



Masonic Cancer Center News

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

From basic science to second chances

Patients benefit when research moves from the laboratory into the clinic

If you had met Duane Cramer in the spring of 2008, it would have been hard to guess that he had run out of options for treating his acute myelogenous leukemia (AML), a fast-growing blood cancer. Even after four rounds of the strongest chemotherapy and full-body radiation, the Blaine resident didn't feel sick.

"Nobody who saw me could believe it," Cramer recalls.

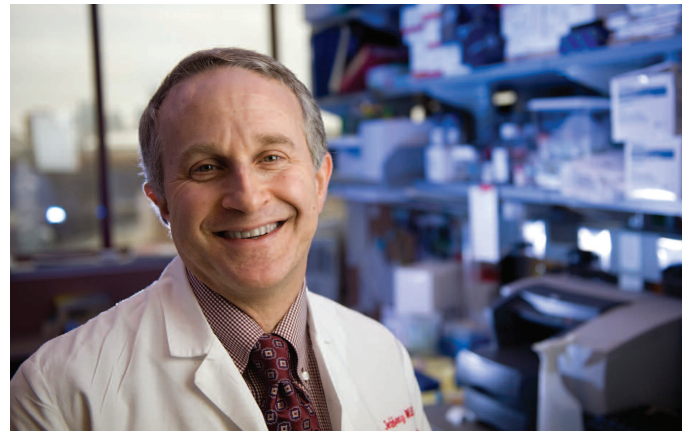
But his blood tests told a different story—cancerous cells remained. Cramer's doctor, Sarah Cooley, M.D., explains, "His choices were to go on hospice or try something experimental."

Fortunately, Cramer was at the right place to try an investigational new therapy available through the Masonic Cancer Center, University of Minnesota. Clinical trials using novel treatments based on ideas straight from the lab—generally reserved for patients for whom standard therapies haven't worked—can offer patients a second chance for remission.

The trial Cramer joined was evaluating the cancer-targeting potential of natural killer (NK) cells, a type of white blood cell that's part of the immune system. The hope was that an infusion of NK cells from a half-matched related donor would clear out Cramer's leukemia before he received a hematopoietic cell transplant (HCT) from the same donor.

"The doctors' honest expectation was that the chances of success were probably somewhere between 20 and 30 percent," says Cramer. "That was better than no chance. After a family consultation, we decided to go ahead with it."

Photo by Scott Streble



Jeffrey Miller, M.D., has taken his research on natural killer cells from the laboratory to clinical trials to treat people with blood cancers.

Putting a natural killer to work

Jeffrey Miller, M.D., the Masonic Cancer Center's associate director of experimental therapeutics, first thought of using NK cells to fight cancer 20 years ago.

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Second chances continued from cover

Sarah Cooley, M.D., is developing strategies for using natural killer cells to treat solid tumors.

At the time, researchers in the field of blood and marrow transplantation—a standard therapy for blood cancers—had discovered that people who relapsed after a transplant could be treated successfully using immune system cells from their original donor. But few scientists had studied NK cells, which protect against viral infections and cancer formation.

Working with Philip McGlave, M.D., deputy director of the Masonic Cancer Center, Miller came up with the idea of capitalizing on NK cells' tumor-killing ability. Taking an idea like this from the laboratory to clinical trials is known as translational research.

Using NK cells isolated from the blood of normal donors (including themselves), Miller and other researchers in his lab studied the cells' basic biology.

"A lot of what I did in the first several years in the lab

was to try to understand

NK cells, how to measure their function, how to see what they do with normal targets and malignant targets," says Miller, who holds the Roger L. and Lynn C. Headrick Family Chair in Cancer Therapeutics.

He also needed to make sure that the NK cells would not damage the normal cells that are given during a transplant—hematopoietic stem cells, the immature cells that give rise to blood cells.

Miller launched his first clinical trial of NK therapy in 1994 with patients who had received HCTs using their own stem cells. "The reality of translational research is that once you take an idea like this and start testing, it takes a long time," Miller explains. "So, 10 years later, in 2003, we came to the conclusion that despite success-

fully activating NK cells in the body, the therapy wasn't good enough to prevent clinical relapse."

In the meantime, NK cells were found to have surface receptors that "turn off" when they recognize cells as "self." Because cancerous cells are actually "self" cells gone awry, NK cells don't always target them as the enemy. This development prompted Miller to try a new protocol using NK cells from a related partially matched donor instead of using the patient's own cells.

In 2005 Miller and his team showed that NK cell therapy for people with AML for whom all standard therapies failed could lead to the cancer's remission. Miller's group treated 32 people, and 10 achieved complete remission.

Based on those promising results, they developed the next generation of that therapy, which incorporates an NK cell infusion into a partially matched HCT and is designed to cure patients with advanced leukemia. Now 39 patients have been treated—including Duane Cramer.

From bench to beach

Cramer received his infusion of NK cells on May 6, 2008. The youngest of his three sons, Brian, served as his donor. Because NK cells can be harvested directly from the blood, donating these cells was no more invasive than a blood draw.

Cramer kept an optimistic attitude and told people he was going to beat his cancer.

"He understood the challenges ahead of him and took it one day at a time," says Cooley, a member of the Masonic Cancer Center and assistant professor in the Department of Medicine's Division of Hematology, Oncology, and Transplantation. "Now he's more than one year out, and he's doing great."

Cooley, who trained with Miller as a student and is now working to develop strategies to use NK cell therapy to treat solid tumors such as breast cancer as well, leads the leukemia trial through which Cramer was treated.

"We've been able to get remission in 50 percent of patients for whom nothing else worked," she says. "That's beyond what we expected."

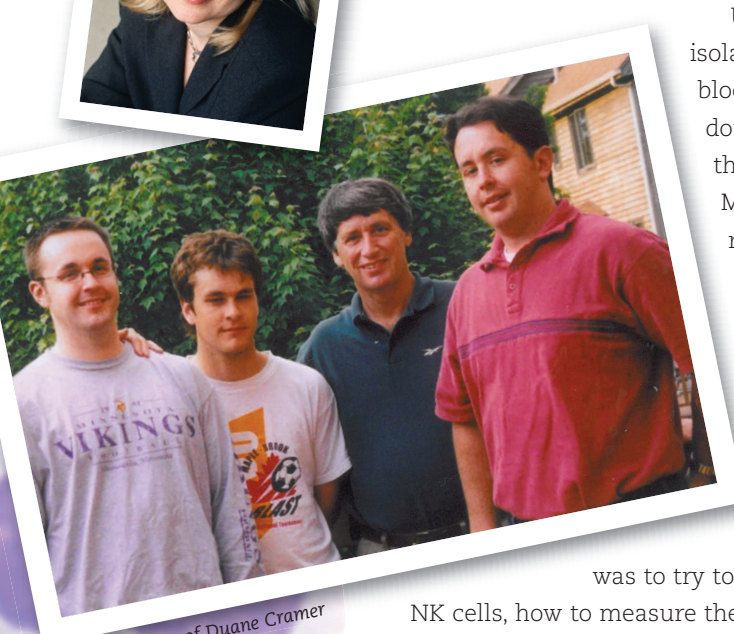


Photo courtesy of Duane Cramer

Duane Cramer (third from left)—with sons Dan, Brian, and Scott—is "doing great" after treatment through a clinical trial at the University, his doctor says.

That's also a motivator for Miller.

"We feel good that the new therapies we brought from the lab to the clinic are helping people," he says. "They're not always curing people ... but the only way to be one step ahead is to go back to the laboratory and understand the failures as well as the successes."

As for Cramer, he believes every day is a blessing. Even though his immune system was still somewhat weakened, he got the go-ahead to travel to Florida last spring.

"I was just happy to be sitting on the beach," he says.

CETI: A jump-start for new cancer therapies

Promising cancer research often stalls out at the concept level because there's no funding to complete it.

To help get more ideas from the lab into the clinic, the Masonic Cancer Center recently created the Cancer Experimental Therapeutics Initiative (CETI). Director Jeffrey Miller, M.D., says CETI is being established to create the infrastructure needed to help move the best basic science research into clinical trials faster and double the number of patients enrolled in clinical trials at the University of Minnesota in the next five years.

Because translational research is expensive, CETI was designed to advance ideas that will eventually be funded by the National Institutes of Health, the major source of funding for sustainable medical research.

But to have a good chance of securing those grants, researchers must already have clinical trials in progress. That's where CETI comes in—and why CETI will rely mainly on private funding and philanthropy to sustain it, says Miller.

"Philanthropic dollars give us the freedom to invest in the future," he says, because the most novel ideas test new boundaries. "But innovation is important to make new strides in cancer therapies."

To learn more about how you can support the Cancer Experimental Therapeutics Initiative at the Masonic Cancer Center, contact Catherine McGlinch at 612-626-5456 or c.mcglinch@mmf.umn.edu.



Bruce Blazar, M.D.

Grant from NIH funds study on chronic graft-versus-host disease

The National Institutes of Health (NIH) has awarded a five-year, \$9.5 million grant to Bruce Blazar, M.D., of the Masonic Cancer Center, University of Minnesota, and two researchers with Dana-Farber Cancer Institute to further their research on chronic graft-versus-host disease (GVHD).

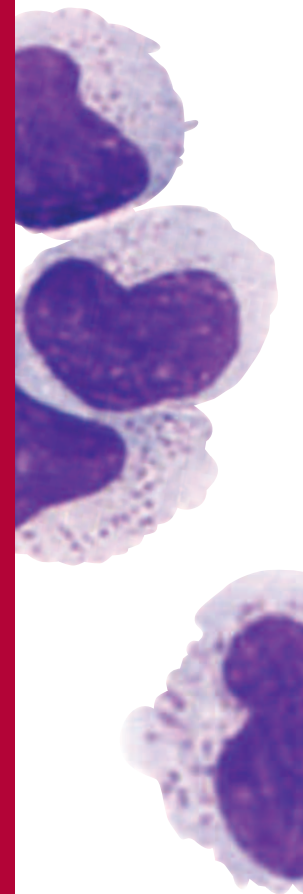
GVHD can occur after a patient undergoes a stem cell transplant for treating blood cancers including leukemia, lymphoma, and multiple myeloma. The transplanted donor cells can perceive the recipient's body as "foreign" and attack the recipient's organs and tissue.

The disease can be either acute, starting within three months of a patient's transplant, or chronic, beginning more than three months after transplant and potentially lasting for years.

The group's previous work resulted in effective new ways of controlling acute GVHD; however, chronic GVHD remains a problem.

"Over the next five years, our goals will include trying to better understand the biology of chronic GVHD, identify the potential for GVHD in patients undergoing stem cell transplant, and begin clinical trials to test new therapy approaches that can prevent or better treat GVHD in stem cell transplant patients," says Blazar, a Regents Professor and leading scientist in the Masonic Cancer Center's Transplant Biology and Therapy Research Program.

Rates of GVHD vary from between 30 to 40 percent among related donors and recipients and twice that for unrelated donor-recipient pairs, according to the NIH. People with GVHD are very vulnerable to infections and can experience other symptoms ranging from mild rashes and diarrhea to life-threatening conditions.



Finding answers

Woman's gifts support research to treat the disease that took her husband's life



Jane Starr hopes her gifts will expedite research into better treatments for adults with leukemia.

Clark Starr, Ph.D., was two months away from retiring when he and his wife, Jane, got devastating news. Clark had myelodysplasia, a disease in which the bone marrow doesn't make enough healthy blood cells. It can progress and become acute myelogenous leukemia (AML).

Clark Starr had spent 43 years as a speech-language pathologist at the University of Minnesota and served as the first chair of the University's Department of Communication Disorders, now known as the Department of Speech-Language-Hearing Sciences. The news meant that instead of treating patients, he'd become a patient himself.

Doctors treated Clark's myelodysplasia for about a year with blood transfusions and growth factors, Jane Starr says. But his disease progressed to AML within a year.

After two rounds of chemotherapy, it became apparent that traditional treatments weren't working for Clark's leukemia, so his care team went back to blood transfusions and growth factors to keep him alive.

Clark Starr died in March 1999, not even two years after he was diagnosed with myelodysplasia. He was 71.

And Jane Starr was frustrated that more couldn't be done for her husband.

"They've accomplished so much with helping children [with cancer] ... but they didn't have any

way to treat [Clark's leukemia]," she says. "And I was really angry about that."

So later that year, Jane Starr approached the University of Minnesota's cancer team to find out what she could do to improve the outlook for adults with leukemia. That's when she learned about leading-edge research on the cancer-fighting power of natural killer cells that Jeffrey Miller, M.D., was conducting. (See cover story.)

That December, Starr made her first gift of \$10,000 to Miller's research. "I wanted it to go somewhere where it would help with acute myelogenous leukemia," she says.

Starr has made similar gifts annually to keep Miller's research moving forward. And she believes the need to continue supporting this work is as great now as it was when her husband died 10 years ago.

"I read the obituaries, and I still see people dying from the same disease," she says, acknowledging that research takes time. But she still wishes it would move faster.

Through her continued contributions to Miller's work, Starr is doing her part to make that happen. She says she's pleased that Miller's clinical trials using natural killer cell therapies have shown promising results and hopes her gifts can help bring this investigational treatment to adults with leukemia who so desperately need it.

"I figure it's money well spent," Starr says.

Reap the benefits of leaving a legacy gift from retirement accounts

Retirement accounts are typically set up to allow people to save money on a tax-deferred basis during their working years. Over time, the value of a retirement account may increase beyond what the owner needs in retirement.

But leaving an IRA or other retirement account in estate plans for a loved one can have serious tax consequences, causing double taxation of the assets.

That's why many donors have found that using retirement plan assets to make a gift to charity can be an ideal way to leave a legacy.

When a person names the Minnesota Medical Foundation as beneficiary of a retirement plan using a beneficiary designation form, the individual's estate receives a charitable estate tax deduction for the full value of the account. Because the foundation is a tax-exempt charity, no income taxes are due on the donated assets.

For more information on making a gift to the Masonic Cancer Center through the Minnesota Medical Foundation, contact our experts at 612-625-1440, 1-800-922-1663, or giftplanning@mmf.umn.edu, or visit www.mmf.umn.edu/giftplanning.

The science of tobacco control

Cancer researchers contribute to historic legislation

President Obama in June signed the Family Smoking Prevention and Tobacco Control Act, giving the U.S. Food and Drug Administration (FDA) the power to regulate tobacco products. The law now prevents cigarette manufacturers from using terms such as “light,” “mild,” and “low;” curbs tobacco marketing aimed at children; and opens the door for eventual limits on carcinogens and nicotine in tobacco products.

This historic legislation may not have existed without the complementary efforts of researchers Stephen Hecht, Ph.D., and Dorothy Hatsukami, Ph.D., at the Masonic Cancer Center, University of Minnesota.

Hecht has spent his career decoding the process by which cigarettes cause lung cancer, from identifying carcinogens to discovering their “biomarkers”—byproducts created when the body metabolizes cancer-causing substances in tobacco. His research helped to establish that light cigarettes are just as harmful as regular ones.

For her part, Hatsukami helped to establish that smokers develop a physical addiction to nicotine, tests newer “reduced toxic or nicotine exposure” products to determine their potential impact on health, and contributed to the Tobacco Control Act.

What impact will this legislation have on tobacco products?

Hatsukami: In recent years, manufacturers have developed a number of new products that are touted as providing less health risk. This act says you have to have scientific evidence to back up those claims so consumers are not misled into thinking they are smoking safer cigarettes, as was the case with light cigarettes. In addition, tobacco companies have to disclose what toxicants are in the products. More importantly, there are provisions that allow the government to reduce the levels of carcinogens and nicotine in tobacco products.

Hecht: One of the big questions is, how much do you reduce the level of carcinogens and nicotine to have an effect? Let’s say you can reduce them by 50 percent. How many products will be knocked off the market? What will that do to tax revenue? Tobacco is not just a scientific issue; there are practical and economic aspects of it.

How do you respond to people who criticize smoking regulation as an infringement on individual freedom?

Hatsukami: Hiding information from the public is an infringement on freedom. I don’t view this as infringing on personal rights so much as providing accurate information and not misleading consumers so they can make an informed decision. It’s also about protecting our youth from using a highly addictive product.

Hecht: If food products had the level of toxicants in them that tobacco products have, the food manufacturers would be thrown in jail. There’s a double standard in how these products are regulated, and it’s all because of money.

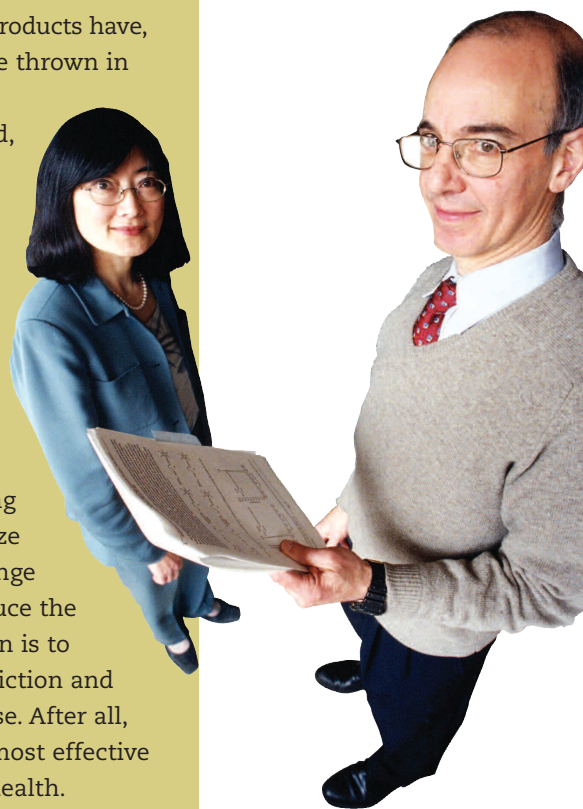
What’s the next frontier in your tobacco research?

Hecht: We want to find the susceptible smoker—identify people who are vulnerable to the harmful effects of smoking and to nicotine addiction.

Hatsukami: We’re also developing ways to help people quit, minimize the toxicity of smoking, and change the tobacco product itself to reduce the potential for addiction. Our vision is to dramatically reduce tobacco addiction and tobacco-related death and disease. After all, reducing smoking is one of the most effective means of improving our public health.



For more of this interview with Dorothy Hatsukami, Ph.D., and Stephen Hecht, Ph.D., visit www.mmf.umn.edu/cancer/mccn.



MCC launches improved clinical trials website

A new website offers accurate, up-to-date information about more than 250 clinical trials currently available through the Masonic Cancer Center, University of Minnesota.

Because finding information about clinical trials is one of the primary reasons patients, their families, and health-care providers visit this site, it has been significantly enhanced. It's now easier to

search for open trials and get answers to questions through our information line.

The Masonic Cancer Center now offers dozens of clinical trials to evaluate emerging therapies, in addition to many other clinical trials focused on cancer prevention and survivorship.

The new site launched in August. Check it out at www.cancer.umn.edu/clinicaltrials.

Center for Prostate Cancer welcomes new leader



Badrinath R. Konety,
M.D., M.B.A.

The University of Minnesota welcomed Badrinath R. Konety, M.D., M.B.A., August 31 as director of its Center for Prostate Cancer and head of the Department of Urology. Konety will hold the Endowed Chair in Uro-Oncology.

Konety comes from the University of California, San Francisco's Helen Diller Family Comprehensive Cancer Center, where he was also codirector of Genitourinary Cancer Epidemiology and Population Science and vice chair of the UCSF Department of Urology.

An active researcher, Konety is an expert not only in urologic cancer surgery but also in epidemiology and biostatistics. His research interests include nerve replacement to restore

erectile function after prostate cancer surgery, management of prostate cancer in older men, evaluation of markers for bladder and prostate cancer, gene therapy for treating prostate cancer, and factors influencing therapeutic outcomes for urologic cancers. He has served as principal or coinvestigator on grants funded by such organizations as the National Institutes of Health, U.S. Department of Defense, American Geriatrics Society, and Centers for Disease Control and Prevention.

Konety has authored more than 100 journal articles as well as numerous review articles and book chapters.

Upcoming events



PSA: Issues in Screening, Diagnosis, and Treatment

Fall 2009 Cancer U: Ask the Experts

6–8 p.m. Thursday, October 29

*A. I. Johnson Great Room, McNamara Alumni Center
University of Minnesota
200 Oak Street SE, Minneapolis*

Speakers will be Masonic Cancer Center researchers Timothy Church, Ph.D., who was involved in a recent national study of the value of PSA testing, and Christopher Warlick, M.D., Ph.D., a urologic surgeon who treats men who have prostate cancer. The program is free but advance registration is requested. Please call 612-624-2620 or visit www.cancer.umn.edu.

Gopher football pre-game reception for breast cancer supporters

5 p.m. Saturday, October 31

*Heritage Gallery, McNamara Alumni Center
University of Minnesota
200 Oak Street SE, Minneapolis*

Supporters of the Masonic Cancer Center who are also Gopher football season ticket holders are invited to this reception before the team takes on Michigan State at 7 p.m. at the new TCF Bank Stadium. There will be a short program at 6 p.m. Space is limited, so please RSVP to Catherine McGlinch at 612-626-5456 or c.mcglinch@mmf.umn.edu.

What does it mean to be a comprehensive cancer center?

The National Cancer Institute (NCI) has renewed the Masonic Cancer Center, University of Minnesota's designation as a comprehensive cancer center for another five years, the longest term possible.

The NCI recognizes different types of cancer research centers, ranging from centers specializing solely in laboratory science to centers with a broad range of research and patient services. The NCI awards the prestigious comprehensive designation only to institutions that make ongoing, significant advances in cancer research, treatment, and education.

NCI-designated cancer centers provide a

setting in which common scientific goals, a collaborative work environment, and shared resources propel basic, clinical, and population research forward faster. They are not only the primary source of knowledge about preventing, diagnosing, and treating cancer, but they also deliver this new information to cancer patients, their families, health-care professionals, and the community at large.

The Masonic Cancer Center is one of 40 NCI-designated comprehensive cancer centers in the United States and the only one in the greater Twin Cities area.



A Comprehensive Cancer Center Designated by the National Cancer Institute

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New programs address long-term health effects of adult cancer survivors

Because of advances in detection and treatment, people today often live many years after a cancer diagnosis.

And as these survivors live longer, trends in "late effects" of cancer treatment are becoming apparent. Survivors may have special health concerns after treatment because the often-harsh therapies needed to kill cancer cells can take a toll on normal cells and organs, too.

The Masonic Cancer Center's new Cancer Outcomes and Survivorship Research Program will tackle these issues head on. Directed by Joseph Neglia, M.D., M.P.H., and Beth Virnig, Ph.D., this program aims to promote collaboration among University investigators conducting survivorship research and educate patients and health-care providers about special health considerations affecting cancer patients and survivors.

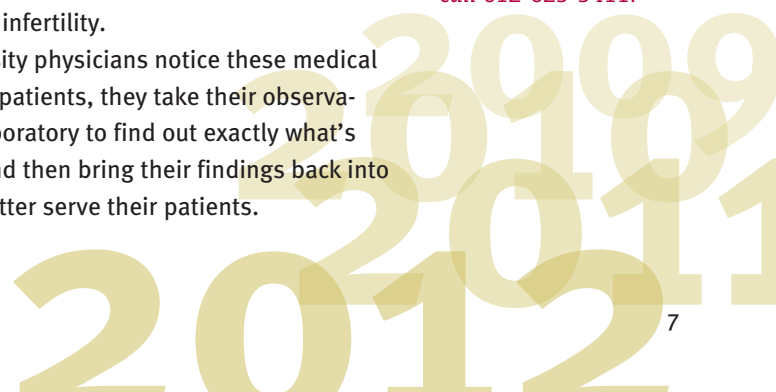
Complementing this research program is the University of Minnesota Physicians-run Long-Term Follow-Up Clinic, which previously was for childhood cancer survivors only but is now seeing survivors of adult cancers as well.

"While we anticipate cancer survivors will lead healthy, active lives, some will develop complications from their chemotherapy and other treatments," says Anne Blaes, M.D., director of the Long-Term Follow-Up Clinic adulthood cancer survivor program.

Some of these complications include second cancers, cardiovascular issues, lung and bone problems, and infertility.

As University physicians notice these medical trends in their patients, they take their observations to the laboratory to find out exactly what's happening—and then bring their findings back into the clinic to better serve their patients.

Learn more about the Cancer Outcomes and Survivorship Research Program at www.cancer.umn.edu/research/programs/cos.html. To make an appointment at the Long-Term Follow-Up Clinic, call 612-625-5411.



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**Director's
note**



With health-care reform debates happening across the country these days, I can't help but think of cancer care as a health-care reform issue in many ways.

Research has led to the development of many new medications to treat different types of cancer. A number of them specifically target an abnormality in the cancer cell and are based on work conducted in basic research laboratories.

Although these new drugs can be expensive, I believe cancer care would become cheaper if we knew right away which tumors would respond to which drugs. That's a research question.

As cancer outcomes improve, another critical question involves cancer survivorship. What can we do to reduce long-term complications of cancer therapy and maximize the quality of life for cancer patients—both during and after treatment? Reducing the impact of cancer therapy on long-term health also has important implications for health-care costs. That's also a research question.

If we ever have a "public option" for health care, I believe that including federal funding for clinical research—in a fashion now used for basic research—could reduce costs in the long term. It would be a wise investment.

The Minnesota Masonic Charities have recently made an investment of their own. As you've probably heard, last year they pledged \$65 million over 15 years to our work. Generous giving from many individuals and organizations (such as the Children's Cancer Research Fund) allow our research teams to pursue a broad spectrum of projects, including population, laboratory, and clinical research.

We're so grateful to have their support—and yours. All of you truly make a difference in what we do.

Sincerely,
Douglas Yee, M.D.

*Director, Masonic Cancer Center, University of Minnesota
John H. Kersey Chair in Cancer Research*

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Masonic Cancer Center

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