nearing the end of it," says Mandel, adding that his team will be preparing a comprehensive report in the coming months. "As we finish the analyses, we'll have enough information to say what is going on and what is driving these cases."

Through music, Zach Sobiech said goodbye to his loved ones. And in the process, the Stillwater teenager's YouTube music video for his song "Clouds" touched people around the world.

Leaving a legacy

The Zach Sobiech Osteosarcoma Fund lifts bone cancer research at the U 'up, up, up'



Photo by J Dunn Photography

Though Sobiech died of osteosarcoma, an aggressive type of bone cancer, on May 20 at age 18, his legacy extends far past millions of YouTube views. The Zach Sobiech Osteosarcoma Fund, created by Zach and his family through Children's Cancer Research Fund, exclusively benefits research at the Masonic Cancer Center, University of Minnesota that's focused on understanding the causes of osteosarcoma and developing new therapies for it.

Proceeds from the sales of Sobiech's music, prints of his lyrics, and specially designed necklaces and key chains all benefit the Zach Sobiech Osteosarcoma

Fund. To date, more than \$500,000 has been raised—from 195,000 people around the world.

Osteosarcoma affects approximately 500 children in the United States per year, but doctors know very little about the cancer, says Brenda Weigel, M.D., codirector of the Masonic Cancer Center's Sarcoma Program and director of the Department of Pediatrics's Division of Hematology/Oncology. She also was Sobiech's doctor at University of Minnesota Amplatz Children's Hospital.

"We know [almost] nothing about the causes or why certain people get it," Weigel says. "If we did, we could come up with better treatments."

University investigators from a variety of different areas, including veterinary science, chemistry, surgery, medicine, and pediatrics, are working together to understand the complexity of this disease.

Currently, University researchers are evaluating the human genome to identify genetic changes that may indicate a greater likelihood of developing osteosarcoma. They've also found that, at a molecular level, naturally occurring canine osteosarcomas are remarkably similar to those that occur in children, meaning that progress toward developing treatments for dogs who have osteosarcoma can speed the development of treatments for people with the same disease.

And they'll only build on their successes with support from the Zach Sobiech Osteosarcoma Fund. "Zach's legacy will live on in many, many ways," says Weigel, "through his songs and his efforts to raise advocacy and awareness of osteosarcoma."

To make a gift to the Zach Sobiech Osteosarcoma Fund or hear his music, visit www.childrenscancer.org/zach.

U cohosting new center dedicated to African American men's health care and research

With a \$13.5 million grant from the National Institutes of Health, the University of Minnesota and University of Alabama, Birmingham are collaborating to better address health disparities in conditions affecting African American men.

The new National Transdisciplinary Collaborative Center for African American Men's Health will target disparities in unintentional and violence-related injuries as well as chronic diseases including cancer, cardiovascular disease, and stroke.

Academic-community partnerships will be integral to the program, particularly for identifying important issues to address and getting treatments and interventions out to people in the community.

Masonic Cancer Center member Badrinath Konety, M.D., M.B.A., chairman of the Department of Urology, will lead the University of Minnesota's portion of the 5-year project.

A new home for discovery

Eighteen Masonic Cancer Center investigators are moving their labs across campus this summer and fall into the new Cancer and Cardiovascular Research Building.

Part of the University's burgeoning Biomedical Discovery District, the facility features state-of-the-art lab space and stunning common areas designed to spark collaborations, as well as a green roof and other special features that promote energy efficiency.



Photos by Stephanie Dunn

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

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Bridging a gap

To learn how you can support patients receiving treatment at the University, contact Cathy Spicola at 612-625-5192 or cspicola@umn.edu.



Facing mounting expenses, a patient dealing with ongoing complications of his blood and marrow transplant (BMT) often had to make a difficult choice—whether to pay his mortgage or buy groceries.

Another young patient's family was about to have its heat turned off because of an outstanding \$1,200 bill it had no way to pay.

One man whose cancer came back twice ended up homeless for weeks, either sleeping in a storage locker or wandering the streets, because he couldn't afford a security deposit for an apartment.

Then the BMT Patient Support Fund stepped in to lend a financial hand. Even relatively small grants have made a huge difference for many patients who have undergone BMTs at the University of Minnesota Medical Center, Fairview and University of Minnesota Amplatz

Children's Hospital, according to the social workers who manage the fund.

It's all thanks to a gift of \$100,000 per year from the Rising Sun Foundation, run by an anonymous Minnesota couple with firsthand BMT experience. The fund provides financial assistance to patients and their families for mortgage payments, food, utilities, insurance premiums, copays, transportation, and additional expenses when other funding is not readily available.

"The disease is bad enough with the scramble to get yourself treated"—without the added financial stressors, says one of the donors.

The donors are grateful for the care they received at the University, and they feel fortunate to have the means to cover their own treatment-related expenses. It only feels right to support others who aren't as fortunate, one says: "I can help others like me who have been there."

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Nicole Endres, *Editor*
Grace Birnstengel and
Barbara Knox, *Writers*
Lisa Haines, *Design*

To find out how your gift can make a difference, please contact:
Cathy Spicola
Director of Development
612-625-5192
cspicola@umn.edu

www.give.umn.edu/cancer
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