A PUBLICATION OF THE MINNESOTA MEDICAL FOUNDATION

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

Medical Bulletin

Innovation and Collaboration

Minnesota researchers explore the enormous potential of stem cells.

DEAR FRIENDS,

We begin a new academic year at the Medical School with a tremendous feeling of optimism and excitement. The students in the Class of 2008 are well prepared, talented, and eager to embrace the task before them.

As you will read in this *Medical Bulletin*, we are asking important questions about how medical students are educated and examining some of our traditional methods to see if they are due for a change. Our new students will live and practice in a different world than those who graduated 50, 25, or even 10 years ago.

Students in the Class of 2008 are entering the Medical School at an amazing time in the history of medicine. They will be able to take advantage of the tremendous research and discovery under way at the Stem Cell Institute, the Lillehei Heart Institute, and the Center for Cardiovascular Repair that you will read about in this issue. The collaboration of faculty in our numerous centers and institutes is reaching a new level—and the results are mind-boggling.

As always, we are deeply grateful to our alumni and to our benefactors who enable our Medical School to be among the very best.

Deborah E. Powell, M.D.
Dean, University of Minnesota Medical School

MINNESOTA
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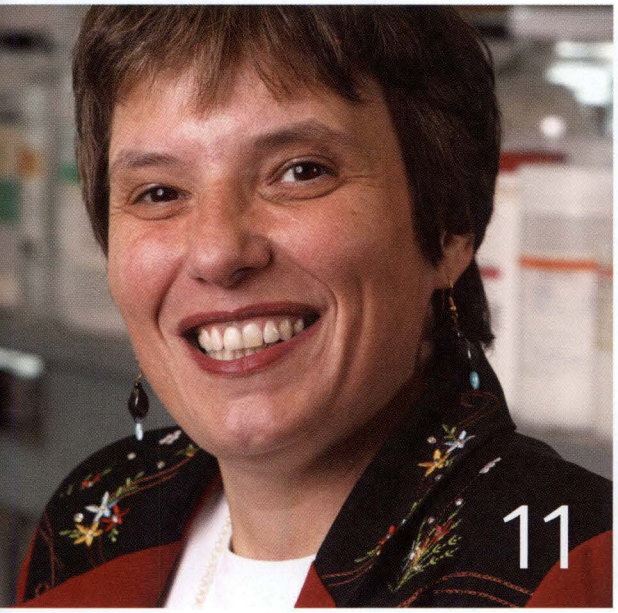
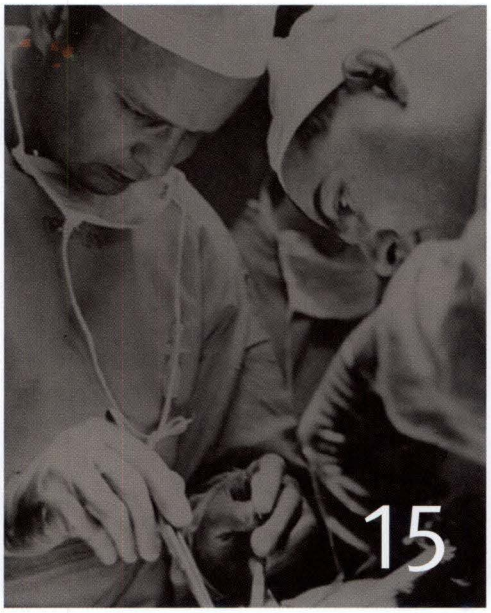
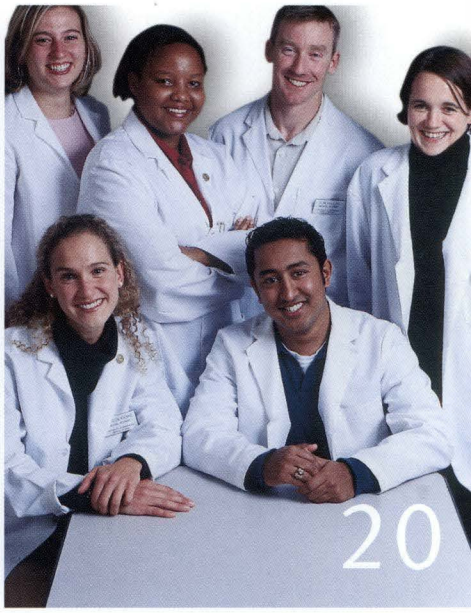
The mission of the Minnesota Medical Foundation is to improve the quality of life for the people of Minnesota, the nation, and the world by supporting the advancement of health-related education, research, and service at the University of Minnesota.

FALL 2004 Contents







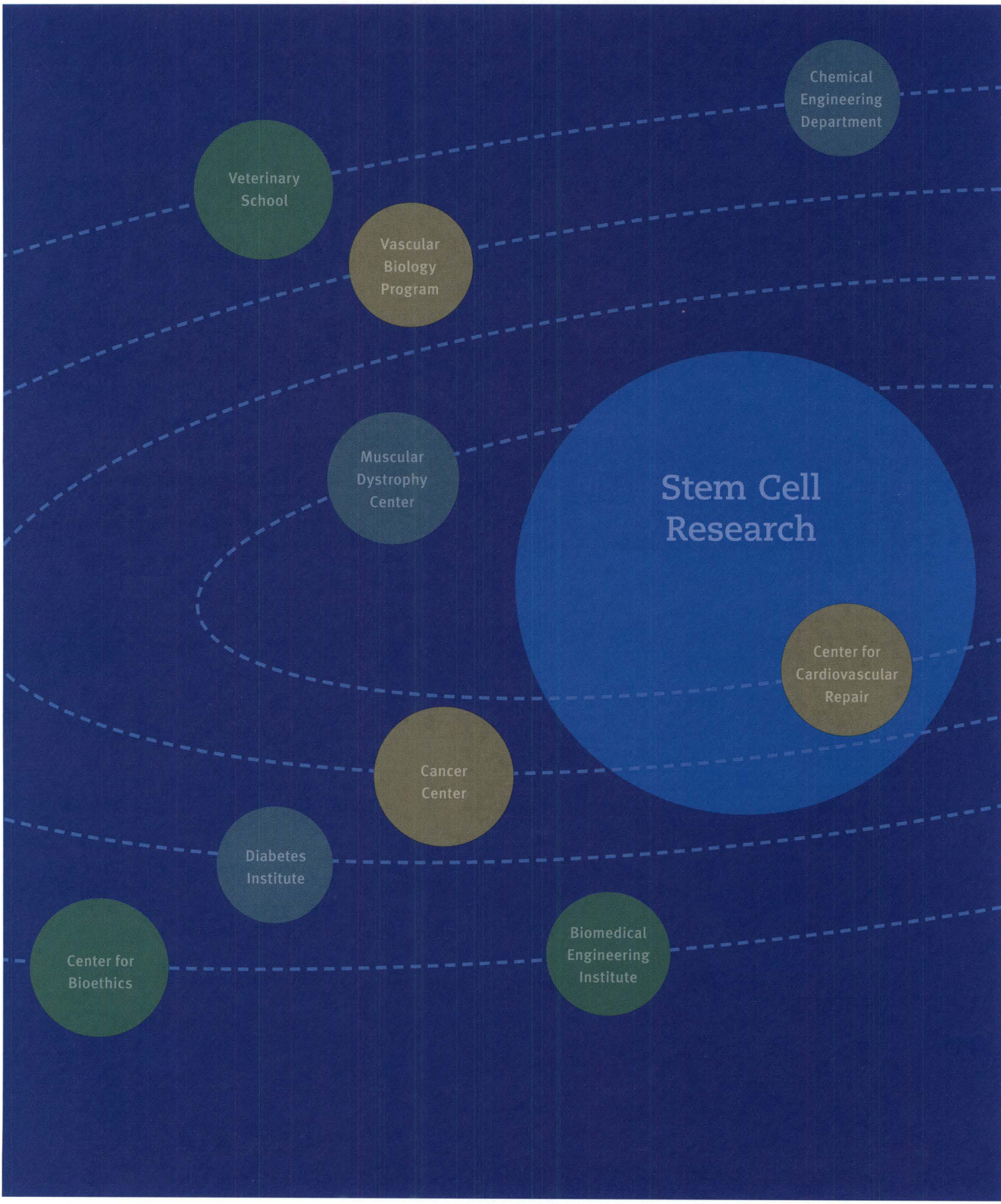
Features

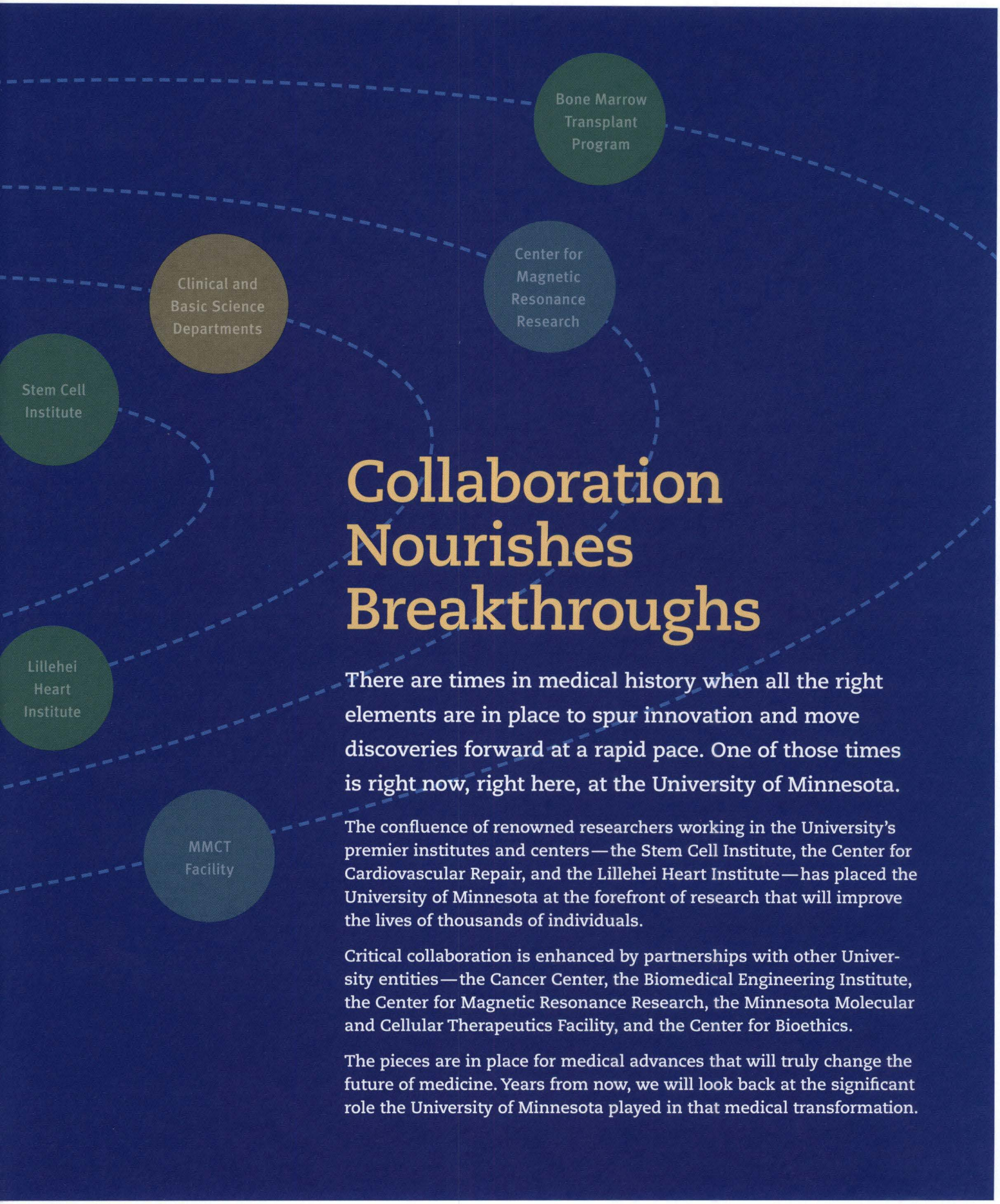
DEPARTMENTS

ON THE COVER

The cover image illustrates the potential of multipotent adult progenitor cells—a rare type of adult stem cell—to be coaxed into becoming other tissue, including liver cells (shown as purple with violet nuclei), endothelial cells (red round cells), and nerve cells (in green, red, and blue).

COVER IMAGE COURTESY OF GERALD J. SEDGEWICK, BIOMEDICAL IMAGE PROCESSING LAB, UNIVERSITY OF MINNESOTA, BASED ON THE RESEARCH OF CATHERINE VERFAILLIE, M.D., PROFESSOR OF MEDICINE AND DIRECTOR OF THE STEM CELL INSTITUTE; AND YUEHUA JIANG, M.D., ASSISTANT PROFESSOR OF MEDICINE


Chemical Engineering Department
Veterinary School
Vascular Biology Program
Muscular Dystrophy Center
Stem Cell Research
Center for Cardiovascular Repair
Cancer Center
Diabetes Institute
Center for Bioethics
Biomedical Engineering Institute



Collaboration Nourishes Breakthroughs

There are times in medical history when all the right elements are in place to spur innovation and move discoveries forward at a rapid pace. One of those times is right now, right here, at the University of Minnesota.

The confluence of renowned researchers working in the University's premier institutes and centers—the Stem Cell Institute, the Center for Cardiovascular Repair, and the Lillehei Heart Institute—has placed the University of Minnesota at the forefront of research that will improve the lives of thousands of individuals.

Critical collaboration is enhanced by partnerships with other University entities—the Cancer Center, the Biomedical Engineering Institute, the Center for Magnetic Resonance Research, the Minnesota Molecular and Cellular Therapeutics Facility, and the Center for Bioethics.

The pieces are in place for medical advances that will truly change the future of medicine. Years from now, we will look back at the significant role the University of Minnesota played in that medical transformation.

"We are at a major hinge in the history of medicine. We will change the way we practice medicine dramatically in the next couple of years because of our abilities to generate and repair tissue, in understanding and predicting human disease."

JOHN WAGNER, M.D.

Professor of pediatrics and scientific director of clinical research for the University's Stem Cell Institute, speaking at the United Nations Genetics Policy Institute Forum on June 2, 2004.

Changing the Future

The University of Minnesota's Stem Cell Institute

RESEARCHERS FROM ALL OVER the world came to the United Nations last June to present the latest scientific and clinical advances in stem cell research. Wagner was one of a handful of leading researchers and one of only two clinicians to address the policy makers at the forum. His role was to explain the next steps in moving adult and embryonic stem cell research out of the laboratory and into patient treatment.

Once approved by the U.S. Food and Drug Administration, the University will begin human clinical trials in the near future—becoming perhaps the first public research institution to do so.

The University of Minnesota's Stem Cell Institute, the world's first, founded in the summer of 2000, is one of the preeminent centers for stem cell research in the world. The institute is poised to lead the field in new discoveries into the next decade. As one of the University of Minnesota Medical School's highest priority programs, the institute has been approved for an ambitious expansion over the next three to six years.

Stem cell research has received international attention because of the exciting potential these cells have to provide the basis for novel therapies replacing or repairing cells, tissues, and organs damaged by disease, injury, and degeneration. They are seen as a potential vehicle for gene therapy, for enzyme replacement in genetic diseases, and for inducing tolerance to organ transplants. Further, they are seen as a key to understanding developmental biology and mechanisms of disease, and as a tool for disease prevention. Studies ar under way to find new treatments and cures for diseases including, among others: heart disease, spinal cord injur Parkinson's disease, cancer, diabetes, cirrhosis of the liver, hemophilia, muscular dystrophy, stroke, and geneti diseases such as Fanconi anemia.

While researchers across the University are actively engaged in stem cell research, three areas symbolize the Stem Cell Institute's program. The institute's director and lead scientist Catherine Verfaillie's innovative work with multipotent adult progenitor cells (MAPCs), Dan Kaufman's work with embryonic stem cells, and John Wagner's translational and clinical research, aimed at bringing stem cell therapies out of the laboratory and

nto the clinic are all at the leading edge of stem cell research worldwide.

Commitment to excellence in adult and embryonic stem cell research

The University of Minnesota's Stem Cell Institute has received considerable international attention for this ongoing work with adult stem cells.

# of Medicine

n 2003, the University made clear its commitment to raise private funds to aggressively pursue embryonic stem cell research alongside its established adult stem cell research program.

Researchers at the University of Minnesota have repeatedly stressed the importance of studying both adult and embryonic stem cells simultaneously. Kaufman explained that a study of one type of cells often improves studies of the other, saying that here at Minnesota, "There is a lot of good feedback between the systems."

Politics

Embryonic stem cell research is controversial because the process that removes the stem cells from a fertilized egg destroys the embryo. Because a fertilized human embryo is destroyed, abortion opponents are critical of the process. Abortion remains

CATHERINE VERFAILLIE, M.D.

Professor of medicine and holder of the Andersen Chair in Stem Cell Biology, McKnight's Presidential Chair in Stem Cell Biology, and Tulloch Chair in Stem Cell Biology, Genetics, and Genomics; director of the Stem Cell Institute

STEM CELL BASICS

Stem cells are unique because they have two key characteristics: They are self-renewing, and they can differentiate into cell types of all three embryonic tissues (endoderm, ectoderm, and mesoderm). Not all stem cells are the same.

The vast potential of embryonic stem cells

Embryonic stem cells are "pluripotent," capable of being coaxed to become any kind of cell in the human body. Embryonic stem cells are derived from what is known as the inner cell mass of the embryo at the "blastocyst" stage—very early in development—approximately a week after fertilization. They were first isolated from humans at the University of Wisconsin, Madison, by James Thomson, Ph.D., in 1998.

The embryonic stem cell lines that are available today were derived from embryos created by in vitro fertilization (IVF) procedures. Because the process of in vitro fertilization often requires more than one attempt, one to ten eggs are typically fertilized for potential implantation in a woman's womb. Once the woman becomes pregnant, any unused fertilized eggs may be discarded at the wish of the couple. Embryonic stem cells are derived from these fertilized eggs if the couple elects to donate them for research.

The promise of adult stem cells

On the other hand, adult stem cells are multipotent. These cells exist in many tissues of the body. Their "normal" function is uncertain, but they may be responsible for the continued growth or repair of a particular organ (for example, the heart or the liver). Under the right laboratory conditions, however, these cells can be transformed into a number of other tissues in the body such as cartilage and liver, heart, or muscle cells. Stem Cell Institute director Catherine Verfaillie, M.D., and colleagues first observed this multipotency at the University of Minnesota in 1997.

Verfaillie and her colleagues were the first to report (in 2002) that adult bone marrow–derived cells can differentiate into cells of all three embryonic germ layers—an important characteristic, previously believed to occur only in embryonic stem cells. This subset of adult stem cells, dubbed multipotent adult progenitor cells, or MAPCs, shows tremendous therapeutic promise. Like embryonic stem cells, they are believed to be capable of becoming many cell types. Some studies have already demonstrated differences between MAPCs and embryonic stem cells. Embryonic stem cells remain the "gold standard," and Verfaillie believes that side-by-side comparison of adult and embryonic stem cells must be done to determine which stem cells are most useful in treating a given disease. MB

a deeply polarizing issue in the United States, and powerful organizations that oppose legal abortions have mobilized against stem cell research.

These groups have successfully limited federal support for the work. On August 9, 2001, President George W. Bush announced that federal funding for embryonic stem cell research would be limited to the 78 human embryonic stem cell lines created prior to that date. While the limitation on funding does not make research on newly developed cell lines illegal, it does make it more difficult.

The National Institutes of Health is the largest source of funding for basic medical research in the world. The policy stipulating that no federal dollars can be spent on embryo research outside of the federally approved cell lines is therefore severely limiting. To date, NIH has approved 22 of the 78 cell lines for research. Wagner says, "The 22 cell lines are not enough because of genetic abnormalities in the existing cell lines and the need for greater genetic diversity."

Competing policies and proposals to restrict or fund stem cell research are constantly being debated. For example as soon as the University announced its commitment to raise private funds to further embryonic stem cell experimentation, state legislators in Minnesota proposed a measure that would block all public funding of the University if research on embryonic stem cells outside the federally approved lines were to proceed. The bill never received a hearing and did not pass. Indeed, proponents of the research attempted to pass legislation making it clear that all forms of stem cell research would be legal in Minnesota. This bill, too, never received a hearing. "Fortunately, the

state legislature has not put in any new hurdles," Kaufman noted.

The situation is similar in other states. *USA Today* reported in April that 33 state legislatures were considering 100 bills either funding or restricting the research. On the November ballot, California voters will decide the fate of a measure entitled "The California Stem Cell Research and Cures Initiative" to invest $3 billion over 10 years in stem cell research in the University of California system. Discussion of stem cell research is a part of the presidential campaign as well.

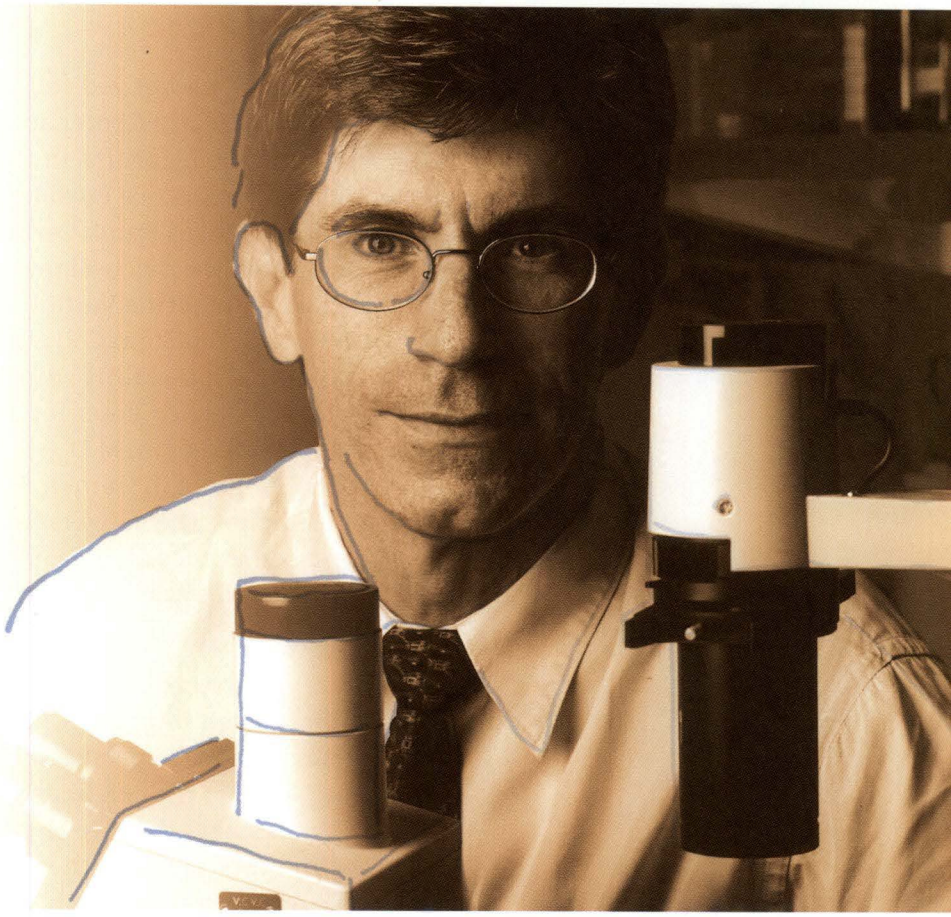
Nuclear transplantation and stem cells

The conference Wagner addressed on June 2, 2004, "Human Cloning Issues in All Its Aspects for the United Nations," was held to inform U.N. representatives about the issues in preparation for a debate scheduled for September. As a result of this debate, the international community may adopt a treaty that the United States and Costa Rica (with the support of many predominantly Roman Catholic nations) proposed that would ban all cloning, reproductive and therapeutic. While there is widespread agreement that reproductive cloning should be banned, attempts to conflate reproductive cloning with therapeutic cloning and, by extension, stem cell research, are seen by those supporting stem cell research as an attempt to deliberately confuse the issue.

Cloning or ("somatic cell nuclear transfer" [SCNT] or "nuclear transplantation" as scientists prefer to call the procedure) is tangentially related to embryonic stem cell research. Stem cell research has been linked to the nuclear transplantation debate because of the hope that one day, the nucleus of a patient's cell could be transferred to a donor egg whose own nucleus has been removed and induced to create a patient's own tailor-made embryonic stem cells—cells that would be seen as identical to the patient's. This would theoretically eliminate the problems associated with organ transplant-like rejection and the need for lengthy regimens of immunosuppressive drugs. However, Wagner has said that any such attempts for clinical treatments are many years in the future. Importantly, no researcher at the University of Minnesota has ever suggested pursuing cloning for reproductive purposes (the process of making an identical "clone" of an individual).

Making the process visible: Responsibility of a public institution

In order to explain the process that led to the University of Minnesota's decision to support expanding embryonic stem cell research beyond



JOHN WAGNER, M.D.

Professor of pediatrics and scientific director of clinical research for the University's Stem Cell Institute

The goal of all the work done at the Stem Cell Institute is to move quickly toward therapies for patients. The work is ultimately about saving lives.

the federally approved cell lines, the Academic Health Center sponsored a series of public forums in the spring of 2004. Senior Vice President for Health Sciences Frank Cerra, M.D., moderated the discussions. Speakers included Catherine Verfaillie, M.D., director of the Stem Cell Institute; Jeff Kahn, Ph.D., M.P.H., director of the University's Center for Bioethics; and Steven Calvin, M.D., co-chair of the Program in Human Rights in Medicine. The conversations were sometimes at odds, mostly cordial, and always forthright.

According to Wagner, "None of the embryonic stem cell lines [created prior to Bush's August 9, 2001, order] were developed specifically for clinical use." Most of the cell lines available to researchers that are eligible for federal funding are either unavailable due to restrictions or genetically abnormal, bringing the number of truly viable cell lines to less than a dozen. According to Kaufman, this figure is optimistic. Further, Wagner adds, "All of the cell lines approved by the president were developed on 'feeder' cells from mice, which affects how they can be used clinically."

If research is to go forward, it is necessary to expand the number of viable embryonic stem cell lines and to do so with the tremendous care and precision necessary to make the new lines viable for clinical (human) use. However, due to federal funding restrictions, all costs related to this research must be supported with private funds.

In short, it is plain to researchers at the University's Stem Cell Institute that if research is to go forward, it will be necessary to expand the number of viable embryonic stem cell lines and to do so with the tremendous care and precision necessary to make the new lines viable for clinical (human) use. The University has committed to supporting this research. However, if the research is to proceed, all costs related to this research must be supported with private funds. Never before has the role of private philanthropy been more important.

In his presentation at the United Nations, Wagner stated, "We can't forget that studies done with ES (embryonic stem) cells seem to always provide insights on how to make studies with adult stem cells better." Ultimately, the goal of all the work done at the Stem Cell Institute is to move quickly toward therapies for patients. Wagner emphasized that the work is ultimately about saving lives.

Taking the lead in clinical trials

The University of Minnesota Stem Cell Institute is uniquely positioned to make rapid and significant progress in this area. First, the depth of the University's program and range of faculty expertise is unparalleled. Unique strengths include the strong research teams focused on various diseases, the ability to work in concert with a clinical research team, and the existence of the University's Molecular and Cellular Therapeutic Facility, which is a National Institutes of Health-designated somatic cell therapeutic facility geared to scaling up cell production necessary for moving these new cellular therapies to a clinical setting.

The first clinical trial for an embryonic stem cell therapy is set to begin in the next year. Wagner is, as of this

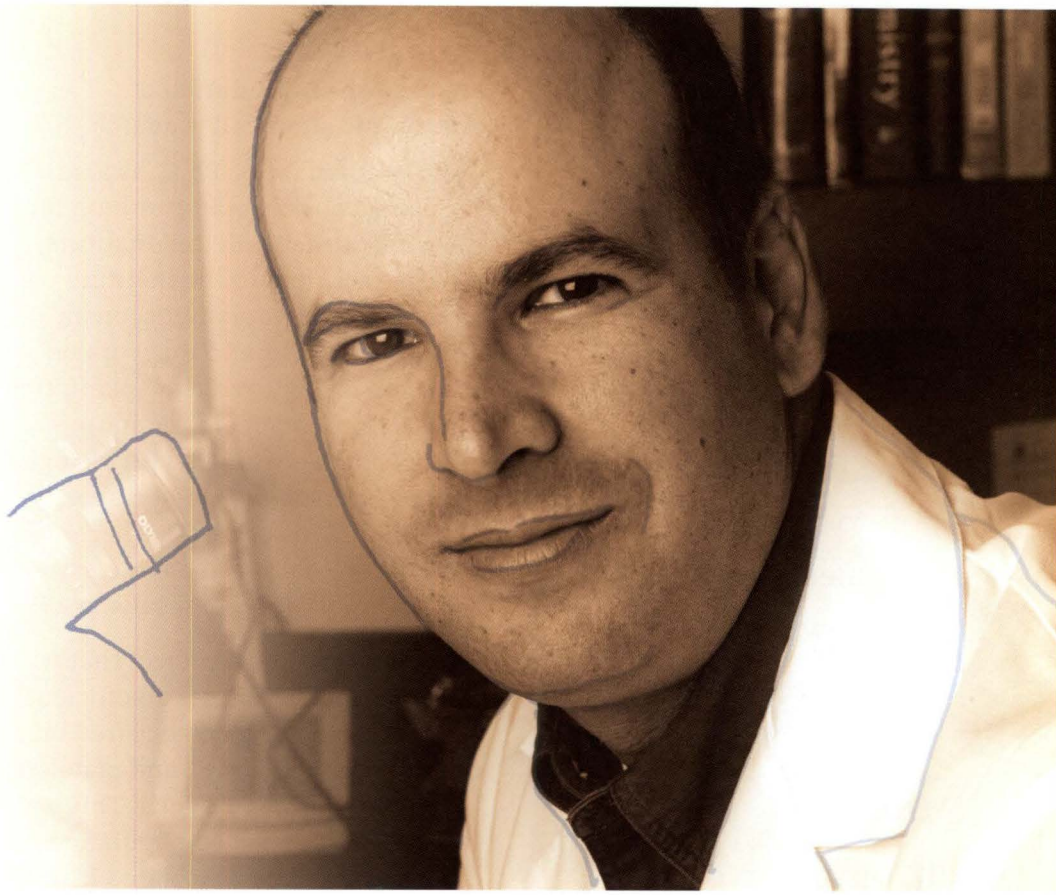
writing, assisting in the trial design for federal Food and Drug Administration approval. The trial is sponsored by Geron Corporation of Menlo Park, California. It follows remarkable animal model results. The trial will test whether treating patients with severe spinal cord injury with injections of neural cells derived from human embryonic stem cells leads to improvement in their conditions.

Designing an effective clinical trial for an investigational new drug (IND) for FDA approval for any new treatment is a long, detailed, and intensive process. Wagner says that spinal cord injuries are a good place to begin because spinal cord injury involves the injection of a single type of cell. He adds, "It would be more difficult, for example, to design a trial for Alzheimer's disease, because multiple types of cells are affected by the disease."

"The University of Minnesota is the place for clinical trials using stem cells because," Wagner says, "all the required elements are in place: the Stem Cell Institute, the National Cancer Institutes (NCI)–designated Comprehensive Cancer Center, a Trauma Center, and the Minnesota Molecular and the Cellular Therapeutics (MMCT) Facility on the St. Paul campus." The MMCT facility provides clinical expertise as well as the regulatory structure to ensure that cells manufactured for therapies meet all of the FDA's current Good Manufacturing Practices (cGMP) requirements.

In addition to trials in spinal cord injury, clinical scientists are also exploring the use of adult stem cells, specifically MAPCs, to repair chemotherapy-induced injury. Stem cells will be injected into the vein and then will "home" to damaged areas, lock in, and replace injured cells throughout the patient's system. Stem cells used in this way, Wagner suggests, "can be thought of as a drug." The challenge now is to design the studies that will determine whether or not such a therapy will be safe and have a positive impact.

Wagner is no stranger to innovation. He led the medical team that, in 1990, performed the first umbilical cord blood transplant in the world to treat leukemia. In 2000, he performed the first transplant with stem cells from a sibling that had been selected as an embryo using genetic technology, through preimplantation genetic diagnosis. This medical breakthrough saved the life of a girl named Molly Nash. Over the past two decades, Wagner's hematopoietic stem cell programs have received national and international attention and considerable grant support.



DAN KAUFMAN, M.D., Ph.D.

Assistant professor of medicine and member of the Stem Cell Institute

The future of stem cell therapy is real, and Minnesota is uniquely positioned to leverage several strengths, including our history and our infrastructure, to help lead medicine in this new direction.

– Catherine Verfaillie, M.D.

FOR MORE INFORMATION

about the Stem Cell Institute or to support critical stem cell research, contact the director of development at 612-626-3379 or visit the Minnesota Medical Foundation Web site at www.mmf.umn.edu.

Pushing the boundaries of embryonic stem cell research

Dan Kaufman, M.D., Ph.D., is also receiving considerable attention for his work at the Stem Cell Institute. He was recruited to the institute from the University of Wisconsin at Madison to expand the work on stem cell biology and transplantation focused on human embryonic stem cells. Kaufman worked with biologist James Thomson at Madison shortly after he and his colleagues became the first to isolate and characterize human embryonic stem cells in 1998.

Kaufman initiated a project that was the first to demonstrate an efficient means to derive blood cells (red blood cells, white blood cells, and platelets) from these human ES cells. This was likely the first purified population of any cell type to be isolated from human ES cells. Recently, his laboratory demonstrated that these human ES cell–derived blood cells are able to survive and grow when transplanted to an animal model. Additionally, he has developed a related project that demonstrated a means to derive functional endothelial cells (that form blood vessels) from ES cells. Kaufman's primary interest in studying human ES cells is to learn the basics of how humans develop from a fertilized egg to an adult organism.

As a researcher whose studies focus on blood development, he is interested in the study of human ES cells because it permits intricate studies of genes and proteins as blood cells develop and is the only method to closely examine these early developmental steps in human beings. These cells promise to show clearly for the first time precisely how humans develop from a single cell to an adult human being.

The future of stem cell research

Stem cell research is one of the most exciting areas of medicine. The University of Minnesota's Stem Cell Institute is at the forefront of this research, committed to studies on both adult and embryonic stem cells and to rapidly moving laboratory innovations to treatments for patients. Stem cells hold incredible promise, not only in furthering understanding of basic biological processes but potentially in curing diseases of all kinds. It is difficult to overstate the potential of stem cell therapies to mitigate many areas of human suffering. Wagner says, "Stem cells offer great promise that could change the practice of medicine—perhaps a revolutionary change unprecedented in history."

Stem Cell Institute director Catherine Verfaillie is confident as she looks to the future. She recently wrote, "Minnesota has the potential to be a real world leader in the nascent field of stem cell research. We have made critical investments, and researchers are hard at work exploring the potential of adult and embryo, animal and human stem cells. From a purely scientific view, it's hard to understand the controversy, but I believe it's healthy to debate the merits of the research. Ultimately, it is up to the scientists to prove the value of this work. While large-scale clinical trials are still years away, we can begin to see work emerging from the lab and making its way into potential therapies for people with life-threatening diseases. The future of stem cell therapy is real, and Minnesota is uniquely positioned to leverage several strengths, including our history and our infrastructure, to help lead medicine in this new direction." MB

BY WOLFE MOLITOR

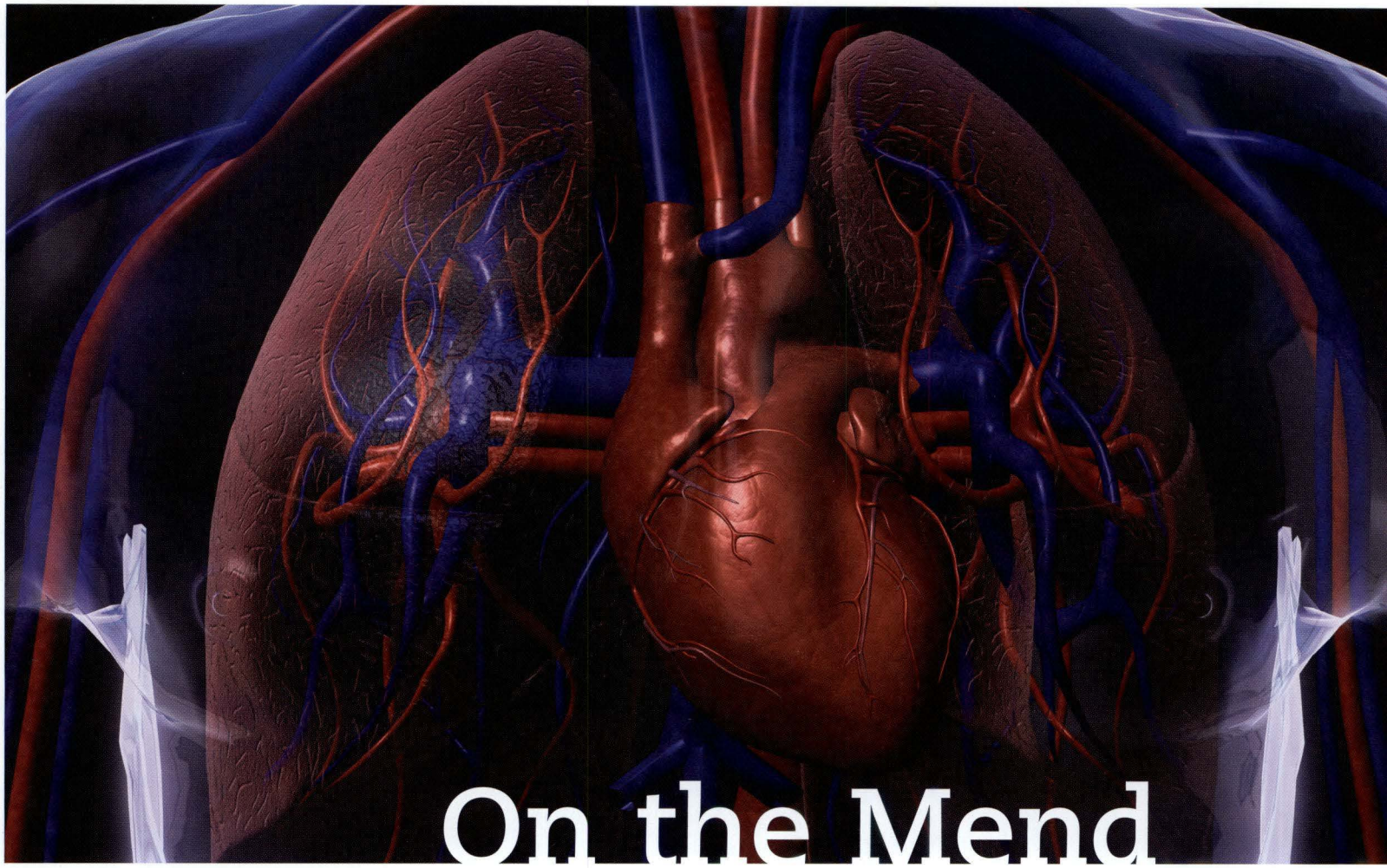


ILLUSTRATION: 3-D CLINIC

On the Mend

The University of Minnesota's new Center for Cardiovascular Repair looks to living cells to fix broken hearts.

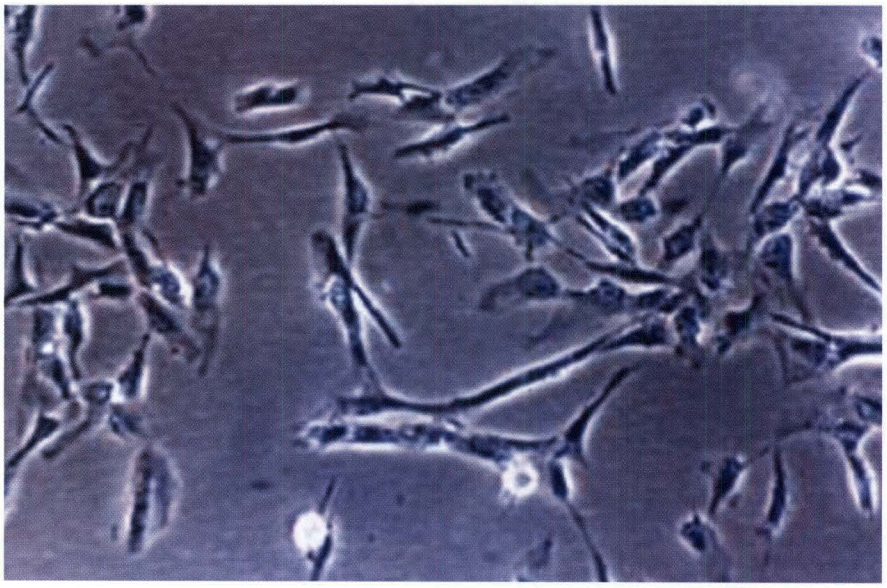
IF YOU SCRAPE YOUR KNEE or break an arm, your body knows just what to do: make more skin or bone to replace the damaged tissue. But it's not that simple if what's hurt is your heart. When cardiac muscle is destroyed by a heart attack, cardiomyopathy, or other illness or injury, there are no replacement parts waiting in the wings.

In some patients, a heart transplant or a mechanical device can help restore at least some of the lost function. But in most instances, the owner of the damaged heart is sentenced to a life of downward-spiraling health as the surviving cells literally work themselves to death struggling to do the job of their fallen comrades.

Soon, however, that picture may change. With the establishment of the Center for Cardiovascular Repair (CCVR) at the University of Minnesota, the stage has been set for moving a revolutionary heart-mending strategy from the laboratory to real life.

Known as cellular cardiomyoplasty, the approach involves infusing living cells from other parts of a person's body into his or her heart, where they implant and begin to restore lost function. This revolutionary approach has been shown to improve heart function in animals and has begun to be tested in humans, with encouraging preliminary results. The rigor of randomized clinical trials is next. Though the technique is still being perfected, researchers hold high hopes that one day soon it will provide a practical means for restoring heart function to the millions of individuals who suffer heart attacks or other forms of heart damage each year.

"This is an exciting field," says CCVR director Doris Taylor, Ph.D., who moved to Minnesota from North Carolina last winter to head the new center. "It's the first opportunity to treat the underlying problem in cardiovascular disease, rather than trying to get the rest of the heart to work better."



Human skeletal myoblasts after a 3-week in vitro culture period (magnification x 40)

A different tack

Taylor should know better than just about anyone what promise this new technology has to offer. In the early 1990s, while working at Duke University, she led the research team that first proved that cells—in that case, skeletal muscle cells—could be used to restore cardiac function lost to heart attack or other illness.

At the time, she had been focusing her research on how genes in skeletal and heart muscle cells are regulated, in hopes of finding clues as to why the skeletal cells can divide while the heart ones generally cannot. Then, she decided to try a different tack. Rather than try to convince heart muscle cells to divide, she thought, why not just move cells that already know how to divide into the neighborhood?

"I was working with muscle, the continuum from white muscle and red muscle," Taylor says, "and the heart is the ultimate red muscle. I decided to take cells from skeletal muscle and transplant it to the heart. It just made a lot of sense."

At first the scientific community was skeptical. "It was not only a novel concept but also not very well believed," Taylor says. "People were saying if it's so easy, why isn't it being done?"

Ignoring the naysayers, Taylor continued her quest. Through trial and error she was able to come up with a winning combination of cells and procedures. In 1998 she and her colleagues published a paper showing an improvement in the function of damaged heart tissue in rabbits after transplantation of leg muscle cells.

Since then, "the field has just exploded," Taylor says. Researchers around the world have been testing variations on the theme, using various types of

cells and procedures, to find the safest and most effective protocols for restoring heart function. Some have focused on muscle cells. Others, including Taylor, are also exploring the use of adult stem cells, which have the ability to take on the traits of other cells around them when they are inserted into various parts of the body, including the heart.

"It really is changing the paradigm for thinking about treating cardiovascular disease," she says.

All the pieces

Shown to effectively improve cardiac function in experimental animals, some of the procedures are rapidly approaching the point where they are ready to be tested through clinical trials.

That, in large part, is why Taylor made the trek from balmy North Carolina to blustery Minnesota last winter. In the fall of 2002, the University of Minnesota and Medtronic, Inc., announced a joint effort to advance cell-based heart repair by establishing the Medtronic Bakken Chair in Cardiovascular Repair. After an international search, Taylor was offered the position along with the opportunity to establish and head the CCVR.

She was delighted to be invited to continue her quest at the University, with its longstanding reputation for innovation in cardiovascular research and collaborative connections with some of the world's premier biomedical businesses. It's an environment she sees as poised for success.

"It's clear that the University has a commitment to leading the field in cardiovascular disease," she says. "All the pieces are in place here to succeed." Those pieces include a cadre of top-notch cardiologists and

My job is to... help bring together what might have seemed like disparate areas of research into a network so that we can move ahead faster and better than anyone else.

surgeons; the Stem Cell Institute, which offers opportunities to collaborate in exploring the use of adult stem cells for repairing not only heart but also vascular tissue; the Biomedical Engineering Institute, which can design almost anything we can imagine; the Lillehei Heart Institute; the Center for Magnetic Resonance Research; the Minnesota Molecular and Cellular Therapeutics Facility, which allows researchers to prepare cells under the rigorous conditions needed for human clinical trials; the surrounding biomedical industry community; and what Taylor refers to as a "strong belief in innovation."

"Literally, you couldn't ask for anything else," she says.

Gathering experts

Since she arrived in Minnesota, Taylor has been gathering experts from various departments and centers to begin moving the cardiac cellular approach to heart repair to clinical application. She's also setting the stage for exploring other avenues

PHOTO: TIM RUMMELHOFF

Doris Taylor, M.D., professor of medicine and physiology, member of the Biomedical Engineering Institute, and holder of the Medtronic Bakken Chair in Cardiovascular Repair

OUTSIDE THE BOX

Nearly 50 years ago, University of Minnesota alumnus Earl Bakken, founder of Medtronic, Inc., revolutionized cardiovascular medicine when he developed the first transistorized, wearable, battery-operated pacemaker at the behest of heart surgery pioneer C. Walton Lillehei, M.D. Last year, the University and Medtronic jointly established the Medtronic Bakken Chair in Cardiovascular Repair as a way to both honor Bakken and show support for ongoing innovation in the field of cardiovascular care.

When Doris Taylor, the first person to repair a damaged heart using skeletal muscle cells, was invited to move her laboratory to Minnesota, one of the things that clinched the deal for her was the opportunity to be associated with the Bakken legacy. Taylor sees holding a chair with Bakken's name on it as both an honor and a challenge.

"I respect him a lot," she says. "He's always thought outside the box, which is something I like to think I do. He certainly changed the world. And if I'm lucky enough to change the world, that will be a wonderful thing."

to cardiovascular repair, including the use of stem cell and other therapies to repair blood vessel damage caused by coronary artery disease, atherosclerosis, and other disorders, and the use of gene-based therapies to treat cardiovascular diseases.

"I think I was hired to be the catalyst," she says. "My job is to be a connector among the various aspects that are here and to really help bring together what might have seemed like disparate areas of research into a network so that we can move ahead faster and better than anyone else and really be the place people think of when they think cardiovascular repair."

One of the current focal points for research at the CCVR is testing the potential of various types of cells to help restore damaged heart tissue. Both muscle cells and adult stem cells implant into heart tissue, but they behave differently once there. For example, stem cells' ability to make a variety of kinds of cells is normally seen as an asset. However, if they are implanted in scar tissue instead of in functional heart muscle, they may make other kinds of cells instead of the needed muscle cells.

"It may be that one cell fits all, but that would surprise me," Taylor says. "It's going to take a true understanding of cells and patients to know how to choose the right cell for the right patient."

Cultivating connections

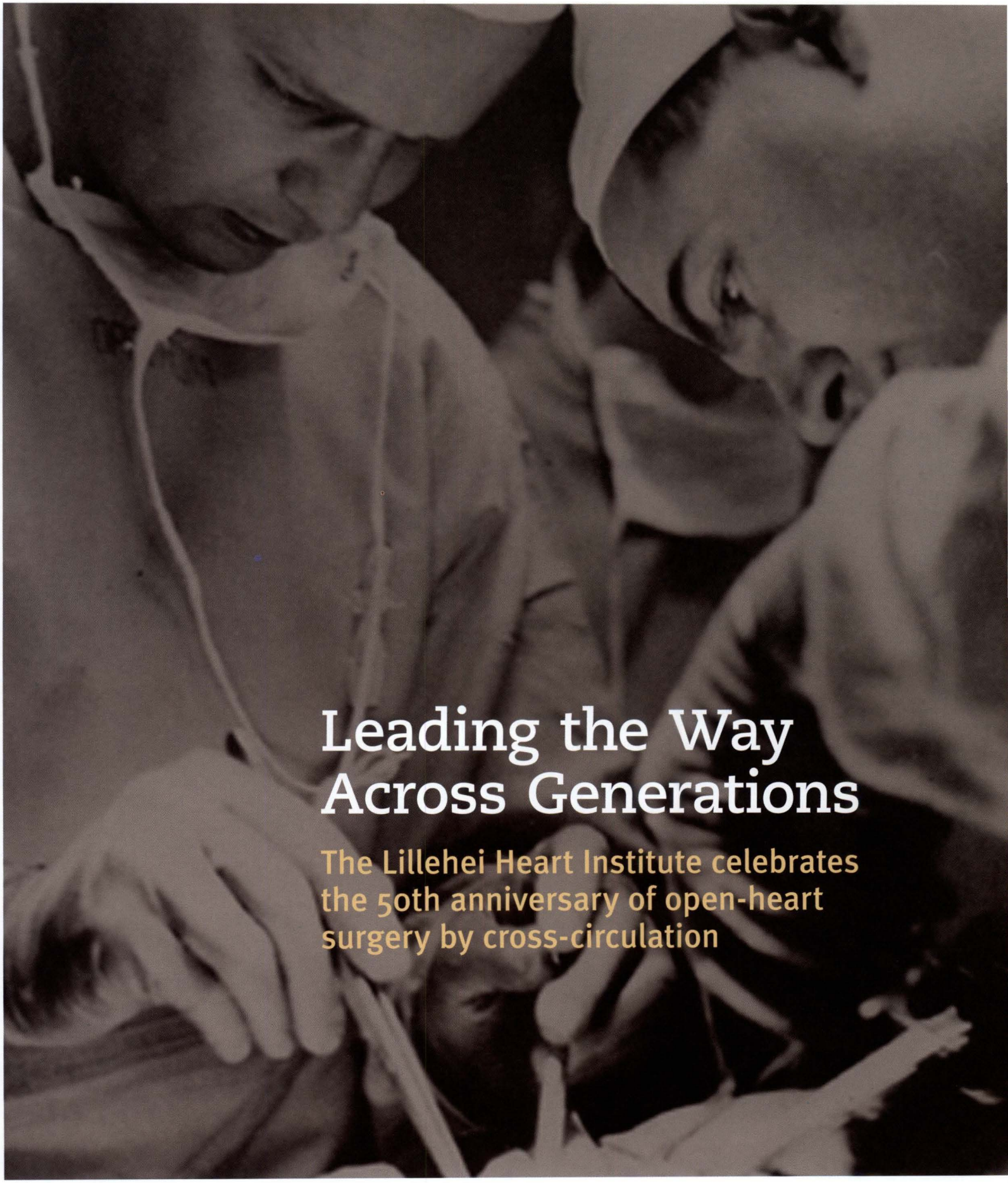
Taylor is also working with various biomedical companies to explore the best way to move cellular cardiomyoplasty from lab to real life. She expects clinical studies at the University to begin fairly soon.

"We've taken the philosophy that we want to move ahead as quickly as is clinically prudent," she says, "Doing it best, rather than first, and improving patients' lives comes first. The truth of the matter is, though, it is fairly straightforward. Nature is doing a lot of the work for us. We don't have to be sidetracked by understanding every little detail. We can take advantage of the fact that nature will do some of it for us."

High on Taylor's list of priorities is continuing to cultivate connections with the private sector, such as the one that made her move to Minnesota possible in the first place.

"Certainly one of our strong goals is to continue to work with the private sector," she says. "I will not have succeeded here at the University if I don't capitalize on the fact that we're in the medical device hotbed and make sure our ideas make it beyond clinical trials to products, that we train people who are capable of participating in the industry, and that we share ideas and resources in both directions. I want to make the University of Minnesota the place companies come when they want to do cell- or gene-based research." MB

BY MARY HOFF



Leading the Way Across Generations

The Lillehei Heart Institute celebrates the 50th anniversary of open-heart surgery by cross-circulation

Fifty years ago at the University of Minnesota something happened that had never been done before. On March 26, 1954, C. Walton Lillehei, M.D., and his colleagues—Drs. Morley Cohen, Herb Warden, and Richard Varco—hooked up the circulatory system of a one-year-old boy with a heart defect to that of his father, essentially using the father as a heart-lung machine to keep his son alive while open-heart surgery was performed successfully to correct the defect.

C. Walton Lillehei, M.D., University of Minnesota alumnus and faculty member, often called the "father of open-heart surgery." He was part of the team that performed the world's first successful open-heart surgery in 1952, developed the bubble oxygenator, collaborated with Medtronic founder Earl Bakken on the pacemaker, and created several artificial heart valves.

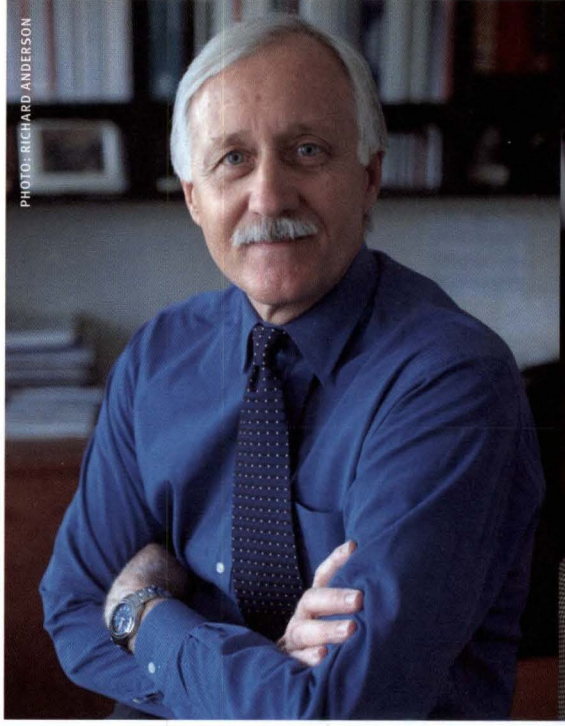
While this was not the world's first open-heart surgery—that had been performed two years before, also at the University of Minnesota, by F. John Lewis, M.D., and his colleagues—Lillehei's innovative use of cross-circulation was the crucial link in the evolution of open-heart surgery to what is now a safe, routine procedure performed hundreds of times a day around the world.

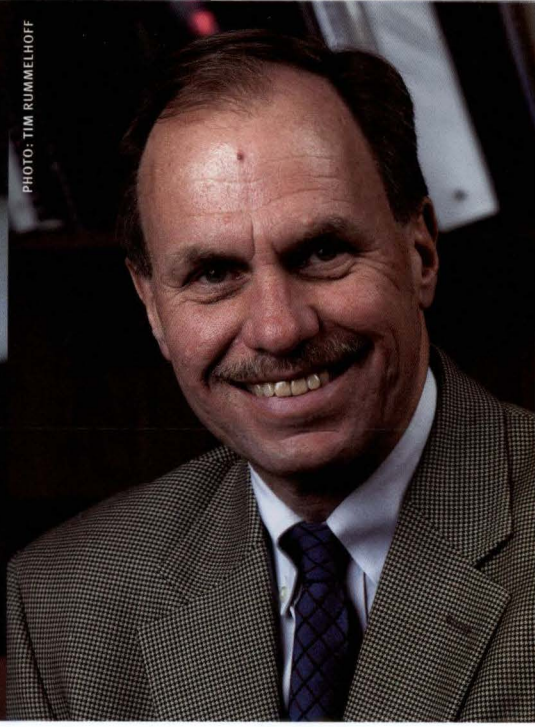
The University of Minnesota and the Lillehei Heart Institute commemorated this seminal achievement in the history of medicine with the 4th Annual Lillehei Heart Institute Symposium October 19–20. The two-day event featured heritage sessions retelling the history of open-heart surgery and related topics, as well as lectures on major topics in cardiovascular surgery by renowned surgeons and physicians from around the world. Talks on future therapies concluded with a keynote speech by Peter Agre, M.D., from Johns Hopkins University, who won the Nobel prize in chemistry last year.

The symposium was not a typical academic event. Invitations were sent to the families and survivors of the first patients who underwent heart surgery at the University. Ceeya Bolman, volunteer chair of the planning committee for the patient portion of the symposium, explains, "Because of the rich heritage in congenital heart disease surgical repair at the University of Minnesota, we hope to open the doors for future educational opportunities for these patients and families, even those who are having procedures done today. In 50 years they'll be sitting where our past patients are now. This was a celebration of the past, but it also marked a new beginning of what we hope to accomplish."

"Back in the 1950s there were a number of seminal events, any of which could have been chosen as the 50th anniversary of open-heart surgery," explains R. Morton (Chip) Bolman, M.D., professor and chief of the Division of Cardiovascular and Thoracic Surgery, director of the Lillehei Heart Institute, and holder of the C. Walton and Richard C. Lillehei Land Grant Chair in Thoracic and Cardiovascular Surgery. "In talking with those who were actually here at the time, we decided the cross-circulation experience was the one event that really catapulted the field of open-heart surgery forward."

The decision was also made to hold the symposium near Lillehei's October 23 birthday rather than in March, to show that the innovative spirit of Lillehei and his colleagues was being honored along with the momentous breakthrough of cross-circulation.





LEFT Leslie Miller, M.D., professor and director of the Division of Cardiology in the Department of Medicine, director of the Heart Failure and Transplant Program, and associate director of the Lillehei Heart Institute

RIGHT R. Morton (Chip) Bolman, M.D., professor and chief of the Division of Cardiovascular and Thoracic Surgery, director of the Lillehei Heart Institute, and holder of the C. Walton and Richard C. Lillehei Land Grant Chair in Thoracic and Cardiovascular Surgery

Lillehei's legacy

"We take very seriously the legacy of the University of Minnesota being the birthplace of open-heart surgery," says Bolman. "Our commitment is to make sure that in a hundred years when we're all gone, there will still be an entity called the Lillehei Heart Institute dedicated to Dr. Lillehei's legacy of innovation in cardiovascular surgery and medicine and in the education of future practitioners."

Peter Bitterman, M.D., professor in the Division of Pulmonary, Allergy, and Critical Care in the Department of Medicine and director of research for the Lillehei Heart Institute, explains the legacy this way: "We strive to carry out the highest quality health care research and prepare the next generation of scientists to eclipse our accomplishments. That's what the Lillehei Heart Institute stands for.

"The other part of the legacy is that you need to recalibrate your vision of what can and can't be done," explains Bitterman. "Our job is to take any human health problem and solve it, whether it's in heart disease, breast cancer, orthopaedic surgery, or bionics for the hand. This is the legacy Dr. Lillehei left us—the idea that we bring together individuals, students, faculty, and scientists to solve problems in human health. He took a problem that was viewed as insurmountable and solved it."

The Lillehei Heart Institute was established three years ago with a generous gift from Kaye Lillehei and the Lillehei family to honor Walt Lillehei's memory and continue his legacy. According to Bitterman, "Kaye Lillehei is very enthusiastic about stimulating bright, young people to pursue cardiovascular and respiratory research using the tools available to them today."

Leslie Miller, M.D., professor and director of the Division of Cardiology in the Department of Medicine, director of the Heart Failure and Transplant Program, and associate director of the Lillehei Heart Institute, says, "Part of our mission is education, but it's not simply to train the next group of itinerant doctors. We feel our job is to truly inspire the next generation and instill in them that same pioneering spirit we have received from Dr. Lillehei."

Collaboration and creativity

The Lillehei Heart Institute was specifically designed as an interdisciplinary institute at the University of Minnesota. In part, the decision was practical—

In talking with those who were actually here at the time, we decided the cross-circulation experience was the one event that really catapulted the field of open-heart surgery forward.

–R. Morton (Chip) Bolman, M.D.

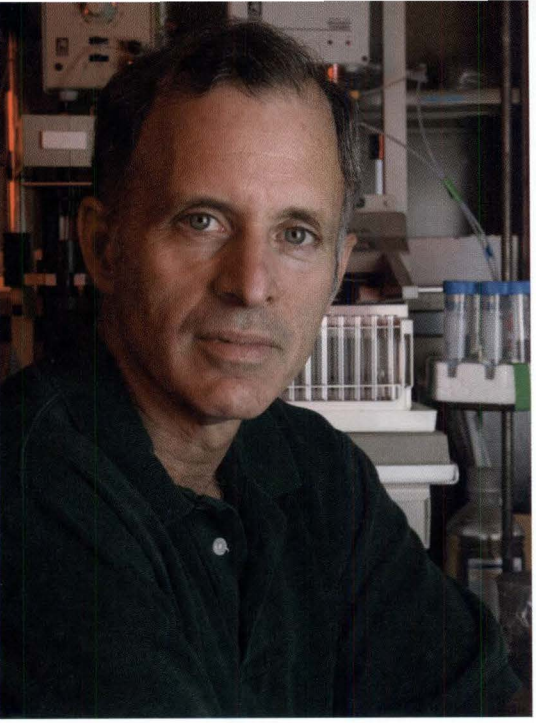


PHOTO: TIM RUMMELHOFF

Peter Bitterman, M.D., professor in the Division of Pulmonary, Allergy, and Critical Care in the Department of Medicine and director of research for the Lillehei Heart Institute

federal research dollars are contingent on recipient institutions having an interdisciplinary structure. But such a structure also fosters greater creativity and collaboration, leading to more rapid discoveries and innovations.

Interdisciplinary research is much more intentional than in Lillehei's day. Bolman explains, "Now we have programs in the Lillehei Heart Institute that are intentionally multidisciplinary and cross not only disciplines within the Medical School, but also in the Institute of Technology and in the entire Academic Health Center, including public health, nursing, pharmacy, and others. We are able to perform sophisticated, basic research without having to duplicate facilities. There was already a lot of interesting cardiovascular research being conducted across the University, and the Lillehei Heart Institute brings it together in a more formal manner."

Miller agrees: "I think the Lillehei Heart Institute is the perfect umbrella organization. There was already a good deal of collaboration between cardiology and cardiac surgery, perhaps better than in many institutions around the country, but I think the Lillehei Heart Institute has taken us to the next step. It has brought together our creative energies and intellectual curiosity both in direct translational patient care and in innovative ideas that point to the future of cardiovascular research and care."

Today's innovations

The medical landscape has changed significantly since Lillehei's day. "We're focusing on specific areas such as heart failure and transplant and pediatric heart disease," explains Bolman. "One of the things we do is very sophisticated valve repair surgery that is relatively unique in the community. High-risk surgery for heart failure includes coronary bypasses and valve surgery, but it also includes ventricular assist devices, used either to allow the patient's heart to recover, after which the device is taken out, or as a bridge to a transplant when the heart doesn't recover and the patient can be placed on a transplant waiting list. I think we've also continued to lead the way in pediatric heart disease, which is really where it started with Dr. Lillehei's initial efforts to correct very simple defects in the hearts of infants and small children."

While the Lillehei Heart Institute will continue to support advancements in these current areas of expertise, new areas of research and exploration have emerged. University surgeons have begun performing heart surgery with a surgical robot that has been used in other types of surgery. Now the Lillehei Heart Institute is trying to help define the device's role in cardiac surgery.

Another key area of exploration is cell-based therapies for myocardial repair. Bolman explains, "We're very interested in seeing whether this is going to be a promising avenue of therapy, which we anticipate it will. But the questions have to be asked and answered, and I think we're ideally positioned to do that. We have the basic research strength here, plus the clinical strength in heart failure, and years of experience with a long track record. I think we have a very good chance of being the ones to answer many of those questions."

Miller has been working with ventricular assist devices for over 20 years and has seen an incredible evolution

We strive to carry out the highest quality health care research and prepare the next generation of scientists to eclipse our accomplishments. That's what the Lillehei Heart Institute stands for.

– Peter Bitterman, M.D.

in their efficiency, sophistication, and durability. His work in this area has now led him to study the molecular basis for heart failure and recovery. He is currently working with two grants looking at basic molecular and gene mechanisms in order to stimulate true cardiac repair.

"Traditionally, we've believed a person is born with a certain number of cardiac cells, and as these cells die, the heart can never regenerate," explains Miller. "We're at the door of a fundamentally different understanding of that concept, which is extremely exciting."

Moving forward

The Lillehei Heart Institute, currently located in the Dwan Variety Club Cardiovascular Research Center, will be embarking on a campaign to build support for its own dedicated space. There is a critical shortage of space for the researchers already recruited, let alone the numerous individuals that the institute would like to recruit in the next five years.

Bitterman explains, "We cannot begin to achieve what the current faculty and student body are capable of achieving without a new, dedicated facility. Creating a facility designed for the sole purpose of supporting investigators committed to the development of new therapeutics will keep these people here rather than leaving for another institution."

The new space will be modeled after the Cancer Center, which has gained national recognition for its success with multidisciplinary research.

The 4th Annual Lillehei Heart Institute Symposium represented an opportunity to celebrate not only the great achievements of the past in cardiovascular research and surgery but also to publicize the current innovations and expertise taking place at the University of Minnesota and show where the University is taking the lead in developing future therapies.

"I think the 50th anniversary of open-heart surgery by cross-circulation was an incredibly important occasion," says Miller. "But of all the things we were celebrating, it is the innovative, pioneering spirit of Dr. Lillehei that we celebrate the most. The testimony to someone's legacy is, Does it endure? Does it re-inspire? Dr. Lillehei took a whole field and opened it up with a multiplier effect in terms of everyone who's been operated on, everyone who's been trained, and all the surgeons they have trained in turn.

"We still feel that spirit here—that someone had the outside-the-box mentality all the time. And I think that's what captivates all of us here at the Lillehei Heart Institute. Dr. Lillehei's spirit of creativity and innovation is something we want to pass on to everyone with whom we're associated." MB

BY ANDREA J. PETERSON

The former Variety Club Hospital, where C. Walton Lillehei, M.D., and his colleagues performed the world's first open-heart surgery by cross-circulation

Cardiac firsts at the University of Minnesota: The first 25 years

1950s Link between dietary fat, serum cholesterol, and heart disease established by Ancel Keys, Ph.D.

1952 World's first successful open-heart surgery using hypothermia performed by John Lewis, M.D., Richard L. Varco, M.D., and Mansur Taufic, M.D.

1954 World's first open-heart surgery using cross-circulation performed by C. Walton Lillehei, M.D.

1955 Bubble oxygenator (prototype for today's heart-lung machine) developed by Richard DeWall, M.D., and C. Walton Lillehei, M.D.

1958 World's first portable pacemaker invented by Earl Bakken, Medtronic, Inc., cofounder, at the request of C. Walton Lillehei, M.D., the first to use it in a patient

1958 World's first artificial heart valve implanted in a human by C. Walton Lillehei, M.D.

1960 Antifibrillation heart drug bretylium developed

1975 World's first implantable pump for internal delivery of the blood thinner heparin developed and inserted by Henry Buchwald, M.D., Ph.D.

FOR MORE INFORMATION

on Dr. Lillehei and the first open-heart surgery by cross-circulation please visit the following Web sites:

Dr. Vincent Gott's tribute:
www.ctsnet.org/doc/3531

Dr. Denton Cooley's tribute:
circ.ahajournals.org/cgi/content/full/100/13/1364

To support innovative research at the Lillehei Heart Institute, contact the Minnesota Medical Foundation at 612-625-1440 or visit the Web site at: www.mmf.umn.edu.

A Vision for Medical Education

Over the past decade, it has become widely accepted that the current structure of medical education—established more than a century ago—needs to be revamped to reflect changes in the American health care system that call for new skills as well as a continuum-of-education approach that integrates all levels of medical education, from pre-med to clinical practice.

Doctors are increasingly called upon to work in interprofessional teams and to keep abreast of the latest information available through the Internet and other innovative technologies. Since joining the University two years ago, Medical School Dean Deborah Powell, M.D., has committed herself to placing the University at the forefront of change. Recently, the *Medical Bulletin* asked her to expand on her vision for medical education in the 21st century.

MEDICAL BULLETIN: Dean Powell, you've made clear that you believe medical education in the United States needs to be transformed in important ways, and that the University should be in the forefront of this change. What led you to this conclusion?

DEAN POWELL: First, it's important to point out it isn't just me who feels there is a need for a new model of medical education. For the past several years there has been a feeling in many quarters that change is needed. The Association of American Medical Colleges (AAMC), the umbrella group that represents the country's 125 medical schools, has called for this. The Institute of Medicine has a series of reports on the quality of care in the United States, the last of which calls for a new paradigm for health professional education. The Accreditation Council for Graduate Medical Education (ACGME) started an outcomes project in 1997 that talked about the need to change the way we evaluate and train residents, and the American Board of Medical Specialties has also called for change in the way we do continuing education and the recertification of physicians.

These trends are starting to come together in a larger vision across the medical education community, questioning if residents and students are being educated to practice in the health care environment in which we currently find ourselves.

MB: Why is that?

DP: Medical schools are fairly traditional. We haven't made many fundamental changes in the past 100 years. We operate in a system now where we have national licensing exams that all students must pass to be licensed. Many faculty feel a great deal of pressure to make sure that students know what may be tested on these exams. We spend a lot of time testing students in basic sciences and clinical knowledge, but only relatively recently have made changes to reflect the need to test for clinical skills. Many important skills like communication have not been part of the training or evaluation. And we are only recently dealing with training for practice, in the skills of practice improvement and how health systems function.

MB: What would medical education look like if it were changed in the ways you envision?

DP: We would spend less time in lectures and on making sure students learn and memorize a large mass of information. Technology is such now that students need more of a framework and an understanding of concepts than ever before. They have to be able to understand and incorporate new information more quickly, and they need to know how to access information when they need it. That means we have to pay much more attention to things like information management and technology. As it is, a lot of our students come to us with those skills or are ready to learn them because they grew up in the Information Age, but many of our faculty are not as ready.

Traditionally medical school has been time- and course-bound—so many weeks are allotted for this subject, so many weeks for that, and these are the courses you must take. But some students come to us with strong backgrounds in, say, biochemistry, and might be able to do research or study advanced metabolism rather than sitting through another chemistry course. We need to individualize medical school education.

We also need to have a better sense of the competencies students should have at each stage of their education and develop ways to measure and evaluate those.

Another thing we haven't done is to educate students enough about the health care system in which they will find themselves practicing. We give them some courses about this in their first or second year of medical school, but that's simply not enough. More and more health care is provided in outpatient settings by interprofessional teams, but the current education has been very segmented. We haven't chosen students who have backgrounds in systems development or team building, and we don't train them to develop those skills.

We also haven't talked enough about quality-improvement techniques. How do you come into a clinical setting and assess and improve it in ways that ultimately improve patient care? Nor have we paid enough attention to the issue of patient responsibility for their own health care. Medicine has been very paternalistic. It has become less so, but there's still work that needs to be done. We have to train our students in how to develop a patient-centered practice. Among other things, this involves an understanding of the increasingly pluralistic nature of our society. Students have to understand the different cultural, ethnic, and social contexts from which their patients come and how those contexts affect their health and treatment programs. This means we need more education in the social sciences than our students typically possess when they come to us.

MB: If you were to rank by order of priority the things you'd like to change, what would that ranking look like?

DP: I would start by trying to identify by area the competencies we want students to graduate with, and then develop an evaluation system we felt confident would assess those competencies sufficiently to ensure we are graduating students who are really ready for the next stage of their education.

The second thing I'd like to work on is individualizing medical education. When we talk about competencies we have to recognize that not every student is going to acquire those competencies at the same time or at the same pace. We have to offer choices and a progression toward those goals that suit the needs of particular students.

Third, we have to look at our prerequisites for medical school. What we want students to learn as undergraduates may be different from what they are required to study now. This might mean requiring a background in systems engineering or information technology or languages.

Then we need to develop in our curriculum the other skills students should have, such as how to develop interprofessional team-based practices.

And we need to assess where students are learning outside the school. If a student learns about evidence-based medicine in a classroom setting or a Web course and then does a clerkship at a place where people don't practice that or aren't interested in patient-

PHOTO: TIM RUMMELHOFF

Traditionally medical school has been time- and course-bound... But some students come to us with strong backgrounds in, say, biochemistry, and might be able to do research or study advanced metabolism rather than sitting through another chemistry course. We need to individualize medical school education.

centered health care, then they don't get reinforcement for the things we want them to learn.

The list could go on and on. We plan to address some of these in overarching steps as well as in smaller pilot projects to give us a chance to see what works and what doesn't work before incorporating new things into the broader curriculum.

MB: If the Medical School faculty have, by and large, been educated in the old system, how will they be able to teach students a new way of doing things?

DP: Some faculty have been exposed to important concepts such as evidence-based medicine. Many feel dissatisfied with the health-care delivery system, and are aware of the ACGME's six core competencies (patient care, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, professionalism, and systems-based practice). They understand the need for our students to be educated in different ways and are willing to try new approaches.

At the same time, the faculty needs some new skill sets. Most are clinicians and not educators by background and need knowledge about education. Many of us are not as familiar with the new technologies as our students are. Most of our faculty want to make this transition, though, of course, some do not. Some feel very strongly that the way we have done things is fine. And that's hard to argue with in some ways. Our students come in with very strong backgrounds, do well on tests, and go on to be successful physicians. You really have to believe the American health care system is not as good as it could be to want to make these changes.

But if you believe we have a problem in American medical education—and I do—then those of us who are responsible for educating the next generation of doctors have a huge responsibility to change the paradigm. I think a key to that is the involvement of concerned health care professionals—across the disciplines. We have a responsibility not to perpetuate old stereotypes.

MB: What is your timeline on this?

DP: I have been at three medical schools and was involved in curriculum reform at two of them. It is very disruptive for faculty. They work very hard, doing research, teaching, and clinical care. I don't think we can rush this and ask already busy people to disrupt their lives and programs to make cataclysmic changes in how they teach. Realistically it will take four or five years.

MB: How will you know if you have succeeded?

DP: That's the $64,000 question because we have to make sure that what we are doing results in a better practice of medicine. Determining that's going to be a long-term project. We have to define an evaluation strategy now and then assess students as we develop a new curriculum to see if they are better able to achieve the competencies we have defined for them.

MB: What's the price of failure in this?

DP: That's an interesting question. Some faculty would say we're not failing now—we're educating doctors who are smart and socially responsible. But the price of failure will be that we have not met our responsibility to make improvements. We will have kept the status quo and that's not acceptable, because it will mean that more patients will be dissatisfied with their care and physicians will be less credible in the task of creating a higher quality health care system. MB

BY RICH BRODERICK

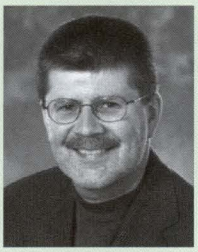
FOR MORE INFORMATION

Visit the Association of American Medical Colleges (AAMC) Web site at www.aamc.org and click "Improving Medical Education," and the Accreditation Council for Graduate Medical Education (ACGME) Web site at www.acgme.org and click "Competencies."

Faculty honored for health research

FOUR UNIVERSITY OF MINNESOTA researchers were awarded the highest recognition of research excellence from the Academic Health Center in June. The AHC Academy for Excellence in Health Research recognizes faculty who have contributed to the quality of the University through nationally and internationally recognized health-related research.

ROBERT HEBBEL, M.D., is an international leader in the investigation of vascular pathobiology of sickle cell disease and leads one of the most productive sickle cell research programs in the world.



MARC JENKINS, PH.D., is one of the world's top immunologists. His method to track T cells and visualize cell-to-cell interactions in vivo helps determine how the immune system keeps people healthy and makes them ill.

ROBERT KANE, M.D., is a world leader in geriatric health care research. His extensive work on aging and outcomes of care has resulted in improved care of numerous individuals.

HON CHEUNG LEE, PH.D., is internationally renowned for his research in calcium signaling. In addition, he has been generous in collaborating with colleagues worldwide and nurturing young researchers.

According to Frank Cerra, M.D., senior vice president for health sciences, "The individuals being recognized have performed cutting-edge research crucial to the development of new drugs and therapies, as well as improved health care. Their research has transformed the fields in which they work." MB

University explores risk factors for type 1 diabetes

University of Minnesota researchers have launched a study that will probe the risk factors and biological events leading to type 1 diabetes, a disease in which the body's immune system mistakenly destroys the insulin-producing beta cells of the pancreas. The hormone insulin is needed to convert glucose into energy.

"In the last 10 years, we've made great strides in predicting who is at greater risk for type 1 diabetes by studying the genetic and immune markers for this disease," says David Brown, M.D., professor of pediatrics and principal investigator. "In this study, we hope to deepen our understanding of why the immune system targets and destroys the beta cells. With this knowledge, we hope to develop ways to safely prevent type 1 diabetes and to preserve the beta cells of people who've recently been diagnosed with the disease."

The University of Minnesota is one of 18 medical centers in the United States, Canada, Europe, and Australia participating in Type 1 Diabetes TrialNet. This network of researchers, labs, and facilities is dedicated to understanding the autoimmune process that leads to type 1 diabetes, preventing the disease, and stopping its progression in those newly diagnosed. MB

Minnesota Medical Foundation names new vice president of development

CARL J. BENDORF was named vice president of development at the Minnesota Medical Foundation, effective August 2, 2004. Bendorf directs all fund-raising activities for the foundation and serves as a member of the executive management team.

Bendorf was most recently assistant vice president for medical center development at the University of Iowa Foundation, where he worked for the last 14 years in a number of major and planned gift development positions and in key campaign planning and institutional leadership roles. He was responsible for all fund-raising for the University of Iowa Roy J. and Lucille A. Carver College of Medicine, University of Iowa Hospitals and Clinics, and College of Public Health. In this role, he led a $263 million campaign, which, with 18 months remaining at the time of his departure, was at 80 percent of goal.

Brad Choate, president and chief executive officer of the Minnesota Medical Foundation, commented, "We are very fortunate to have attracted someone of Carl's caliber to the foundation. He will be integral to the realization of our long-term strategic plan and related philanthropic goals."

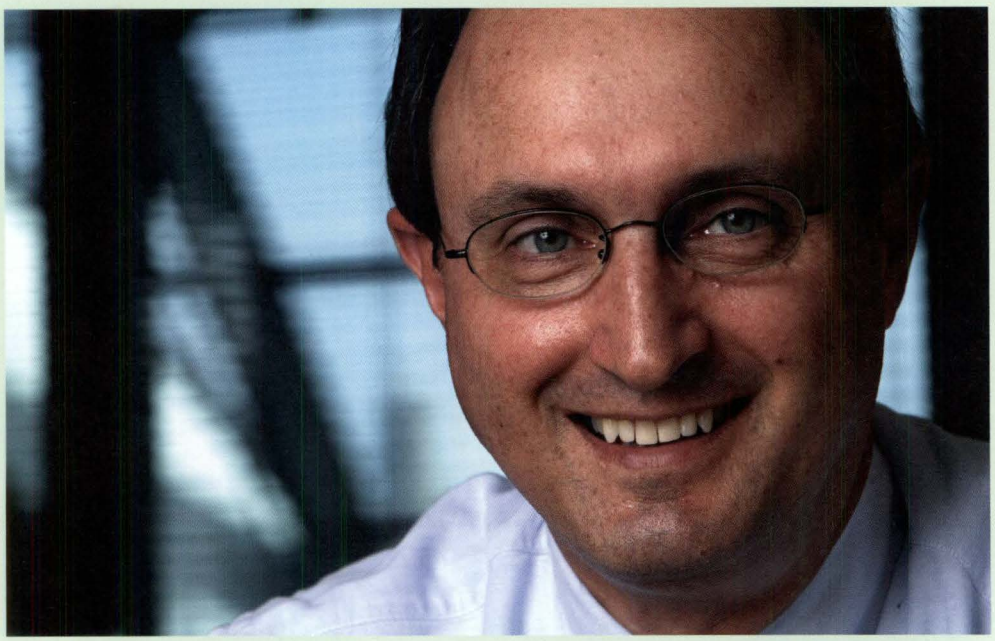


PHOTO: TIM RUMMELHOFF

Bendorf is well known in the fund-raising community for his accomplishments at Iowa and for his professional activities. In 2002–2003 he was the development track chair and on the steering committee of the Association of American Medical Colleges, Group for Institutional Advancement, and in 2000 he was the co-organizer of the Big Ten Planned Giving Conference. In 2002, Bendorf served as president of the Eastern Iowa Planned Giving Council. He has been a frequent guest lecturer with the Iowa Nonprofit Resource Center and has made presentations to the Iowa Pharmacy Association, Iowa State Bar Association, American Association of Collegiate Schools of Business, and International Assembly of the Council for Advancement and Support of Education. He has also contributed articles to *Planned Giving Today*. MB

University designated as Midwest Training Center in Surgical Robotics

The University of Minnesota Center for Minimally Invasive Surgery has been designated the Midwest Training Center in Surgical Robotics by Intuitive Surgical. One of 11 training centers in the country, the Center for Minimally Invasive Surgery will provide the infrastructure and expertise to train surgeons in robotic technology.

Some of the benefits of surgical robotics include reduced trauma to the body, less anesthesia, often less blood and need for transfusions, less post-operative pain and discomfort, smaller risk of infection, shorter hospital stay, faster recovery, and less scarring.

Intuitive Surgical develops and commercializes products that are designed to provide surgeons with the flexibility of traditional open surgery while operating through tiny ports. MB

New target for breast cancer therapy discovered

University researchers have identified a new molecular target that when inhibited blocks cancerous tumor growth in the breast. Although molecular targets for cancers have been identified in the past, this one appears to be a "major hub" for tumor growth activity. The research was published in the journal *Cancer Cell*.

The molecular target is an essential component of the protein synthesis machinery in normal cells and is necessary for cell viability and growth. However, when its activity becomes unregulated, tumors may form. One way of preventing tumor growth is to block the key proteins that drive cancer, but as lead researcher Vitaly Polunovsky, Ph.D., says, "There are many different proteins that cooperate to cause and maintain cancer, some of which are not yet identified. What is exciting about this study is that we've identified a critical target, one that is able to stop other cancer-causing proteins from working up and down the line."

The researchers believe the results of the present investigation will spearhead future studies aimed at targeting the protein synthesis machinery as a way to prevent and treat breast cancer. MB

University establishes nation's first endowed chair in sexual health

The University of Minnesota has announced the nation's first endowed chair in sexual health as part of an ongoing initiative within the Program in Human Sexuality to provide research, education, and patient care in this field. More than 260 donors pledged a total of more than $1 million toward the endowed chair.

Eli Coleman, Ph.D., director of the University's Program in Human Sexuality in the Medical School's Department of Family Practice and Community Health, described the program as one of the oldest, largest, and well-recognized human sexuality centers in the country.

"The Program in Human Sexuality at the University of Minnesota has been on the cutting edge of research, education, and patient care for 35 years. In Minnesota we have a tradition of strong public health informed by science and guided by principles of equity and social justice." MB

Gene associated with lupus identified at University

University of Minnesota researchers have identified, for the first time, a gene variation associated with systemic lupus erythematosus, a complex, inflammatory autoimmune disease that affects multiple organs. The gene variation is found in approximately 16 percent of healthy Caucasians in the United States. However, nearly 23 percent of lupus patients carry this variant, which has also been associated with risk for type 1 diabetes and rheumatoid arthritis. The study was published in the *American Journal of Human Genetics*.

"This appears to be a very important gene for lupus," says Timothy Behrens, M.D., principal investigator, "and this is the first time we have identified a variant that predisposes to many different autoimmune diseases. We hope that this discovery will lead to the identification of other genes associated with lupus and other immune disorders."

Behrens believes that dozens of genes may be responsible for lupus and that discovering the combination of these genes will be important to developing better diagnosis and treatment of the disease. MB

President's Column

AS WE USHER IN A NEW academic year, the Medical School welcomes 165 talented individuals to the Class of 2008, and the Medical Alumni Society board resumes its meetings on alumni programs and awards.

Since the spring of 2004, the board has also taken on an enhanced consultative role with the Medical School dean, Deborah Powell, M.D. At each board meeting, the dean presents one or two important issues for an exciting, in-depth, roundtable discussion.

The dean's first topic was changes in the physician workforce and the preparedness of University of Minnesota Medical School graduates for practice. The lively dialogue brought forth many issues important to alumni today, like the effects of the increase in malpractice insurance and the decrease in compensation for primary practice on a student's specialty choice, efficiently and effectively using physicians and the skill sets they bring to the workforce, and training physicians for academic medicine versus private practice. The board appreciates this opportunity to speak for our fellow alumni and the fact that the dean is listening. We hope to share more feedback from alumni in the future, both through our topical discussions with the dean and through this section of the *Medical Bulletin*.

Alumni involvement is critical to the success of our great alma mater. An impressive 30 percent of our fellow alumni participate by giving financially, much of it to scholarships for current students.

Hundreds of alumni also participate by volunteering for the Medical School. Through the highly successful Connections Mentoring program, for example, Twin Cities physicians re-energize their interest in medicine while supporting the development of the next generation of committed physicians.

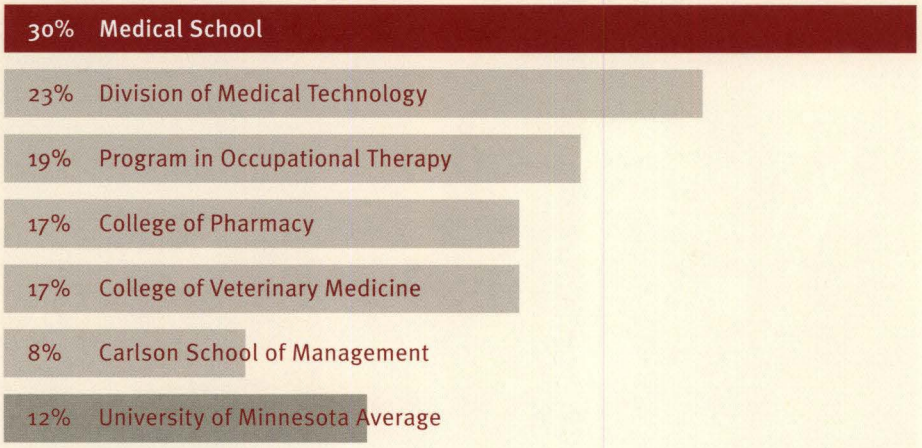
If you would like to contribute to the Medical School and help its students, please contact Emily Heagle in the alumni office at 612-624-9161 or 800-922-1663, or send an e-mail to MAS@mmf.umn.edu. For more information about the Medical Alumni Society and its programs, visit the Minnesota Medical Foundation Web site at www.mmf.umn.edu/alumni.

Best regards,

Richard A. Carlson, M.D., '72
President, Medical Alumni Society

Did You Know?

Alumni of the Medical School are generous philanthropists. Our alumni have the highest giving rate of any University of Minnesota school or college. Here's just a sample:



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Update your alumni records by visiting the Minnesota Medical Foundation Web site at www.mmf.umn.edu/alumni and click on "Update Records," or contact Sue Clark in the Alumni Office at 612-626-0619 or 800-922-1663.

TO BE A DOCTOR

Minneapolis *Star Tribune* writer Gail Rosenblum and photographer Judy Griesedieck followed students in the Medical School Class of 2004 since the first day of class four years ago. The four-year series of stories ended July 13, but the complete series is still available online. Read the "To Be a Doctor" series online by visiting http://www.startribune.com/doctors.

Reunion Weekend 2004

RIGHT Class of 1954 Co-Chair Dr. Bob Geist and Dr. Richard Magraw, '43

BELOW 2004 Diehl Award recipient Dr. Jim Boulger (second from right) celebrates with 1998 Diehl Award recipient Dr. John Sanford, '48, and his wife, Julie Moller Sanford, and Virginia Kremen.

THE MEDICAL SCHOOL Reunion Weekend in May was a great success. More than 300 alumni and their 200 guests from eight celebrating classes attended a number of events throughout the weekend.

The festivities began with Alumni Day at the Medical School, where alumni from the classes of 1942 through 1994 enjoyed a tour of the new Center for Minimally Invasive Surgery; a research presentation by Doris Taylor, M.D., director of the Center for Cardiovascular Repair; and lunch in the newly renovated Coffman Memorial Union.

Distinguished alumni and friends were honored at the Alumni Recognition Banquet on Friday evening, and the weekend ended Saturday evening with the grand finale of individual class dinners at the McNamara Alumni Center.

"Our 40th class reunion was wonderful," said reunion attendee and 40th reunion class chair Jim Lehmann, M.D. "This was the most meaningful of all our gatherings."

Thanks to all of you who participated in the event!

Plans are already under way for next year's reunion weekend, to be held May 20–21, 2005. The Medical School graduating classes of 1945, 1950, 1955, 1965, 1970, 1975, 1980, and 1995 are invited to reconnect with classmates and check out the latest developments at their alma mater. As the date approaches, information will be posted on the Minnesota Medical Foundation Web site at www.mmf.umn.edu/reunions, or call the Alumni Office at 612-624-9161 or 800-922-1663. MB

Call for mentors

CONNECTIONS
MEDICAL STUDENTS COMMUNITY PHYSICIANS

IF YOU LIVE in the Twin Cities area, we invite you to strengthen the connection between today's medical students and community physicians by serving as a mentor.

"I think mentoring is an incredibly worthwhile endeavor," says Rosemary Kelly, M.D. "I have already encouraged other physicians to become involved. In the mentoring relationship, the medical students have enthusiasm and the physicians have experience. The combination of these assets is dynamic and unpredictable, which makes it so interesting. There is much to be gained, by the mentor as well as by the medical student."

You can visit the Minnesota Medical Foundation Web site at www.mmf.umn.edu/alumni and click on "Volunteer" and then "Connections Mentor Program" to fill out the online mentoring registration form, or you can request a form by contacting Emily Heagle at 612-624-9161 or e.heagle@mmf.umn.edu. Registrations are due by Friday, November 5.

We look forward to initiating the program for this year's first-year medical students at a kickoff breakfast from 7 to 9 a.m. on Friday, November 19, at the McNamara Alumni Center on the Minneapolis campus. We hope to see you there! MB

In Memoriam

ARNETTA M. BROWN, M.D., Class of 1937, St. Petersburg, Florida, died May 21 at age 89. She is survived by her five children.

WILLIAM J. CARR, M.D., Class of 1952, Shoreview, Minnesota, died March 19 at age 77. Dr. Carr was a founder of Silver Lake Clinic and charter member of Unity Hospital. He is survived by his wife, Ann, and four children.

ELMER K. GEORGE, M.D., Class of 1937, Missoula, Montana, died February 13 at age 90.

RUTH JOLLY HAUCK, M.D., M.P.H., Class of 1947, Gardnerville, Nevada, died February 17 at age 79. Dr. Hauck practiced medicine in California. She was preceded in death by a daughter and is survived by her husband, Gerard, and two children.

HENRY H. KAVITT, M.D., Class of 1937, Portland, Oregon, died June 17 at age 90. Dr. Kavitt served in the army in North Africa during World War II. He was preceded in death by his wife, Margaret, and is survived by two children.

ERVIN A. KJENAAS, M.D., Class of 1948, Park Rapids, Minnesota, died March 30 at age 80. Dr. Kjenaas served in the army in Korea. He is survived by his wife, Mary Ann, and six children.

RICHARD J. LESSARD, M.D., Class of 1955, Maplewood, Minnesota, died April 22 at age 74. Dr. Lessard spent his career working in St. Paul, Minnesota, and Fargo, North Dakota. He is survived by his wife, Mary, and four children.

ARTHUR J. MOSS, M.D., Class of 1937, Los Angeles, died July 14 at age 90. He served in the army during World War II. Dr. Moss was the former head of the UCLA Medical School Department of Pediatrics and chief of the Pediatric Cardiology Division. He was preceded in death by his wife, Alice, and is survived by three children.

ROBERT J. MURTAUGH, M.D., Class of 1955, St. Paul, Minnesota, died March 27 at age 76. Dr. Murtaugh served in the army before attending medical school. He is survived by his wife, Adeline, and two children. Memorials are being directed to the Minnesota Medical Foundation Scholarship Fund.

G. NICHOLAS ROGENTINE JR., M.D., Class of 1962, Bethesda, Maryland, died May 24 at age 67. Dr. Rogentine spent his career practicing medicine in Bethesda. He is survived by his wife, Carole, and two children.

ARTHUR J. RUSHAY, M.D., Class of 1957, Hudson, Wisconsin, died April 26 at age 76. He is survived by his wife, Jean, and three children.

ROBERT E. T. RYDELL, M.D., Class of 1955, Minnetonka, Minnesota, died April 15 at age 79. He served in the army in World War II. Dr. Rydell was on the staff of the Minneapolis Veterans Administration Medical Center for 31 years. He is survived by his wife, Susan, and a son. Memorials are being directed to the Minnesota Medical Foundation.

LLOYD A. SCHLAEPPI, M.D., Class of 1961, Redington Shores, Florida, died June 1 at age 65. Dr. Schlaeppi served in the army for 29 years, retiring as a colonel. He is survived by his wife, Sharon, and a son.

RICHARD L. SWANSON, M.D., Class of 1959, Medford, Oregon, died February 24 at age 74. He served in the army during the Korean War. Dr. Swanson had a solo ENT practice in Medford for 36 years before retiring in 2000. He is survived by his wife, Marjorie, and three children.

A. BOYD THOMES, M.D., Class of 1942, Minneapolis, died July 4 at age 88. He served in the navy during World War II. Dr. Thomes was a former clinical professor at the University of Minnesota and had a private practice in downtown Minneapolis. He was preceded in death by his wife, Maris, and is survived by four children.

ROBERT B. TUDOR, M.D., Class of 1937, Bismarck, North Dakota, died May 22 at age 91. He served in the Army Medical Corps in Europe during World War II. Dr. Tudor spent his career practicing pediatrics in Bismarck. He is survived by his wife, June, and three children.

ALSO NOTED

JONATHAN D. WIRTSCHAFTER, M.D., Minneapolis, died August 9 at age 69. He came to the University of Minnesota in 1977 with joint appointments in the Departments of Ophthalmology, Neurology, and Neurosurgery. He held the Frank E. Burch Chair in Ophthalmology from 1990 until 2001, when he stopped his clinical practice to devote more time to teaching and research, and to his family. He continued teaching and conducting research until shortly before his death.

Wirtschafter trained 13 fellows in neuro-ophthalmology. Most recently, he was involved in a trial to permanently and non-surgically treat blepharospasm, spasms of the muscles around the upper and lower eyelids, a condition he researched and treated throughout his career. He was the founder and first president of the Benign Essential Blepharospasm Research Foundation and the first volunteer for an injection therapy for blepharospasm treatment trial. The annual Wirtschafter Lectureship in Ophthalmology at the University of Minnesota was started in his honor in 2003. Dr. Wirtschafter is survived by his wife, Carol, and five children.

Class of '43 alumni share power of healing

Written by Kay Fate, condensed from the Cloquet, Minnesota, *Pine Journal,* July 1, 2004.

Ask anyone who's been at a job for any length of time what the most drastic change has been, and you'll probably get a one-word answer: technology. Nowhere are improvements more vital, it seems, than in the field of medicine, and in the 1950s two local doctors were savvy enough to recognize that.

Frank Anderson and Albert Olson were boyhood friends in Cloquet. They lived a block apart and went to school together from seventh grade on, through college and then medical school.

"I always said I only had one friend, and that was Olson," Anderson laughed. "We go way back." Their route to Owatonna—and their eventual founding of the Owatonna Clinic—took many turns.

"(Olson) went to be an engineer at Duluth, to what's now the University of Minnesota–Duluth," Anderson said. "Then he saw those engineers with their spyglasses, you know, standing out in the cold, and he didn't want to do that."

"I wanted to be a forester," Anderson continued, "but I met with a guy and was told that most of the jobs were office jobs. I didn't want that. So, we both decided to be doctors at the same time."

After graduating from the University of Minnesota Medical School in 1943, both men served in the army before beginning their own practices, Anderson in Little Falls and Olson in Owatonna.

Back home in Cloquet for the holidays in 1948, the two friends ran into each other. "I had a good practice in Little Falls," Anderson said. "There was a state-of-the-art hospital there, and I was going to build a house on the Mississippi."

But Olson's partner, a man named Dr. Dewey Morehead, had gotten sick, and Olson had been struggling for a year, trying to juggle all the patients on his own. Olson convinced his friend to visit Owatonna, where Anderson found "a beautiful office and a beautiful town." The two men began their joint practice at 111 Main Street on January 1, 1949.

Five years later, their practice had outgrown their location, so the men found a lot suitable for building, and the Owatonna Clinic's foundation was laid. Six additions were added throughout the years, "and they've been remodeling ever since," Anderson said.

When Anderson retired in 1987, after more than 40 years in medicine, the Owatonna Clinic had 17 physicians. Today it has 50. "We just planned to practice together," he said, "and it just got bigger."

Advances in public health, both men agree, are responsible for the improved health of today's population.

"Public health has meant clean water, adequate sewage and garbage disposal, and a generally adequate diet for most people," Anderson said. "Foods now have vitamins added, so you don't get scurvy or rickets. Now the milk is pasteurized, so you don't get brucellosis."

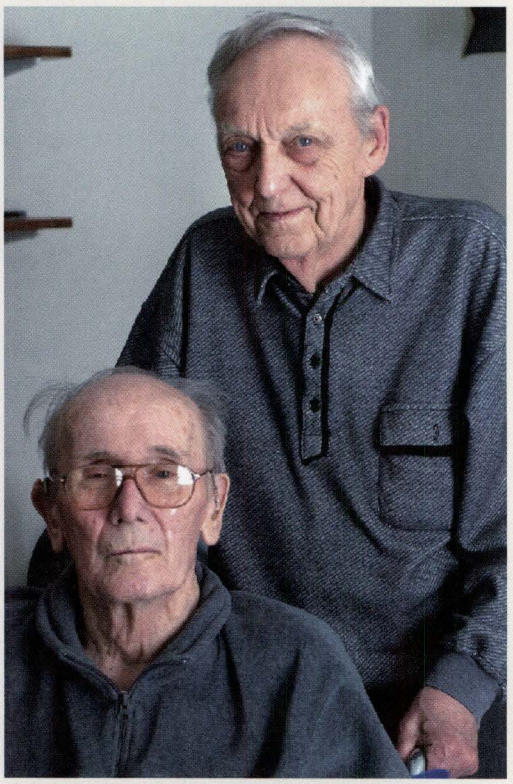

PHOTO COURTESY OF *OWATONNA PEOPLE'S PRESS*

Frank Anderson, M.D. (standing), and Albert Olson, M.D. (seated), practiced "with the times."

The push for better public health in the early 1940s was critical, Anderson said. "The main influence (of improving standards) was that you didn't die when you were a kid."

The immunization for smallpox had "been around for years," Anderson said, "and as kids, my brother and I got tetanus and diphtheria shots. We were really the first generation to have those available. Not a lot of kids got immunized, but it was advertised." Preventive shots for measles, mumps, polio, and pertussis were all developed after Anderson and Olson became physicians.

An advancement in the treatment of infectious diseases arrived just before World War II, with the development and use of sulfa. Penicillin came shortly after the end of the war.

Which was better?

"Oh, don't even compare them," Anderson said. "Sulfa was marvelous compared to what we had, which was nothing. And," he added, "it was less expensive than penicillin."

There were tuberculosis asylums scattered around the state until the development of "good drugs for TB," Anderson said. "The thing they used to do was push air into the lung, to compress the lung so it heals."

There was, he said, "a hiatus of medical advances during the war." Instead, efforts were concentrated on the war itself. That began to change in the late 1940s.

Anderson continued to tick off the list of medical improvements that made his job easier—and his patients healthier.

"A guy over in England figured out how to do hip replacements," he said, "and that changed dramatically how old people healed." A hip fracture 40 years ago was "pretty much a death sentence because you couldn't move around, you stayed in bed, and then you developed pneumonia or other infections. Or your skin broke down," causing other problems.

"Of course, there are the advances in heart surgery. And you can't ignore X-rays," he said. "Then they did all the injections of dye and watched where it went to find the problems, and then we go to CAT scans, then the MRIs."

"It's magic," he said. "It's just magic for guys like me and Olson. We had the smallpox vaccine, tetanus and diphtheria, and that's it."

Now, he said, it's microsurgery that is the medical marvel.

"They've been doing all this big stuff," Anderson said, "and now they're doing all this microsurgery, operating inside" the body through tiny incisions. It's all part of the advancement in medicine, he realizes.

Both men agree advances in public health are responsible for the improved health of today's population. "You have to practice with the times," Anderson says.

"You have to practice with the times, and that's the deal," he said. "That's why we hired a board-certified surgeon. Here we were, 40 miles from Mayo, 60 miles from the University of Minnesota. We had to offer these people a qualified surgeon."

Did he make house calls?

Anderson practically scoffed at the question. "Well, of course. Most people didn't have cars then. Older people usually didn't drive at all."

He brought out the two black medical bags that accompanied him wherever he went. He opened them, displaying the medications and equipment they held.

Olson, who suffers from Parkinson's disease, now lives at Prairie Manor Nursing Home in Blooming Prairie. Anderson visits him at least twice a week. "I tell him his medical bags were twice as big because he was twice as strong," Anderson said.

"We had all the medicines in there," Olson said. "It held all the things that we had to use—you didn't want to not have the one thing you might need" on a house call.

"When I came down here to practice with him in 1949," Anderson said, "he had a schedule of people he would visit every week or two. Usually, they were old, but he just called on them, to check on them." Olson agreed that his role then was much like that of a clergy today, making visits at home.

Medical advancements aside, Anderson has some advice. "We should be our own best doctor," he said. "A good doctor won't mind if you ask for a second opinion."

Olson reflected on a career that lasted nearly 50 years. "Well, we did what we could," he said. "We didn't cure them all, but we did our best." MB

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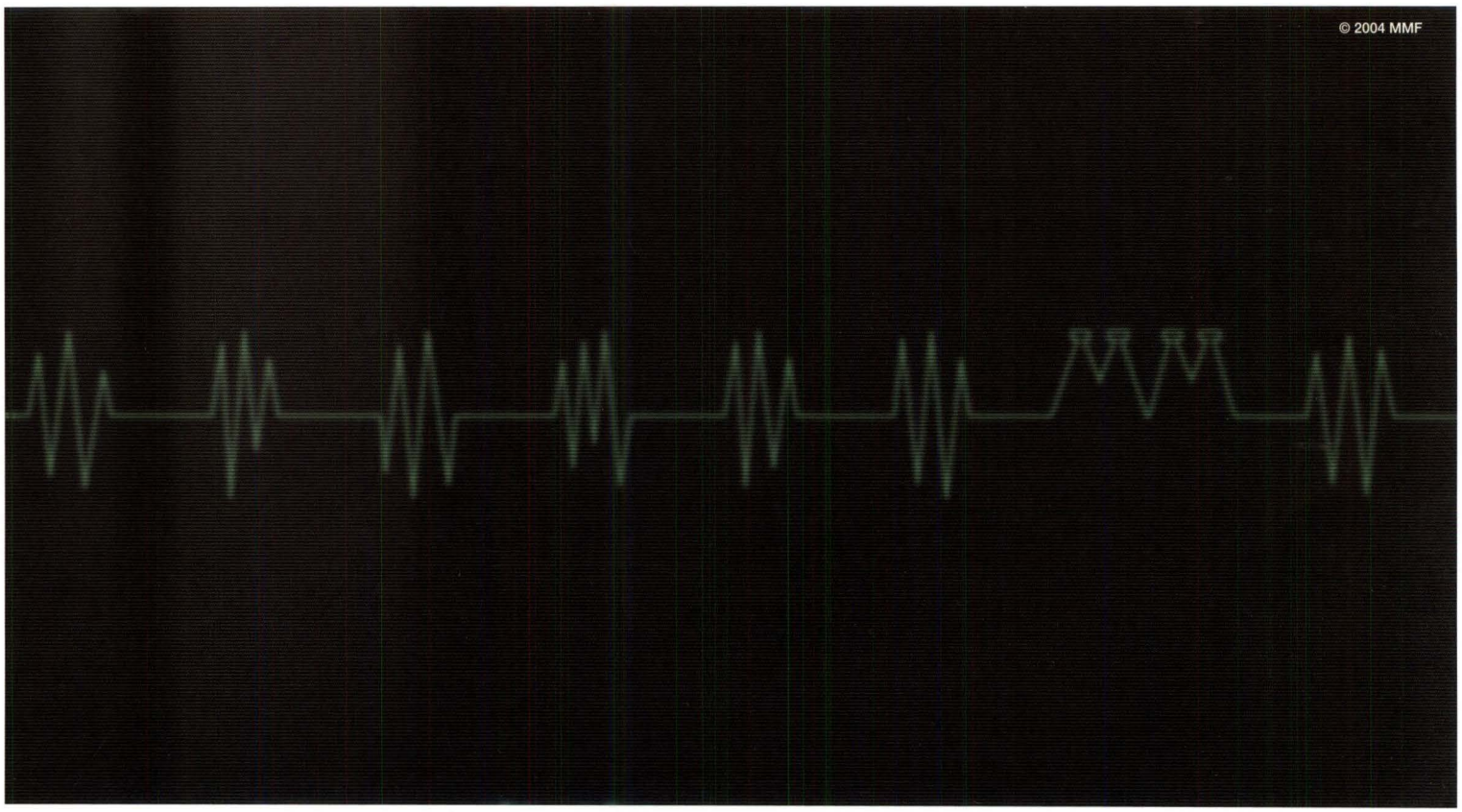

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