

# Mayo Magazine

AUTUMN 2008

Individualized medicine  
at Mayo Clinic

# One OF A kind

**ALSO INSIDE:**  
Aging and cancer  
Growing new ideas  
The innovation center story



# Mayo Magazine

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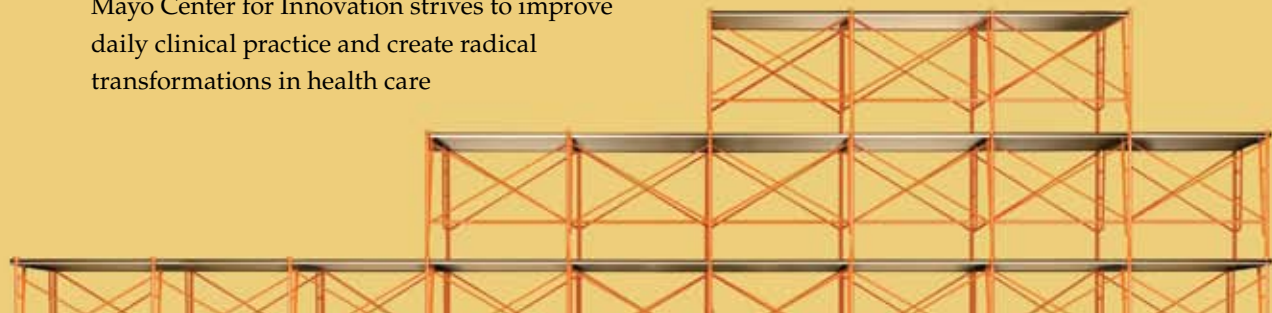
Trustees honor three Mayo Clinic named professors



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# The CAMPAIGN for MAYO CLINIC

In this issue of *Mayo Magazine*, we feature two of our campaign initiatives: **CANCER** and **INDIVIDUALIZED MEDICINE**. The section that follows will give you a snapshot of Mayo's efforts in these two very important fields of study. How is Mayo continuing to improve its methods to diagnose, treat and cure cancer? What is Mayo doing to advance the concept of individualized medicine — treating each person based on his or her own genetic blueprint? How are Mayo researchers advancing the field of pharmacogenomics — tailoring treatment and saving lives? How does studying the immune system give us clues into the intricacies of the aging process? And how is Mayo partnering with its benefactors to assure that the life-robbing diseases of today are a thing of the past for the next generation? By focusing on our core value: **THE NEEDS OF THE PATIENT COME FIRST**.

More than 100 years ago Mayo revolutionized medicine with this simple, yet powerful, statement. We're poised to do it again in the 21st century.

This special section on cancer and individualized medicine is the first in a series of special sections highlighting Mayo's advancements in practice, research and education. Through the completion of The Campaign for Mayo Clinic in December of 2009, each issue of *Mayo Magazine* will contain the stories that highlight our campaign initiatives.

With your help, we can build a world of medicine  
without walls, without boundaries.

Funds raised as of publication date





## Mayo Clinic individualized medicine revolutionizes health care

Over the past decade, we've all read news stories about "decoding the human genome," and perhaps wondered how (or if) it might benefit us individually. Yes, it's great that scientists have now mapped all those millions of genes that make up human DNA — but can anyone draw a map of MY genes and apply that knowledge in a way that helps my doctor keep me healthier?

To the right and on the bottom of the pages that follow, you'll ► meet patients whose unique medical problems illustrate the many facets of individualized care at Mayo Clinic.

The short answer is: We're getting close. Researchers and physicians around the world are using the rapidly growing knowledge base surrounding genomics to tailor methods of diagnosis, treatment and follow-up for individual patients, as well as genetically similar groups (members of a distinct ethnic population, for instance). This movement toward "individualized medicine," as it is commonly called, represents a paradigm shift in medicine. As many physicians and patients have discovered, the "one-size-fits-all" model of medical care often fails a significant percentage of patients who do not respond to a specific drug or treatment. Individualized medicine focuses on understanding an individual's genetic makeup and carefully tailoring drugs and treatments to take advantage of individual genetic tendencies.

That's why Mayo Clinic has made individualized medicine one of its top initiatives. In a recent interview with *Mayo Magazine*, three of Mayo's leaders in the field of individualized medicine, Glenn Forbes, M.D., Franklyn Prendergast, M.D., Ph.D.,

and Andre Terzic, M.D., Ph.D., talk about building Mayo's individualized medicine priority. Here they address the kinds of changes individualized medicine will bring to current methods of providing care, the challenges we need to overcome, and the potential applications of this new science beyond the examination room.

#### **What will individualized medicine look like at Mayo Clinic?**

Individualized medicine will provide the means to determine disease susceptibility, define prevention measures and enable targeted therapies to promote wellness. It's about lifelong care as we predict, prevent, treat and cure disease from childhood to adulthood. It's about moving from the concept of taking care of people when they're sick to partnering with people for their wellness throughout their lifetimes and the lifetimes of the next generation. It's individualizing the delivery of care, acknowledging the differences among us and catering to the needs of each patient. Individualized medicine is the 21st century application of the

*(continued on page 4)*



"Mayo has so many good people who have vision, creativity and ideas. What we really need is to place the right tools in their hands so they can deliver the kind of care our patients deserve and expect."

— Glenn Forbes, M.D.



#### **Second chance for patient with a rare genetic disorder**

Heather Hinton is more than 6 feet tall. She has long fingers and toes and a slender face. These features may not be extraordinary, except in her case, they're caused by Marfan syndrome, an inherited disorder of the connective tissues.

One evening Mrs. Hinton experienced excruciating back pain. She took her pain seriously, knowing that aortic dissection — which causes back pain — is a complication of Marfan syndrome.

She soon learned that her entire descending aorta — the part running from the heart to the neck and down to the abdomen — had dissected, meaning the layers of the aorta separate or tear.

Mrs. Hinton heard about the Marfan Clinic at Mayo Clinic and made an appointment with Thoralf Sundt III, M.D., a cardiovascular surgeon whose interest and expertise lies in aortic surgery.

Mrs. Hinton's aorta was repaired with a synthetic polyester fiber. "In a subsequent operation, we grafted the ascending and arch portions of the aorta and replaced her aortic and mitral valves," explains Dr. Sundt. This is a proactive measure to prevent further dissection.



“In terms of applying individualized medicine in ways that stretch beyond traditional patient care, we are only limited by our imaginations.”

— Franklyn Prendergast, M.D., Ph.D.

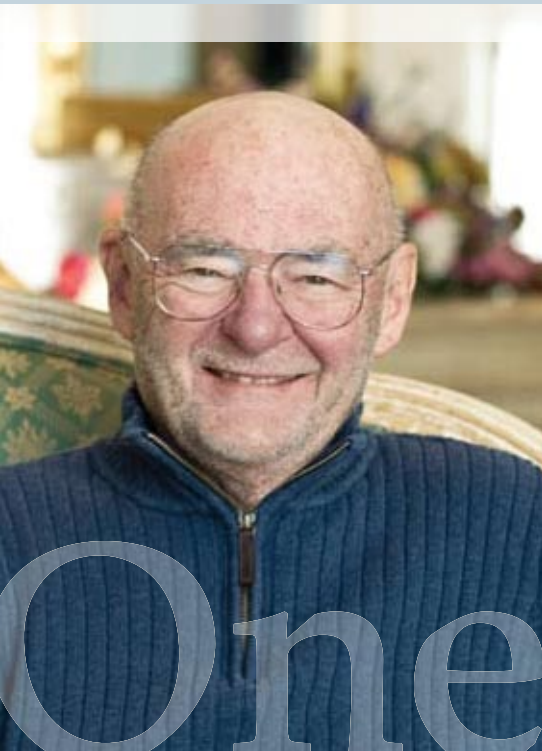
Mayo brothers’ foundational statement that has become the Mayo Clinic core value: the needs of the patient come first. Individualized medicine is a powerful tool for discovering and meeting the needs of each patient — providing safe, effective treatment that works in concert with his or her body for the best possible outcome.

Mayo has an advantage in building individualized medicine because our culture is one of teamwork. It’s always been that way. Success lies in our collaboration and comprehensiveness. That comprehensiveness says that individualized medicine is not just a matter of genetics and genomics, it’s about the collective new science being integrated into our practice, and it’s about proactive partnering with our patients to address individual medical needs.

#### What is Mayo doing today to prepare for tomorrow’s practice of individualized medicine?

We are approaching individualized medicine in a slightly different way from other institutions. Others are focusing only on prediction and pre-

vention; Mayo is focusing on the entire spectrum of health care. Individualized medicine merges all life sciences to create a community of practice. What this means is that before we can predict or prevent disease, we have to be able to assess risk. From there we have to understand fundamental biology in order to predict disease. From prediction, we can move to prevention and early detection. And from detection, we have to understand specific disease susceptibilities. For example, how many different diseases really are there under the label of cancer? From diagnosis and disease stratification, we have to be able to predict the outcome of diagnosis, which is prognosis. And then we have to be able to develop tailored treatments and monitor the safety and effectiveness of those tools. Mayo is looking at the whole spectrum of health care in order to understand the root cause of disease and offer personalized solutions. Built on the Mayo Clinic Model of Care, implementation of individualized medicine will advance innovation within a transformative health care delivery system.



#### Defying the odds

Andy Walch married his longtime sweetheart in a Mayo Clinic chapel just before his surgery to remove a life-threatening brain tumor. The five-year survival rate for his type of tumor was less than 3 percent. Because the odds were stacked against him, Mr. Walch instigated the wedding and got his “house in order.”

No one would have guessed he would be around six years later with no signs of tumor recurrence.

“We are in an era of classifying tumors,” says Joon Uhm, M.D., a neuro-oncologist at Mayo Clinic. “We can identify molecular features, receptors and genetic markers. These patterns offer clues as to treatments. Genetics has revolutionized neuro-oncology.”

Mr. Walch knows his doctors are passionate about helping him, so he took a chance on a clinical trial following his surgery and radiation treatments.

“I’m happy to have defied the odds and I hold a record for long-standing defeat against glioblastoma,” he says. “In the process, my doctors have become my friends. Their passion for medicine and my health has made a real difference.”

In order to accelerate this state-of-the-art care approach, we need to hone our skills. We already have a highly integrated discovery engine, meaning we have a very robust research program with many connections throughout the world of investigation. And we already have highly integrated tools and the experience needed to translate research discoveries into drugs and treatments for patients in the real world. Now we just need to work to make these attributes even stronger.

#### **What are the challenges to implementing individualized medicine?**

There are always going to be the ongoing technological challenges of making medicine personal. However, the scientific challenges of trying to break down the vast amounts of genomic data and the very complex networks of interacting disease systems in order to yield a complete, holistic picture of a patient as an individual person are real, tangible and substantial.

Yet, there is much more to it than just these complexities. Globally,

medicine is unraveling genetic puzzles, meaning we now understand more about ourselves genetically. This deeper understanding of who we are as human beings raises ethical questions regarding what is ethical and responsible as it pertains to this new, intimate knowledge about and use of a person's genetic makeup. The medical community is trying to help define the proper level of privacy and confidentiality. And as medicine enters an era when we can predict as well as prevent some afflictions, we have to give more consideration to how we use that information in appropriate and responsible ways. The ethical implications are profound, and Mayo Clinic has a moral imperative to show leadership in these considerations. For example, if medical science can predict the likelihood (but not certainty) of an individual developing a disease, whom and when do you tell? And especially if you're not absolutely certain it's going to happen, should you reveal this information at all? We have a profound responsibility to ensure that personal information is used responsibly.

*(continued on page 6)*



**“We already have a highly integrated discovery engine ... highly integrated tools and the experience needed to translate research discoveries into drugs and treatments for patients ...”**

**— Andre Terzic, M.D., Ph.D.**



### **Living with non-Hodgkin's lymphoma**

After Margaret Adams was diagnosed with stage IV non-Hodgkin's lymphoma, she underwent intensive chemotherapy and radiation therapy.

The treatment worked and Ms. Adams' cancer had been dormant for nearly a decade when it recurred. This time around, her Mayo Clinic oncologist, Gerardo Colon-Otero, M.D., tried a new radioactive iodine treatment called BEXXAR, used for patients with CD 20 positive, B-cell, follicular non-Hodgkin's lymphoma who relapse following chemotherapy.

“BEXXAR is an intravenous monoclonal antibody that's directed against the proteins located in lymphoma cells,” says Dr. Colon-Otero. “The antibodies are coupled with a radioactive iodine substance. Monoclonal antibodies identify the bad cancer cells and attach to them; then the radioactive iodine gives off radiation and kills them.”

Targeting the cancer cells directly versus treating large areas with radiation and using different types of chemotherapy worked for Ms. Adams ... and many other Mayo Clinic patients.

### What are the applications of individualized medicine beyond traditional patient care?

Individualized medicine will become a lifelong partnership between physician and patient. In today's world, you wait until you're sick to go to the doctor. In tomorrow's world, you may choose to proactively visit your doctor, or you may "go to the doctor" by simply going to the computer on your kitchen countertop and gathering the information you need to help answer health questions. One great example of how Mayo is addressing this type of virtual office visit is through the Enterprise Learning System (ELS) being built by Mayo. When completed, this will be another tool for dissemination of information and knowledge. The ELS will be especially useful for people in parts of the world who can't afford quality health care. The potential is to be able to use the accumulated skills of Mayo providers to help make remote diagnoses.

In terms of applying individualized medicine in ways that stretch

beyond traditional patient care, we are only limited by our imaginations.

### Why should benefactors consider supporting Mayo's vision of individualized medicine?

Over the years, Mayo Clinic has been blessed with benefactors who exhibit not only extraordinary generosity, but also exceptional vision and commitment to helping us create the medicine of tomorrow. Most benefactors expect their gift to continue advancing the science and improving the health of future generations long after they're gone.

Supporting individualized medicine is a solid investment in the future health of individuals, families, communities and, indeed, humanity. There is no doubt that genomics, pharmacogenomics and other components of individualized medicine represent the best hope for unlocking the mysteries of diseases that were previously thought incurable: cancer, Alzheimer's disease, diabetes and heart disease, to name just a few. The

amazing advances in understanding genetic markers that have been made in the past five to 10 years are just a taste of what is possible as researchers and physicians begin to apply new knowledge and new tools to the diagnosis and treatment of their individual patients.

Mayo has so many good people who have vision, creativity and ideas. They have the drive. What we really need is to place the right tools in their hands so they can deliver the kind of care our patients deserve and expect. Our benefactors can help with that.

Some of our needs start with discovery and research. We can benefit from partnerships that help us expand and align our world of discovery. Logistically, we need help in collapsing our data repositories. That's a technical way of saying that Mayo has as many as 1,000 separate areas of information that we need to somehow combine, cross-reference and categorize. We need to link all of that information together so we can see all the relationships between and among the data.



### Boy meets girl, boy saves girl

It's the stuff of Hollywood movies — boy meets girl, boy likes girl, girl moves away. Years later, they meet again and love is rekindled.

Such is the story of Janice and Charlie Lowe. The couple were sweethearts in 5th grade in West Virginia until Janice's family moved to Florida. Years later they reconnected at a Florida State University football game, rekindled their childhood romance and married. Later they had a son, Zachary.

Two years after Zachary's birth Mrs. Lowe began to feel ill. She was nauseated a lot. She thought she was pregnant. Turns out, she was in renal failure. She was diagnosed with Goodpasture's syndrome, a rare kidney disorder that occurs in less than one in a million people. She needed a kidney transplant and as luck would have it, Mr. Lowe turned out to be a perfect match. Most often, the donor is a blood relative.

"We've had a connection our whole life, but it was amazing to think that he would give an organ out of his body. It couldn't be more wonderful," says Mrs. Lowe.



We also need to train and retrain our people to work in different ways in tomorrow's health care world. How do we develop curricula? How do we develop the tools necessary to provide care to the patient of tomorrow?

These are just some of the areas that are essential for moving the practice of individualized medicine forward. ■

## Volunteers take the lead

As a testimony to Mayo Clinic's compelling vision that individualized medicine will be a key component to the future of medicine, Mayo's most steadfast supporters are backing Mayo's efforts to build a program of tailor-made medicine.

Bill Marriott, Jr., chair and CEO of Marriott International, along with his wife, Donna, recently contributed \$15 million to the program whose goal is to translate medical breakthroughs into tailor-made treatments. This gift is in addition to a previous gift of \$10 million, also slated for individualized medicine.

James Barksdale of Barksdale Management Corporation and chair of the Mayo Clinic Board of Trustees, along with his wife, Donna, recently gave \$15 million to the program.

This \$40 million commitment will boost Mayo's efforts to one day treat patients based on their genetic makeup versus the way medicine is currently practiced by using a predetermined set of guidelines based on what works for the majority of the population. Genomic research is at the heart of individualized medicine, and Mayo researchers are closer than ever to translating what's known about the human genome into personal health solutions for each patient who comes to Mayo for care.

Individualized medicine is a strategic priority that is vital to Mayo's mission. With the accelerating pace of scientific discoveries, Mayo expects that individualized medicine will find the best answer for every patient and lay a solid foundation for future practice, education and research. The goal is to integrate new science into personalized health care.

Building on the Mayo Clinic Model of Care, successful implementation of individualized medicine will advance Mayo's culture of innovation. For patients, this means providing patient-specific, lifelong management of health and disease through application of new science to predict, prevent, treat and cure.

The needs of the patient mandate individualized medicine at Mayo Clinic. The overall outcome is the well-being of each individual through the continuum of life. ■



Mr. and Mrs. Bill Marriott, Jr.



Mr. and Mrs. James Barksdale



## It takes a village

If it takes a village to raise a child, then 3-year-old Ellen Hagen's village is populated by Mayo Clinic teams. Ellen's caregivers have included specialists from more than 15 Mayo disciplines. Identified by ultrasound before she was born, a hole in Ellen's diaphragm allowed her liver, spleen and intestines to migrate up to her chest cavity, pushing her heart to the right side and limiting space for her lungs to develop.

Delivered six weeks prematurely, she was just 36 hours old when pediatric surgeons discovered the entire left side of Ellen's diaphragm was missing. Surgeons sewed in a Gortex diaphragm to close the hole. Two months later, tests revealed that Ellen had abnormal brain development and a muscular disorder.

Ellen's doctor, Mary Rahrick, M.D., participates in care conferences with Mayo caregivers from multiple disciplines to implement ongoing care plans for Ellen. This integrated team demonstrates how important coordination, creativity and resourcefulness are to Ellen's care.

"I am grateful for medical professionals like Dr. Rahrick who see the potential of special needs children instead of their limitations," says Mrs. Hagen.

# smarter

How pharmacogenomics innovations are changing cancer care



This distinguished trio of Mayo Clinic physicians and scientists — oncologist Matthew Goetz, M.D., (left), oncologist James Ingle, M.D., (center) and physician-scientist Richard Weinshilboum, M.D. — helped make an important discovery about the way in which genes and other medications influence the effectiveness of the breast cancer-fighting drug tamoxifen.

In 2007, breast cancer survivor, Carol Wray, searched the Internet to learn about her condition and to confirm that she was benefitting from the latest, cutting-edge research. Her research led her to Mayo Clinic oncologist Matthew Goetz, M.D., whose own research discovery had suggested the importance of genetic makeup in her cancer treatment. The link between this physician-scientist and patient illustrates Mayo Clinic's enduring commitment to translating basic research to patient care, and a new generation of Mayo scientists advancing the field of pharmacogenomics.

#### **A founding center for pharmacogenomics**

To understand Mrs. Wray's story and Dr. Goetz's accomplishments, one must look back almost 30 years to the groundbreaking work of Mayo Clinic physician-scientist Richard Weinshilboum, M.D. In 1980, Dr. Weinshilboum published the findings about his breakthrough discovery that the activity level of an enzyme, thiopurine methyltransferase (TPMT), is controlled by a common genetic polymorphism, or gene variation. His research solved the mystery of why the same dose of an anti-cancer drug, 6-mercaptopurine (6-MP), cured some children with acute lymphocytic leukemia, but killed others. Dr. Weinshilboum's now-historic research into the most common cancer in children opened the curtain on the essence of pharmacogenomics: one's genetic makeup can account for the difference in how individuals respond to the same dose of the same drug.

The TPMT blood test subsequently developed at Mayo Clinic has been a standard here since 1991. It saves lives by identifying children who should receive one-tenth of the normal dose

of 6-MP. In 2002, Dr. Weinshilboum testified at the first hearings conducted by the U.S. Food and Drug Administration (FDA) on the incorporation of pharmacogenomics into drug labeling. Based on his testimony, 6-MP was the first drug to have pharmacogenomic information on its label.

Dr. Weinshilboum's research helped establish Mayo Clinic as a pioneer in the field of pharmacogenomics and inspired other researchers. One of Dr. Weinshilboum's lectures motivated Dr. Goetz, who was training in medical oncology at the time, to launch the career that made him the second Mayo Clinic pharmacogenomics researcher whose discovery prompted the FDA to consider changing a drug's label.

"During the last 20 years, oncologists have simply accepted toxicity as something that goes along with chemotherapy," says Dr. Goetz. "But this respected scientist [Dr. Weinshilboum] was telling us that it's possible to predict, before you treat a patient, how they might respond to a given drug and thus avoid both severe toxicity and underdosing by determining the function of common genetic polymorphisms."



*"Dr. Ames' laboratory provided me with the training essential to understand the pharmacology and pharmacogenetics of drug metabolism."*

**— Matthew Goetz, M.D.**

Shortly after Dr. Weinshilboum's lecture, Dr. Goetz began training in the laboratory directed by Matthew Ames, Ph.D. In his laboratory, Dr. Ames has conducted pharmacology studies for cancer drugs developed by the National Cancer Institute.

"Dr. Ames' laboratory provided me with the training essential to understand the pharmacology and pharmacogenetics of drug metabolism," says Dr. Goetz. "It was at that time that we came up with the idea of studying the metabolism of tamoxifen."

This laboratory continues to play a key role in the research team's ongoing efforts to further understand the pharmacology and pharmacogenetics of tamoxifen.



“I just thought we’d be a lot smarter about gene technology in 10 years, so I archived the tissues.”

— James Ingle, M.D.

### Continuing the reputation for innovation

Many women who have surgical treatment for estrogen-receptor (ER)-positive breast cancer consider tamoxifen a miracle drug. An anti-estrogen drug, tamoxifen almost halves the recurrence of cancer and reduces the mortality rate by one-third in women with early breast cancer. One important gene responsible for the drug’s metabolism is CYP2D6. Emerging data, including some first reported by Mayo investigators led by Dr. Goetz, indicate that tamoxifen, for full effect, must be converted by CYP2D6 to endoxifen.

A common side effect of tamoxifen is hot flashes. During the past 10 years, physicians have prescribed antidepressants to relieve hot flashes. However, the same enzyme, CYP2D6, responsible for conversion of tamoxifen to endoxifen, is inhibited by many antidepressants. Dr. Goetz and his collaborators within the Pharmacogenetics Research Network (PGRN), hypothesized that women who lacked the CYP2D6 enzyme would have higher rates of breast cancer recurrence and, therefore, should not take tamoxifen because their endoxifen levels would be too low to prevent recurrence of the cancer. To prove the hypothesis, the research team needed large numbers of DNA samples with corresponding

clinical data from women treated with tamoxifen. They also needed to know whether these women were treated with drugs that inhibited CYP2D6.

### Eureka, DNA archives

Ordinarily, designing a new clinical trial would take at least a decade to produce results. But Dr. Goetz discovered that Mayo Clinic and the North Central Cancer Treatment Group (NCCTG) had exactly what he needed to expedite the research — a bank of DNA from tumor samples of 250 breast cancer survivors who had each taken tamoxifen for five years following surgery.

Kudos for accumulating the samples belongs to Mayo Clinic breast oncologist James Ingle, M.D. In the 1980s and 1990s, Dr. Ingle conducted multiple tamoxifen studies to develop best-practice guidelines.

Dr. Ingle speaks modestly about his contribution. “I just thought we’d be a lot smarter about gene technology in 10 years, so I archived the tissues,”

he says. “It was fortunate that we designed our studies with the strict eligibility criteria that made them useful for these studies.”

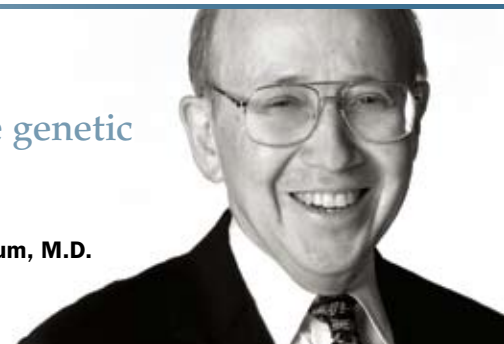
Says Dr. Goetz: “Dr. Ingle’s foresight was amazing because people simply did not save tissues in those days. He had samples from a population of patients who had taken tamoxifen alone with 15 years of clinical follow-up. Other groups may have had the same idea, but it was Mayo Clinic who had the required resources.”

More than 200,000 women in the United States develop breast cancer each year. Approximately 70 percent have ER-positive cancer. Many are prescribed tamoxifen following surgical treatment. The study was first published in *The Journal of Clinical Oncology* in December 2005 and again in *Breast Cancer Research and Treatment* in 2007. The findings, which have been verified by several other groups of researchers, showed that women treated with tamoxifen who inherited a common genetic change in the CYP2D6 gene or who were co-administered medications that inhibited the CYP2D6 enzyme had a nearly threefold higher risk of relapse when treated with tamoxifen for five years.

**In 2007, Carol Wray discovered that she was one of those women ...**

“It won’t be long before we have genetic information on every patient.”

— Richard Weinshilboum, M.D.



### A savvy patient

Purely through happenstance in the course of her research, Mrs. Wray was sent a Web article that claimed a woman's genetic code might counteract the action of tamoxifen.

"Over the years, I noticed how some drugs seemed to have no effect on me," says Mrs. Wray. "So when I read this, I thought, 'They're talking about me.'"

Mrs. Wray's observations were astute. The CYP2D6 enzyme is involved in the metabolism of up to 25 percent of all drugs. Her suspicions were confirmed after she learned that Dr. Goetz had presented his findings regarding tamoxifen and CYP2D6 to an FDA advisory committee that was considering a labeling change for tamoxifen because of his discovery. She called Dr. Goetz and arranged to send a blood sample to Mayo Clinic for the CYP2D6 test. On her own initiative, Mrs. Wray then got her prescription changed from tamoxifen to Arimidex, one of a newer class of anti-estrogens called aromatase inhibitors, which she could metabolize.

"I was so thankful to Mayo," says Mrs. Wray. "I wanted to verify that I had done the right thing, so I made an appointment to see Dr. Goetz."

Mrs. Wray traveled from Virginia to Mayo Clinic in Rochester, Minn., where Dr. Goetz confirmed that she was getting excellent care, and, through perceptiveness and tenacity, she had reduced her risk of breast cancer recurrence.

### A collaborative future

The future of pharmacogenomics lies in the nationwide collaboration of scientists. One example is the Pharmacogenetics Research Network (PGRN), which is supported by the National

Institutes of Health. PGRN investigators study the effects of genes on human response to a wide variety of drugs and add their discoveries to a growing collection of integrated data, available to all, that links genotypes with clinical response.

Dr. Weinshilbom and his colleague, Liewei Wang, M.D., Ph.D., have shown striking common variations among major ethnic groups, which have important consequences for drug metabolism. For example, the TPMT variant is very common in people of European descent but has not been found in Chinese, Korean or Japanese people. Dr. Wang has recently sequenced cell lines from three major ethnic groups with more than 1 million genetic markers across the genome. She now can scan across the entire genome to ferret out other genes that might help to predict drug response.

Surprises are inevitable. In 2005, Dr. Wang's research team showed that people who have genetically low TPMT have no enzyme because it is rapidly destroyed or collected in a structure called an aggresome. Recently, a team of Mayo Clinic researchers including Dr. Goetz, Dr. Ingle, Thomas Spelsberg, Ph.D., John Hawse, Ph.D., Xianglin Wu, M.D., Ph.D., and Malayannan Subramaniam, Ph.D., also discovered a new mechanism involving endoxifen metabolism. Their findings have been submitted for publication. Additionally, Dr. Goetz and Dr. Ames recently received funding to study the pharmacogenetics of tamoxifen in breast cancer patients who were treated either with tamoxifen or anastrozole.

"I take some pride in the fact that two of the four public hearings that the FDA has held to consider changing the label of a drug due to pharmacogenomic advances deal with discoveries



Breast cancer survivor Carol Wray (pictured above) is one of many women who lack an enzyme needed to allow the anti-cancer drug tamoxifen to work effectively.

made at Mayo," says Dr. Weinshilbom. "It won't be long before we have genetic information on every patient. However, no single institution can do this alone. It will take collaboration rather than competition to develop the technology and knowledge base that will move this field forward."

Mayo Clinic is well-positioned to continue its history of innovation through practice, education and research. The collaborators who are putting the puzzle pieces together at Mayo Clinic are pioneering pharmacogenomics researchers and bright, young scientists, who have access to extensive banks of DNA tissue and correlating clinical records — an unparalleled assemblage of medical experts and information. ■



# Spicing up your life

New therapies help aging immune systems fight cancer

**J**oseph Lustgarten, Ph.D., studies how the aging immune system responds to cancer. A native of Colombia, he earned his doctorate at Weizmann Institute of Science in Rehovot, Israel. He recently joined the research faculty at Mayo Clinic, coming from Sidney Kimmel Cancer Center in San Diego. Aside from a passion for immunology and immunosenescence (the inevitable decline of the immune system as the body ages), Dr. Lustgarten has a zest for soccer (which he plays avidly with his three sons) and a love of good food.

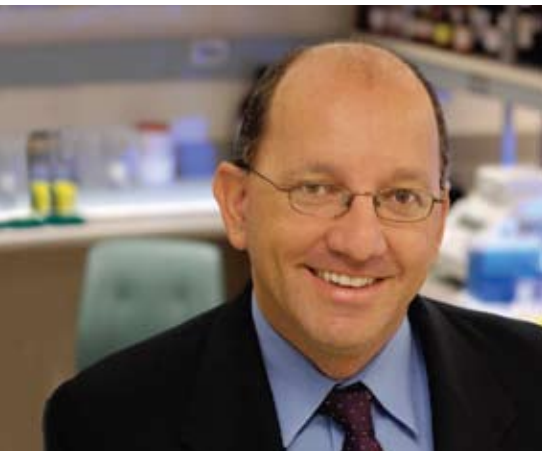
His proclivity to use culinary metaphors in discussing his research, therefore, should be no surprise. “An

older person just doesn’t have the same vigorous immune response as a youngster,” says Dr. Lustgarten. The efficiency of the immune system declines during the aging process, especially after about age 65. Lymphocytes — the umbrella term for the B and T cells that patrol the body looking for invaders, including infections and cancerous tumors — respond less vigorously to threats. “We need more spices to boost the aging immune system to help it suppress tumors,” he says.

Dr. Lustgarten and his colleagues are looking for those “spices,” those potential therapies to help an aging immune system control cancer tumor growth, combat cancer metastasis or prevent tumors from recurring. In their best-case scenario, these researchers envision the development of universal strategies to effectively stimulate anti-tumor immune

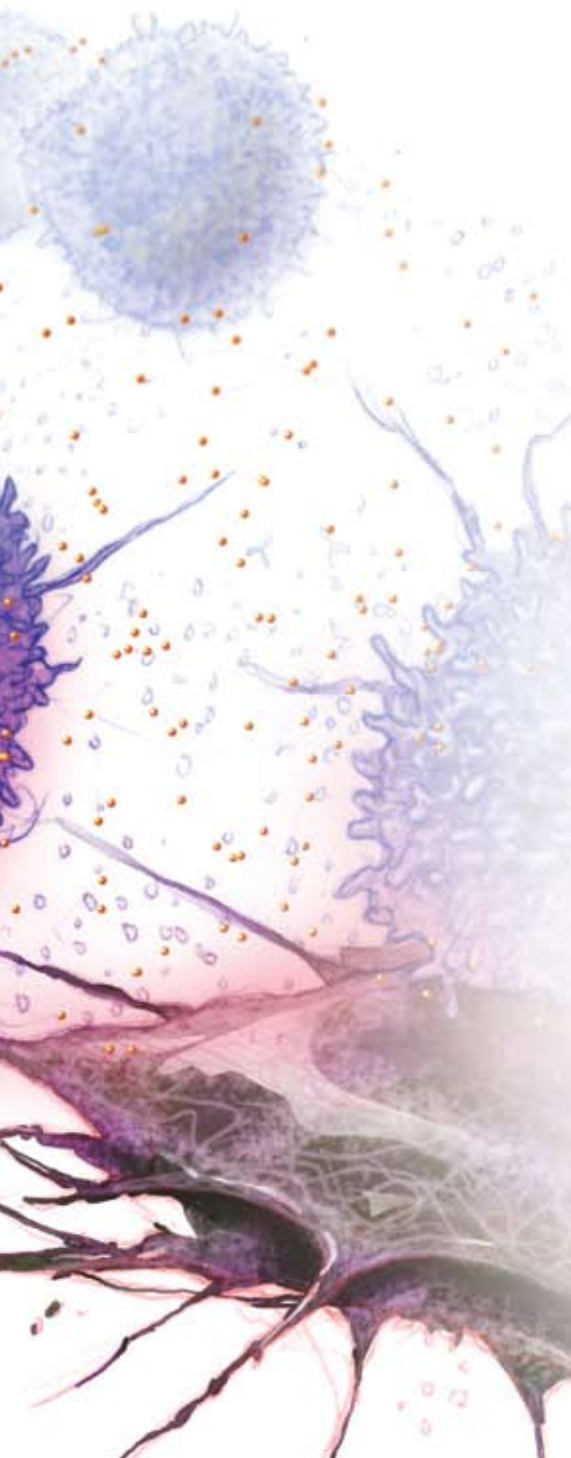
“We need more spices to boost the aging immune system to help it suppress tumors.”

— Joseph Lustgarten, Ph.D.



Joseph Lustgarten, Ph.D.

T cells (large blue spheres below) attack a cancer cell (spiny shape on lower right) as part of the immune response. Mayo research data suggests that immunizations with the adjuvant CpG-ODN (tiny yellow dots throughout) jumpstart the immune system to promote tumor immunity in both younger and older individuals.



responses in the young and old: a one-therapy-treats-all approach that could be administered more efficiently, and also be more cost-effective.

### Changing the focus

Dr. Lustgarten's research is bucking a trend. Most work in cancer immunology uses models involving younger populations with more robust immune systems. Given that some prevalent cancers, including breast, prostate and colorectal, mainly affect older populations, the focus on young people might seem almost incongruous and a bit illogical, especially to someone born into the baby boom generation.

"Everyone is aware of this predicament, but very few laboratories or research institutions want to deal with it," says Dr. Lustgarten. "That's because it is very expensive to do the preclinical research necessary to get a potential therapy into human trials, and it is challenging to do clinical trials with the elderly." Dr. Lustgarten's work seems even more urgent now that people are living longer. In the United States, the number of people 65 years or older is expected to increase from 35 million in 2000 to 71 million in 2030.

Dr. Lustgarten's work focuses on two major questions: "First, what is the basic biological process the immune system goes through as it declines with age?" he explains. "And then once that is known, how can we develop strategies to increase immune function in the elderly as a means of treating cancer?"

Already he has found that T regulatory cells in the aging immune system accumulate in higher-than-normal totals. T regulatory cells are considered peacekeepers. They regulate the immune system's other lymphocytes, preventing a scenario

where those lymphocytes might run amok and attack all the healthy, normal cells in the body. The immune system's ability to distinguish "self" and "non-self" (friend from foe) is exquisite, yet complicated. T regulatory cells also have an important role in shutting down immune responses after the invading organism, whether a virus or tumor, has been quelled. Dr. Lustgarten and colleagues have demonstrated a direct correlation between the expansion of T regulatory cells and immune deficiency in older people. That is, the elderly have too many T regulatory cells. Dr. Lustgarten thinks that reducing the number of T regulatory cells may be a critical component to restoring immune responses in older people.

In research that builds on these findings, Dr. Lustgarten is manipulating the immune system by targeting antigen-presenting cells (APCs). An analogy is volleyball players who set up the ball for a teammate to spike: APCs process invader substances (antigens), increasing their vulnerability to recognition and destruction by helper T cells. Research indicates that by targeting APCs with different types of adjuvants (immunological agents that increase antigenic response), the immune system can mount anti-tumor responses. Dr. Lustgarten and colleagues recently demonstrated that not all adjuvants stimulate APCs. However, they showed that immunizations with the adjuvant CpG-ODN could manipulate young and aging immune systems to induce tumor immunity. These findings hold promise for developing universal anti-tumor vaccinations — for the young and old. The adjuvant CpG-ODN may just be one of the right "spices." ■

# Helping those in need

Spreading knowledge and fostering hope

When Janelle Hail, CEO of the National Breast Cancer Foundation, Inc., faced breast cancer 28 years ago, the diagnosis was a shock. She was living a healthy lifestyle, she didn't smoke or drink and she exercised. Yet, along with her diagnosis she learned that breast cancer doesn't discriminate.

She found no support network outside her family and friends. Breast cancer was not talked about. It was considered to be an old woman's disease. When she went in search of information about what she faced, there was nothing.

At age 34, Ms. Hail faced a disease that today, affects one in eight women. Determined to help other women face down breast cancer, she created the National Breast Cancer Foundation. Ms. Hail's vision was that the foundation would be there for women, to educate them about breast cancer and provide free mammograms for underserved women.

"We encourage women to not operate out of fear of what they might find, but to face head-on what they are dealing with. We encourage women to use preventive care in every way they can," says Ms. Hail.



Janelle Hail

The National Breast Cancer Foundation supports women's cancer outreach programs at Mayo Clinic. Drs. Pruthi, Gorman and DePeri lead those efforts at Mayo Clinic's three locations. ▼



## Sandhya Pruthi, M.D. — dispelling fear

By bringing awareness and assistance to underserved and uninsured women in the Rochester, Minn. area, Dr. Sandhya Pruthi, director of Mayo's Breast Diagnostic Clinic in Rochester, is dispelling fear through knowledge. Her program provides hands-on learning tools, screenings and written materials at Hawthorne Education Center, part of the city's public school system. Interpreters are provided in several native languages.

The goals of the program are to develop health literacy of mammogram screening, provide clinical breast exams and help coordinate and schedule mammograms. Through her direct participation in the community, hundreds of women have utilized the program that began in 2007. "The women we are helping have little or no knowledge that screening and early detection can alleviate much of the fear and mystery associated with cancer," says Dr. Pruthi.



Ms. Hail credits a mammogram for saving her life. “Early detection saved my life. That’s why I’m here now,” she says.

Ms. Hail is pouring her passion for fighting breast cancer into concerted efforts to beat the disease. As CEO of the National Breast Cancer Foundation, one of America’s most highly recognized and respected charities, Ms. Hail is well-positioned to make a difference. She is particularly impassioned in her

work with those who care about women. Mayo’s philosophy of caring fits perfectly with our goals,” she says.

The relationship between Mayo Clinic and the National Breast Cancer Foundation began in 2005 with a gift to support mammogram screenings and education efforts in Minnesota and Florida. Successful implementation of the initial program led to subsequent gifts and growth of the program to include the Arizona campus.

“Mayo was a natural fit. They provide the services that we desire, but more importantly, we want to work with those who care about women. Mayo’s philosophy of caring fits perfectly with our goals.”

— **Janelle Hail, CEO of the National Breast Cancer Foundation**

pursuit of reaching out to women who have no assistance. The foundation chose to work with Mayo Clinic to accomplish this goal.

“Mayo was a natural fit. They provide the services that we desire, but more importantly, we want to

“When we began our philanthropic relationship with Mayo, they were so willing to work with us. The doctors and nurses are always helpful,” she says.

Mayo Clinic’s three locations, Arizona, Florida and Minnesota, appeal to the National Breast Cancer

Foundation. “The multiple sites allow us to move our program into three states and reach three populations. It’s really a nice fit for both sides,” says Ms. Hail.

The impact has been dramatic. The National Breast Cancer Foundation has provided over \$1 million to the Women’s Cancer Program at Mayo Clinic, under Mayo’s leadership of Sandhya Pruthi, M.D., in Rochester, Elizabeth R. DePeri, M.D., in Florida and R. Scott Gorman, M.D., in Arizona.

Ms. Hail also emphasizes that Mayo Clinic’s culture of education is a major factor in the successful relationship. “If you don’t educate women about breast cancer, they won’t get their mammograms,” she says.

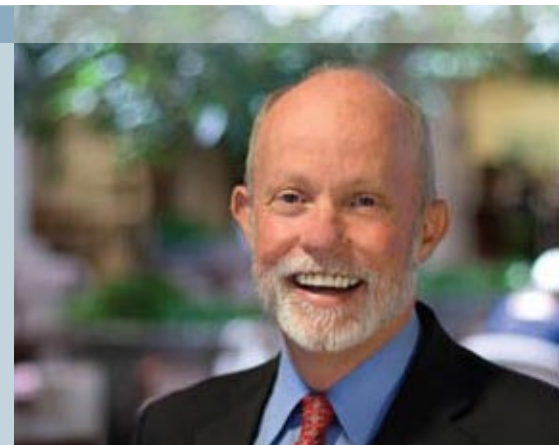
She inspires breast cancer survivors with her weekly blog, which she signs with the moniker “Live Life” at [www.nationalbreastcancer.org](http://www.nationalbreastcancer.org). Through its extensive online community, the National Breast Cancer Foundation provides caring support and encouragement to women and their families as they face breast cancer.

Ms. Hail’s vision for the National Breast Cancer Foundation is to “cover

### **R. Scott Gorman, M.D. — making connections**

By working with a local community health center in Phoenix, Ariz., Mayo Clinic is providing diagnostic mammography and enhanced screening mammography to underserved women in metropolitan Phoenix. By providing on-site mammography services at Mountain Park Community Health Center, Mayo Clinic is improving both the continuity of care and the timeliness of care for Mountain Park patients.

“Mountain Park’s lack of diagnostic mammography is their number one women’s health issue,” says R. Scott Gorman, M.D., Health Disparities Physician Lead, Mayo Clinic in Arizona. “Through the outstanding teamwork of Mayo Clinic Cancer Center and its radiology team, we have been able to better serve Mountain Park’s needs by providing both an updated mammography unit and physician staff to support it.” The program will eventually expand to provide a base for research aimed at better understanding of ethnic variations in mammography results.



the entire United States.” The foundation isn’t far off. It currently operates in 41 states and partners with more than 60 hospitals. “In another year, year and a half, we will have that accomplished. And then we will expand internationally, which we have already started.”

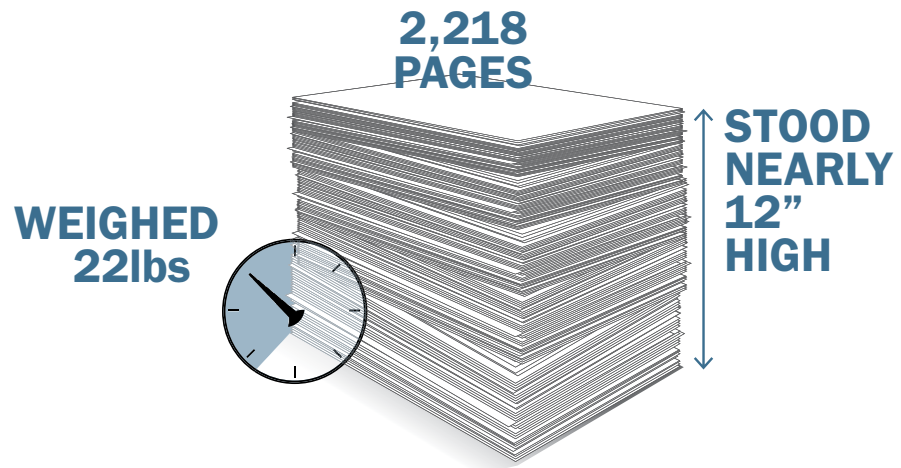
The foundation’s activity with Mayo Clinic will also continue to grow. “The reason that we support Mayo is because of their excellent reputation. The people at Mayo are a joy to work with,” says Ms. Hail.

Today the National Breast Cancer Foundation extends women’s lives through education about breast cancer and free mammograms for those in need as they offer Help for Today ... Hope for Tomorrow®. ■

## NCI grant renewal a labor of love

When finished, the document weighed in at more than 22 pounds and stood nearly a foot high. Completion of the 2008 Cancer Center Support Grant (CCSG) renewal was a heavy task and a tall order for the more than 120 Mayo employees who contributed to its creation. But it was a labor of love for many who know that with grant approval, their part in the grant process will assure the cancer center’s ongoing designation by the National Cancer Institute (NCI), at least for the next five years when they have to do it all over again.

The 2,218-page grant requests nearly \$50 million in funding from the NCI. If approved, the bulk of that funding will go to support scientific leadership and shared resource services that enable cancer center members to conduct superior, cancer community-leading research. There are currently 16 shared resource facilities that fall within the cancer center. The number and diversity of these shared facilities speaks to advanced capabilities in cancer research and the marked growth and expansion of cancer center programs. ■



### Elizabeth DePeri, M.D. — closing the care gap

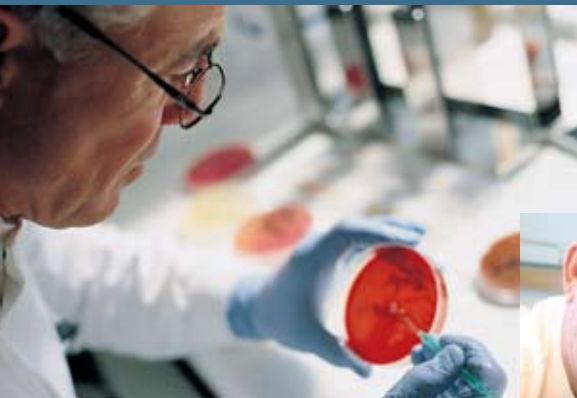
In northeast Florida, free diagnostic services are available to women who have been screened for breast cancer by their county health departments. Of 150 multicultural women utilizing services in the last year, 18 were diagnosed with breast cancer and referred to the appropriate resources for care. All women were financially disadvantaged, medically uninsured or underinsured, and many belong to minority ethnic and racial groups.

“Through this community partnership, women were provided the necessary care that they might otherwise avoid seeking due to financial concerns,” says Elizabeth DePeri, M.D., radiologist and division head for the Breast Imaging Section, Mayo Clinic Florida. Dr. DePeri’s program provides access to patient navigator services, timely reviews of screening films and diagnostic procedures and a rapid diagnosis. The program has elevated the level of preventive women’s health care in the Jacksonville area.

# The CAMPAIGN *for* MAYO CLINIC

The 21st century brings overwhelming challenges and miraculous opportunities. Your support can help us achieve what we all need — breakthrough cures and pioneering treatments to relieve suffering and improve lives. Together, we can.

It doesn't take much to feel like a million. For more information on investing in the medicine of tomorrow, visit: [www.mayoclinic.org/campaign](http://www.mayoclinic.org/campaign)



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It was a routine job for a longtime customer. Jerry Spoerl, a refrigeration contractor, was repairing a refrigerator at a center for homeless and low-income families operated by the United Methodist Outreach Ministries. He was working in the breaker box when suddenly he was struck by an electric arc “like a bolt of lightning.” His shirt caught on fire and the flames spread across his face, arms and hands. Mr. Spoerl was rushed to the Arizona Burn Center, fortunately just a few blocks from the accident. He suffered second- and third-degree flash burns over 28 percent of his body. “When they let me in to see him, he looked like a mummy,” says his wife, Marilyn. “Every inch of his torso was wrapped. He had little slits for his eyes, nose and mouth. But I was so thankful he was alive.”

The accident occurred on May 30, 2006. The medical team at the burn center saved Mr. Spoerl’s life, but his hands were severely injured, and it was unclear if he’d ever be able to return to work.

“I grew up on a farm,” he says. “I’ve always used my hands, for everything, all the time. In my refrigeration business it’s vital to me to have the mobility of handling tools and working with small things. Without my hands, I wouldn’t be able to run my business. I wouldn’t be able to participate. I would have to sit back and find another way to approach life.”

As he talks, Mr. Spoerl is twirling and bending his fingers. He is regaining the use of his hands. Most important, he is back at work. His unfolding story — he’s still in hand therapy and will undergo more reconstructive surgery — goes to the heart of Mayo Clinic’s mission. It is about people and institutions working

Jerry Spoerl’s recovery from severe burns illustrates Mayo teamwork at its best. Jerry and his wife Marilyn are pictured at left.

# led with care

How classic Mayo teamwork saved Jerry Spoerl’s hands



hand-in-hand to care for patients. It's about educating and training the next generation of physicians, nurses and therapists. It's about medical research that will enhance patient care in the years to come. And it's about the generosity of Mayo's benefactors who understand and support all of the above.

### **The power of collaboration**

Surgeons at the burn center grafted skin from Mr. Spoerl's leg over the deep burns on his hands to replace the skin that was lost or damaged and to protect against infection. The grafting saved his hands, but they were badly distorted, especially his right hand.

Mayo Clinic has a long association with Maricopa County Medical Center, which is home to the Arizona Burn Center. Since 1991, Mayo Clinic's plastic and reconstructive surgical residents based in Rochester, Minn., have been going to Maricopa to train. The residents train there because in Phoenix, a city of 3 million people, they gain experience with an array of patients with congenital defects or traumatic injuries requiring complex reconstructive surgeries. In 2003, the collaboration grew stronger when Mayo Clinic

"In the Mayo environment there's such great opportunity for collaboration and communication," says Cecelia Skotak, Mr. Spoerl's certified hand therapist. "He and I and Dr. Smith sit down together. We talk about what Dr. Smith and the surgical team can best handle and what Mr. Spoerl and I can best handle, therapeutically. In other words, we talk about how we can achieve the best functional outcome for him based on the needs of his daily life. It's a very interactive process."

### **"Thank you for giving my husband back his hands"**

The thumb on Mr. Spoerl's right hand would not spread open. The index finger was hyperextended, pointing stubbornly upward and unable to align with his other three fingers. The ring and little fingers were curved and would not straighten. "I couldn't grab a glass of water. I basically couldn't open my hand enough to clamp onto anything," Mr. Spoerl says.

On April 25, 2007, Mr. Spoerl had surgery on his right hand. The surgery, combined with an ongoing rigorous regimen of therapy that includes wearing elaborate splints

**"I know how important research and education are to patients like me. I know all of this goes into the care I'm receiving. Without this level of care, I don't know what I would have done." — Jerry Spoerl**

reconstructive hand surgeon Anthony Smith, M.D., became involved in monthly clinics with patients at Maricopa's Arizona Burn Center.

"After evaluating Mr. Spoerl's injuries a number of times in the burn clinic, it became clear to me that he would require complex reconstructive surgery, including microsurgery, as well as ongoing hand therapy to regain the use of his hands," says Dr. Smith. "It's the integration of our hand surgery service with ongoing occupational hand therapy that allows us to take care of the most severe injuries. For this reason, after discussion with Mr. Spoerl and his wife, and with Drs. Daniel Caruso and Kevin Foster, the co-directors of the Arizona Burn Center, Mr. Spoerl's care was transferred to Mayo Clinic."

each night, has helped Mr. Spoerl regain almost full motion of his right hand. "I'm very pleased. I actually feel like I can just about do most anything now," he says. In the months to come, follow-up surgeries will be performed to release scar tissue in the webbing between his right thumb and index finger and to address similar issues with his left hand.

The partnership between the patient and his medical team is paying off. "Mr. Spoerl has recently been able to take on a large contracting project, which is very exciting," says Ms. Skotak. "His hands reflect that he's a hands-on type owner. He comes in with dirt on his hands. He is building up callus. That's something I love to see because it tells me he's using his hands."

A key player on Mr. Spoerl's medical team is his wife. She is his at-home hand therapist. "Because of the scar tissue, it's a constant battle to stretch the skin. It's like slipping into an undersized glove and not being able to close your hand," explains Mr. Spoerl. Every night since his injury two years ago, Mrs. Spoerl massages his hands with lotion to help soften the scar tissue. Then she helps him apply his splints, which are custom-made of plastic, suede, tension devices and Velcro. "We no longer sleep with fluffy blankets," she says. "The Velcro sticks to them."

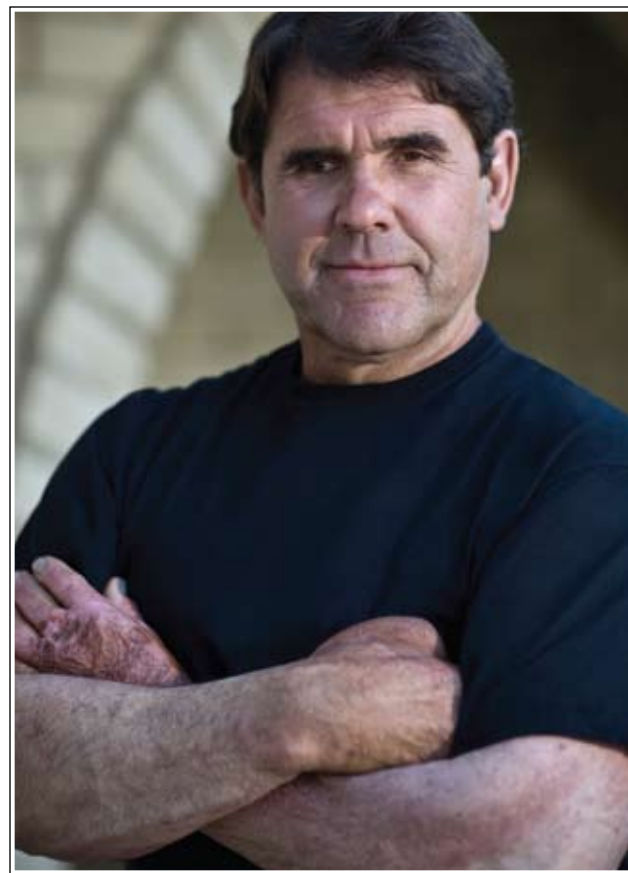
For her part, Mrs. Spoerl is simply grateful her husband is alive and back doing what he loves. "I don't know what Jerry would have done without Mayo Clinic. He's a workaholic. He has to work. He has to do something with his hands," she says. "Thank you for giving my husband back his hands."

#### **"Heal the sick, advance the science"**

Mr. Spoerl's story is part of a continuum of patient care that reaches back more than a century and is propelled forward by Mayo Clinic's ongoing commitment to medical education and research. His near-death experience and courageous struggle to regain a normal life make Mr. Spoerl's story inherently compelling. The background details of his care — the development of plastic and reconstructive surgery at Mayo Clinic, the training of surgeons in microsurgical techniques, the meticulous preclinical investigations in neurophysiology that hold promise for advanced prosthetic systems — are more technical and less emotional. But it is precisely Mayo Clinic's focus on the details, year after year, day in and day out, that lead to outcomes like Mr. Spoerl's.

One of the founders of Mayo Clinic, Charles H. Mayo, M.D., was a pioneer in surgical skin grafts in the 1890s. In 1911, Mayo Clinic formed the division of plastic surgery, one of the first medical institutions to recognize this type of surgery as a specialty. In the late 1940s, in an effort to improve the care of World War II soldiers with devastating head and neck injuries, the War Department recruited Mayo surgeon John Erich, M.D., a leading authority on traumatic injuries to facial bones, to train fellows in the emerging specialty of plastic surgery. Dr. Erich also participated in the founding of the American Board of Plastic Surgery as a way to develop a certification process for plastic and reconstructive surgeons.

In education, Mayo Clinic has one of the largest and longest-running training programs for plastic and reconstructive surgeons in the nation. In research, Mayo Clinic



is engaged on the forefront of plastic and reconstructive procedures in the areas of tissue engineering, allographic facial and limb transplantation and advanced prosthetics systems. And because of Mayo Clinic's long commitment to rare as well as common diseases and disorders, it is a leader in patient care and research related to HHS (hypothener hammer syndrome), an uncommon but severely debilitating and painful condition caused by reduced blood flow to the hand.

In 1926, Dr. Charles Mayo wrote an essay on medical education that captures the integration of clinical practice, education and research underlying the care of each and every patient at Mayo Clinic. "There are two objects of medical education: to heal the sick and advance the science," he wrote.

Mr. Spoerl has spent enough time at Mayo Clinic to see Dr. Mayo's words in action. He's seen how medical students and residents learn and prepare for a lifelong profession of caring for patients and how his surgeon is continuously engaged in teaching and research. "I know how important research and education are to patients like me," he says. "I know all of this goes into the care I'm receiving. Without this level of care, I don't know what I would have done."

**“I don’t know what Jerry would have done without Mayo Clinic. Thank you for giving my husband back his hands.” — Marilyn Spoerl**



#### **A microcosm in the Mayo Clinic universe**

Dr. Smith sees plastic and reconstructive surgery as a microcosm for Mayo Clinic and he talks about the integration of patient care, education and research by putting his own specialty into perspective. “My practice — hand surgery — is very narrow when you look at the clinical spectrum of reconstructive surgery across Mayo Clinic’s three sites,” he says. “As surgeons we are fortunate because we see the big picture every day. My colleagues at Mayo Clinic in Arizona, Drs. Bill Casey and Alanna Rebecca, do reconstructive surgery literally from the top of the head to the bottom of the foot, and we work hand-in-hand with colleagues across multiple specialties ranging from surgical oncology to cardiac surgery to transplant surgery.”

In research, Dr. Smith has been part of Mayo Clinic’s involvement as the clinical partner on a research project at Arizona State University (ASU). The project, led by Ranu Jung, Ph.D., co-director of the Center for Adaptive Neural Systems at ASU, and funded by the National Institute of Biomedical Imaging and Bioengineering at the National Institutes of Health, is focused on advanced prosthetic systems. The goal: to develop prostheses for people who

have lost a hand because of disease or traumatic injury. The device will have a neural interface that allows a person’s own nervous system to directly engage the prosthesis to make it function much like a normal hand.

On the education front, Dr. Smith has championed a Phoenix program in plastic and reconstructive surgery headquartered at Mayo Clinic, which involves Mayo Clinic residents rotating at other Phoenix hospitals. It will be part of a very robust educational environment at Mayo Clinic, which offers 249 residencies and fellowships in 27 areas, from anesthesia, family medicine and internal medicine to genetics, neurology and surgery.

#### **Imagine what we can accomplish together**

It is ultimately Mayo Clinic’s benefactors who make a difference in the lives of patients like Mr. Spoerl. Our benefactors are transforming how we educate and train the next generation of physicians, nurses and allied health professionals and they are driving the medical discoveries that save and change lives.

The family members who recently endowed Mayo Clinic’s newest residency program in plastic and reconstructive surgery, through the Powers Family Foundation, have never met Mr. and Mrs. Spoerl, but they know deeply, just as Mr. Spoerl does, how important it is to your livelihood and sense of self-worth to work with your hands. Their passion is multiplied many times over by the thousands of benefactors who give to Mayo Clinic every year.

“Our benefactors are people who want make a difference, whether their gift supports a residency training program, efforts to advance individualized medicine or research in cancer or Alzheimer’s disease or cardiovascular disease,” says Dr. Smith. “And if they’re concerned about their gifts making a difference, they don’t have to worry. I’m privileged every day to see how their gifts are touching the lives of our patients now and forever.” ■



# Reconstruction **zone**

How regenerative medicine restores injured bones and nerves

Growing demand from the U.S. military for new therapies to treat battlefield injuries fuels the innovation behind regenerative medicine — the concept of growing new tissue and bone. Although this new technology is being developed for military application, its findings are helping the civilian population, as trauma patients and those who have injuries resulting from disease benefit from these developments. **Mayo Clinic is on the front line of this effort.**

Michael Yaszemski, M.D., Ph.D., oversees Mayo Clinic's regenerative medicine collaboration with the U.S. military. With 30 years' combined military service in both active and reserve roles, including a stint in the Iraq War, his participation is a natural fit. To top it off, he was recently promoted to brigadier general in the Air Force Reserve, a title bestowed to only four Mayo physicians before him, including Drs. Will and Charlie Mayo.

According to Dr. Yaszemski, even though the human body is incredibly resilient, it can only regenerate to a certain point. Massive structural bone and nerve damage can leave gaps that cannot be overcome by the natural healing process. Fortunately, innovations in regenerative medicine, led by Dr. Yaszemski and his team, are guiding new treatments to heal injuries once believed insurmountable.

"War is such a sad thing, but one of the good things that can come of it is innovations that benefit the civilian population," he says.

## **Back-and-forth benefits**

To meet the clinical needs of patients facing the challenges that regenerative medicine addresses, Mayo Clinic researchers are applying their knowledge of and passion for discovery to clinical solutions in this novel area of medicine. In true Mayo fashion, problems identified in the clinic are taken to the laboratory for study and translated back into clinical practice.

“The clinical needs of patients are driving our laboratory discoveries,” says Dr. Yaszemski. “We continuously re-evaluate our treatment methods, keeping the patient’s needs at the forefront of our process.”

### Building bridges and scaffolds

Regenerative medicine at Mayo combines the body’s natural regenerative qualities with synthetic biomaterials. The combination facilitates the repair or restoration of damaged tissue or function by using synthetic compounds to bridge large defects or gaps to allow for natural cell formation. The program focuses on three areas: bone, peripheral nerve, and central nervous system and spine.

The science of regenerative medicine centers on building “scaffolds.” These scaffolds, comprised of synthetic biomaterials, serve as support bridges or anchors for new cells. The structures support the body in the healing process much like a painter uses scaffolding for support while he works.

In both instances, scaffolds connect two points.

Dr. Yaszemski says the scaffolding method “applies equally to nerve cells in creating new nerves as it does to bone cells in creating new bone.”

### Converging career paths

Dr. Yaszemski was a polymer chemist before he became a surgeon. And although he cannot pinpoint what drew him to medicine, his career change did not end his work with polymers. Essentially, polymers are supporting structures, much like scaffolds. They are large molecule compounds that are composed of repeating structural units.

The use of Mayo’s library of novel synthetic polymers, all developed at Mayo, is central to Dr. Yaszemski’s work and is critical to the success of the regenerative therapy program. Mayo holds 10 patents on various polymers; several have been licensed for commercial application. Each material was developed for specific clinical needs.

“When we develop polymers, we control the properties that go into making them,” says Dr. Yaszemski. “Therefore, we can design and use them as the situation dictates, using them in the manner that will best help the patient.”

### Polymer properties

Prior to polymers, physicians relied on metal materials and ceramics to repair bone injuries and nerve grafts. Although these repairs were effective in many applications, rejection, infection and incompatibility were common problems.

The use of polymers alleviates most potential problems. Polymers are biocompatible; they can reside in the body without triggering autoimmune response. They are also biodegradable, which eliminates the need for implant removal if replacement is necessary. The unique qualities of each polymer allow for custom tailoring. For example, the polymer-based scaffolds can be used for controlled delivery of antibiotics, cells and chemotherapeutic agents.

This ability for customization allows for a wide array of applications. And polymeric scaffolds can be molded for physical implantation in a patient, through a surgical procedure. In such an instance, 3-D images from CT scans provide patterns for the scaffold.

Advances in materials allow scaffolds to be injected as liquid, a less-invasive implantation. Such an application is important in dealing with metastatic bone cancer where a patient may experience a bone defect but not have an open wound. Rather than subjecting the patient to surgery, a liquid scaffold may be injected into the defect. Once in place, a bonding agent may be applied to the scaffold converting the liquid to solid.

Polymer technology also may have useful preventive medicine applications. Patients who have degenerative bone diseases, such as osteoporosis, may receive proactive treatment to prevent fracture. In such a procedure, polymeric material would be injected into degenerated bone in order to strengthen the bone.

Clinical trials for polymer scaffold therapies will begin within the next year, according to Dr. Yaszemski. ■

### The Campaign for Mayo Clinic

As a result of the broad impact of musculoskeletal disease and musculoskeletal trauma, Mayo Clinic is making research in this area a campaign priority. The Campaign for Mayo Clinic seeks to raise \$1.25 billion for research, practice and education in many areas including musculoskeletal disease and trauma.

In the United States alone, musculoskeletal conditions cost society an estimated \$254 billion every year. One out of every seven Americans has a musculoskeletal impairment. The number of people affected by arthritis is expected to reach 60 million within 10 years. Each year, musculoskeletal conditions result in more than 100 million office visits and 25 million emergency visits. Together, we can change these statistics.

Benefactor opportunities exist to support this important research. For more information about The Campaign for Mayo Clinic, visit: [www.mayoclinic.org/campaign](http://www.mayoclinic.org/campaign)

## Collaborating for soldiers and civilians

Nowhere is the application for regenerative medicine greater than for injured veterans. Veterans of the wars in Afghanistan and Iraq have sustained debilitating injuries from roadside bombs and other explosive devices. Some soldiers are victims of devastating bone and nerve injuries. The need for solutions is driving collaboration among the U.S. military, Mayo Clinic and other leading medical centers.

The Armed Forces Institute for Regenerative Medicine (AFIRM) leads the medical center consortium. Funded by the Army Medical Research and Materiel Command, AFIRM works in conjunction with the Office of Naval Research and the National Institutes of Health.

Mayo Clinic is lending its expertise in bone and peripheral nerve regeneration to this effort. Other medical centers focus on head and face trauma, burns, transplant and other conditions. Most collaborators in AFIRM have been professional colleagues for years with longstanding working relationships.

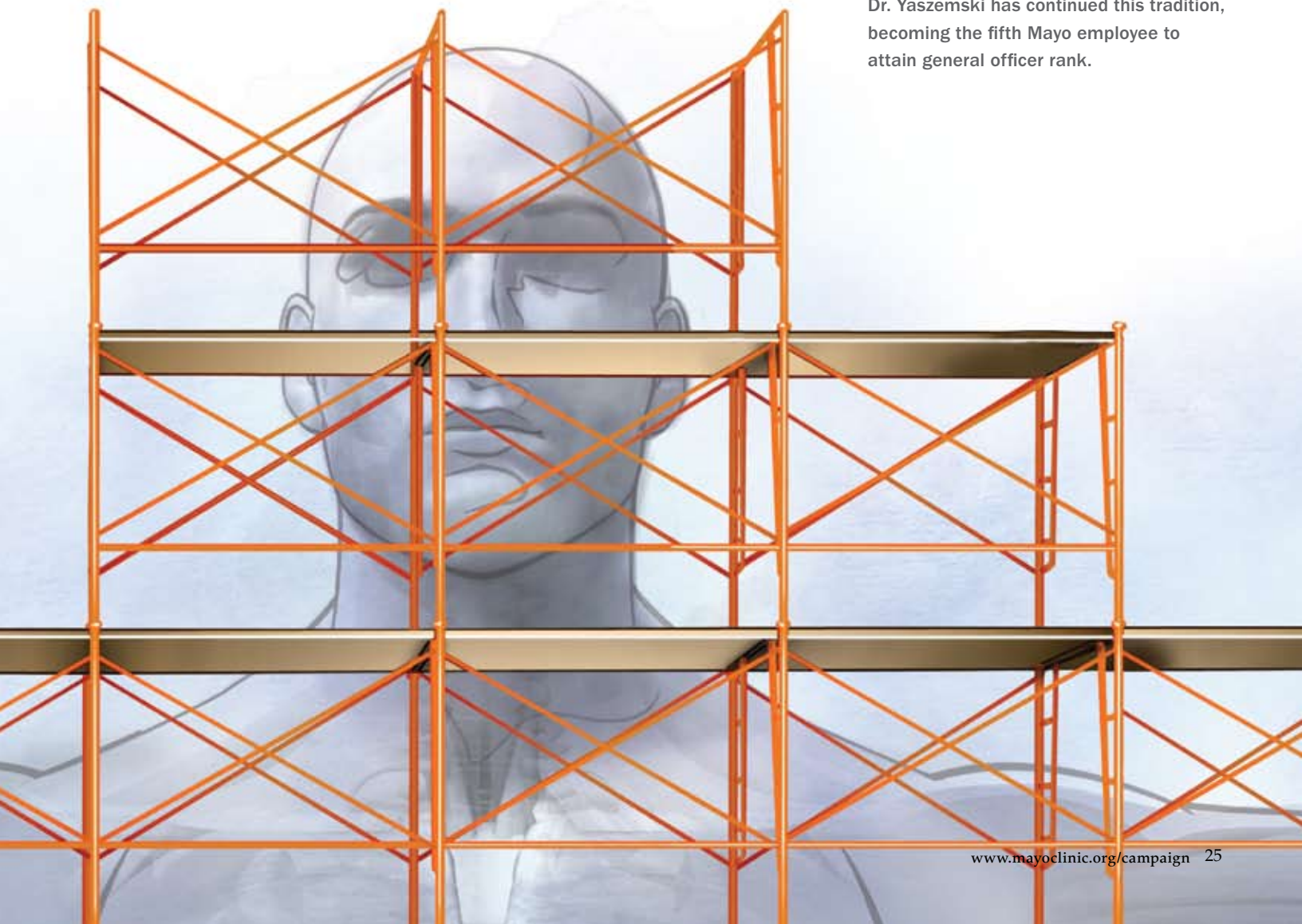
Michael Yaszemski, M.D., Ph.D., serves on the project's executive committee and also is the nerve program leader and bone program co-director.

"Communication is the key to the success of this program," says Dr. Yaszemski. "My military experience provides access to useful information in the clinic; conversely, my clinical role provides access to information that is important in military communications. The combination of both helps facilitate good communication." ■



### MAYO CLINIC MILITARY SERVICE

Mayo Clinic physicians have a long and distinguished history of military service and leadership. In 1863, William Worrall Mayo, M.D., was appointed as examining surgeon for the draft board. Drs. Will and Charlie Mayo followed in their father's footsteps during World War I. Both achieved the rank of brigadier general. Dr. Yaszemski has continued this tradition, becoming the fifth Mayo employee to attain general officer rank.





leadership

empathy

connect

principle

transfer



design

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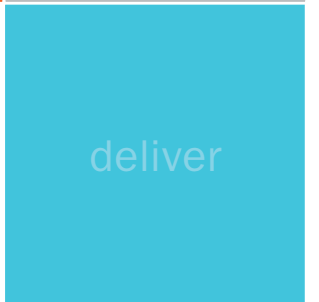
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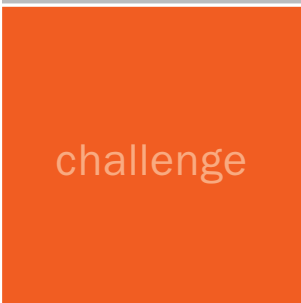
challenge

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enable

# MAYO CLINIC CENTER FOR INNOVATION

Despite the immense change occurring in health care today, academic health centers are lagging behind industry in their ability to orchestrate major innovation. While unprecedented change is taking place in medications, surgical procedures, and medical devices, true innovation in patient care is lagging. Innovation in health care delivery poses a dilemma. How does a health care institution continuously refine and improve its day-to-day practice, and simultaneously pioneer radically new approaches to care delivery?

INSPIRED BY THE PAST. INNOVATING FOR THE FUTURE.

### Exploring the future while improving the present

Nearly a decade ago, Mayo Clinic stepped into the innovation arena to resolve this dilemma. "It started as an initiative in the Department of Medicine with what we called, the Program in Innovative Health Care Delivery," says Nicholas LaRusso, M.D., then chair of Mayo's Department of Medicine, a department comprised of 600 physicians and scientists. "Our initial work led to the development of the SPARC program. SPARC (see-plan-act-refine-communicate), is an acronym for one methodology Mayo uses to bring new innovations to practice. Over the years, Mayo has gained extensive experience with innovation, developing new design tools and strategies to deepen understanding of patient needs and to create new services to improve patient care. Innovation as a department-based initiative has now matured and evolved into an organization-wide effort. This year, the Mayo Clinic Rochester Executive Board advanced its commitment to innovation by creating the Mayo Clinic Center for Innovation, naming Dr. LaRusso the center's director and Barbara

that take time and effort. Mayo Clinic's culture of teamwork is uniquely suited for innovation, and sets Mayo apart from other health care institutions. "The Center for Innovation will build on the strengths of Mayo's patient-centered care model and unwavering dedication to teamwork," says Dr. LaRusso.

### Making connections

At the core of innovation work is the need for health care providers to connect with the experiences and emotions of the people they serve. This includes exchanging expertise inside and outside of Mayo Clinic. Within Mayo, the role of the center is to cultivate relationships among departmental and institutional leaders to promote innovation across patient care, education and research. Outside the organization, Mayo connects with leading organizations in health care and other industries to identify key innovation opportunities and to work collaboratively to develop, test and implement solutions. As these diverse experts work to solve specific health care problems, new opportunities for innovation evolve.



**"At Mayo Clinic, innovation is about discovering and**

Spurrier the senior administrator. SPARC has been integrated into the center as its research and design unit.

### Mayo's journey to define innovation

The hallmarks of Mayo Clinic's innovation journey are teamwork, collaboration and participative management. Above all, Mayo is driven by a deep commitment to put the needs of the patient first. To design clinical experiences that will truly meet people's needs, organizations must understand those needs. Innovation has numerous connotations. According to Dr. LaRusso, "At Mayo, health care innovation is about discovering and implementing new ways to deliver better health care. The center's core mission is to transform the way health care is experienced and delivered."

The concept of innovation is not about fads, shortcuts or immediate gains. Innovation is a discipline that follows a methodology and incorporates design-specific processes

### A safe space to grow new ideas

The Center for Innovation uses a design-centered approach where patient needs drive the process in a culture of experimentation, risk-taking and learning.

To enhance competency and to enable a culture of innovation to flourish across Mayo Clinic, the center is providing tools, resources, educational programs and expertise. "It's a responsibility we take very seriously at the Center for Innovation," says Ms. Spurrier. "Our intention is that within five years, we will all understand what innovation is and the role it plays in our daily work."

A temporary space for the Center for Innovation has been designed on the 17th floor of the Gonda Building. Much like a giant incubator, the center offers a unique space for nurturing new ideas, enabling them to grow, mature and evolve until they are ready for the clinical setting. The Center for Innovation creates safe space for new ideas to blossom

without interfering in the day-to-day operations of a clinical area. The center is an efficient solution to the dilemma that has hampered innovation in health care environments — enabling Mayo to improve daily clinical practice, and at the same time, create transformations in health care.

**Organizing for innovation**

Successful innovation is all about diverse perspectives. Mayo’s ability to work with other world-class organizations is key to the center’s success. Already the Center for Innovation has established relationships with Blue Cross Blue Shield of Minnesota, IBM, Purdue University, Steelcase, IDEO, GE Healthcare, Ascension Health, Cisco, and Microsoft.

“The current health care delivery system is complex, disconnected and focused on disease care rather than health care,” says Ms. Spurrier. “The Center for Innovation is in collaboration with innovation experts to design transformative solutions to solve vexing problems. Their advice is to define a few bold concepts, understand consumer needs, prototype

concept — integrated medical practice. The same concepts of teamwork and collaboration that established Mayo as a world-renowned name in medicine are the concepts of innovation that are enabling Mayo to renew itself for the future. By building a team with innovation expertise that is multidisciplinary, collaborative, open-minded and passionate, Mayo is organizing for an innovative future. It’s not an easy process. It requires confidence, bold moves, reframing old ideas and generating new ideas, to spur a culture of creativity.

“The new Center for Innovation has been launched to continually generate new ideas. As long as we maintain our values and principles, everything else can change,” says Glenn Forbes, M.D., chief executive officer, Mayo Clinic Rochester.

Mayo Clinic Center for Innovation promotes connections between what we will be doing tomorrow and current day-to-day clinical practice across Mayo departments, divisions and committees. As an enterprise, it goes beyond Rochester including Arizona, Florida and Mayo Health

implementing new ways to deliver better health care.”

— Nicholas LaRusso, M.D.



like crazy and gain experience. We approach our work with a think big, start small and act fast attitude,” she says. “To begin, the Center for Innovation has developed key agendas, focused around disease prediction, prevention, earlier intervention, wellness, and tools and technologies to help people maintain a Mayo Clinic connection from afar. We want to make it easy for people to experience all that Mayo Clinic can be for them — anywhere and anytime. There are many ways we can extend the Mayo Clinic Model of Care in partnership with patients, families, communities and local physicians so people do not always have to travel to our physical sites,” says Ms. Spurrier.

**Building on who we are**

Mayo Clinic is no stranger to innovation. Dr. William Worrall Mayo and sons, Drs. William and Charles Mayo, founded their medical practice in the late 1800s around an innovative

System. “We think of the Center for Innovation as having four components to it,” says Dr. LaRusso. The structure allows for cross-fertilization of ideas without overwhelming clinical areas and it provides protection for new ideas to evolve. By working closely with leadership from the Mayo Clinic Health Policy Center and others, the center will translate into action the cornerstones for building a new vision of health care in America. ■

# Silver lining

## Generous gift expands Lung Diseases Research Program

**T**he adage, every dark cloud has a silver lining, is appropriate when discussing Mayo Clinic's aggressive Lung Diseases Research Program.

The thriving program at Mayo today is vastly different from the startup program of just seven years ago. The catalyst for growth was Robert N. Brewer.

Diagnosed with idiopathic pulmonary fibrosis (IPF) — a condition that involves gradual scarring of lung tissue and leads to an eventual inability to transfer oxygen to the bloodstream — Mr. Brewer came to Mayo Clinic seeking help and treatment. Sadly, his condition was too progressive and eventually fatal, but that reality didn't stop him from seeing the possibility of a silver lining for others.



Andrew Limper, M.D.

### Generosity + vision = results

"He was a very generous and forward-thinking individual who conceived of funding a program that would establish a clinical and basic research program at Mayo to address pulmonary fibrosis and interstitial lung disease," says Andrew Limper, M.D., director of the program. "Mayo was very lucky to be the beneficiary of Mr. Brewer's vision."

Mr. Brewer's gift of \$3.3 million planted the seed for a now-booming lung diseases program, one of the best in the nation. "The initial investment took a really good clinical care program for patients with interstitial lung disease, and helped build a really great working team of clinical physicians, investigators and basic scientists who have developed some amazing projects to address the challenges faced by those with interstitial diseases," says Dr. Limper. "The initial work in bringing this group together really helped us to become engaged in efforts to fight interstitial diseases on a national level."

Prior to this funding, Mayo's interstitial lung diseases program found itself in a common catch-22 experienced by many in the research world: The program had not developed to the extent that it could compete for funding from the National Institutes of Health (NIH) and it couldn't grow until it received substantial funding. The Brewer Foundation changed that.

### A national presence

Today, the thriving program has successfully competed for membership in the Lung Tissue Research Consortium, part of an NIH effort to promote the collection of human tissues



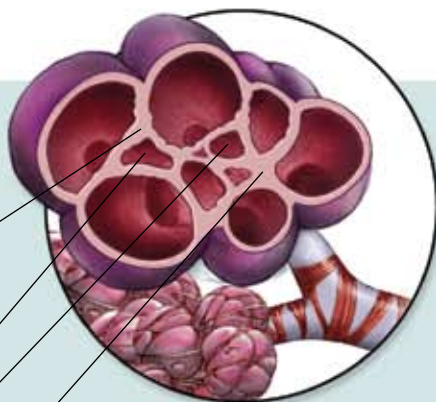
### ABNORMAL ALVEOLI ▶ (figure 1)

Thickening of tissue  
between air sacs  
(interstitium) irregular

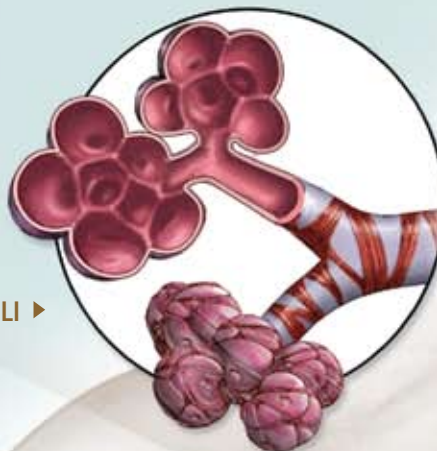
Abnormal air spaces

Alveolar shaped  
(honeycombing) irregular

Large areas of fibrosis



### NORMAL ALVEOLI ▶



to study idiopathic pulmonary fibrosis. This is a real step forward in the research of this disease since animals have not proven reliable in modeling the disease in humans, according to Dr. Limper. Membership in the consortium allows Mayo to work in collaboration with the University of Colorado, the University of Michigan and the University of Pittsburgh to collect and study these tissue samples. The group is making good progress in understanding the basis of interstitial lung disease.

In addition to the wealth of biopsied tissue now available for study, complete blood work and corresponding DNA information on this set of patients have been accumulated and stored.

Mayo's program is also now fully engaged in the NIH IPF Treatment Network. This network consists of 12 centers across the country actively studying IPF through clinical treatment trials. Jay Ryu, M.D., is the principal investigator for Mayo. Two trials are under way at Mayo as a result of participation in the IPF Network; a third trial is planned. "Participation in this network allows Mayo Clinic and other major investigators across the country to be at the table together," says Dr. Limper. "It allows us to put our minds together about how to address this disease. This is collaboration at its best."

Involvement in this important network puts Mayo in a lead role when promoting topics for research on idiopathic pulmonary fibrosis to decision makers at the National Institutes of Health who may not otherwise give this disease the same priority enjoyed by more common conditions garnering more public attention and support. ■

The term **pulmonary (lung) fibrosis (scarring)** refers to scarring and thickening of the interstitium, the tissue between the air sacs (alveoli) in the lungs (see figure 1). The lungs become stiff and do not function well. If scarring progresses, breathing can become difficult, and the lungs' ability to transfer oxygen to the blood can be impaired.

# Reaching out

Bringing quality medical care to the poor



For Randy Miles and 11 other first- and second-year Mayo medical students, nothing compared to their experience, yet nothing could have prepared them for it either. Such life-defining moments must be lived to be appreciated. The dozen would-be doctors traveled from Mayo Clinic to Haiti as part of Project Medishare, a relief organization that brings quality medical care to poor regions of the world. The poorest is Haiti.

“At first I just toyed with the idea of going, but after I learned more about the program, I was absolutely compelled to go,” says Mr. Miles. “There is so much need and I knew that by working as a team, we could accomplish so much for so many. These people need our help; we were obligated to go.”

## Few hands, big hearts

During their weeklong assignment in Haiti, the Mayo Clinic team assessed or examined more than 600 patients. The majority suffered from hypertension, gastrointestinal problems and skin infections. “It was definitely a learning experience,” Mr. Miles says. “Fortunately, there wasn’t time to dwell on the overall conditions in which these people were forced to live. That would have been too hard. Instead, we turned our focus to the job at hand and provided care to as many people as possible in the time we had. At the end of the trip, we all felt good about the care we provided.”

During their weeklong assignment in Haiti, Randy Miles (pictured above) and 11 other Mayo medical students helped assess or examine more than 600 patients.





Mayo medical student, Elisabeth P. Aponte

### Mentors make the difference

The students were accompanied and guided by Mayo physician Walter Franz, M.D., and Family Medicine resident, Chad Lowe, D.O., who also helped prepare students for their trip by exposing them to the history, culture and language of the country.

Mr. Miles had additional mentors in Col. and Mrs. James Miller, benefactors responsible for awarding him the first-ever Miller Scholarship — given to medical students whose parents served in the military. Mr. Miles' military heritage began with his grandfather, who served in the Korean War, and continued with his father whose service came at the end of the Vietnam War.

"I am truly honored to be the first recipient of the Miller Scholarship. I only hope I can make a fraction of the sacrifice that my father, grandfather and Col. Miller have made," says Mr. Miles. "Actually, I don't see it as a sacrifice at all, but rather as an honor and a duty to serve. I hope one day I can make this kind of difference to someone in need."

Perhaps for 600 people in Haiti, Mr. Miles has already achieved his goal of making a difference. ■



Col. James Chris and Shirley Miller

### Nurturing intellectual growth

Col. James Chris Miller understands the hardship that can befall families left behind in the wake of war. He's seen what happens when a soldier is lost and family members struggle not only with grief, but with the harsh economic reality of survivorship.

"During my 20 years in the Air Force, I attended many funerals and I always wondered how in the world those young widows would be able to support their children, much less get them through college," says Col. Miller.

Time spent pondering these types of questions led Col. Miller to a personal promise he's worked hard to keep. Upon retiring from the military in 1975, Col. Miller bought and developed ranches and oil and gas properties. These investments made him wealthy enough to fulfill that promise he made so many years ago.

He and his wife, Shirley, now help military families by providing scholarships to the children of deceased military personnel of any service or rank so that they may attend any accredited undergraduate college in America. The Military Officers Association of America administers the undergraduate scholarships.

Col. and Mrs. Miller also recently gave \$4 million to be split among graduate programs at all five schools of medicine at Mayo Clinic, his alma mater Harvard Business School, and at the Harvard Medical School and the Harvard School of Divinity.

The memories of all of those young widows and their children spur their giving. The Millers want those military children, who have paid such a high price for our freedom, to have the opportunity to learn that what matters in this world is acknowledging and nurturing the intellectual growth of the human mind and spirit. ■

# Common bonds

## Genetic discoveries are revealing a worldwide connection in Parkinson's disease

**T**he results on his computer screen were easy to get excited about, but Owen Ross, Ph.D., a geneticist at Mayo Clinic, resisted. He didn't want to believe, just yet, that he had discovered a surprisingly common genetic risk factor for Parkinson's disease in people of Han Chinese descent. So, he did what he always does in situations like this; he tried to prove the data wrong.

An exceptional fallibility test was right at hand — Mayo Clinic's worldwide network of collaborators who were also searching for genetic factors in Parkinson's. He contacted a subgroup from that network, researchers in Singapore, Taiwan, Japan and Seattle, each of whom had DNA samples from Asians and Han Chinese, and asked them to test their samples for the association he observed. Over the next couple

of months, the confirmations came via e-mail. The results were staggering. Collectively, the group examined DNA from more than 2,000 Han Chinese, half of whom have Parkinson's. Their work showed that a mutation in one gene, LRRK2, doubles the risk of the disease in Han Chinese carriers.

Even more surprising, the mutation, LRRK2 R1628P, was found in 3 percent of the disease-free study participants. More than 1 billion people in mainland China are of Han descent, which means that more than 30 million people in that country alone may carry the mutation. An overwhelming majority of these mutation carriers will not develop Parkinson's, but the discovery is noteworthy because it creates another window into understanding this enigmatic disease.

More than 6 million people worldwide have Parkinson's, according to the Michael J. Fox Foundation. The disease affects people differently as it progressively destroys cells in a part of the brain that coordinates movement. Current therapies only address symptoms, not its progression, and as Parkinson's advances, patients also can develop dementia and other non-movement-related symptoms.

"Our genetics research is reinforcing the notion that there isn't just one form of Parkinson's, especially from a therapeutic perspective," Dr. Ross says. "Mutations in five genes have now been shown to cause Parkinson's. In LRRK2 alone, seven different mutations have been identified that cause or increase the risk of disease. Whether they cause disease through the same mechanism is as yet unknown. For example, mutations can result in a gain or loss of protein function or production, and you can see how these alternate scenarios can affect therapeutic strategies."



Owen Ross, Ph.D.

Mayo Clinic researchers' search for genetic factors in Parkinson's disease involved some truly global networking. Asking colleagues from Singapore, Taiwan, Japan and Seattle to test DNA samples from people of Asian and Han Chinese descent, Mayo researchers discovered that a mutation in one gene doubles the risk of the disease in Han Chinese carriers.

### The human family

The path to this discovery began in the late 1980s with a substantial genetic contribution from family reunions held in the United States. Zbigniew Wszolek, M.D., then a neurologist at the University of Nebraska, began working with families in the Midwest who had unusually high incidences of Parkinson's, in the hopes of finding the genes that caused the disease in these families.

"Families are more spread out in the United States," says Dr. Wszolek, who joined Mayo Clinic in 1998. "The reunions made it possible to meet everyone, build clinical histories, obtain DNA samples and so forth."

Dr. Wszolek continued meeting with the families, and he worked with collaborators in Canada and Europe to recruit other families. Eventually, they amassed data and samples from several families, and in late 2004 and 2005, they made two landmark discoveries — that six LRRK2 mutations were a major cause of familial Parkinson's disease, and that these mutations could cause the disease in people with no apparent family history of disease.

Since then, Mayo Clinic researchers have been working with investigators in nearly 20 countries to determine LRRK2's influence on Parkinson's and to find new genes. Their results and findings from other researchers show that LRRK2 mutations are present in populations across the globe and are a significant factor in Parkinson's worldwide.

"In the beginning, I only expected to find the cause in a small number of families," Dr. Wszolek says. "But these results illustrate the power of the genetic approach and how starting with something small can sometimes lead to something that is large and very powerful."



Zbigniew Wszolek, M.D.

### Creating the future

Perhaps the most powerful discoveries from LRRK2 remain to be unearthed, say Drs. Wszolek and Ross, who believe that, with future genetic discoveries, the treatment of Parkinson's will become more individualized and more effective.

"In the future, a patient will present with symptoms, and a physician will order a test to find the mutations present in that patient and then prescribe a combination of therapies that target those genes," Dr. Ross says.

Today, with no therapy that slows the progression of Parkinson's, that vision may seem improbable, but Dr. Wszolek says history shows that discoveries build off each other.

"Look what happened with antibiotics," he says. "For a while all we had was penicillin, but it opened a door, and now we have a whole range of antibiotics to address all sorts of infections. The same scenario may happen in Parkinson's. Once we develop an effective therapy for one form of the disease, it may make it easier to create new therapies and treat the whole range of disease forms." ■

# K. Sreekumaran Nair, M.D.,

Mayo Clinic endocrinologist and director of Research Resource of the Mayo Clinic Center for

**E**nergy powers everything in our lives — our homes, our cities, even the simplest cells in our bodies. And just like everywhere else, when our cells burn fuel, the consequences mount over time.

*Mayo Clinic endocrinologist K. Sreekumaran Nair, M.D., Ph.D., has been studying this body process for more than three decades, trying to understand the effects of fuel consumption, aging, muscle metabolism and diabetes. He's not looking for eternal youth, but a way to increase quality of life, particularly as more people live into their 80s and 90s.*

*That goal has taken Dr. Nair across several countries and continents, including his birthplace in Kerala, India; New Zealand; Europe; and, for the last 24 years, the United States. He joined Mayo Clinic in 1994, and in 1999 he received the Murdock-Dole Professorship in Nutrition. Research occupies most of his time, but he continues to see patients, and he is a leader in Mayo Clinic Center for Translational Science Activities (CTSA), a National Institutes of Health (NIH)-funded center designed to rapidly translate laboratory discoveries into improved patient care.*

*Mayo Magazine recently talked to Dr. Nair about his research.*

**Kerala is one of India's most diverse states and your medical career has taken you around the globe. How have these experiences made you a better physician and researcher?**

Kerala is not only diverse; it has the highest literacy rate in India, nearly 100 percent, as well as the country's highest life expectancy and highest prevalence of diabetes, so there's an interesting parallel between where I grew up and my research.

My travels have given me a broad perspective about my fellow human beings. I feel we are all bound by a common thread. This has definitely influenced my judgment as a physician and as a researcher. Now, with society becoming more global, I feel well prepared to talk to people from anywhere in the world.

My laboratory has also brought the world to me. I've had trainees from 10 different countries, and I continue to keep in touch with them and learn from them.

**What attracted you to endocrinology and the study of aging?**

Hormones always kindled my imagination, and during my internal medicine residency I was impressed with endocrinology because most diagnoses can be made very logically, and they offer definitive treatment. The treatments often make a big difference in patients' lives, and it's very satisfying to be part of that.

I became interested in aging through my practice. I focus mostly on diabetes, and I became curious about genes that make people more susceptible to diabetes as they age. I could see a common pathway that causes aging and diabetic complications. The mitochondria help cells metabolize fuel and

# Ph.D.

## Translational Science Activities



K. Sreekumaran Nair, M.D., Ph.D., Mayo Clinic endocrinologist, has been studying the effects of fuel consumption, aging, muscle metabolism and diabetes for more than three decades. He's not looking for eternal youth, but to increase quality of life as we age.

convert it to a form called ATP (adenosine triphosphate) that all cells can use for their functions, but this process damages DNA, proteins and cells over time. So, I became fascinated with the idea of creating a buffer to prevent or reduce this damage.

I also want to know how and why aging occurs. More knowledge about those topics will have a tremendous impact. There's a huge demographic shift happening worldwide, with fertility rates decreasing and life spans increasing. So, the quality of life for our worldwide, aging population is a very important topic.

### What is normal aging?

That's a huge question, and the answer is we don't know yet. But we do know a few important things. For example, cells and DNA can't replicate indefinitely. They become damaged over time, partly as a result of the normal process of metabolizing energy. For that reason, many people, including myself, don't expect human life expectancy to go much beyond 120 years.

### We can't live much longer than 120. Can we live better up until that theoretical limit?

Frailty is one of the biggest barriers, and energy metabolism is an important factor in this, as well. A muscle's ability to metabolize fuel and convert nutrient energy to ATP declines with age. This reduced ability to produce ATP affects all cell functions and adversely affects muscle functions, leading people to adopt more sedentary lifestyles, contributing to many metabolic and cardiovascular disorders. Decline in activity hastens muscle aging and frailty, not just in humans but in many species. In fact, in species like worms, we can almost predict their demise based on declines in their activity. To offset aging it's critical that we prevent the decline in our activity levels.

But a lot of evidence shows that deliberate exercise training can reduce the muscle mitochondrial damage that aging causes. Aerobic exercise seems to delay the decline of the mitochondrial function even as we age, and new research suggests this may slow age-related declines in physical activity and performance. So, it's vital for people to exercise as often as possible.



### **Do you follow that advice?**

I do the best I can, especially with my Indian background and two parents who suffered from type 2 diabetes. I keep my BMI (body mass index) below 23. I do aerobic exercise five days a week and flexibility and joint exercises every day. I do strength training when I can.

The combination is important because aerobic exercise improves your mitochondrial functioning, maintains perfusion to vital organs and improves insulin action, and flexibility and strength training make it easier to perform aerobic exercise.

### **Is activity the only prescription available for successful aging?**

Caloric restriction prolongs longevity in animals but similar caloric restriction studies are not practical in humans. On the other hand, we have overwhelming evidence that preventing obesity allows people to live longer and better lives. In my lab, we've looked at circulating hormones, like testosterone, DHEA (dehydroepiandrosterone) and others, which decline with age. But replacing them artificially seems to have little, if any, benefit. Studies are also in progress to determine whether certain longevity genes can be stimulated by chemicals, but we are a long way from having any panacea for youth.

That's why the focus has really shifted to keeping activity levels high. People will only do that if they are motivated, and I think knowledge motivates people. So we need to really invest in educating people about the benefits of exercise. It's so incredibly important. With the help of philanthropy, we have made a huge visionary step

forward at Mayo Clinic by building the state-of-the-art Dan Abraham Healthy Living Center. I consider this a landmark investment in the welfare of our staff that may inspire other institutions all around the world.

### **Do we need to learn more about the benefits of exercise?**

Absolutely, and one reason is to find the molecular and metabolic pathways it invigorates. Once we do that, we can develop medicines that target those pathways and, for example, help someone with paralysis or other disability that prevents them from exercising. We have a major program, funded in part by NIH, studying how exercise slows aging.

### **Is there an age when the benefits of exercise are inconsequential?**

The earlier you start, the better, but it's never too late. I recommend that people start exercising regularly in their 30s. But even people in their 80s can improve their muscle mass and their mitochondrial function. The problem is motivation because the gain is not immediate. That's why it's useful to have a trainer to help us do this gradually. The same is true about starting a healthy diet. It's important to get some advice before trying it.

### **Recently you received an honorary doctorate from Karolinska Institute, the organization that awards the Nobel Prize. What was that like?**

Awards are not the reason I do research. There is an enormous delight in finding the truth and helping my fellow human beings, and discoveries are huge enhancers for the mind and spirit. But it feels good to know people value my work.





**You came to Mayo Clinic 14 years ago. What influence did that have on your career?**

Coming to Mayo is one of the best decisions I've made in my life. The environment is remarkable for someone like me, a physician engaged in research. I take questions that emerge from my patient-care activities to the lab, find the cause and strive to bring the solution back to patients. There is no better place than Mayo for this. That's the whole purpose behind our Center for Translational Science Activities (CTSA), and our skill in this area is one of the reasons our CTSA was one of the first centers to receive funding from the NIH.

**Other medical centers around the country have translational research. What makes Mayo different?**

Many centers have outstanding resources, but their focus is mostly on basic science research. We also have outstanding basic science, but our focus is on our patients. It's always been that way, and it's what we're designed to do. We have a very lengthy tradition and, with our CTSA, we have the infrastructure in place to allow any physician to conduct high-quality, patient-centered research.

**Mayo's CTSA is also mobile. Can you tell us about that?**

We not only facilitate complex human research protocols throughout Mayo Clinic; we now have a vehicle that we can take anywhere, outside Minnesota's Olmsted County, into minority communities and so forth, to perform clinical research. It makes it easier for people to participate in our research, and it helps us recruit more diverse people for our studies. It's especially important today, as we need to make medical research more inclusive and study popula-

tions that are more representative of society as a whole. To my knowledge, Mayo is the first institution to have a mobile clinical research unit, and I think many others will follow us.

**You hold the Murdock-Dole Professorship at Mayo Clinic. How important has philanthropy been to your career?**

From an overall perspective, Mayo can't perform research without philanthropy, especially with the way Medicare payments have declined over the last several years. But for me personally, just about every study starts with philanthropy and Mayo's internal funding for research.

This support allows me to do studies in the lab and develop ideas and techniques that eventually receive NIH funding. I've been continuously funded by NIH for the last 23 years, largely because of philanthropy.

I'm very impressed by and grateful for the support of our benefactors. We try to give our patients the best care in the world, and I think that inspires a lot of them to give. At the same time, I know they want to see a return on their investment, and our record of NIH support makes a strong case for the value of their giving. ■

# Stewardship report

The many ways you can support Mayo's mission

These stewardship pages highlight Mayo Clinic recognition groups. Many benefactors belong to one or more of these groups to enhance their philanthropic experience.

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## Philanthropic Partners

Philanthropic Partners is the top tier of Mayo Clinic benefactors. This elite group was established in 2004 and represents the foremost supporters of Mayo Clinic — those who have contributed \$10 million or more cumulatively. Philanthropic Partners have shaped the course of our history — and include Dr. William J. and Hattie D. Mayo and Dr. Charles H. and Edith G. Mayo.

## Principal Benefactors

The designation of Principal Benefactor was established in 2003. Principal Benefactors are individuals and organizations who demonstrate distinctive leadership by committing \$1 million to \$9,999,999 to Mayo Clinic. From throughout our history, Principal Benefactors have supported Mayo Clinic in maintaining the medical programs and facilities so essential to the highest quality of patient care.

**Contact: James Hodge**  
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## Major Benefactors

The designation of Major Benefactor began when Mayo Clinic Department of Development was established in the early 1970s. Major Benefactors are recognized as those who have made generous contributions of \$100,000 to \$999,999 to support the mission of Mayo Clinic as we carry on the important work of the Doctors Mayo, "to heal the sick and to advance the science of medicine."

**Contact: Cynthia Nelson**  
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## The Mayo Legacy

Established in 1990, The Mayo Legacy is an organization of patients, staff and friends who make planned gifts to support the Mayo Clinic mission. The Mayo Legacy includes members whose gifts advance medical progress by supporting facilities and programs in medical care, education and research.

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## The Doctors Mayo Society

The Doctors Mayo Society was established to honor Mayo Clinic Alumni who provide philanthropic support for Mayo programs. The Society is open to members of the Mayo Clinic Alumni Association, Mayo Clinic Administrative Voting Staff and public members of Mayo Clinic Board of Trustees.

## Mayo Alumni Laureates

The designation of Mayo Alumni Laureates honors benefactors who are alumni of Mayo Graduate School, Mayo School of Graduate Medical Education or Mayo Medical School, as well as their spouses, who provide philanthropic support of \$100,000 or more. We are honored to maintain a permanent record of all Laureates.

**Contact: Robert Giere**  
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## Mayo Annual Giving Program

The Annual Giving Program emphasizes the importance of significant annual support and the need for a strong financial base to meet the challenges and opportunities each year. Membership is renewed each year with a gift commitment of \$1,000 or more.

**Contact: Jim Isaak**  
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For more information on philanthropy at Mayo, please visit: [www.mayoclinic.org/development](http://www.mayoclinic.org/development)

MEMBER OF THE MAYO LEGACY: **Ann Carroll**

# Giving my estate to Mayo Clinic

If Mayo Clinic had a fan club, Ann Carroll would be its president. Her entire adult life has centered on Mayo, first as an employee for more than 20 years, and now as a volunteer and benefactor. In her volunteer role, she helps visitors navigate the sometimes-complicated campus. As a benefactor, she has made her estate plans with Mayo in mind assuring that the next generation of Mayo patients will enjoy this place of hope and healing as much as she has.

Ms. Carroll is all about Mayo. For more than two decades, she administered care as a nurse anesthetist helping to calm and monitor patients before and during surgery. "I was fortunate enough to spend my whole career working with people who provided exceptional care. I was able to do that for many years until, unfortunately, I had to go on disability for health reasons. Still, I wasn't ready to give up being a part of the Mayo Clinic family, so I signed on to volunteer," she says. "I now see that my role as a volunteer is similar to my role as a nurse anesthetist. I still help to calm people."

Today, Ms. Carroll spends her time directing visitors, lending a sympathetic ear or administering her own form of healing by way of a smile. "Sometimes people just need someone to talk to. This is a big place and people are often here for not-so-pleasant reasons. It makes me feel good to know that I am helping those who are hurting," she says.

And her selfless service to others will continue long after she is gone.

Through The Mayo Legacy program, Ms. Carroll has left her entire estate to Mayo Clinic as directed in her will. Her planned charitable gift will establish an endowment to fund research. This means Ms. Carroll has chosen to rely on the experts at Mayo to distribute the funds as they see fit and in the research area of greatest need when the time comes.

*"The best investment I can make is in helping to secure the future of Mayo Clinic. I have spent my whole life here and I know for a fact that the people who work at Mayo are hard-working, dedicated, conscientious people who accomplish what they set out to achieve," she says. "The more people contribute, the more good that can be done." ■*



Ann Carroll

MAJOR BENEFACTORS: **Max and Thelma Biegert**

# Partnership yields success

Owning and operating a railroad after retirement was not in Max and Thelma Biegert's plans. They had two successful business ventures under their belt and were enjoying a retirement filled with travel. However, little did they know a risky investment would lead to one of the biggest commercial adventures of their lives.

The Paradise Valley, Ariz., couple had two options: walk away from their investment and take a loss, or assume the challenge that The Grand Canyon Railway posed. Twenty years later, the once-defunct railroad is now a well-known tourist destination.

During their 58-year marriage, the Biegerts have been equal partners in life and in business. They founded three successful companies in three different industries. They attribute the success of their aviation, daycare and railroad businesses to teamwork.

Says Mr. Biegert, "We discuss things, work out strategies and implement ideas. From the business side, it has worked out well because we can bounce ideas off each other."

While their teamwork approach made for a successful work environment, it was also necessary to survive in industries neither initially knew much about.

"It seems like everything we start out to do we know nothing about," says Mrs. Biegert. "Fortunately, Max has the ability to hire people who do, and he gives them free reign to operate."



Thelma and Max Biegert

With the railroad, the Biegerts certainly purchased something that they knew little about. What they had in 1988 was 20 miles of tracks and the vision of reviving a railroad that had not operated since 1968. They stuck to their winning teamwork formula and maintained their determination to see the project through.

Last year, that formula was validated when they sold the railroad, an enterprise that now includes 65 miles of track, a 300-room hotel, a 385-seat restaurant and an RV park. Their success led to their induction into the National Railroad Hall of Fame, joining a legendary group that includes Abraham Lincoln and J.P. Morgan. Mrs. Biegert became the first female honoree.

The Biegerts insist that they are now permanently retired. Even

though they no longer build successful business partnerships they still apply their winning formula — now to philanthropic partnerships.

Last year, the Biegerts established an endowment that supports neuroscience research at Mayo Clinic. Their gift was inspired by the care they have received at Mayo, their observations of how Mayo is run, and its reputation as a world-renowned medical institution. But plain and simple, they support Mayo Clinic because it helps people.

"We are so happy that Mayo is in the Valley. It's a wonderful resource available to all. We are proud to support the great work that they do," says Mrs. Biegert. ■

PRINCIPAL BENEFACTOR AND MEMBER OF THE MAYO LEGACY: Irene McKenney

## A face off with diabetes

At 5 feet 4 inches tall, she's a formidable prizefighter in the battle against diabetes. She's had to be: her loved ones have depended on her.

Irene McKenney's ever-expanding repertoire of diabetes information is an impressive wealth of personal knowledge. Over the years, she has helped two of her five children manage the disease, as well as her now-deceased second husband.

Caring for those with diabetes has been a way of life.

"I remember my grandparents' generation and when they talked about people with diabetes, it was like a death sentence," says Mrs. McKenney. "Before the days of insulin, all they could do to treat diabetes was to avoid foods containing sugar."

Over the years, she had no choice but to amass an almost encyclopedic knowledge of diabetes. "My daughter was two and my son was eight when they were diagnosed with juvenile diabetes. By that time, beef and pork insulin had been invented. But my daughter was allergic to it," she says. "Luckily, at about that time, human insulin came out. Since then, varying types of insulin have been developed to control blood sugar on a more even keel. Controlling blood sugar is a magician's game, especially with children. Food intake, exercise, emotions and insulin must all be in balance to prevent diabetic coma or insulin reactions. Yet I never kept my personal fears of diabetes



Irene McKenney

or its possible consequences from encouraging my children to participate in anything they wanted to do."

Mrs. McKenney's caring and compassion extends to others who have the disease. Her wish is that other children and their families don't have to endure the constant cycle she and her loved ones endured — the rigid, repetitive schedule of checking blood sugar and adjusting insulin. She knows all too well the sometimes teeter-totter emotions that can result from this all-consuming routine. "My goal is to make life better for children with diabetes," she says. And so, she and her late husband, Martin, support diabetes research at Mayo Clinic with the Dr. Martin and Irene McKenney Mayo Clinic Endowed Fund for Diabetes Research. "I give to advance research at Mayo Clinic because I know

the funding will be used by capable people who will do their very best to enhance our understanding of this disease," says Mrs. McKenney.

"Mayo's concern of always putting the patient first is carried out in their research. Mayo does a lot of research in diabetes, and I admire the way everyone works together for the good of the patient," she says.

"The treatment of diabetes has come a long way with the invention of the insulin pump, but there's still a long way to go. You can never forget you're a diabetic, not one day or even one hour of your life. It's always with you," she says. Her wish is that, someday, those who have the condition can leave it behind. ■

# News at Mayo Clinic

## The Mayo Legacy meeting, Aug. 21-23, 2008

The 13th meeting of The Mayo Legacy was held Aug. 21-23, 2008 in Rochester, Minn. This year's theme was *Translating Discovery to Patient Care*. Attendees had the opportunity to hear the dramatic story of separating conjoined twins, Abbigail and Isabelle Carlsen, as told by their surgeon Christopher Moir, M.D., and his surgical team. At the end of the presentation, the Carlsen twins made a surprise appearance with their mother, Amy Carlsen.

During Friday's session, attendees were given the opportunity to listen to a variety of medical presenters discussing the latest advancements in medicine and research. In addition, a number of exciting "behind the scenes" tours of Mayo Clinic research and patient care facilities were offered.



Christopher Moir, M.D.

Attendees also had the opportunity to listen to Denis A. Cortese, M.D., Mayo Clinic president and CEO, speak about the Mayo Clinic Health Policy Center.

On Friday evening, Legacy members were the first to see *My Brother and I ... The Founding of Mayo Clinic*, a PBS-quality documentary, highlighting the lives and values of Dr. Will and Dr. Charlie Mayo. The film included rare home movies, vintage photos and family artifacts. Funded with a generous gift from John T. and Lillian G. Mathews, the founding benefactors of Mayo Clinic Heritage Hall, the film featured original music, beautiful cinematography and interviews with people who knew the brothers. As a special highlight, the film was narrated by broadcast icon Garrison Keillor, who donated his service to the project.

On Saturday morning, Diane Jelinek, Ph.D., led a discussion panel featuring students from the Mayo Graduate School of Medical Education. Attendees were able to interact with the students and ask questions about their education and experiences at Mayo Clinic.

The event concluded with a keynote address by Father Nick Mezacapa, M.Div., Rector of Calvary Episcopal Church followed by a special send-off performance by the Honors Choir of Southeastern Minnesota.

The next meeting will celebrate the 20th anniversary of The Mayo Legacy and will be held May 6-8, 2010 in Rochester, Minn.



Abbigail and Isabelle Carlsen

## Trustees honor three Mayo Clinic named professors

Named professorships at Mayo Clinic represent the highest academic distinction for a faculty member. Faculty are appointed to a professorship through nomination and endorsement of their peers and then confirmed by Mayo Clinic senior leadership. Appointed individuals are recognized for distinguished achievement in their specialty areas and service to the institution.

These professorships are named in honor of benefactors. The gift funds, which may be unrestricted or focused on a specific medical area, are held in endowment. All income from the endowed professorships supports Mayo Clinic programs in medical education and research.

**Daniel Berry, M.D.**, is a professor of orthopedics and chair of the Department of Orthopedic Surgery at Mayo Clinic in Rochester.

Dr. Berry received the B.A. degree at Dartmouth College in New Hampshire and the M.D. degree at Harvard Medical School. He completed an internship in general surgery at New England Deaconess Hospital in Boston and residencies in the Harvard Combined Orthopedic Residency at Children's Hospital in Boston, Brigham and Women's Hospital, and Massachusetts General Hospital. He completed a fellowship in hip surgery in Europe and a fellowship in adult reconstructive surgery at Mayo Clinic.

Dr. Berry is a member of many professional societies and has served as president of the American Association of Hip and Knee Surgeons, Mid-America Orthopedic Association and Mueller Foundation of North America. He is a director of the American Board of Orthopedic Surgery.



Daniel Berry, M.D.



Larry Pease, Ph.D.



William Tremaine, M.D.

Dr. Berry has been elected Teacher of the Year by the residents of the Orthopedic Surgery Resident Training Program at Mayo Clinic. He has lectured and published extensively and has won awards for research on hip and knee replacement. Dr. Berry is widely recognized for his clinical contributions, extensive research publications and leadership in the field of orthopedics.

**Larry Pease, Ph.D.**, is the chair of the Department of Immunology and a professor in the Department of Immunology and the Department of Biochemistry and Molecular Biology. He is the theme leader for the Immunology, Transplantation and Infection Disease Theme and program co-leader for the Immunology and Immunotherapy Program. His other leadership roles include membership in the Department Chair Advisory Council, the Three Shields Coordinating Committee, the Medical-Industry Relations Committee and the Clinical Immunology Program Executive Committee.

Dr. Pease earned the Ph.D. and the M.S. degrees in zoology from the University of Michigan. Dr. Pease is a two-time recipient of Teacher of the Year for Mayo Graduate School and also received the Dean's Merit Award. Throughout his career, Dr. Pease has mentored numerous trainees.

Dr. Pease is a member of many professional societies and serves on the editorial board for *Immunogenetics* and, along with four colleagues, holds a United States patent for "Dendritic Cell Potentiation."

**William Tremaine, M.D.**, is a consultant in the Department of Internal Medicine and Gastroenterology, a professor of medicine and director of the Mayo Clinic Office of Human Research Protection.

Dr. Tremaine received the M.D. degree from the University of Mississippi School of Medicine and completed a residency at Mayo Clinic in the Department of Medicine. He joined the staff of Mayo Clinic in 1981 and is a recipient of the Henry S. Plummer Distinguished Physician Award, Department of Medicine, and the 2007 Mayo Clinic Distinguished Clinician Award.

Dr. Tremaine is a member of many professional societies and has lectured extensively. He is widely published and serves as a section editor of the journal *Inflammatory Bowel Diseases*. Dr. Tremaine is a member of the Grants Review Committee of the Crohn's and Colitis Foundation of America. His primary clinical interest is inflammatory bowel diseases.

**Mayo students earn law degrees from Sandra Day O'Connor College of Law at Arizona State University**

In crossing the stage to receive her J.D. last spring from the Sandra Day O'Connor College of Law at Arizona State University (ASU), Lindsay Evans fulfilled half of a promise she made in 2000 at her high school graduation in Madison, Tenn.

"I don't remember saying this, but my mom says she has a videotape of me saying I wanted to be a doctor and a lawyer," said Evans, 26.

In two years, when Evans earns a degree from Mayo Medical School, she will have achieved that goal through a unique partnership between the two schools. Evans is the second person to graduate from the law school in Tempe, Ariz., under the M.D.-J.D., a synergistic program that spreads the learning of medicine and the law over six years.

Brian Wilhelmi is the first, having earned his law degree in May 2007. Wilhelmi joined Evans at the law school's convocation on May 9, 2008, to walk with other graduates of his entering class.

"It was wonderful seeing my old friends, who are going to be anything from politicians to academics," said Wilhelmi, 27, who is back in Rochester this semester, after spending the summer at a Washington, D.C., law firm.

Evans, currently on rotation at Mayo Clinic Hospital in Phoenix, said she learned to think differently at law school and was exposed to brilliant professors and fascinating topics in the intersection of law and science.

"I took courses in medical malpractice, health law, elder law, and it was all so integrated to the practitioner," she said. "There's a business element to medicine that a lot of students aren't exposed to, and I am so thankful that I was offered this opportunity."

The Sandra Day O'Connor College of Law ([www.law.asu.edu](http://www.law.asu.edu)) at Arizona State University was founded in 1967 and renamed for the retired U.S. Supreme Court justice in 2006. It is the only fully accredited law school in the Phoenix area, boasts an Indian Legal Program that is arguably the best in the nation, and houses the Center for the

Study of Law, Science, & Technology, the oldest, largest and by far the most comprehensive law and science center in the country. ASU is one of the premier metropolitan public research universities in the nation.

**Mayo Clinic ranked among top pediatric hospitals**

Mayo Clinic has been honored in *U.S. News & World Report's* 2008 Edition of America's Best Children's Hospitals, published online and in the magazine's June 9 issue. Mayo was ranked in three specialties: Neurology and neurosurgery, Digestive disorders, and Heart and heart surgery.

Mayo Clinic has been ranked as among the top pediatric hospitals every year since *U.S. News & World Report* began its rankings. Last year was the first time children's hospitals were considered separately from the overall Best Hospitals ranking, which is published annually in July. This year's rankings are the first to evaluate pediatric subspecialties.

"The recognition we receive is a real tribute to the great team of care providers we have at our children's hospital. Lots of people extend themselves every day to provide the best care possible for children and adolescents," says Phil Fischer, M.D., medical director for Mayo Eugenio Litta Children's Hospital. "The fact that our relatively small children's hospital within a hospital is favorably compared to large freestanding children's hospitals is a testimony to the great care our staff provide to children each day. Even while we are still growing and improving, our patient-focused, family-centered, team-based care has gained a favorable national reputation."



Lindsay Evans and Brian Wilhelmi



### Mayo Clinic recognized as benchmark in report

Mayo Clinic has been recognized as the national academic medical center benchmark in the recently released “Dartmouth Atlas of Health Care.” This report tracks the care of patients with chronic illnesses during the last two years of their lives, examining the variability of this care both for quality and cost. According to the report, “It [Saint Marys Hospital] is not the least costly hospital, but it enjoys a strong national reputation for quality, while simultaneously keeping utilization and costs relatively low. It is part of a well-organized health care system.”

Institutions such as Mayo can give better care at a lower cost because they don’t overtreat patients, especially those who are chronically ill. The lead author of the report, John Wennberg, M.D., Ph.D., has challenged people to learn how organizations such as Mayo use fewer resources and spend less per capita than their peers while receiving high marks on quality measures.

According to the report, control of excess use is the most critical factor in controlling health care costs in our country. One element in Mayo’s success in this area is salaried physicians who practice as an integrated group.

A *New York Times* editorial on April 10 said, “Few will be surprised to discover that doctors in high-expenditure institutions are typically paid on a fee-for-service basis, which means they earn more if they do more. Mayo Clinic doctors, by contrast, are on salary and have no financial incentive to do anything more than the patient clearly needs.”

A summary of the report is available online at <http://dartmouthatlas.org>.



Harvey Mackay

### The Doctors Mayo Society meeting Sept. 12-13, 2008

*Building the Future of Medicine* was the theme for The Doctors Mayo Society (TDMS) meeting held in Rochester, Minn. on Sept. 12-13, 2008. A reception and dinner launched the meeting on Friday evening, hosted by Miguel Cabanela, M.D., chair of The Doctors Mayo Society, and Dr. John and Joan Joyce, honorary chairs of the meeting. Harvey Mackay, internationally known author and inspirational speaker, delivered the keynote address on excellence and staying competitive in today’s global business climate.

Saturday’s scientific presentations highlighted virotherapy as a cancer treatment, surgical options for prostate cancer, new perspectives on aging, a new treatment option for cardiovascular disease, and spinal cord regeneration. On the nonscientific front, a “fit and healthy” cooking demonstration was held at the Dan Abraham Healthy Living Center demonstration kitchen. Afternoon activities included a premiere screening of the documentary *My Brother and I ... The Founding of Mayo Clinic*, and tours of Mayo Clinic research facilities, the Dan Abraham Healthy Living Center, and Mayo Clinic art and history.

The meeting concluded Saturday evening with a buffet dinner, followed by a theater presentation of *The Mystery of Maud Mellish*. Author and actress Megan Cole created and performed this one-woman play, based on historical facts, writings, and the memories of those who knew and worked with Maud Mellish.

### Mayo hospitals receive Blue Cross Blue Shield of Minnesota awards

Saint Marys Hospital and Rochester Methodist Hospital each received a Blue Cross Blue Shield of Minnesota “Recognizing Excellence for Hospitals” program award for 2007. This new program is open to hospitals participating in either of the following quality initiatives:

- The Blue Distinction Hospital Measurement and Improvement Program, which measures self-reported data from the Centers for Medicare and Medicaid Services, and the Agency for Healthcare Research and Quality.
- The Leapfrog Group, which measures self-reported data relating to computer physician order entry, ICU physician staffing, evidence-based hospital referral/high-risk treatments and the Leapfrog Safe Practices Score.

Saint Marys Hospital and Rochester Methodist Hospital participated in both initiatives and won awards based on participation in the Leapfrog Group initiative.

In addition to Saint Marys Hospital and Rochester Methodist Hospital, two Mayo Health System sites — Austin Medical Center and Fairmont Medical Center — each received awards for participating in the Blue Distinction Hospital Measurement and Improvement program.

Mayo received four of the 13 awards presented to Minnesota hospitals.

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### ON THE COVER

Behind each one of these smiling faces lies a unique person with a genetic blueprint that's also one of a kind. Now that scientists have mapped all those millions of genes that make up human DNA, Mayo Clinic researchers are drawing on that knowledge to advance the field of individualized medicine.



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