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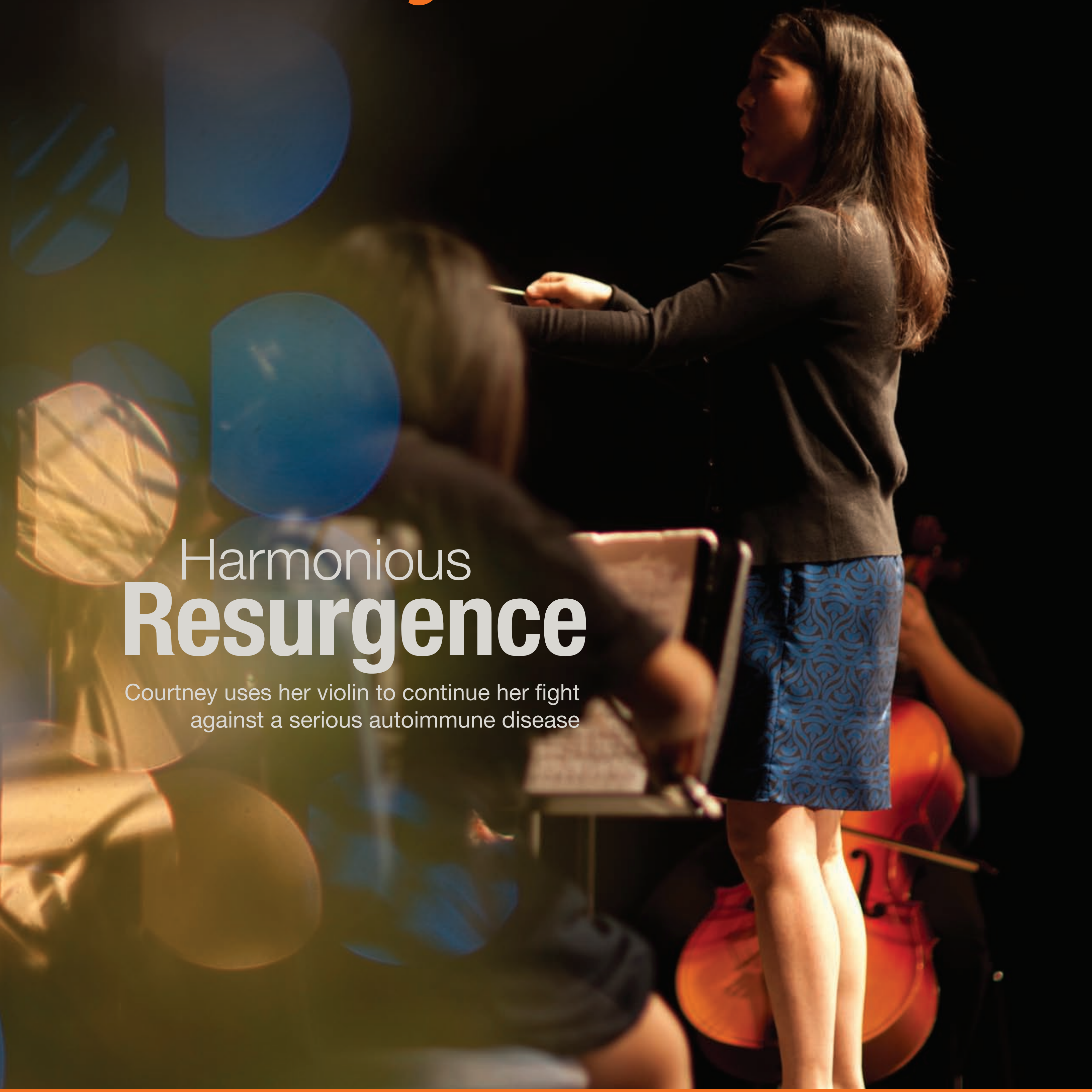

Harmonious Resurgence

Courtney uses her violin to continue her fight against a serious autoimmune disease

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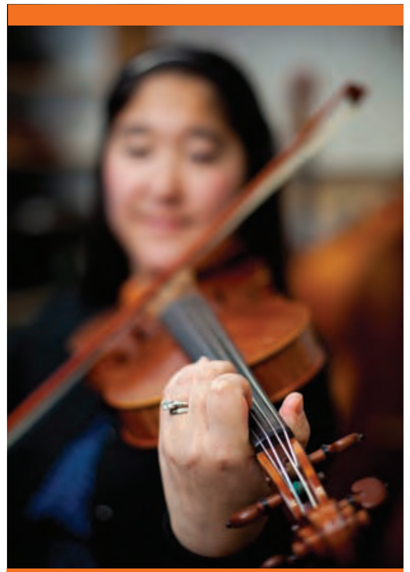

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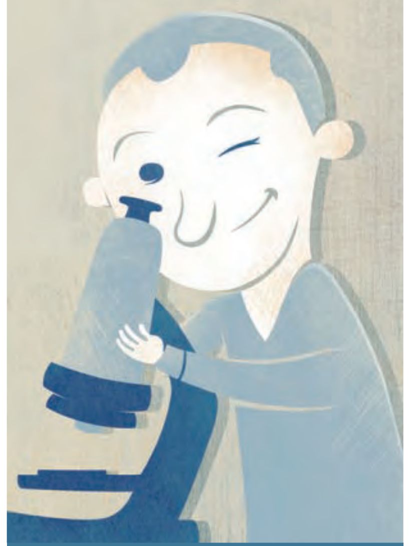

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HARMONIOUS RESURGENCE

Courtney Engel relied on her passion to help her fight a serious autoimmune disease. She received a standing ovation.

IN PURSUIT OF INNOVATION

Breakthroughs are about more than chance. They emerge from minds prepared by hard work and open to new possibilities.

BIG HEARTS LITTLE HANDS

Three little girls prove that you don't need a lot of money to be a philanthropist.

Paying It Forward

Christopher Gregory was of Polish and Irish descent, but after his unfortunate death at the too-young age of 19, he's become something more. Christopher was an organ donor. He gave the gift of life to Jorge Bacardi, a Mayo Clinic patient and benefactor from the Bahamas. According to Eric Gregory, Christopher's father, that makes Christopher a little Bahamian, too.

Or maybe Christopher has become a citizen of the world.

The dedication of the Gabriel House of Care at Mayo Clinic in Florida drew more than 200 people from three countries. The 30-room facility provides affordable, extended-stay lodging and a supportive environment for visiting cancer and transplant patients.

The project was conceived not long after the lives of Christopher Gregory and Jorge Bacardi came together on March 28, 2008. Sadly, that's the day Christopher died following a brain aneurysm.

Within weeks of receiving Christopher's gift, Jorge Bacardi vowed he would do his utmost to repay it and, at the same time, do something to honor his Mayo Clinic physicians and help others in need of transplant care. So he and his wife, Leslie, as well as his siblings, led the fundraising drive to create Gabriel House of Care, which opened in April 2011. While the house is the result of many gifts given, the dedication event was, in many respects, a celebration of receiving.


William Rupp, M.D., chief executive officer of the Florida campus, and Edward Asher, executive director of the agency that will manage Gabriel House of Care, thanked the Bacardis and every other benefactor who helped make the house a reality. From left to right: Dr. Rupp, Mr. Edward Asher, Eric Gregory, Grace Gregory (partly hidden), Leslie Bacardi, Jorge Bacardi.

Mr. and Mrs. Bacardi shared their gratitude for their Mayo Clinic caregivers, Christopher's gift of life and the generosity of his parents, Eric and Grace Gregory, who've welcomed the Bacardis into their lives. The Gregorys, in turn, described the healing power of the Bacardis' gift. "It makes my wounded heart soar," Grace Gregory said.

In many ways, the story behind its creation is a foreword for the Gabriel House of Care. A series of unfortunate events — Christopher's passing and Jorge Bacardi's congenital lung disease, curable only by transplantation — brought together two seemingly disparate lives. From those difficult beginnings springs a house that brings together people from all over the world, not only making it easier for them to receive lifesaving care, but making it easier for them to support one another at a time when support is almost as important as medicine itself.

That ongoing support and care will create something that is timeless, something that may even match the inspirational story that led to the creation of the Gabriel House of Care. That's what Eric Gregory believes, and it's hard to argue with him.

"Jorge, I will make you this promise," Mr. Gregory said in front of the dedication crowd. "Someday 10 or 12 years from now there'll be a little boy or a little girl who's not even born yet who's going to walk out the door with a new heart or new lungs. That child will go out into the world and live a great life. They will pay your gift forward. Maybe 40 or 50 years after their transplant, they'll serve the purpose that God has for them. Maybe they'll be a great transplant surgeon or maybe they'll be a great philanthropist. We won't be here. But we'll watch. Me, you and Chris; we'll see it from heaven." ■

A World Beyond Cancer

The pouring rain beat on Chuck Howard's car as he maneuvered it through the congested parking lot of the hospital near his hometown of Largo, Fla. Easing the car into a space, he hurried inside to where his wife, Gail, waited for him, and together they walked to the doctor's office for her appointment.

Then their lives changed forever.

Gail had stage 3 lung cancer, they learned, and there was little hope. She had a 10 percent chance of surviving five years and probably less than a year left to live.

"The doctor told us to take a trip to France or do something else that we always wanted to do — and to do it fast," says Chuck, a tall man with a soft-spoken voice and a sparkle in his eyes.

In a way, they followed the advice. They agreed that travel would be the best way to spend Gail's remaining days. They took a trip. But it wasn't to Paris. It was to Mayo Clinic's campus in Jacksonville, Fla., where they met oncologist Gerardo Colon-Otero, M.D., who confirmed the grim diagnosis. But he did more than that. He agreed to treat Gail, and in a way that would support the couple's desire to see as much of the world as possible before she died.

Almost immediately, they were off, traveling to Hawaii, where they departed for a five-week cruise that took them to Kiribati, Bora Bora and a host of other island nations in the Pacific. A pattern soon developed. Chuck and Gail would check in with the doctor every three months and then depart on another voyage. Gail made it beyond the one-year prognosis, and then she passed the five-year mark. In all, she lived more than a decade with her disease. And it would be fair to say she saw a good bit of the world, too.

In fact, she saw almost all of it. The Howards decided to visit every country in the world or get as close to that goal as possible. They visited 146 countries and all seven continents before Gail passed away in 2007.

"That's why I think Gail's story is so important," Chuck says. "She showed that there's life even after the worst cancer diagnosis you can get. She may have died from cancer, but it didn't defeat her because it didn't stop her from living."

To this day, Chuck doesn't know how to explain Gail's remarkable survival, but he says there was one constant, besides the travel. "Dr. Colon was there from day one, until the last half-hour before Gail passed away," Chuck says. "He made a personal visit, not a doctor's visit, on that last day. He's smart and caring, but he's more than that. He's a humanitarian, and I don't know how he's able to do everything he does."

To express his appreciation for his wife's care, Chuck established the Gail Lynn Howard Fund for Lung Cancer Research. This endowment fund honors Colon-Otero and supports lung cancer research at Mayo Clinic. Its proceeds are supporting the lab of Alan Fields, Ph.D., whose team has discovered that a family of genes, called protein kinase c (PKC), has a surprisingly prominent role in lung cancer. Their work launched a clinical trial studying a new treatment for lung cancer — an arthritis drug that targets a PKC gene. In laboratory studies, this drug blocks the gene's cancer-inducing activity.

Photography by Mr. Howard

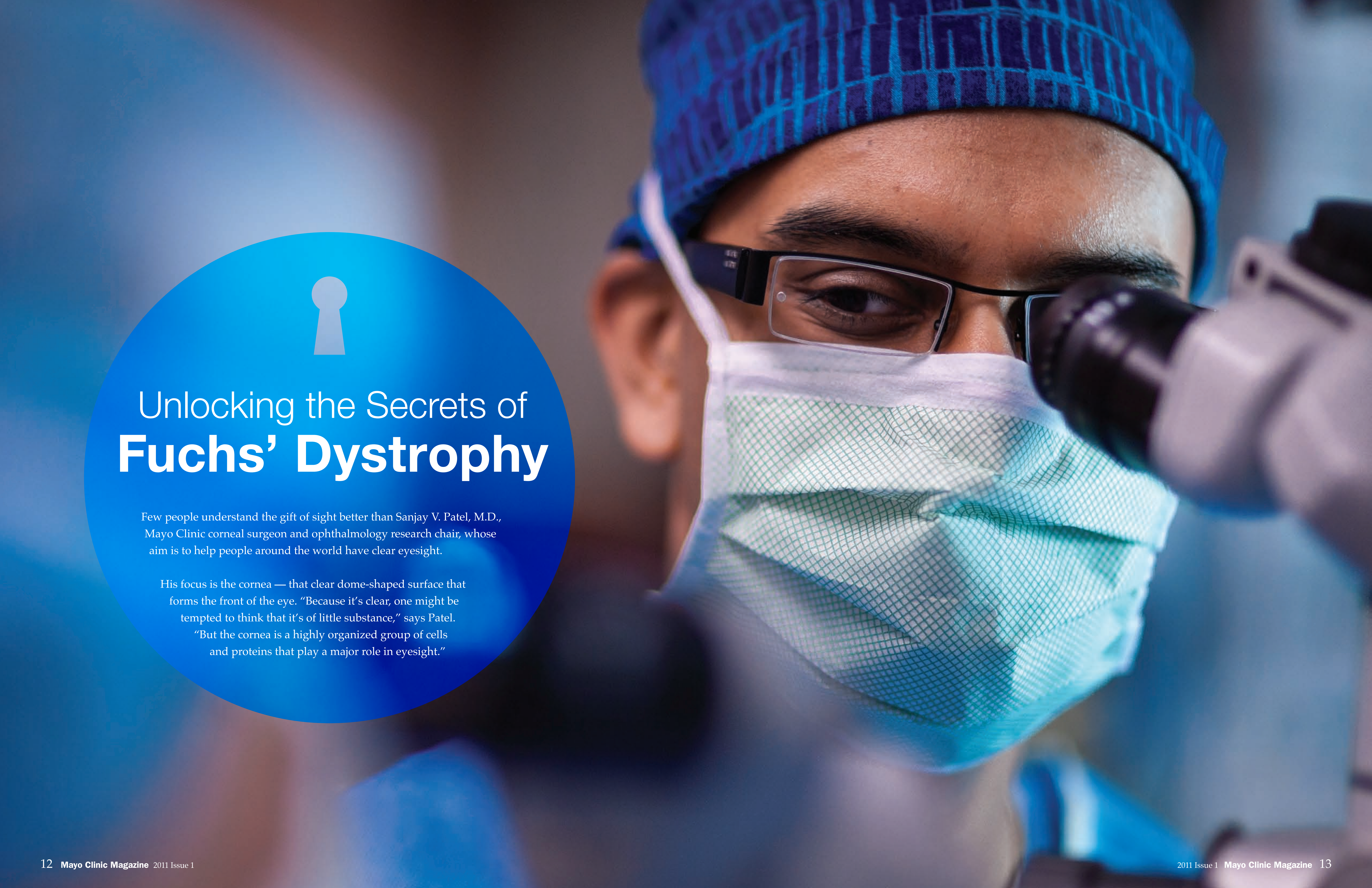
> "She showed that there's life even after the worst cancer diagnosis."

That news brings hope to Chuck. His gift, he says, is his way of helping others avoid Gail's fate. While a cure for all cancers is important to him, it's equally important to spread a message of hope. Life needn't end with a cancer diagnosis.

After Gail's passing, he continued to travel the world. He's closing in on his goal of visiting all of the world's countries and at last count, he'd seen more than 195.

And he's found a new companion, too. In 2010, he married Kathy Sears. Kathy shares his love of travel and knows cancer's touch all too well, having lost her mother to lung cancer. For that reason, the gift to Mayo Clinic is a source of strength and pride for her as well.

It's easy to look back on how things began, with a typical rain-soaked day in southwest Florida and a diagnosis that destroys hope. It's easy to marvel at the mysterious turns a life can take. But maybe that's not the point. Maybe the point is to never look back at all. After all, as Chuck Howard can tell you, it's a big world, and who knows what lies around the next bend? ■



Unlocking the Secrets of Fuchs' Dystrophy

Few people understand the gift of sight better than Sanjay V. Patel, M.D., Mayo Clinic corneal surgeon and ophthalmology research chair, whose aim is to help people around the world have clear eyesight.

His focus is the cornea — that clear dome-shaped surface that forms the front of the eye. "Because it's clear, one might be tempted to think that it's of little substance," says Patel. "But the cornea is a highly organized group of cells and proteins that play a major role in eyesight."

Research to Prevent Blindness

Since it was founded in 1960, Research to Prevent Blindness (RPB) has been a catalyst in vision research, responsible for spawning a vibrant community of eye research institutions and for initiating the movement that led to the creation of the National Eye Institute. RPB has been instrumental in developing an army of eye researchers and is connected through its financial support to nearly every major treatment for eye diseases in the past half century.

For more than three decades, RPB has been a loyal benefactor of ophthalmology research at Mayo Clinic, with support now totaling more than $2.6 million. Many of the advances in research in ophthalmology at Mayo Clinic can be attributed to generous support from RPB.

Patel's specialty is corneal surgery and Fuchs' (FOOKS) dystrophy, a slowly progressive hereditary disease of the cornea. In advanced cases, Fuchs' causes the loss of clear eyesight in otherwise healthy people. Its symptoms emerge gradually, typically in people 40 and over, causing blurry vision, glare, halos and loss of contrast perception in both eyes. Tiny bumps or guttae (GOO-tay), that develop on the inside surface of the cornea are the hallmark of the condition. Eventually, the cornea swells, which results in worsening of vision and, in severe cases, painful blisters on the outer surface of the cornea. The exact cause of Fuchs' dystrophy remains unknown. The only treatment option is corneal transplantation.

Mayo ophthalmology — a tradition of teamwork

Mayo Clinic in Rochester, Minn., is ranked among the best hospitals in ophthalmology by *U.S. News & World Report*. With a staff of more than 30, including ophthalmologists (working in all ophthalmic subspecialties), optometrists, Ph.D. researchers and ophthalmology residents, Mayo provides the ideal environment to integrate clinical research with patient-centered care. The Mayo team does more than 120 corneal transplants a year, primarily for patients with Fuchs' dystrophy.

Through a National Institutes of Health (NIH) grant, Patel is investigating the feasibility of a new transplantation technique for Fuchs' dystrophy. He's also interested in discovering what causes the disease, because identifying the underlying disease process may lead to the development of new kinds of treatments.

"We have several clinical studies investigating corneal transplant outcomes, grading and prospective evaluation of corneal changes in Fuchs' dystrophy; so for me it's not just laboratory research," says Patel. "My work with the disease extends from the laboratory to the operating room."

A genetic key

Keith H. Baratz, M.D., who is also a corneal surgeon at Mayo, studies Fuchs' dystrophy from a different angle — the genetics of the disease. In the *New England Journal of Medicine*, Baratz recently reported the discovery of the first gene associated with the most common form of Fuchs' dystrophy. "Discovering a gene association means the gene is somehow implicated in the disease, but it doesn't necessarily mean that it's the gene that causes the disease," says Baratz. "This is a first step in identifying the pathology of the disease. The ultimate goal is to discover how the disease occurs and then find a treatment to slow its progression." Working together, Patel and Baratz are now focused on ways to merge the two areas of study.

Extending treatment worldwide

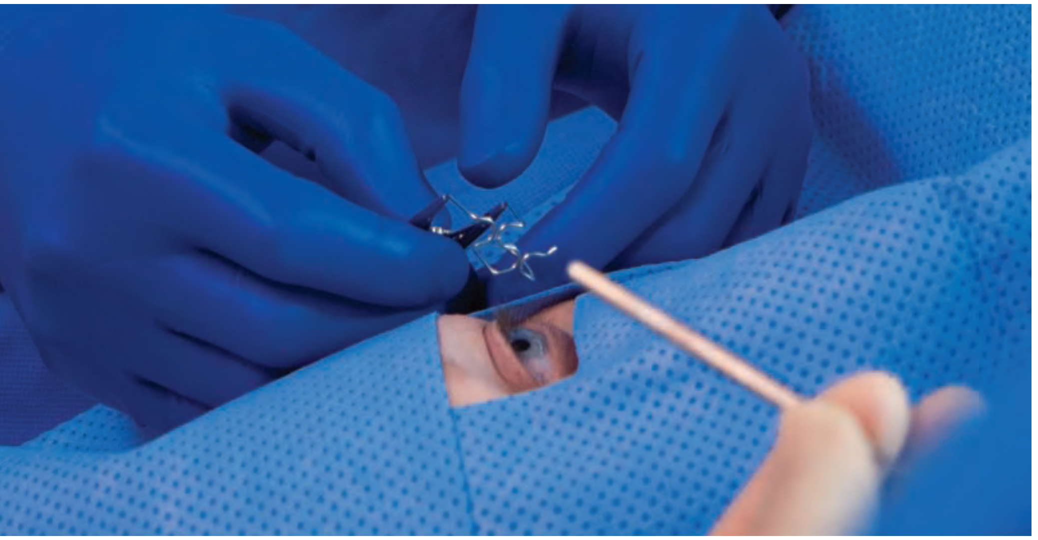
Although severe corneal disease rarely results in blindness in the United States, it is the second leading cause of vision loss and blindness in adults and children worldwide. A wide variety of infectious and inflammatory eye diseases cause corneal scarring that ultimately leads to blindness.

"In the U.S., we are able to treat conditions of the cornea such as Fuchs' dystrophy and other diseases by transplanting human donor tissue. This is made possible because we have an excellent eye banking system that gathers and distributes corneal donor tissue, but that's not the case in much of the rest of the world where eye banking facilities are not available," says Patel. "So we need to ask: How can we improve corneal transplantation for the rest of the world? How can we expand our donor pool?"

Regenerating healthy cells

The real promise seems to rest with Patel's current research initiatives with corneal cell regeneration and transplantation, and the development of an artificial cornea. "By having an 'off-the-shelf' corneal replacement readily available, vision could be restored to millions of people in developing countries," Patel says.

> "Vision could be restored to millions of people."



The field of stem cell research and regenerative medicine has enormous potential for improving patient care across common and challenging patient conditions. Regenerating cells for therapeutic repair involves the convergence of three strategies:

1. Replacement with surgical transplantation of tissue or organs
2. Regeneration using stem cells
3. Rejuvenation through the self-healing process

Corneal treatment has traditionally used a replacement strategy — replacing diseased tissue with donor tissue. Corneal endothelial cell regeneration offers the next frontier of therapy for diseases of the corneal endothelium, such as Fuchs' dystrophy. Patel has successfully regenerated human corneal endothelial cells in the laboratory and recently published a model to study transplantation of these cells to human corneas in the laboratory. "Further development of this technique has the promise of expanding the donor pool, because cells from one donor could potentially be used to treat multiple recipients," says Patel. In addition, he is investigating new methods of freezing the cells to enable longer preservation times, which could help expand the donor pool worldwide.

Work is also under way to develop an artificial cornea — a hybrid of collagen and silica that rejuvenates into living tissue. This project, which is a partnership between Patel and the University of Minnesota, involves cell regeneration of the corneal stroma, which is the layer that forms the main substance of corneal tissue. "An artificial cornea would be a tremendous benefit to the rest of the world," says Patel, "because infection and inflammation, which causes corneal blindness, is so prevalent worldwide."

Support is critical

Benefactor funding is critical to these types of innovative breakthrough projects. "Support from foundations such as Research to Prevent Blindness gives us a head start on these projects, and eventually many of these projects become self-sustaining through NIH and other funding sources," says Patel.

As research in cell regeneration continues to evolve, the need for surgical intervention may one day become obsolete. "My aim would be to put myself out of business as a surgeon," he says. "The ultimate treatment would be to use eyedrops capable of regenerating healthy cells to treat diseases such as Fuchs' dystrophy without creating a surgical incision. We're a long way from that, but that's what we should be striving for." ■

Life. In Focus.

Peg Wepner knew the time had finally come. At 56, the schoolteacher from Sturgeon Bay, Wis., had been coming to Mayo Clinic for more than 10 years since being diagnosed with Fuchs' dystrophy. She was all too familiar with the disease. Her mother had been diagnosed with it when she was in her late 60s. Back then, less was known about Fuchs' dystrophy, but doctors did know it was genetic.

Every year Peg met with her Mayo ophthalmologist and surgeon, Sanjay V. Patel, M.D. There was never pressure for corneal transplant surgery. "Whenever you're ready, Dr. Patel would say."

Eventually, Fuchs' dystrophy began disrupting Peg's life. Her depth perception had become a problem, and she could no longer distinguish the edges of stairsteps. Night driving was particularly difficult; oncoming headlights were jagged blurry bursts of light, so she began driving less and less. Every morning she'd wake to eyesight as cloudy as if she were looking through watered-down milk. During the day, she'd use saline drops for the blurriness. But they never helped for long. She loved sewing, but couldn't thread a needle, much less evaluate what she'd sewn. And as a seventh grade teacher of family consumer science, this situation was unworkable.

Then, in the doctor's office, she couldn't see the large E on the eye chart.

"It took a while for me to decide it was time for surgery, but it wasn't the thought of surgery itself that held me back," says Peg. "It was the idea around the donor gift that took me more than nine months to wrap my head around. It humbles you to accept a gift of this magnitude. I couldn't stop thinking about the thoughtful generosity of two families, to give such a gift, never knowing what it meant to the recipient. It still amazes me."

Less than 24 hours after Patel performed a partial thickness corneal transplant on one of Peg's eyes, she was seeing 20/45. Her second surgery was just as successful. Today, she's living the life she loves and giving back to all those who made it possible by participating in eye research. Peg participates in ongoing research into Fuchs' dystrophy — not only for herself and her mother, she says, but also for her three children and their futures.

"For anyone who may be facing this disease, I think it's important to first find a corneal specialist that you're comfortable with," says Peg. "Every person's experience with the disease is unique, and each person has a different story to tell. Learn as much as you can about it. There are support groups for people with Fuchs' that can be helpful. Research advances are happening every day, and new procedures are being developed that make the future exciting." ■

Harmonious Resurgence

COURTNEY USES HER VIOLIN TO CONTINUE HER FIGHT **AGAINST A SERIOUS AUTOIMMUNE DISEASE.**

Last August, Courtney Engel stood backstage contemplating a violin recital she was about to give in Eau Claire, Wis. A crowd of maybe 100 people would be nice, she thought. But after the first hundred took their seats, people kept filling the lobby and entering the concert hall.

They arrived from Washington, D.C., San Diego, the Twin Cities and all over the country. Some hadn't seen Courtney, 29 at the time of the recital, since college, and a few hadn't even known that she was an accomplished violinist. By the time Courtney took the stage and played her opening notes, 300 people were in the audience.

Word of the recital had spread and Courtney's friends and admirers responded enthusiastically. It was her first time on stage as a soloist since she'd suffered a devastating loss of vision after developing neuromyelitis optica (NMO).

Sometimes called Devic's syndrome, NMO is an uncommon autoimmune disease similar to multiple sclerosis. NMO sets the body's own immune system against the optic nerves or the spinal cord, resulting in inflammation and often life-threatening damage. Its cause is unknown.

Courtney and her husband, Jake, had many reasons for deciding to give the recital. Preparing for the concert lifted her spirits and gave her a creative goal after months of fighting the disease. She wanted to reward her friends and family members who had endured with her while the outcome of her condition was uncertain. And she loved the music — she has played the violin since the age of four.

Most of all, though, Courtney committed to the concert out of gratitude and a deep desire to raise awareness about NMO. With the help of her caregivers at Mayo Clinic, she received an accurate diagnosis and underwent treatment that halted the unchecked advance of her NMO. Mayo Clinic is one of the world's leading centers for the study and treatment of NMO, and Courtney's recital raised $14,000 for its research. Her yearlong odyssey with NMO had left her, at last, ready to give back and move forward.

Looking back

Courtney noticed something wrong with her eyesight at the close of summer 2008. This was two months after her marriage to Jake Engel and a few days before she was to resume her work as an orchestra director and teacher at John Muir Middle School in Wausau, Wis. The field of vision of her left eye was gradually shrinking. "It started going dark on the top and sinking down," she remembers. "It took a couple of weeks for it to go down to nothing." After her local eye clinic couldn't diagnose the problem or recommend any treatment, she obtained a referral to Mayo Clinic.

"I went to Mayo on Thanksgiving weekend in 2008, and I was there pretty much all day in Ophthalmology and Neurology getting tests and seeing doctors," Courtney says. The tests showed that Courtney's blood contains an antibody called NMO-IgG, which is found in the blood of the majority of people with NMO.

Neurologist Mark Keegan, M.D., contacted Courtney with the NMO diagnosis. In the past this diagnosis meant a high probability of disability or death within five years, but now — thanks to research and treatments pioneered at Mayo Clinic — patients' prospects are much brighter.

> "Without a supportive and loving network of family and friends behind you," she adds, "this disease would be nearly impossible to deal with."

Courtney began a series of treatments involving the exchange of her blood plasma for new plasma that did not contain the NMO-IgG antibody responsible for the inflammation of her optic nerve. In addition, she started a regimen of medications that suppress the immune system. Over time, "these drugs produce lots of side effects, including risks of infection, some kinds of cancer and problems during pregnancy," says Sean Pittock, M.D., a Mayo neurologist who assisted in Courtney's treatment. Courtney knew that there was no cure for the disease, but she held hope that the progress of her NMO had been halted.

Throughout her ordeal, although exhausted by plasma treatments and aware of the seriousness of her disease, Courtney had been coming to terms with the loss of her vision by calmly continuing to teach. "After the first attack, I felt better — not completely better emotionally, but I believed I was going to get through it," she says. She led her classes and directed the school orchestra. Then, however, there came an unexpected second attack.

In February 2010, on the night of a school orchestra concert, the vision in Courtney's right eye began to dim. "I was up on stage, and I thought things were darker, but I wasn't really sure," she recalls. "We went out to eat afterward, and I kept asking Jake for help because I was having trouble reading the menu. I was terrified. What happens if I wake up in the morning and can't see anything? And that's what happened."

Plasma exchange restored some vision to her right eye, and she now describes its acuity "as if I'm looking through a frosted window. I can see colors, I can see shapes, but everything is kind of blurry." She never regained vision in her left eye but has experienced no attacks since that winter of 2010. Courtney still teaches at John Muir Middle School — many of her students barely notice her vision loss. Eventually she stopped performing in the Central Wisconsin Symphony Orchestra because she could no longer read standard sheet music.

Lacking that ability, Courtney prepared for her fundraising recital by laboriously memorizing each work on the program, two measures at a time. The concert totaled about a thousand measures. Her reward for all of that time spent in practice was the satisfaction of contributing to Mayo's NMO research efforts. "It's Mayo that found my diagnosis and is leading NMO research," Courtney says. "As an orphan disease, there's not much funding going into it. The people at Mayo Clinic took care of me and I know they'll do the most with the money that we raised." But it doesn't stop there. "Without a supportive and loving network of family and friends behind you," she adds, "this disease would be nearly impossible to deal with."

New hope through research

Mayo's approach to NMO research — which draws from experts in genetics, pathology, neurology, and the translation of laboratory advances to patient treatment — has brought recognition that NMO differs from multiple sclerosis in crucial ways and is responsive to immunosuppressive treatment. Someday, with continued support from funding organizations like the Guthy-Jackson Charitable Foundation and individuals like Courtney, Mayo researchers may find a way to suppress the harmful NMO-IgG antibody while leaving the rest of the immune system strong.

"Courtney embodies the strength of character necessary to get through a very tough disease," neurologist Pittock says. "She shows a great sense of hope in the future by continuing life as normally as she can. It's incredible that she goes into the classroom and teaches music and leads an orchestra. She symbolizes the rapid advances we've made in understanding her disease. Now we want to find a cure." ■

Mayo Clinic and NMO

For years NMO, an immunological disorder occurring in 1 in 100,000 people that damages the optic nerves and spinal cord, was considered a variety of multiple sclerosis (MS) and therefore merited the same treatments.

In 2004, however, Mayo Clinic researchers discovered an antibody marker in most NMO patients that is not present in people who have MS. Since then, it's become clear that NMO demands specialized treatments and affects the body differently than MS. The clinic broke new ground in 2006 by developing a revised set of diagnostic criteria for distinguishing NMO.

When Mayo physicians diagnose NMO in a patient, they begin a double-edged course of treatment. Patients receive corticosteroid medication to immediately relieve the inflammation of an ongoing NMO attack. And to remove the cells that are attacking the body's own tissues and help prevent future attacks, patients undergo plasma exchange — a periodic replacement of the liquid component of blood that contains antibodies. "Many NMO patients who experienced severe spinal cord attacks used to develop respiratory failure and many would die, but plasma exchange can prevent that," says Brian Weinshenker, M.D., a Mayo neurologist who often treats NMO patients.

When the disease targets the optic nerves, as in Courtney's case, vision in both eyes is at risk. Most NMO patients continue to receive treatments to suppress the immune system for several years to prevent unpredictable harm to the eyes or spine. "Right now we have no cure for the condition," Weinshenker says, "just ongoing treatment."

He is optimistic, though, that research at Mayo Clinic and elsewhere may someday lead to more effective treatments. In the future it may be possible to neutralize the specific antibody that causes NMO damage, which will make it unnecessary to suppress the patient's entire immune system. The funds that Courtney raised through her recital edge the clinic closer to that goal. ■

In Pursuit of Innovation

> In the fields of observation, chance favors the prepared mind.
>
> Louis Pasteur (1854)

Where do important ideas in medicine begin? Although much has been written about the role of serendipity in medical research and scientific discovery, most modern day experts in innovation and creativity agree with Louis Pasteur. Sudden flashes of insight or breakthroughs don't just happen. They emerge from minds prepared by hard work and open to new possibilities.

So-called chance discoveries are usually the outcome of relentless perseverance. It's not serendipity so much as sagacity — the ability to take utterly dissimilar facts and recognize their connection to the pattern of information emerging before us.

The stories behind Mayo's medical discoveries are often fascinating and full of wonder. Yet, we forget at times that years of study and thoughtful observation go into each discovery and the new ideas it generates. It's impossible to relate them all, so we've arbitrarily selected these five. In the short vignettes presented here, you may recognize the role of chance, lucky encounters, unexpected surprises, the timely collision of ideas and even the unlikely connections that sometimes play a part in Mayo Clinic discoveries.

A Startling Discovery

Why do cancer cells spread? The answer must be somewhere in the cells themselves, right? After all, their behaviors are the oddest thing about cancer cells. They grow uncontrollably and travel where they shouldn't. Even their shape is odd.

"That's the traditional way of thinking about cancer metastasis, where the cells leave their site of origin and form tumors throughout the body," says Panos Anastasiadis, Ph.D., who has studied that lethal process for more than two decades. Recently he made a startling discovery. And he did so by looking not at the cancer cells, but outside them.

Anastasiadis found a gene that regulates the permeability of blood vessels, making them "tight" or "leaky." Different versions of the gene appear to make blood vessels especially permeable, which may promote metastasis, he believes, because cancer cells move into — and out of — blood vessels to spread throughout the body.

His early studies support this hypothesis, but they suggest something even more far-reaching. The gene also may have a role in several serious conditions, such as heart defects, strokes and other vascular-related diseases.

So, what's next?

"In the short term, we think we can use this mutation as a marker, to help predict the likelihood that a tumor will metastasize," Anastasiadis says. "But further out, we think we can develop drugs to correct the leakiness, and now it seems those treatments may have applicability beyond cancer. It's a fascinating story and one that emerged after four years of work. So, it just proves that you have to be persistent."

> "In the short term, we think we can use this mutation as a marker, to help predict the likelihood that a tumor will metastasize."

An Unlikely Connection

The body's most mysterious organ, the brain, is a ripe place for discoveries, and recent research by neuroscientist Guojun Bu, Ph.D., at Mayo Clinic in Florida is a great example.

Bu has spent the last 20 years studying cholesterol transport and its role in memory, Alzheimer's disease and other dementias. Earlier this year he discovered that memory is significantly impaired in mice with genetically engineered brains that lack a critical receptor for cholesterol called LRP1. That discovery, however, wasn't the big surprise. In fact it confirmed his long-standing hypothesis.

The surprise was that in addition to poor memory, the experimental mice were obese, twice the weight of their "normal" counterparts, and they ate with reckless abandon. They were also insulin resistant, which we know is a precursor to diabetes.

This finding suggests that it may be possible to combat not just dementias, but also obesity and even diabetes with a genetic therapy that amplifies LRP1's appetite-suppressing signals. Bu intends to continue examining those possibilities in future studies.

To him, the results are "a small justice" to obese people, providing more evidence of a genetic link to obesity, as opposed to just lifestyle factors.

A Needle in the Haystack

A Mayo research team recently identified a protein with a hefty one-two punch: it can predict which pancreatic cancer patients will likely respond to chemotherapy, and, at the same time, it can kill tumor cells. The protein is called FKBP5.

So how did Liewei Wang, M.D., Ph.D., and Zhenkun Lou, Ph.D., and their colleagues find this one protein out of the millions and millions in the universe of our bodies? Persistence. Talent. Experience. Teamwork. Technology. And lots of each.

"Not until we used the unbiased approach of genomewide association study did a red flag go up on that protein," says Wang.

This high-throughput computerized technique, which analyzed cell lines from 300 people, quickly identified FKBP5, a protein present in many people with pancreatic cancer. The FKBP5 protein was a new target never before suspected to be involved in cancer.

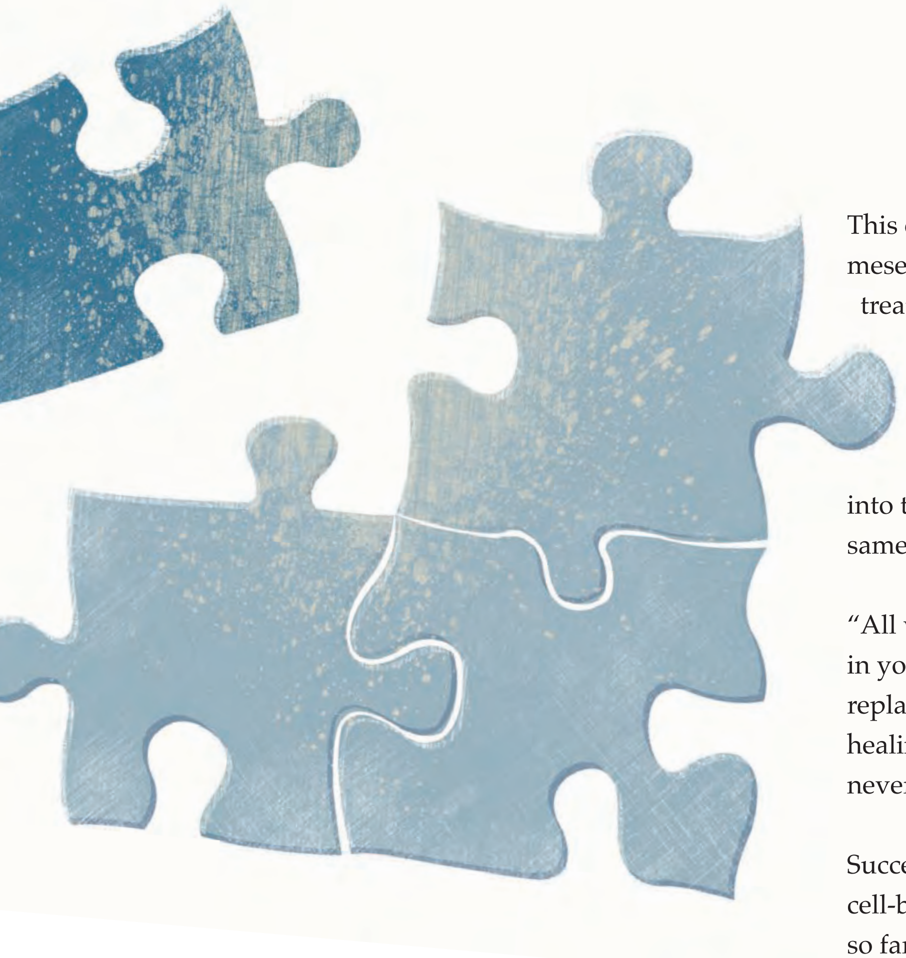
Wang brought her findings to Lou, a colleague and a cell biologist who happens to be her husband. She asked him to help validate her hypothesis that FKBP5 was important to control cancer cells.

Lou got busy and tested the protein to see how it affected a common cancer signaling pathway involving a gene called AKT. Then, in one of his experiments, Lou noticed that AKT activity had changed. That's when he knew they had something special: confirmation that FKBP5 had strong cancer-fighting characteristics.

This finding may lead to the first new drug option for pancreatic cancer since 1996.

Partnering among high-throughput geneticists, statisticians and basic biologists is an increasingly successful model of doing science. Wang says, "Together we add another layer of information, and we take another step closer to the goal: longer survival and the right drug for the right person."

This finding may lead to the first new drug option for pancreatic cancer since 1996.



A Hallway Exchange

Have you ever been stumped by a jigsaw puzzle, then someone walks in, drops a piece in place, and suddenly you see what you hadn't? That's the kind of chance encounter that led to a one-of-a-kind test using stem cells to treat people who have amyotrophic lateral sclerosis (ALS).

Mayo scientist Allan Dietz, Ph.D., had perfected a way of quickly growing safe, stable stem cells that fight inflammation and help cells heal. Mayo physician-scientist Anthony Windebank, M.D., had long studied ALS and was interested in using stem cells to treat it, but he had no cells deemed pure and safe enough to test in humans. Each had something the other needed, but didn't know it, until they happened to chat in the hallway.

This exchange led to the first-in-human trial of mesenchymal stem cells derived from fat for the treatment of ALS. Windebank needed about 10 million cells to begin, so Dietz harvested a half-teaspoon of fat from a subject with ALS, grew the cells in his lab and gave them to Windebank's research team to inject into the fluid space around the spinal cord of that same patient.

"All we're really doing is taking cells already in your body, building an army of them and replacing them to enhance the body's natural healing processes," says Dietz. "But this has never been done before."

Success in these tests will set the stage for a cell-based therapy for ALS, a disease that has so far resisted all treatments tested in humans. This particular stem cell has even more tricks up its sleeve — a sort of built-in GPS, the ability to home in on diseased tissue. "Stem cells are perfect for the job because they can cross the blood-brain barrier, which has always limited our ability to get drugs to the damaged area," Windebank says. This could make it a highly effective delivery mechanism for the treatment of a number of autoimmune or other diseases.

A Backward Look

"Breast cancer is still the number one cancer of women," says Richard Weinshilboum, M.D. "Of the approximately 200,000 to 250,000 women who will develop breast cancer this year, about 70 to 80 percent will have cancers that respond to estrogens. In these women, estrogen makes the cancer grow. We want to turn off those estrogen effects."

One drug, tamoxifen, has been around for about 20 years. Tamoxifen can cut the recurrence rate by half for women with these kinds of tumors. Half a million women would not be alive today without tamoxifen.

But not everybody responds to tamoxifen.

Tamoxifen is supposed to get in and block the receptor for estrogens, but, surprisingly, tamoxifen itself isn't the agent. Rather it's the machinery of the body that converts tamoxifen into something that does the work of blocking that estrogen receptor. For genetic reasons, about 5 to 10 percent of women with European ancestry don't have that conversion machinery.

"We were able to prove this from research done by my colleague Dr. Ingle in the 1980s," says Weinshilboum. James Ingle, M.D., of Mayo Clinic, studied women on tamoxifen for 15 years. Weinshilboum's team was able to go back to those tumor samples to extract DNA. Results showed that the women who couldn't convert tamoxifen into an active estrogen receptor blocker had fared much worse through the course of their illnesses.

As a result, we now have an alternative drug, aromatase inhibitors. These drugs work by blocking the body's ability to make estrogens. "We believe our studies and findings with tamoxifen and endoxifen are vital in making a positive difference in the care of women with certain kinds of breast cancer," Weinshilboum says.

> "Breast cancer is still the number one cancer of women."

Making Good Ideas into Great Discoveries

Perhaps the critical question in medicine is less about where important ideas begin, and more about how those ideas survive to eventually become breakthrough approaches and new treatments.

To pursue a big idea or the possibility of a medical breakthrough is neither a quick nor an easy process. It takes years of perseverance and uncommon dedication. And always behind the fascinating stories of medical discovery are the tireless minds and passionate hearts of a network of researchers, educators and clinicians who raise new questions and believe in new possibilities.

Without support, however, questions and possibilities remain just that — good ideas. Largely through the support of grants and generous private donations, good ideas are nurtured through arduous paths to become medical breakthroughs. ■

If These Walls Could Talk

Honoring Our Benefactors

Philanthropy at Mayo Clinic began with its founders, and the tradition of giving continues to be a hallmark of Mayo's practice today.

> Mayo benefactors are people from around the world and all walks of life. Their generosity supports Mayo's belief that health care is for the good of all people and the needs of the patient come first.

Philanthropic recognition levels honor benefactors who offer their partnership and support to Mayo Clinic.

This outpouring of generosity strengthens Mayo's accomplishments in research, education and patient care. Without philanthropy, Mayo's mission could not be sustained.

◆

Mayo honors benefactors throughout its campuses in a variety of ways. The names of the people and organizations displayed represent unique stories of giving.

◆

Featured in the Halls of Benefactors located at all campuses in Minnesota, Florida and Arizona are the names of those whose giving totals more than $100,000. Each name is hand engraved on quarried slate from Vermont and Pennsylvania. Each slate piece is different in its veining, which represents the uniqueness of the individuals and organizations represented.

◆

Patients, families and visitors see marble from around the world. The different colors, textures and reflections impart a sense of security and well-being.

◆

A green marble wall in Rochester honors the foremost benefactors of Mayo Clinic. The individuals and organizations named here represent many generations, many places and many walks of life. They share a commitment to helping achieve a healthier future by investing their gifts in the facilities and programs of Mayo Clinic.

Mayo recognizes that each benefactor brings a story with their gift. To capture some of the stories and honor Philanthropic Partners, customized storyboards are located in prominent locations throughout the Mayo campuses.

◆

Electronic recognition kiosks are located in high-traffic areas on the Mayo Clinic campuses. These "electronic family albums" honor members of recognition groups and alumni societies.

◆

For all levels of gifts, Mayo expresses its gratitude. ■

Big Hearts
Little Hands

You don't need a lot of money to make an impact on the lives of Mayo Clinic patients. Philanthropy has a long-standing history at Mayo Clinic. After all, Mayo Clinic itself was established through the generous philanthropy of its founders, Drs. William J. and Charles H. Mayo and their wives, Hattie and Edith. There was a time when the word "philanthropist" conjured up images of only the very wealthy. But these days, something is changing. Social research shows a skyrocketing interest in the number of young children and teenagers involved in philanthropy.

In this story, we introduce you to three philanthropic young girls who are putting their entrepreneurial skills to work to help Mayo Clinic.

Emma Field
Age: 8

What she's doing: Raising money to help advance Mayo Clinic's melanoma research efforts.

Why she's doing it: Emma's father, David, lost his battle with melanoma on Aug. 28, 2009. After watching her dad go through his treatments at Mayo Clinic, Emma decided she wanted to do something to try to help her father's oncologist, Svetomir N. Markovic, M.D., Ph.D., find a cure for the disease that had taken her father. "Dr. Markovic was so good to my dad," Emma says. "My mom said that he treated him like his brother. This experience has made me realize that I like to help other people. And even though I'm sad that I don't have my dad anymore, this makes me feel happy."

How she's doing it: After her father's diagnosis, Emma and her family became involved in their local chapter of the American Cancer Society. As they were preparing to participate in last year's Relay for Life event in their hometown of Langdon, N.D., it was Emma's job to design T-shirts for the 25 members of "Team Scrappy." Why? Because "Scrappy" was a nickname Emma's father had earned during his high school wrestling days.

As she was designing the T-shirts, Emma decided that she was going to try to sell them to help raise money for melanoma research at Mayo Clinic in order to, in her words, "help find some answers for people with melanoma."

She made good on that recently when she came to Mayo Clinic to surprise Dr. Markovic with a check for $1,000 — money she'd raised from her T-shirt sales. She's not done, though. This year, Emma says she intends to more than double her initial contribution. "We raised $1,000 last year, so this year I want to raise that goal to $2,500," she says.

Svetomir N. Markovic, M.D., is the Charles F. Mathy Professor of Melanoma Research at Mayo Clinic.

Maria Keller

Age: 9

What she's doing: Donating new and used books to children with cancer at the Mayo Clinic T. Denny Sanford Pediatric Center.

Why she's doing it: "I really want kids who don't have books to own their own," Maria says. "And after I'd learned of the need for books on the different children's units at Mayo, I decided I wanted to help. By giving books to the kids at Mayo, maybe that will make them forget about their illness for maybe even just a few minutes. If the books can do that, I think that's a huge gift that I can give to them."

How she's doing it: Maria is quite an entrepreneur. At the age of 8, she founded Read Indeed, a 501c3 nonprofit literacy organization with the lofty goal of donating 1 million books by her 18th birthday. A year later, at the age of 9, Maria is already nearing the halfway point.

She's collecting her books the old-fashioned way — by holding book drives. Others around the country are jumping on board to help, including schools, businesses and even professional basketball teams like the Minnesota Timberwolves, which donated 1,200 books to Read Indeed. Maria then donated those 1,200 books to Mayo's Pediatric Center.

Katie Boland

Age: 10

What she's doing: Raising money to buy presents for children who are hospitalized at Mayo Clinic over the holidays.

Why she's doing it: Katie suffers from nocturnal frontal lobe seizures, which began when she was only 2 years old. She started coming to Mayo Clinic five years ago after other medical centers had failed to help.

During the family's first visit to Mayo, Katie was required to stay at Saint Marys Hospital. It was during the holidays, and she occupied her time with craft projects while doctors performed EEG tests. Occasionally during her stay, Katie would venture out to the hospital's "kids room" to make snow globes with the other children. After an opportunity to see and meet other kids who were going through the same thing, Katie told her mom, then and there, that she wanted to raise money to buy presents for kids who have to stay at Mayo Clinic during the holidays.

How she's doing it: Like any good young entrepreneur, Katie started her fundraising efforts close to home — with her grandparents. "Katie was not shy about talking with people about her fundraiser," says her mom, Sara Boland. "As soon as she knew that she could help raise money for Mayo Clinic, she got on the phone and called her grandparents to ask if they would donate money. She then asked our neighbors and many other people we know, including my co-workers, who were quite amazed by her little entrepreneurial personality and her excitement about what she was raising money for." ■

Brains Together for a Cure

MAYO EMPLOYEES AND FRIENDS EMBARK ON A GRASSROOTS EFFORT TO HELP RAISE MONEY AND AWARENESS **FOR BRAIN TUMOR RESEARCH AT MAYO CLINIC.**

Shelly Kuhlmann knew something was wrong with her husband. In 2005, he started getting crippling headaches.

“Mike had never been one to get headaches and these were headaches that totally took him down,” Shelly says. “But there were only a few so we never thought much of it.”

Four months later, Mike told his wife that he thought he needed new glasses because his computer screen at work was getting hard to see. A short time later, he got another headache, but this one wouldn’t go away.

“The pain was in the front of his head between his eyes, and again we thought it was nothing,” Shelly says.

"That's when we learned about the mass in his brain," she says. Mike was diagnosed with glioblastoma, the most common and most aggressive brain tumor. With treatment, doctors gave him one to two years to live. Without treatment, six months. Tops.

He was scheduled for a series of chemotherapy and radiation treatments at Mayo Clinic's Rochester campus and along the way participated in several clinical trials. After his diagnosis, the Kuhlmanns lived from MRI scan to MRI scan as doctors worked to slow the tumor's growth.

"He never had an MRI that was clean," Shelly recalls. "There was always something growing." Mike had surgery in July 2007, but by then the tumor had done too much damage. He lived for another year before finally succumbing in August 2008. The following May, still mourning the loss of her husband, Shelly received more bad news. Her brother had been diagnosed with the exact type of brain tumor that had taken Mike just months before. This time, however, surgery wasn't an option. Her brother passed away a short time later.

From tragedy comes opportunity

After suffering such pain and loss, Shelly might have isolated herself from the rest of the world as she came to terms with her new reality. But she didn't.

During one of her husband's clinical trials, Shelly had come to know Sue Steinmetz, who works as a clinical trial coordinator for Mayo Clinic. After the deaths of Shelly's husband and brother, the two women, along with Mayo employees Deb Sprau, Faith Omberg and Sue Hruska (who was battling a brain tumor of her own) formed an organization called Brains Together for a Cure. The group's mission is simple: To promote awareness of brain tumors and the need for effective treatments. Four months after forming their new nonprofit organization in 2007, they made good on that mission by holding their first event — a fundraising walk at the Rochester Community and Technical College Field House. It attracted 527 participants and raised more than $38,000.

The organization, which is not affiliated with Mayo Clinic and whose founders do all of its work in their spare time, has held the same fundraising walk every year. Last year Brains Together for a Cure achieved Mayo's Major Benefactor status by raising a combined total of more than $228,180 for brain cancer research at Mayo Clinic. ■

Working Toward a Cure

Mayo Clinic neurologist Joon Uhm, M.D., who also serves on the Brains Together for a Cure Scientific Review Board, says a lot is known about brain tumors and what makes a brain tumor cell do what it does. What's not yet known, he says, is how to stop that behavior.

"A big challenge is getting the drug delivered into the brain," Uhm says. "The brain lives beyond the firewall, so to speak, of something we call the blood-brain barrier. So even if we have a drug that will kill cancer cells, it's of no use unless we can get it to the site where it's needed. And even when we get an effective drug, it may stop one disease process, but the tumor will now use something else to make up for it. So a big challenge is to come up with the effective combination of therapies that will then become the effective treatment. And how do we do that without combining toxicity and side effects to the patient?"

Uhm says that as of yet, we don't understand the direct cause of brain tumors. "But if we can get at that," he says, "it will be better than a cure because it could lead to prevention."

"It would be nice if we could say, 'Stop doing this, or stop doing that, and you'll be less likely to get a brain tumor,'" Uhm adds. "But science hasn't identified a clear environmental or lifestyle link with brain tumors. Right now all we can say is that what most tumors — brain, lung, prostate, it really doesn't matter — have in common is that they all cause damage to a person's DNA. Now, what causes that damage in the first place? It could be the things we eat or environmental exposures. We just haven't identified that in brain tumors yet." ■

> "A big challenge is getting the drug delivered into the brain."

One of the mainstays of the group was co-founder Sue Hruska, who after a four-year fight, lost her own battle with brain cancer on July 11, 2010.

During last year's walk, the group, including Hruska's husband, Ed, donated $1,111.11 in her honor.

> “Sue was a very positive person,” **Sue Steinmetz says.** “Even when she had reoccurrence after reoccurrence, she was still one of those people who gave inspiration to everybody else. This group meant so much to Sue, and I want to make sure that we carry the torch for her.”

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> “A big challenge is getting the drug delivered into the brain.”

Life's Blueprints

The doors of the hospital opened on hallways that led to an unfamiliar world. Don Hughes would walk the length of those hospital hallways more than once as he waited for his father to come from surgery. His father was undergoing a lung transplant, and Don was gaining a new perspective on life.

During his father's illness, Don had learned about lung transplantation. Now he also learned what it meant to drop everything when the call came to say an organ was available. He understood how to live between a suitcase and a hotel. And, most importantly, he knew how to face a long, uncertain night on a waiting room couch.

Don's father had been in his 50s when he'd turned to Mayo Clinic for answers to an ongoing cough and related health issues. Doctors diagnosed his condition as idiopathic pulmonary fibrosis — a debilitating lung disease, without a known cause, which makes the lungs stiff, scarred and progressively unable to oxygenate the body.

Like many others with this type of lung disease, Don's father eventually required a lung transplant. After the successful transplant in a New York City hospital, the elder Mr. Hughes lived a much-improved life until passing away in December 2008.

Yet the ordeal revealed to Don and his wife, Linda, a perspective much broader than the hallways of a hospital. They saw into the reality of the sacrifices caregivers make during the transplant process, and they gained a unique perspective on the mission of the Village at Mayo Clinic, a hospitality facility for transplant and cancer patients, located on the Phoenix campus.

"If a person couldn't afford a room close to the medical facility it would be really tough," says

> “Everyone has their hardships, but also their blessings. We’ve been blessed to be able to give. This is something our hearts have been nudged to do.”

Don. “Commuting isn’t a real option for people so sick they require a transplant.”

During his father’s illness, Don felt the struggle of people who couldn’t afford the extended stays and the associated costs of staying nearby when loved ones were undergoing medical care. He could see how such situations add to a family’s stress and make it difficult for them to meet people going through the same experiences.

And it solidified in him the need for a facility like the Village at Mayo Clinic — so Don and Linda were moved to make a gift in their father’s honor.

It takes a Village

“We weren’t taking this gift lightly,” Linda says. “We committed to praying and considering what to support and how much of a gift we would commit to.”

Linda recalls meeting with a development officer and reviewing material on the Village at Mayo Clinic. “When I saw the information about the casitas at the Village my jaw dropped,” she says. “I knew in my heart it was the right fit. But I also knew the decision had to come from Don.”

After discussing what it would mean to others going through experiences like their own, Don and Linda agreed the project was an opportunity. At that point, the decision was about what aspect of the Village at Mayo Clinic project the couple would support: a kitchen or a veranda?

“We chose the kitchen because that is where families gather — either to chat or eat,” Don says. “Plus, my dad loved food.”

Don thought about how a facility like the Village would have helped his family when they went through the transplant process.

“The project is so rewarding — and not only for those who are using it,” he says. “It’s great for us as well. Hearing stories about the people staying at the Village is so rewarding.”

Passing it on

Faith and family are the bedrock of strength for Don and Linda Hughes.

“We feel strongly about the call for generosity,” says Linda. “‘From everyone who has been given much, much will be demanded; and from the one who has been entrusted with much, much more will be asked.’ Everyone has their hardships, but also their blessings. We’ve been blessed to be able to give. This is something our hearts have been nudged to do.”

“We were fortunate to have wonderful role models for giving,” adds Don. “I have memories of my parents donating their time to events to help others, and my grandmother did the same. My belief is if there are ways to help other people and if we can do it, we should do it.”

Looking into the future Don and Linda hope to continue supporting projects focused on helping people who are suffering.

“It feels like the right thing to do, and God willing we’ll be able to continue helping people,” says Don.

It’s a perspective Don and Linda Hughes plan to pass down to their daughter, Flynn. And when she’s old enough they’ll involve her.

“It is our hope to model for Flynn what we have seen through our parents. We want to teach her to give — not just give back,” said Linda. ■

Surrounding Diabetes

Discovered more than 90 years ago, insulin still plays a critical role in the fight against diabetes.

> "Even though the landscape of diabetes management has changed dramatically, insulin remains as essential today as the day it was discovered. If there's one thing I want people to take away from this story, it's that the work being done at any given moment could provide the next breakthrough."
>
> Arthur Ainsberg, in a presentation about the discovery of insulin to the Mayo Clinic Historical Committee on Nov. 19, 2010.

During the fall of 1919, Russell Wilder, M.D., joined the staff of Mayo Clinic as an associate in the Division of Medicine. Widely considered one of the most influential endocrinologists of his time, Wilder was placed in charge of Mayo's patients with diabetes.

Shortly after insulin was discovered in 1922, Wilder was part of a small group of experts who gathered in Toronto, Canada, to conduct a clinical evaluation of this medication. In the years since, insulin has helped millions live a normal life, both in quality and length. Yet an effective cure for diabetes remains just out of reach, something researchers at Mayo Clinic continue to work hard to change.

Where Are We Today?

“What everyone’s still trying to figure out is how to get insulin into the body the right way,” says Robert Rizza, M.D., Mayo Clinic’s executive dean of research and past president of the American Diabetes Association. “What does it take to repair a person’s insulin-secreting cells? Why do they die? How do we stop them from dying? And if someone has diabetes, how do we treat it to prevent problems or complications?”

Tough questions. They’re questions the medical profession has been trying to answer for more than a century.

“Right now, we’re looking at therapies to regulate metabolism, the liver, the muscles, fat and cells,” Rizza says. “How can we make the cells live? What makes them die? And we’re now beginning to understand why insulin-secreting cells do what they do.”

Stephen Russell, M.D., Ph.D., director of Mayo Clinic’s Molecular Medicine program, and someone who has lived with type 1 diabetes for the past 28 years, says that a perfect solution to diabetes will likely be one of several approaches.

“One approach is an artificial pancreas, a machine that mimics the pancreas by measuring blood glucose constantly and delivering insulin at an amount that’s commensurate with a person’s blood sugar,” he says. “There’s a lot of science going into that area right now. The other approach is to replace the pancreas by transplant. But that’s not practical for most patients.”

The alternative to pancreatic transplant, which Mayo is working on, concerns regenerative medicine. More specifically, Mayo researchers want to generate cells that can sense glucose, release insulin into the body and function just as the other cells in the pancreas do. That’s where Mayo’s Yasuhiro Ikeda, D.V.M., Ph.D., comes in.

An iPS Approach

From his lab in the Guggenheim Building on Mayo’s Rochester campus, Ikeda has spent the past few years looking for a successful way to take skin cells from a variety of sites on the human body and convert them into cells that produce glucose and insulin. So far, however, the technology that uses induced pluripotent stem cells (iPS) — normal adult cells that have been coached to act like stem cells — hasn’t been without its own set of problems.

“As soon as we transplant the cells into mice, they don’t work so well,” Russell explains. “Plus, they tend to form tumors. So that’s the next hurdle. How do we actually turn these iPS cells into good, functioning cells?”

Ikeda is trying to solve that riddle by carefully selecting the cells that he uses.

“Before transplanting the cells, we make sure to choose only completely differentiated cells,” Ikeda says. Limiting the genes that are used at the start of the process also seems to help reduce the growth of tumors.

Despite these scientific hurdles, both Russell and Ikeda say Mayo remains committed to developing the iPS technology because, if successful, it will mean an almost limitless supply of cells that could be used to treat patients with diabetes.

Preventing Diabetes with Lifestyle and Diet

Lifestyle and diet are key factors. Mayo Clinic endocrinologist K. Sreekumaran Nair, M.D., Ph.D., is a leading researcher on muscle metabolism and its role in aging and diabetes. While it might sound overly simple, Nair’s research shows that a person’s lifestyle and diet are major factors in the onset of diabetes and that the interaction of lifestyle with genetic predisposition is likely the underlying mechanism of type 2 diabetes.

“Diet and exercise are important,” Nair says. “We know that exercise can increase insulin action on fuel metabolism; so we’re doing studies with exercise and its interaction with cell mitochondria (where all fuel metabolisms occur). Knowing the molecular pathways through which exercise enhances fuel metabolism offers the potential to target drugs to improve insulin action even in people who can’t exercise. We’re investigating the muscles and the liver while focusing on insulin deficiency and insulin resistance. We’re making a lot of advances, but we still don’t know the exact mechanism responsible for insulin resistance and the islet cell failure that leads to type 2 diabetes. There’s no one gene that causes diabetes. If there was, we could target that.”

Nair, Ikeda and Russell remain optimistic that work being done in their labs, and in other labs throughout Mayo, will eventually lead to an effective cure.

“What I’ve seen since I became diabetic approximately 28 years ago is that everything just gets better,” Russell says. “Insulin gets better. The devices and disposable injection pens get better. The glucose monitoring devices get better. Everything has undergone incremental improvement. Now these new approaches have the potential to offer a cure. I’m very optimistic about the future.” ■

A Decade of Discovery

“Currently, one of every three Medicare dollars is spent on diabetes-related treatment in our country,” says Robert Rizza, M.D., Mayo Clinic’s executive dean of research. “When we look at the quality-of-life impact of diabetes, combined with an annual price tag of $170 billion nationally, elevating and expediting the ability to tackle this disease isn’t only the right thing to do, it’s a health and economic imperative.”

On Oct. 5, 2010, Mayo Clinic, the Minnesota Partnership for Biotechnology and Medical Genomics and the state of Minnesota announced a new initiative aimed at finding optimal treatments for, and ultimately curing, diabetes within the next 10 years. The initiative, called “Decade of Discovery,” will build on the diabetes research and treatment strengths of both Mayo Clinic and the University of Minnesota.

Those involved say the initiative could help improve the health and quality of life of the more than 24 million Americans who struggle with the medical, financial and emotional effects of diabetes. In doing so, they say it will also help position Mayo Clinic and the state of Minnesota as a global leader in pioneering medical discovery and treatment, while reducing health care costs and generating economic opportunities.

The Whole-istic Approach

PHYSICAL MEDICINE AND REHABILITATION

> “Rehabilitation is to be a master word in medicine.”
>
> William Mayo (1925)

Physical Medicine and Rehabilitation — Helping people live better

Patients arrive with a variety of problems. They have pain — pain in the neck, in the back or shoulders. They have injuries sustained in accidents or disorders of the nervous system that cause trouble with walking, speaking or even thinking. Sometimes they are older adults meeting new physical challenges. Sometimes they are children coming with their parents or parents escorted by their children. A sea of patients swirls together each day in Mayo Clinic’s Department of Physical Medicine and Rehabilitation (PM&R). The PM&R team specializes in returning movement and function to people whose lives are limited by disease or injury.

“It’s what we do best: bring together a wide range of medical specialists focusing their expertise on the different challenges a person might face,” says Kathryn Stolp, M.D., “We pull together these varied talents in ways that our patients can use each day.”

Stolp, a physiatrist who has researched neuromuscular disease, spasticity management and multiple sclerosis care, found herself drawn to physical medicine and rehabilitation while in medical school. “A rehab doctor spoke with us about polio, braces and quality of life after illness, and I thought, ‘That is what I want to do!’” she says.

As of May 1, 2011, Carmen Terzic, M.D., Ph.D., (pictured) was appointed chair for Mayo’s PM&R department.

> “It’s what we do best: bring together a wide range of medical specialists focusing their expertise on the different challenges a person might face.”

Dr. Kathryn Stolp (pictured) served as department chair for the past eight years.

Mayo’s PM&R department is one of the oldest in the country, and it evolved from a venerable medical tradition. “Our specialty grew out of the consequences of people who were increasingly surviving catastrophic injuries,” Stolp explains. The world wars and polio epidemics of the 20th century left behind disabled but otherwise healthy people who needed to return to their families, communities and places of work. The experts in physical medicine and rehabilitation — called physiatrists — helped them compensate and adapt.

The rehabilitation experts of today’s PM&R department at Mayo follow a philosophy that stresses returning to social participation regardless of the problem a person experiences. “That’s important because we work from a wellness rather than sickness point of view,” Stolp says. “If a person is paralyzed in one leg, we don’t want them to say they’re sick and someone else has to take care of them. They aren’t sick; they just have a paralyzed leg. We look not only at ways to treat the paralysis, which is not always possible, but also at its consequences in their daily life. We ask people, ‘What do you want to do?’ We put their goals first. Then we figure out ways to get them there, no matter what’s working or not working in their body. We guide them to achieve their most optimal level of function.”

Mayo's PM&R approach differs from the traditional medical model in another important way. "Traditionally the physician is in charge, and the patient does what the physician says," Stolp says. "Not in PM&R. Although we educate people on what their best choices are, the person with the condition is the head of the team. They tell us their goals, and we help them get there. We do what we can to optimize the quality of people's lives because there is no limit to wellness, quality of life and happiness."

PM&R experts focus on problem solving to produce customized treatments. Many are involved: physiatrists, physical, occupational and speech therapists, psychologists, social workers, dietitians and clergy, depending on the needs of the person being served. They start with the basics of daily function, controlling pain, eating, sleeping comfortably and dealing with bowel and bladder control. Next they concentrate on giving people adequate range of motion for their joints. Then they build strength, aid with mobility and help improve communication.

Rehabilitation experts often use assistive technologies and adaptive ingenuity to help people compensate in other ways. PM&R's depth of expertise in its interdisciplinary teams makes this range of assistance possible. Patients contribute much to the process, as well. "One of the things I like is how much we learn from our patients, who create new ways to cope and bring these ideas back to us," Stolp says. "There have been great ideas over the years, including a mechanism powered by bungee cords to help a paralyzed man pull up his own pants."

> "We do what we can to optimize the quality of people's lives because there is no limit to wellness, quality of life and happiness."

At the other end of the technology spectrum lies PM&R's use of virtual reality programming to educate patients and their families, electrical signaling to treat muscle disorders, a remote telerehabilitation therapy available online and an exoskeletal robotic system that helps paralyzed people relearn how to walk. PM&R can help patients work miracles. Its emphasis on wellness, self-directed treatment, and care not always cure, often keeps PM&R's work out of the medical spotlight. "Because not all medical schools include PM&R training, there are even physicians we work with, as well as nurses and social workers, who don't know what we do," Stolp says.

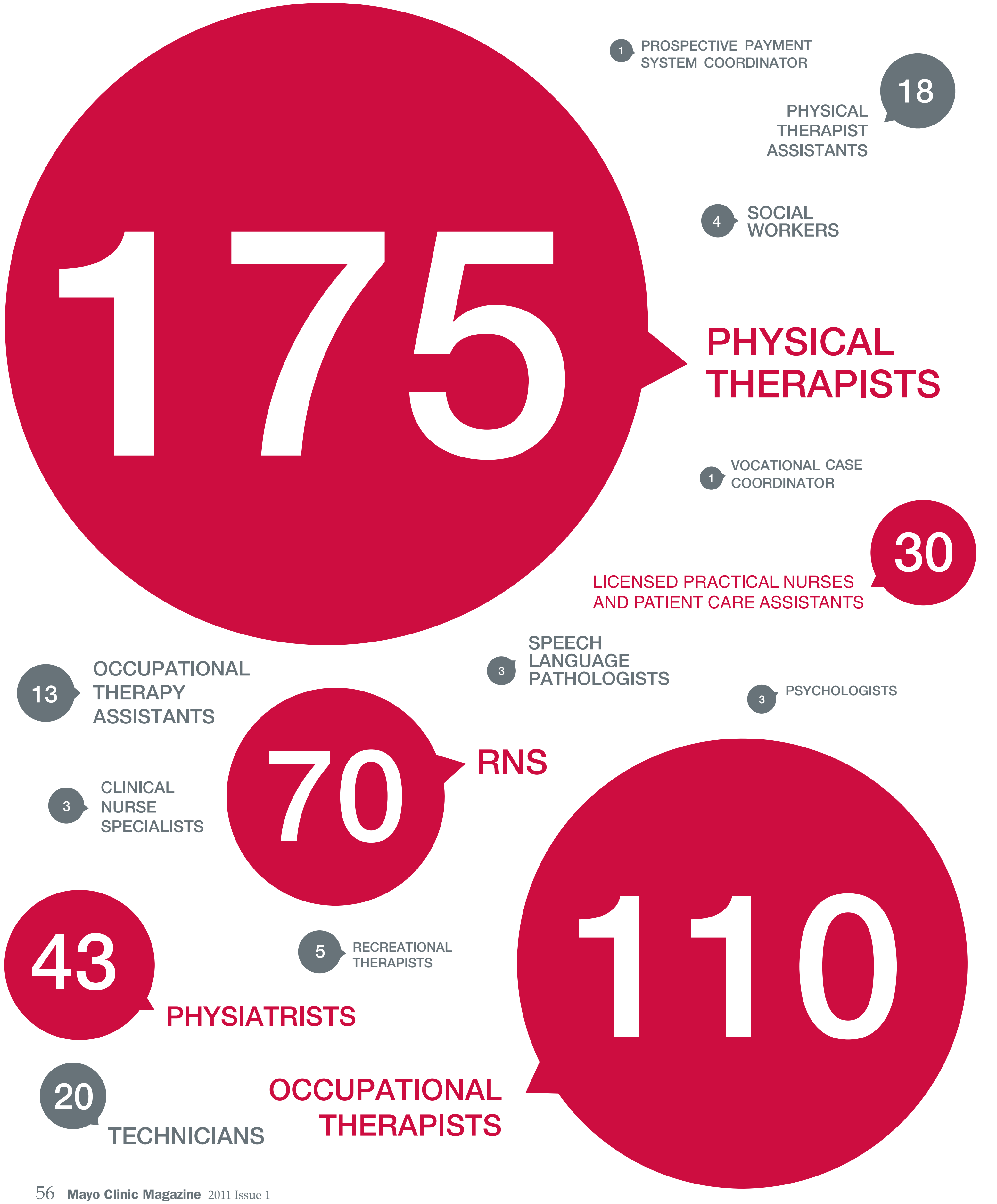
For those who don't understand what PM&R does, Stolp has a simple explanation. "What's meaningful to PM&R is being able to help people meet their own goals, using not only the resources of Mayo Clinic but also those extending beyond and into the community," she says. "We see patients achieve their own goals, and it's rewarding, like watching your children grow up."■

> "I decided that was my dream. And now I live my dream each day."

When asked what influenced her choice of medical specialty, Stolp replied, "Stories about Helen Keller and children's movies, such as *Heidi* and *Pollyanna*, where someone learned to walk again, were inspirational. My father was a dentist and exposed me to various aspects of medicine. He also introduced me to a book called *The Man in the Iron Lung*, about a man who'd lived with the sequelae of polio. I knew I wanted to help people like that — those who found ways to make the best of their lives no matter their physical condition."

She paused to reflect, "I always wanted to be a physician. I was 10 years old when I learned that women could be physicians. I decided that was my dream. And now I live my dream each day."

PHYSICAL MEDICINE AND REHABILITATION PROFESSIONALS



Happenings

Benefactors Support Mayo Clinic

To support **Mayo programs**, gifts from benefactors included in Mayo Clinic's 2010 financial statements **totaled $208 million**. An additional **$151 million** was pledged in trusts, estates and other commitments that will be realized in the future. Support from grateful **patients, foundations, corporations** and other organizations is essential to Mayo Clinic's ability to carry out its mission in practice, **education and research**, and to provide outstanding facilities and technology.

A Mayo Clinic memoir

Mayo is renowned for treating rare and complex medical conditions. One patient who knows this better than most is Thomas A. Long, a retired University of Cincinnati professor of philosophy, who has been treated at Mayo Clinic since 1954.

Mr. Long chronicles his experiences in his memoir, *If This Isn't Cincinnati, It Must Be Mayo*. His story begins in the pre-antibiotic year of 1937 in Cincinnati, where as an infant he struggles with childhood osteomyelitis and related illnesses. The focus of the narrative ultimately shifts to Mayo, where he undergoes a series of lifesaving surgical procedures.

For over 50 years since, Mr. Long has remained a patient of Mayo Clinic. His memoir brings personal experience to bear on the long-term consequences of infection and what it has meant to be treated by Mayo physicians for over half a century.

Mayo Clinic receives $100 million gift to support proton beam therapy program

Longtime Mayo patient and philanthropist Richard O. Jacobson has given a $100 million gift to help establish the Mayo Clinic Proton Beam Therapy Program. This is the largest outright gift in the clinic's history, as well as the largest gift Mr. Jacobson has made to any institution.

Mayo's program will include new facilities on the Rochester and Phoenix campuses; the Rochester building will be named in Mr. Jacobson's honor.

Proton beam therapy represents an advance over traditional radiotherapy to treat some cancers. Mayo's program will use the most advanced intensity-modulated technology, known as pencil beam scanning, which few centers now use. With this technology, patients may experience fewer short- and long-term side effects.

"My dream has always been to establish a major new facility for Mayo Clinic," says Mr. Jacobson. "I began going to Mayo for my care when I was a child and continue to get my care there. Mayo Clinic makes a profound impact on people."

A Belmond, Iowa, native, Mr. Jacobson is founder of Jacobson Companies, headquartered in Des Moines, Iowa.

Board welcomes new trustees

Three new members joined the Mayo Clinic Board of Trustees in February 2011.

Veronique Roger, M.D., M.P.H., is a consultant in the Division of Cardiovascular Diseases with a joint appointment in the Division of Epidemiology. She is director of the Mayo Clinic Center for the Science of Health Care Delivery, chair of Health Sciences Research and a professor of medicine and epidemiology. **Jeffrey Bolton,** Mayo Clinic chief financial officer, was named internal trustee for a four-year term. **Robert Brigham,** chair of administration at Mayo Clinic in Florida, was elected to a one-year term as internal trustee.

> In August 2010 the trustees named Samuel A. Di Piazza, Jr. as a new public trustee. He is the former CEO of PricewaterhouseCoopers International Limited. He was elected to a four-year term.

Named professorships

Named professorships represent the highest academic distinction at Mayo Clinic. These professorships recognize outstanding physicians and scientists for their contributions to research and teaching. A professorship bears the name of the benefactor or honors an individual important to the benefactor.

Gift funds are held in endowment, and all income supports medical education and research. Faculty members are appointed to named professorships through nomination and endorsement by their peers and then confirmed by Mayo Clinic senior leadership. The following professorships were named in 2011:

The **HH Sheikh Khalifa Bin Zayed Al-Nahyan Professorship in Infectious Diseases Honoring Walter R. Wilson** was established by His Highness President of the United Arab Emirates Sheikh Khalifa Bin Zayed Al-Nahyan and the Khalifa Bin Zayed Al-Nahyan Foundation of Abu Dhabi. He is the eldest son of Sheikh Zayed Bin Sultan Al-Nahyan, former president of the United Arab Emirates and a Mayo benefactor who provided support for the Mayo Clinic Zayed Cardiovascular Center. The Al-Nahyan family shares many values with Drs. William J. and Charles H. Mayo: respect for the individual, decision making by consensus, and support for education and research as the keys to a better future.

Larry Baddour, M.D., recipient of the award, is chair of the Division of Infectious Diseases, Department of Medicine. He holds the academic rank of professor of medicine. His research has focused primarily on cardiovascular infections and skin and soft tissue infections. He has investigated several aspects of both native tissue and medical device infections that involve the cardiovascular system, including infective endocarditis, pacemaker and defibrillator infections, and vascular graft infections. Regarding skin and soft tissue infections, he provided the initial description of recurrent cellulitis complicating saphenous venectomy in coronary bypass graft patients in 1982 and an early description of breast cellulitis complicating breast conservation therapy.

The **Joseph I. and Barbara Ashkins Professorship in Surgery** was established in 1986 by Dr. and Mrs. Ashkins, of Dunedin, Fla. Dr. Ashkins was a prominent surgeon at Milford Hospital in Massachusetts. After the couple retired to Florida, friends introduced them to Mayo Clinic, and they developed a lasting patient and benefactor relationship at Mayo Clinic's campuses in Rochester and Florida. For more than 25 years, the Ashkins have provided support for cancer research as well as programs and facilities, medical care, education and research at Mayo Clinic. When Dr. Ashkins died, the couple's tradition of philanthropy continued through a generous planned gift from his estate.

Claude Deschamps, M.D., recipient of the award, is chair and a consultant in the Department of Surgery at Mayo Clinic. Deschamps has served in journal review and editorial activities for publications including *Cancer, Annals of Thoracic Surgery* and *Journal of Thoracic and Cardiovascular Surgery*. Twice he has received the Excellence in Teaching recognition at Mayo Medical School. Deschamps's clinical interest is general thoracic surgery, and his research interests are lung and esophageal physiology and pathophysiology.

The **Vernon F. and Earline D. Dale Professorship** was established in 1977 through a gift from the late Earline Dale of Onalaska, Wis. Vernon Dale was a visionary and entrepreneur who started and ran several successful business ventures. At age 13, he opened a bicycle repair shop. He later sold Harley-Davidson motorcycles, opened Dale's Super Service Garage and started the Onalaska Transportation Company in Wisconsin. He was the general manager of Bump Pump Co. and partner in Metallics, a company that manufactured nameplates. He later founded and was president of Outers Laboratories, a manufacturer of outdoor recreational equipment and gun-cleaning supplies.

Gary Sieck, Ph.D., recipient of the award, is chair of the Department of Physiology and Biomedical Engineering, dean for research academic affairs and deputy director for research. Dr. Sieck, who holds the academic rank of professor of physiology and anesthesiology, is also the director of the Biomedical Engineering Program, Mayo Graduate School. His research focuses on neuromuscular physiology. In skeletal muscles, he has explored neuromuscular plasticity related to spinal cord injury and muscle weakness associated with intensive care and age-related sarcopenia. In airway smooth muscle, he has examined abnormalities in intracellular calcium regulation and excitation-coupling associated with asthma and chronic obstructive pulmonary disease.

The **Carol M. Gatton Professorship in Digestive Diseases Research** honoring Peter Carryer, M.D., was established by Carol "Bill" Gatton. A military veteran, Mr. Gatton entered the U.S. Army as a second lieutenant and completed two years of active duty in 1956. He worked in the banking business for a short while before embarking on a career in automobile dealerships.

In 1985, the Gattons established the Bill Gatton Foundation, with a philanthropic focus on various charitable and educational organizations. Honored as Principal Benefactors, both the Gattons and their foundation have provided generous support to Mayo Clinic.

Reflecting Mr. Gatton's entrepreneurial spirit and desire to support digestive diseases research at Mayo Clinic, this professorship symbolizes his immense gratitude and respect for Peter Carryer, M.D., with whom he established a close relationship over the years. Carryer served as a consultant in the Division of Gastroenterology and

Hepatology, Department of Internal Medicine, at Mayo Clinic in Rochester and held the position of board and operations chair of Mayo Health System. He retired in June 2010.

Keith Lindor, M.D., recipient of this award, is a consultant in the Division of Gastroenterology and Hepatology at Mayo Clinic in Rochester. Lindor serves as dean of Mayo Medical School and holds the academic rank of professor of medicine, Mayo Clinic College of Medicine. He has served as the senior associate editor for *Clinical Gastroenterology and Hepatology* and on numerous committees for the American Association for the Study of Liver Disease. He is on the editorial board of *Gastroenterology* and the *Journal of Clinical Gastroenterology* and is editor-in-chief for *Hepatology*.

The **David F. and Margaret T. Grohne Research Professor of Therapeutics for Cancer Research** was established through the generosity of David F. and Margaret T. Grohne of Wilmington, Ill., and Sarasota, Fla. Mr. Grohne is chair of the board of Independence Tube Corp., where Mrs. Grohne also served as secretary. The company, headquartered in Chicago, manufactures structural steel tubing. The Grohnes have provided support for Mayo Clinic in Arizona and Rochester, including gifts to pulmonary and medical research.

P. Leif Bergsagel, M.D., recipient of the award, is a consultant in the Division of Hematology and Oncology, Department of Internal Medicine, with a joint appointment in Basic Sciences, Research Laboratories. Bergsagel's research focuses on multiple myeloma, monoclonal gammopathy of undetermined significance, amyloidosis and Waldenstrom's macroglobulinemia. His research has been funded by the National Cancer Institute, the Leukemia and Lymphoma Society and the Multiple Myeloma Research Foundation, among other organizations. He holds the academic rank of professor of medicine.

The **Whitney MacMillan, Jr., Professor in Neuroscience** was made possible by Whitney MacMillan, Jr., who is a long-standing patient and friend of Mayo Clinic. He became a Mayo Principal Benefactor by the establishment of this professorship. Through this professorship, his generosity extends across future generations of patients and families. His support helps sustain the ideals of Drs. William J. and Charles H. Mayo and ensures that Mayo always will provide the best in care, focusing on the needs of the patient.

Gregory Cascino, M.D., recipient of this award, is chair of the Division of Epilepsy in the Department of Neurology. Cascino's work and research with epilepsy emphasizes the care and management of patients with intractable epilepsy, with the goal of rendering them seizure-free without treatment-induced adverse effects. He is the principal investigator for the National Institutes of Health-funded study entitled "Epilepsy Phenome Genome Project." This large-scale, multi-institutional, collaborative research project is aimed at advancing the understanding of the genetic basis of the most common forms of idiopathic and cryptogenic epilepsies.

The **John T. and Lillian Mathews Professorship in Neuroscience** was established by John T. and Lillian Mathews. Their Mayo Clinic relationship dates back more than 40 years. In 1992, the couple endowed this professorship in neuroscience to advance the diagnosis, treatment and prevention of strokes and neurological diseases. The Mathews have had a significant philanthropic impact on the Mayo Clinic campus in Rochester. Their gifts enhance the architecture of the campus and communicate the values of the institution. They are the founding benefactors of Mayo Clinic Heritage Hall, and their generosity supports museums at Mayo Clinic locations in Rochester, Minn., Jacksonville, Fla., and Scottsdale and Phoenix, Ariz. Additionally, the Mathews funded renovation of the Mayo Building lobby — which now bears their name.

Robert D. Brown, Jr., M.D., M.P.H., recipient of this award, is chair of and consultant in the Department of Neurology. His clinical and research interests include cerebrovascular disorders, such as ischemic stroke and transient ischemic attack evaluation and management vascular malformations, intracranial aneurysms, acute stroke management and stroke prevention. Among his awards at Mayo Clinic are the Distinguished Clinician Award, Individual Award for Excellence, Karis Award, Outstanding Faculty Award from the Mayo School of Continuing Medical Education and the Recognition for Excellence in Inpatient Teaching. The American Heart Association gave him its Stroke Leadership Award.

The **Alfred D. and Audrey M. Petersen Professorship in Cancer Research at Mayo Clinic in Jacksonville** was established by Alfred and Audrey Petersen in honor of their close relationship with William J. Maples, M.D., and E. Eugene Page, Jr., M.D. Through the Morean Petersen Foundation, the Petersen family also has provided support for the hospital at Mayo Clinic's campus in Florida and for cardiovascular, colon cancer and musculoskeletal research. The Petersen family's personal experiences with cancer and the care they have received at Mayo Clinic resulted in this newly endowed professorship.

Robert Smallridge, M.D., recipient of this award, is chair of the Division of Endocrinology, Department of Internal Medicine, deputy director of Mayo Clinic Cancer Center and a consultant in the Division of Endocrinology, Department of Internal Medicine, at Mayo Clinic in Florida. His clinical interests include biomarkers of thyroid cancer, pregnancy and thyroid disease, as well as pituitary tumors. His research focuses on thyroid cancer clinical trials and mechanisms of thyroid cancer pathogenesis.

Support for patients and families

The American Brain Tumor Association (ABTA) has pledged financial support to Mayo Clinic for a brain tumor nurse educator to provide one-to-one coaching and education to patients and their families. Education is critical to help brain tumor patients and their families better understand and cope with the diagnosis and its treatment.

"We have always admired Mayo Clinic's philosophy of putting the needs of the patient first. This philanthropic support reflects a shared commitment to ensuring that optimal education and resources are available to patients and families facing a brain tumor diagnosis," says Elizabeth Wilson, ABTA executive director.

"We are grateful to our Minneapolis-based volunteers who host an annual fundraising event that enables the ABTA to help Mayo brain tumor patients and their families in a profound way." ■

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