Cleveland Clinic

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PHILANTHROPY SPARKS INNOVATION | SPRING 2015

Personalized Precision

HOW TARGETED THERAPY CHANGES CANCER CARE

Conquering Chronic Illness

A Life Shaped by Crohn's Disease

INSIDE:

PYRAMID

IDEAS ON FINANCIAL, ESTATE AND GIFT PLANNING

Generations of Giving

In Gratitude

From left: Jeffrey and Stacie Halpern, Sydell Miller, Lauren and Steven Spilman

Hundreds of thousands of patients have entered Cleveland Clinic's main campus through the Sydell and Arnold Miller Family Pavilion and world-renowned Cleveland Clinic Miller Family Heart & Vascular Institute. Designed to promote healing and collaborative care, the 10-story building, opened in 2008, was made possible by a transformational gift of $70 million from Sydell Miller and her daughters in Cleveland Clinic's last fundraising campaign.

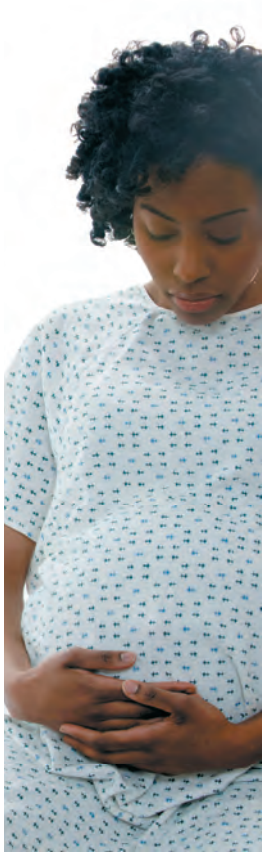
Mrs. Miller and her daughters, Stacie Halpern and Lauren Spilman, have served in a variety of volunteer leadership roles and supported multiple programs and institutes at Cleveland Clinic in both Ohio and Florida. In 2012, Mrs. Miller was named a Distinguished Fellow, the highest lifetime honor bestowed on select individuals making extraordinary contributions of service and resources to further Cleveland Clinic's mission.

"From generation to generation, our philanthropic values have been molded by witnessing acts of giving by my parents," Sydell Miller says. "By participating together as a family and leading by example, we are teaching the next generation. We have learned from our grandparents and parents," say Lauren and Stacie, who add that along with their husbands, they are fostering the next generation to "leave the world a better place."

"Cleveland Clinic stands for world-class medical care in our community and around the globe, and we as a family support its mission and are proud of our long affiliation."

Photo courtesy of Cleveland Clinic

contents



Medicine Chest

Philanthropy at Work

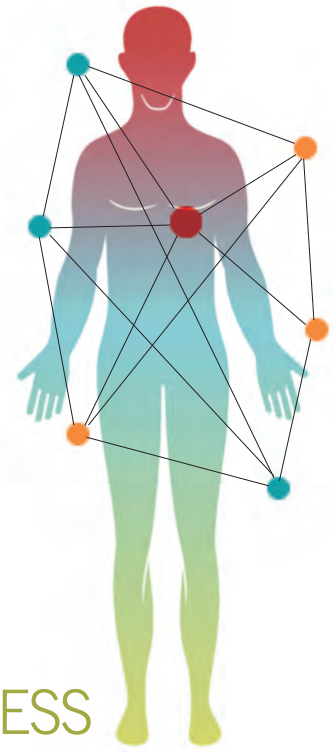
THE POWER OF EVERY ONE

PERSONALIZED PRECISION

Game Changer

Cover: Michael Northrup

Return to Table of Contents



• CLINICAL CARE

CONQUERING CHRONIC ILLNESS

COMPLEX, CHRONIC MEDICAL conditions are the No. 1 cause of death and disability in the U.S. and account for 75 percent of all healthcare spending. Seeking better ways to address these conditions, Cleveland Clinic has established the Center for Functional Medicine.

Led by Mark Hyman, MD, a best-selling author and internationally recognized expert in the field, the center focuses on discovering the underlying causes of illness. "Think of it as connecting the dots of disease," Dr. Hyman says. "It's looking at the root causes, not just the symptoms. And it's really looking at the body as a whole organism rather than looking at specific organs."

Functional medicine builds on conventional diagnostic tools, taking into account a patient's medical history and genetic, environmental and lifestyle factors. It seeks connections among seemingly disparate problems, including mental and emotional.

"The right nutrients, light, air, water, sleep, movement, connection, love, meaning, purpose — all are ingredients for creating healthy humans. We need to improve the health of patients, not solely manage their symptoms," Dr. Hyman says.

Research is intrinsic to the center's work. Current clinical trials are comparing standard treatments for asthma, inflammatory bowel disease, type 2 diabetes and migraines with those used in functional medicine.

"By witnessing the extraordinary clinical results from applying this new operating system to chronic disease, I am clear this must be the model for medicine going forward," says Dr. Hyman, who is committed to educating other physicians. "We cannot otherwise get to the solutions for our healthcare crisis or solve the problem of chronic disease." — *Elaine DeRosa Lea*

• RESEARCH

THE HEART OF PREECLAMPSIA

PREECLAMPSIA CAN BE a serious, and frightening, pregnancy complication. Now, a surprise discovery may lead to a test that predicts preeclampsia and to better treatments.

High blood pressure that comes with preeclampsia often restricts blood flow to the fetus, resulting in low birth weight. The condition is estimated to occur in 5 to 10 percent of all pregnancies in the world. The causes are unknown, but severe preeclampsia can produce serious risks to both the mother's and the baby's life. The only cure is to deliver the baby, which means a preterm birth and the risk of numerous complications.

In 2012, Cleveland Clinic researchers discovered that an enzyme, CORIN, may play a role in preeclampsia. Led by Qingyu Wu, MD, PhD, a professor of molecular medicine at the Lerner Research Institute, the team unexpectedly found that CORIN, normally present in the heart, also appears in the uterus of a pregnant woman. The discovery was named a Top Research Finding in 2012 by the National Heart, Lung, and Blood Institute.

Follow-up research by Dr. Wu's team and collaborators has shown that CORIN levels are low in pregnant women with preeclampsia. They also discovered two separate mutations that impaired CORIN levels in two families affected by preeclampsia.

Now, Dr. Wu's team is trying to figure out how the mutations impair CORIN function, as well as why CORIN levels are low in pregnant women who have preeclampsia but do not have the mutations.

"Ultimately, we want to see how we can benefit patients," Dr. Wu says. "But before we can do that, we have to understand how the process works. If we can predict which group of women will have the disease later on, [they] can be monitored more closely, or we can give them drugs to control their blood pressure." — *Melanie Padgett Powers*

• RESEARCH

PROCESSED PROBLEMS

CHECK THE FOOD LABELS in your grocery store, and you'll see that the use of additives in processed food is widespread. Unfortunately, these additives may contribute to the development of Crohn's disease and other forms of inflammatory bowel disease (IBD), say Cleveland Clinic researchers.

One culprit is maltodextrin, researchers found. When fed to gut bacteria, the modified corn starch used to smooth and thicken food products makes that bacteria much stickier, causing cells to clump together. These "biofilms" mimic the stickiness of bacteria found in the intestines of people with IBD, says Christine McDonald, PhD, Assistant Professor at the Cleveland Clinic Lerner College of Medicine and a member of Lerner Research Institute's Department of Pathobiology.

"In a normal, healthy intestine, you have a large amount of bacteria, but it doesn't actually stick to the surface of the cells," Dr. McDonald says. "There's this little gap — but in IBD patients, that gap is either much narrower or missing."

Follow-up lab research replicated the same stickiness and narrowing of the gap between bacteria and the intestinal surface. In addition, people who ate maltodextrin and were then infected with salmonella did not eliminate bacteria as well as those on a normal diet.

"We think maltodextrin is not only decreasing your natural defenses against bacteria, but also promoting different bacteria to stick to your intestines and be happy there," Dr. McDonald says.

Her team found maltodextrin in approximately 60 percent of packaged foods at a supermarket. A follow-up survey of 200 people showed 98 percent ate food with maltodextrin every day. It's unclear why some people develop IBD and others do not, but diet may be one piece of the puzzle, along with other risk factors, such as genetics, she says.

Next, Dr. McDonald wants to see whether a healthier diet can reduce IBD symptoms for those who have had their disease "reset," either with a colonic resection or a fecal transplant. By promoting a healthy microbiome-friendly diet, she says, "we might be able to maintain the presence of the healthy bugs and keep the ones associated with disease from setting up shop." — *Melanie Padgett Powers*

• MY STORY

Doctor Grateful for Her Mended Heart

A HEALTHY DIET and regular exercise helped keep Margaret Spear, MD, of State College, Pennsylvania, fit for most of her life. An internal medicine physician and now retired Director of University Health Services at Pennsylvania State University, she practiced what she preached, even training to become a yoga instructor.

But she wishes she had had a physical exam sooner. For 35 years, she went without one. When she eventually had an exam, the doctor ordered an echocardiogram. She was diagnosed with mitral regurgitation, a complication of mitral valve prolapse, a condition she'd had for a long time. Four years later, as the valve disease worsened, she was told that she might need surgery. She decided to go to Cleveland Clinic for a second opinion.

"I went to Cleveland Clinic's website to find a doctor because I wanted to establish a relationship before I needed surgery," she says. She chose William Stewart, MD, who told her she would probably need surgery in three to 10 years. But in January 2014, she became acutely ill and was hospitalized near her home with bacterial endocarditis, an infection of the inner surface of the heart.

After recovery, she saw Dr. Stewart. "I thought he'd say, 'Let's keep monitoring.' Instead, he said, 'This changes everything. You need to have surgery soon. Having had one infection, your risk now is much higher.' I was surprised. When I look back on it, though, it was important that I really trusted him. And I had known that this was the place I would have surgery, and I valued his recommendation of a surgeon, as well."

She says there were many things about Cleveland Clinic that made that true. "One was the way Dr. Stewart spent time with me and answered all my questions. Also, every time I called his office, within two rings, a human being answered, not a taped message. It's those little things that you might expect of a small practice in a small town but don't necessarily expect or get at a massive tertiary care center like Cleveland Clinic."

Only a few months after Marc Gillinov, MD, who holds The Judith Dion Pyle Endowed Chair in Heart Valve Research, repaired her mitral valve, Dr. Spear, now 65 and retired, passed rigorous testing to become a certified Iyengar yoga instructor.

"Initially, I thought I couldn't go through that," she says. "But my recovery was so smooth, it became clear how quickly it would be possible to continue and achieve this personal goal."

She says her husband, Alan, sums it up best: "You had a problem. We went to Cleveland. They fixed the problem." — *Elaine DeRosa Lea*

Top left: Ilyast/Getty Images; bottom left: Jose Luis Pelaez Inc/Glow Images
Top: Milanfoto/iStock; right: Courtesy of Margaret Spear, MD

ON TRACK TO SAVE LIVES

Ryan and Beccy Hunter-Reay

Indianapolis 500 Winner Ryan Hunter-Reay and his wife, Beccy, with their son Ryden

When Indy 500 champion Ryan Hunter-Reay lost his mother, Lydia, to colon cancer in 2009, he was distraught to learn from her doctors that she could have prevented the disease through screening or perhaps survived it by seeking help earlier. Instead, she waited a year after having symptoms before seeing a doctor. By then, her disease had advanced to stage IV.

"It all starts with awareness and prevention," he says, noting that standard medical advice is to have a colonoscopy at age 50. "If you have regular testing, like a colonoscopy, you can catch cancer in stage I or II. If you get the right care, you can overcome it. My mom, who was a nurse, was at stage IV because she missed that colonoscopy. She was 53."

Soon after his mother passed away, Ryan and his wife, Beccy, residents of Fort Lauderdale, Florida, established Racing for Cancer, a nonprofit organization focused on education, prevention and detection.

"The first step is being proactive," Mr. Hunter-Reay says. "People make time to get their cars serviced, and they should also get their doctor appointments."

Recently, Racing for Cancer joined with AutoNation, America's largest automotive retailer, in making a $2.5 million gift to Cleveland Clinic Florida's new Maroone Cancer Center.

Both organizations initially gave $1 million; however, AutoNation then pledged another $500,000 — amounting to $1,000 for each lap that Mr. Hunter-Reay made in winning the Indianapolis 500 in May 2014.

"The real reason for our support is that Cleveland Clinic Florida has all of the services under one roof," Mr. Hunter-Reay says. "That was a big challenge with my mom. It essentially was a black hole for us because we had no idea where to go or who to talk to. We drove all over South Florida for her chemotherapy and other care. Cleveland Clinic would have solved that problem because their specialists are all within the same facility."

"The first step is being proactive," Mr. Hunter-Reay says. "People make time to get their cars serviced, and they should also get their doctor appointments."

In addition, he says, "The Maroone Cancer Center is a brand-new, world-class facility with the latest and greatest technology, and the design is really based around the comfort of the patient."

He lauds Maroone Cancer Center Director Steven Roshon, MD, for his role in planning the center and Cleveland Clinic Florida Capital Campaign Co-Chair Mike Maroone, who "really looks after the community. When he told me about the plans for the center, I thought that any project Mike Maroone is high on, I want to get on board. We haven't looked back."

The lobby of the new Egil and Pauline Braathen Center is named in honor of Mr. Hunter-Reay's mother.

"I think that when she passed away, I knew that one day, I wanted something named after her," he says. "This is the perfect way to do it. Her name is the first thing that greets you when you enter this beautiful building, and it really hits home for me because the system that Cleveland Clinic Florida put into place fixes so many of the issues she went through. Having her name there is not just a stamp. There is so much more that goes into it, and that's what I'm proud of."

— Elaine DeRosa Lea

Photo courtesy of AutoNation

BACK IN THE SWING AFTER HEART SURGERY

Brad Comport

In warmer months, retiree Brad Comport spends his days on the golf course in Harbor Springs, Michigan, a lakeside resort. He credits heart surgery at Cleveland Clinic for making that active lifestyle possible.


Brad Comport

"We feel deep gratitude for my care," says Mr. Comport, who, with his wife, Patricia McDuffee, has made planned gifts supporting heart research at the Sydell and Arnold Miller Family Heart & Vascular Institute.

The former Hudson, Ohio, resident and corporate controller at The Davey Tree Expert Co. remembers feeling his heart race as far back as when he played sports in high school. However, doctors at that time found nothing wrong.

It wasn't until a medical exam in 2000 that a doctor said, "Uh-oh. You have a heart murmur. I want you to have an echocardiogram," Mr. Comport says. While in the waiting room, he picked up a copy of *U.S. News & World Report* magazine featuring its "Best Hospital" rankings and read that Cleveland Clinic was listed No. 1 for heart care. Though the doctor had referred him to a local specialist, Mr. Comport instead called a friend who was a patient at Cleveland Clinic. Within an hour, Cleveland Clinic called him, and he made an appointment.

Once there, he was seen by cardiologist Maran Thamilarasan, MD, who diagnosed a congenital heart defect — a bicuspid aortic valve. Over time, this led to premature buildup of calcium on the valve, as well as enlargement of the aorta. Eventually, Mr. Comport was told, he would need valve replacement.

For the next three years, Dr. Thamilarasan monitored Mr. Comport's condition until it was necessary for him to have surgery. His first aortic valve replacement was in 2003 by Toby Cosgrove, MD, now CEO and President of Cleveland Clinic. The second was in 2012 by Kenneth McCurry, MD.

"There isn't a day that goes by that I'm not thinking about Cleveland Clinic," Mr. Comport says. "We made our gift to help perpetuate Cleveland Clinic's excellence in patient care, so that others who need it can experience what we did."

— Elaine DeRosa Lea

NOTEWORTHY GIVING

American Greetings


Morry Weiss

In 2021, Cleveland Clinic will celebrate its 100th anniversary. That same year, another Cleveland institution and a longtime Cleveland Clinic supporter, American Greetings Corp., turns 115.

Like Cleveland Clinic, American Greetings is recognized nationally and internationally and has a history of community support, says company Chairman Morry Weiss. For more than 30 years, American Greetings has contributed significantly to fundraising campaigns and a wide variety of programs and projects at Cleveland Clinic. The company most recently committed to Cleveland Clinic's historic $2 billion The Power of Every One Centennial Campaign.

"We're very supportive of Cleveland and all the places where American Greetings associates live," Mr. Weiss says, referring to the company's employees.

"We focus on healthcare and education, making certain that the people who work and live here benefit," he says. "We conduct a lot of surveys of our associates to learn what's important to them in the community, and we try to be responsive, not only with our dollars, but by volunteering our time."

Mr. Weiss, who also participates in other professional, educational and nonprofit organizations, is a member of Cleveland Clinic's Board of Trustees. He has served on Cleveland Clinic's finance and marketing committees, which help guide strategic planning and growth. He emphasizes the need for Cleveland Clinic's campaign in securing its future.

"The Power of Every One campaign is a huge undertaking, and we are reaching out to corporate Cleveland to meet our goal," he says.

Volunteering time is essential to the nonprofit organizations that American Greetings supports, he says. "The truth is that philanthropy, in terms of dollars given, is important. But giving of your own time is terribly important, too. Our role includes taking time to encourage others to give and explain why Cleveland Clinic is important to our community and that much of the community's success in education or healthcare would not have been possible without philanthropy." *— Elaine DeRosa Lea*

Left: Courtesy Brad Comport; top right: Courtesy American Greetings

PICTURING A HEALTHIER TOMORROW

Ronald J. Ross, MD, FACR


Ronald J. Ross, MD, FACR

For Dr. Ronald J. Ross, the experience of walking through the hospital as a new medical student and seeing sick patients initiated a lifelong desire to help others, which he has accomplished through a landmark radiology career and his passion for community-focused philanthropy.

Starting in the 1970s, Dr. Ross was internationally recognized as one of the leaders of the "radiology revolution," leading to new radiological diagnostic modalities that advanced and improved medical care for patients. He also was widely recognized for having had the first head and whole-body CT scanner used in private practice in the United States and the first MRI facility for clinical use in the world. He published the first report of multiple sclerosis lesions in the brain which were enhanced with contrast material and published the first journal article on clinical MRI.

"Looking back at early MRI, the images were low resolution and the scan was slow, but MRI opened up a whole new world of visualizing parts of the body in ways which could not be seen before," Dr. Ross says.

In addition, he published the first scientific article that included CT scans, EEGs, neurological testing and neurological examinations of patients who were professional or amateur boxers. This work, which he did more than 30 years ago, laid the foundation for recent research into concussions and neurological disorders related to sports and combat injuries.

Over the past 25 years, Dr. Ross has served on more than 40 committees and boards for Hillcrest Hospital and Cleveland Clinic. Now Emeritus Director of the Department of Radiology at Hillcrest Hospital, he chairs Cleveland Clinic's Quality, Safety and Patient Experience Committee and the Hillcrest Hospital Board of Trustees. He has been a member of Cleveland Clinic's Board of Directors since 2006 and a member of the Board of Trustees since 1997. He also lends his time and experience to The Power of Every One Centennial Campaign, serving as Honorary Chair with his wife, Helen Ross.

Dr. Ross credits his career as a natural pathway to volunteering and the philanthropic activities that he and his wife have undertaken in the community. One of their first experiences in philanthropy was a donation of "CPR Resusci-Annie" training mannequins to local schools, allowing for teaching thousands of students lifesaving skills.

In 2005, the couple established the Ronald and Helen Ross Distinguished Chair in Pediatric Cardiology, which was the first endowed chair at Cleveland Clinic Children's.

"All along we've wanted to improve the health of people who are now ill, or young people we hope will not become ill," Dr. Ross says.

In 2014, the Helen and Ronald Ross, MD, FACR, Center for Cardiac Pulmonary Rehabilitation and Wellness opened at Hillcrest Hospital, providing expanded space for rehabilitation, employee fitness and meeting/education space. They also committed a leadership gift to the new health education campus under construction at Cleveland Clinic in partnership with Case Western Reserve University.

Dr. Ross credits his parents with setting an example for him to give what one can. One of the most important awards he has received, he says, is the Distinguished Fellow award from Cleveland Clinic, recognizing his and Mrs. Ross' philanthropic activities benefiting the health system and its patients. The Distinguished Fellow is the highest lifetime honor bestowed upon individuals who have made extraordinary contributions of service and resources to further the mission of Cleveland Clinic.

— *Elizabeth Lear*

Don Gerda/Cleveland Clinic

A LIFE SHAPED BY CROHN'S DISEASE

Dana Marshall-Bernstein

When she was 3 years old, Dana Marshall-Bernstein was diagnosed with Crohn's disease, an autoimmune disorder that attacks the digestive system. Now 26, she strives to live life on her own terms, despite years of surgeries and treatment regimens.

"Crohn's has affected my whole life — every second of every day of my life," she says. "When I go to the doctor, I say, 'This is what you do for a living, but this is what I do to live.' It's not something I can take a break from, like a five-minute breather, or go on vacation and say, 'I'll deal with this on Monday.' It gets very tiring."

However, she adds, because she grew up with Crohn's, it is the norm for her. "I don't miss some unknown world."

Her mother, Cari Marshall, recalls the difficulty of finding appropriate medical care close to their home in Las Vegas as her daughter was growing up. They traveled frequently to California hospitals.

"Three or four years ago, we were running out of resources," she says. "But my parents were from Cleveland, and I grew up hearing about Cleveland Clinic."

A relative put the family in touch with Feza Remzi, MD, Chair of the Department of Colorectal Surgery, who also holds the Rupert B. Turnbull, MD, Chair in Colorectal Surgery. "He said, 'I can help you, but I can't come to you,'" she says. "We decided to make the journey."

Dana's father, Ed Bernstein, has been "thrilled" with the level of care that Dana has received at Cleveland Clinic, noting that he had successful heart valve repair there, as well.

Dr. Remzi has given them reason to hope, Cari Marshall says. In the past, they went from crisis to crisis as Dana's condition worsened. "No one before him ever said, 'Here's the plan,'" she says. "Before, there was no plan."

To help her daughter and thousands of other people dealing with Crohn's, Cari became executive producer of a new documentary about Dana, *Semicolon: The Adventures of Ostomy Girl*. Dana is co-executive producer, and Cari's friend Robin Greenspun is director/producer. It was shot at Cleveland Clinic and debuted in Las Vegas on March 15 and at the Cleveland International Film Festival on March 25.

In addition, Cari and Ed each launched a family foundation to raise money for medical research. Together, they established a personal fundraising page on Cleveland Clinic's website: *giving.ccf.org/goto/dana*.

Dana Marshall-Bernstein and Feza Remzi, MD

"Crohn's has affected my whole life — every second of every day of my life. When I go to the doctor, I say, 'This is what you do for a living, but this is what I do to live.'"

– Dana Marshall-Bernstein

The family also hosted an event in Las Vegas with the goal of attracting support for establishing a national Center for Excellence in Inflammatory Bowel Disease.

All of their initiatives have raised more than $550,000 as of April 23.

"Cleveland Clinic is a worldwide leader in the field of inflammatory bowel disease treatment and research, and we truly believe that this research has the potential to prevent other young people from going through the struggles that Dana faces," Ed says. — *Elaine DeRosa Lea*

Kristoff Lutchman

VELOSANO BIKE TO CURE GEARS UP FOR SECOND EVENT

In its first year, the VeloSano Bike to Cure weekend drew 800 riders and nearly 12,000 supporters from all 50 states. Patients and their families and friends, healthcare professionals, and members of the business community all came together to advance cancer research at Cleveland Clinic. Now, supporters, riders and volunteers are being recruited for the second annual communitywide initiative to be held July 17–19.

VeloSano, meaning "swift cure," was launched through a major gift from Stewart and Donna Kohl. The inaugural event in 2014 was a resounding success, raising nearly $2 million for research into cancer genomics and novel immunologic treatment approaches.

Among VeloSano's most dedicated supporters is UN1TUS, an athletic apparel company in Solon, Ohio, that specializes in American-made products for teams and individuals. The company is owned by Sensical Inc., which produces custom graphics and material-conversion products for the automotive industry along with point-of-purchase signs and displays.

After seeing VeloSano television ads in 2014, Jack Haas, President and CEO of Sensical Companies/UN1TUS, reached out to event organizers about becoming a sponsor.

"We were inspired to partner with VeloSano because of a team member who is battling pancreatic cancer," Mr. Haas says. "Our partnership allows us to not only give back and support her, but also support and encourage the many others fighting a similar battle with this devastating disease." In her honor, the company also formed "Team Christi" to ride in the event.

In 2014, UN1TUS provided items including T-shirts for volunteers, bags and contents for riders, and signs for the VeloSano Bash event. This year, the company again is contributing these items and also is creating, managing and supporting the VeloSano Shop online and producing the merchandise. Further, UN1TUS recently made a major outright gift which, along with its prior giving, raised its participation level from "Contributing Partner" to "Supporting Partner."

To learn more about VeloSano and to register as a volunteer, rider or virtual rider, please visit VeloSano.org. If you are interested in becoming an event sponsor, please contact Nicole Peters at 216.445.1805 or petersn3@ccf.org. — *Elaine DeRosa Lea*

Mueller Design

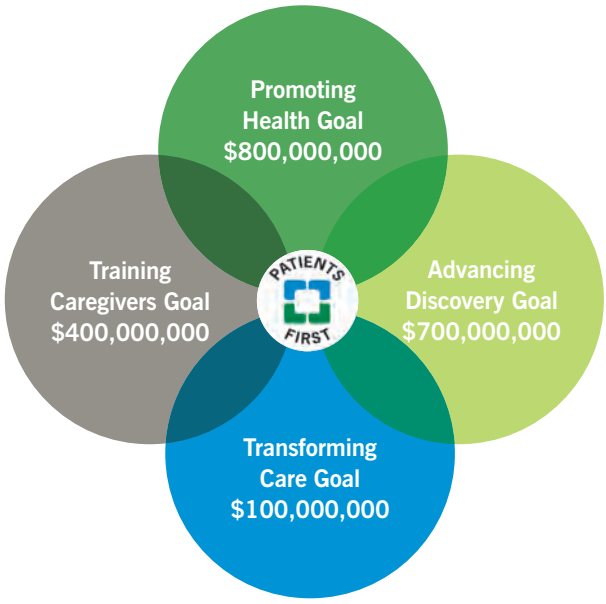
Return to Table of Contents

Cleveland Clinic

The Power of Every *One*.

CENTENNIAL CAMPAIGN

CENTENNIAL CAMPAIGN COMMITMENTS



CAMPAIGN GOAL $2 BILLION

AMOUNT COMMITTED AS OF APRIL 30, 2015: MORE THAN $720 MILLION

It's been a busy time since June 9, 2014, when Cleveland Clinic launched its historic $2 billion campaign, The Power of Every One. There is so much going on, and we are pleased to share some highlights:

• We ended 2014 with an impressive $255 million raised throughout the year, thanks to more than 49,000 supporters making nearly 64,000 gifts. To date, we are over one-third of the way toward achieving our campaign goal.

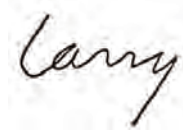
• Plans for the new health education campus, located on an 11-acre parcel between Euclid and Chester avenues and 93rd and 100th streets, are moving forward. The City of Cleveland has approved the design, and construction is scheduled to start this year. We will need generous philanthropic support to help build this innovative vision of interprofessional health education.

• On Feb. 19, Cleveland Clinic Florida opened the Egil and Pauline Braathen Center. This was made possible by the Braathens' largest gift to date: $30 million from Mrs. Braathen, a grateful patient and longtime supporter. In addition to the expanded Pauline Braathen Neurological Center, the building also houses the Maroone Cancer Center, established with the help of generous gifts from the Maroone family.

• At our main campus in Cleveland, ground was broken Sept. 29 on a beautiful new building for outpatient cancer care, which is scheduled to open in 2017. This 377,000-square-foot building will allow patients to receive their care conveniently in one location. You will be hearing much more about this in the coming months — philanthropy will be important to this project. Please take a moment to read about our innovative cancer research that is giving patients hope and helping to transform their care. (Page 11).

Speaking of cancer research, and looking toward events in 2015, we are excited to announce our second annual VeloSano Bike-to-Cure Weekend, July 17–19. The inaugural ride in 2014 raised nearly $2 million for cancer research at Cleveland Clinic and drew 800 riders from 21 states, Canada and Abu Dhabi as well as 700 volunteers! Nearly 12,000 individuals from all 50 states and 23 countries, more than 90 percent of whom had not given to Cleveland Clinic before, supported our effort. Please consider joining us once again this year, or for the first time, by volunteering, riding or supporting our riders. You can find all the information on our website, velosano.org.

You will be hearing more from us in the months ahead, and we are hoping to hear from you, too. *Thank you* for all that you do on behalf of Cleveland Clinic and the patients of today and tomorrow, here and around the world! Please visit our powerofeveryone.org website to learn more about the amazing research, patient care and medical education at Cleveland Clinic and how you can join our efforts to reach our campaign goal.



Larry Pollock
Campaign Co-Chair

Stewart Kohl
Campaign Co-Chair

On Saturday, Feb. 21, 430 guests, including about 70 new contributors, attended 'S Wonderful — An American in Paris Ball in Palm Beach. Among those enjoying the evening were, from left, Sydell Miller, Pauline Braathen and Donald Trump.

The Campaign for Cleveland Clinic Florida, part of Cleveland Clinic's The Power of Every One campaign, supports growth, innovation and excellent patient care in South Florida.

EGIL AND PAULINE BRAATHEN CENTER OPENS

More than 250 guests gathered at Cleveland Clinic Florida on Feb. 19 for an opening celebration inaugurating the Egil and Pauline Braathen Center, the first phase of the Cleveland Clinic Florida expansion strategy. A historic $30 million gift by Pauline Braathen helped establish the center, which includes the expanded Pauline Braathen Neurological Center and the Maroone Cancer Center.

Mrs. Braathen's gift, the largest in Cleveland Clinic Florida's 27-year history, helped support construction of the five-story, 144,000-square-foot building. On March 2, the Braathen Center began providing patients clinical services, including radiation oncology, hematology/oncology, neurology, neurosurgery and physical therapy.

"The Egil and Pauline Braathen Center will serve as an example of outstanding medical architecture and a template for the future," Toby Cosgrove, MD, CEO and President of Cleveland Clinic said at the event.

The center includes a laboratory, pharmacy, patient resource center, wig studio, café and art therapy studio as well as facilities for pain management, diagnostics and physical and occupational therapy.

MAROONE FAMILIES' GIVING TOPS $10 MILLION

Cleveland Clinic Florida Campaign Co-Chairs Al and Mike Maroone and their families made a multimillion-dollar commitment to the construction and programs of the expanded cancer center. The portion of the Braathen Center that houses oncology is named the Maroone Cancer Center in recognition of the families' significant philanthropic support over the years, which has topped more than $10 million.

"We are so grateful to the Maroone family for their generous support of Cleveland Clinic Florida," says Wael K. Barsoum, MD, President, Cleveland Clinic Florida. "Their gift will allow us to develop a robust set of programs to support patients and their caregivers as we bring the cancer resources of the world-renowned Cleveland Clinic in Ohio to our community and to the patients who travel here from around the world."

"Cleveland Clinic stands for world-class healthcare," says Al Maroone, the retired founder of Maroone Auto Group, which was sold in 1997 to Republic Industries (now AutoNation). "Our family is proud of our long-standing affiliation with this fine institution."

The family's gift furthers Cleveland Clinic Florida's fundraising campaign and supports programs providing comprehensive cancer services in one location.

"Cancer touches nearly everyone at some point, directly or indirectly," says Mike Maroone, Cleveland Clinic Florida Capital Campaign Co-Chair. "We recognize the tremendous need in our community and have great respect for Cleveland Clinic's holistic approach to care for patients and their families. Cleveland Clinic Florida is poised to play a leadership role in enhancing cancer care."

Celebrating the grand opening of the Egil and Pauline Braathen Center are, from left, Steven Roshon, MD; Toby Cosgrove, MD; Al, Kit, Monica, and Mike Maroone; and Wael K. Barsoum, MD.

Return to Table of Contents

PERSONALIZED PRECISION

From diagnosis to treatment, every aspect of how researchers and clinicians approach cancer is changing for the better. Find out how genetics and targeted therapies are transforming the field of cancer care.

By Laura Putre

PHOTO ILLUSTRATION BY MICHAEL NORTHRUP

LESS THAN A GENERATION AGO, cancer treatments did their work with an ax rather than a scalpel, destroying good cells along with bad. Chemotherapy drugs were one-size-fits-all. As a result, many patients endured debilitating side effects from toxic doses of medication that did not always help.

> TO MAKE A CELL RENEW ITS DIFFERENTIATION PROGRAM TAKES SOME GOOD SCIENCE AND GOOD PHARMACOLOGY.
> –Yogen Saunthararajah, MD, MPH

Recent advances in genetics and new treatments are transforming that approach — dramatically — to the benefit of patients.

Designed to target very specific genetic mutations, cancer treatment is becoming more exact and effective. Cleveland Clinic physician-scientists are collaborating across disciplines on projects that offer the promise of improved precision in treatment. They are examining the genomics of individual tumors to see how they function. They're studying ways to reprogram cancer cells to prevent their deadly spread. In all cases, the goal is the same: Develop targeted therapy that stands a much better chance of improving patients' health while keeping harmful side effects to a minimum.

Yogen Saunthararajah, MD, MPH

Fighting Cancer Through the Side Door

Certain healthy cells, like spies in old movies, have a natural self-destruct switch that flips on when they're in trouble or no longer needed. The biological term for this is apoptosis. Traditional cancer treatments trigger this switch to stop malignancies from growing.

However, more than 50 percent of cancer patients lack that switch in their cancer cells, thanks to an alteration in the p53 "self-destruct" gene. In these patients, traditional cancer treatments fail.

"It's like you're trying to press the brake, but the brake pedal is gone," says Yogen Saunthararajah, MD, MPH, of Cleveland Clinic's Taussig Cancer Institute.

Dr. Saunthararajah's research bypasses the self-destruction route. Instead, he proposes using targeted treatments to change how cancer cells function through a process called differentiation.

Think of differentiation as "specialization," he says. "When cells specialize, they shift their focus from dividing to performing a very specific assigned task."

This process is the body's natural control of growth, he notes. So cancer cells have to avoid specializing. "Until recently, we didn't really understand quite how cancer cells did that."

One of the drugs Dr. Saunthararajah studies to prompt differentiation is called decitabine. As a chemotherapy drug, decitabine typically is used in high doses to stress cells. In his study, however, the drug is used in much lower, nontoxic concentrations to signal cancer cells to specialize.

The team published a clinical trial in the March issue of the *Journal of Clinical Investigation* showing that differentiation with decitabine can slow the progress of blood cancer. Forty-four percent of patients in the study had significant tumor reduction, accompanied by a significant improvement in the blood counts needed for health. About half of those patients sustained the improvement in blood counts for more than three years.

Return to Table of Contents

The method had been proved effective in treating a rare leukemia called APL, "but this clinical trial showed that we can use differentiation broadly," Dr. Saunthararajah says. At the proper doses, decitabine isn't poisonous, and it can work even when p53 is missing.

The next step is to elicit differentiation in solid-tumor cancers: pancreatic, lung, ovarian, breast and brain. With funding from the National Institutes of Health and the U.S. Department of Defense, he and his team are working to improve the drug so that it penetrates solid tissue.

Prompting cells to specialize is more subtle than trying to force a cell to self-destruct, Dr. Saunthararajah says. "You can make a cell self-destruct in all sorts of ways — by poisoning it, by beating it, by radiating it. There are a gazillion crude ways. But to make it renew its differentiation program takes some good science and good pharmacology. The payoff is much kinder, gentler therapy that is more effective."

Predictions and Pathways

Just as preventing cancer growth requires a change in thinking, so does the way in which clinicians predict how individual patients will respond to a particular therapy.

For instance, if 100 lung cancer patients undergo chemotherapy, only about 30 to 40 of those patients will have a significant response to treatment. Mohamed Abazeed, MD, PhD, wants to know why.

"We can do a much better job of identifying predictors," says Dr. Abazeed, Associate Staff Physician in Cleveland Clinic's Department of Radiation Oncology. The hope is that with better predictors to guide physicians, patients can receive the optional therapy more quickly and can avoid side effects of a medication that is not likely to work for their cancer. Their goals are to select patients who are most likely to benefit from particular treatment regimens. In patients with tumors that are predicted to be resistant to current therapies, Dr. Abazeed's team is working to develop combination treatments that may reverse that resistance.

Dr. Abazeed and his team have been studying predictors in patients with a variety of solid tumors.

Using a method called patient-derived xenografting, Dr. Abazeed's team also leads research into providing new testing platforms for targeted treatments.

Mohamed Abazeed, MD, PhD

Traditionally, tissue samples for testing new drugs are developed in the lab through a "cell line," in which cells from the original tumor grow into new tumor tissue. But there are drawbacks to the artificial setting. "You lose the original heterogeneity of the tumor and the expression profile of the microenvironment where the tumor came from," Dr. Abazeed says.

In the patient-derived xenograft method, tissue samples from a patient's tumor are grafted onto a host in the lab to better replicate the actual physiological conditions. Think of it as a three-dimensional likeness of the real thing, whereas a cell line sample is a shadow of the real thing.

This form of xenografting could allow researchers to test the effects of different treatments in an

> "WE CAN DO A MUCH BETTER JOB OF IDENTIFYING PREDICTORS."
>
> –Mohamed Abazeed, MD, PhD

environment that most closely resembles the original patient tumor. Ultimately, Dr. Abazeed not only is working on better predictors, but also on techniques that can improve the pathway to targeted treatments.

What Follows Sequencing

Access to treatment presents another barrier in cancer care, but one that the current work aims to lessen. The cost of genomic tumor sequencing used to be out of reach for all but the most affluent, but it has dropped dramatically in recent years. Gradually, the procedure is becoming more accessible to a larger number of patients.

However, obtaining results from such sequencing is just the first step. Without targeted therapy for a particular genetic alteration, or an accessible clinical trial, genomic data remains raw information.

That's why Davendra Sohal, MD, MPH, Associate Staff Physician in Cleveland Clinic's Department of Hematology and Oncology, is focusing his efforts on rethinking how clinical trials are conducted. Doing so could help make life-saving treatments accessible to more patients more quickly.

Currently, many clinical trials are decided by location and are not made available to everyone who meets the genetic and disease criteria. "If you sequence tumors from 10 patients, and one patient has alteration A, another B, and another C, trials for those drugs could be in different corners of the country," Dr. Sohal says.

To highlight the need for widespread availability of targeted therapies, Dr. Sohal is leading a multidisciplinary study that systematically tracks outcomes of cancer patients who undergo sequencing. The team presented early results at the American Society of Clinical Oncology's gastrointestinal conference in January.

"I think there's a growing realization, as we learn more from studies like ours, that, yes, you can sequence 1,000 genes, but if only five to 10 percent of the patients are receiving a drug, they need to do a much better job in terms of getting a therapy to them," Dr. Sohal says.

Another hurdle to providing targeted therapies is a scarcity of diagnostic tissue for certain cancers, including biliary (bile duct) and pancreatic cancers. Researchers need viable lab specimens to identify key genetic alterations and develop drugs to target them. Patients with these types of cancers, frequently diagnosed in the late stages of the disease, often are too ill to tolerate chemotherapy.

> "IF YOU SEQUENCE TUMORS FROM 10 PATIENTS, AND ONE PATIENT HAS ALTERATION A, ANOTHER B, AND ANOTHER C, TRIALS FOR THOSE DRUGS COULD BE IN DIFFERENT CORNERS OF THE COUNTRY."
>
> –Davendra Sohal, MD, MPH

"The options are quite limited, and the outcomes are quite poor," Dr. Sohal says. "The science is way behind some other cancers." A targeted therapy, if one is available, may be the best hope.

To improve research prospects in these areas, Dr. Sohal is leading an effort to create a biorepository of pancreatic and biliary cancer specimens. Currently, the tumor samples are solely from Cleveland Clinic patients, but a reciprocal relationship with other institutions is part of the long-term plan.

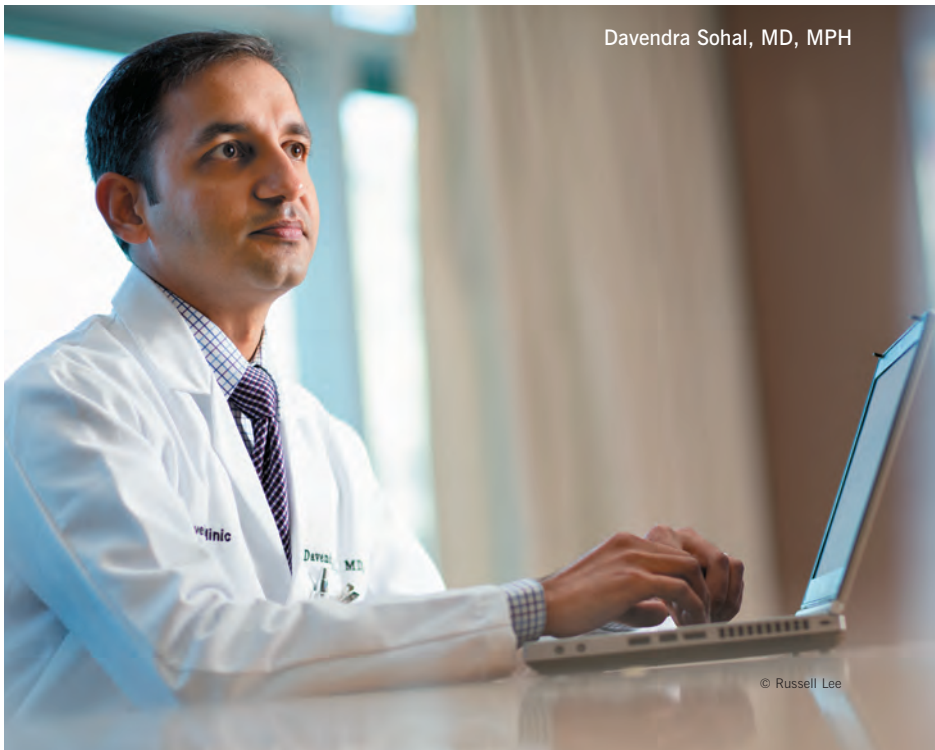
"There are a couple of exciting, hopeful drugs that might work in these diseases, but we need to do the studies and find out for sure," he says.

Drug Discovery Duo

The technology behind personal genetic tumor profiling has seen tremendous growth. The field offers an opportunity to create precision treatment strategies for individuals based on the unique characteristics of specific tumors.

That's where academic medical centers such as Cleveland Clinic can help. Teams of scientists and physicians collaborate closely to develop new therapeutic approaches — and patients benefit.

For example, Jennifer Carew, PhD, and James Phillips, PhD, the members of a drug discovery team in the Taussig Cancer Institute's Department of Translational Hematology and Oncology Research, have complementary skill sets. As a translational researcher with expertise in cancer biology and pharmacology, Dr. Carew identifies proteins or



Davendra Sohal, MD, MPH

Return to Table of Contents

> A LOT OF INVESTIGATIONAL DRUGS ULTIMATELY FAIL TO EARN FDA APPROVAL BECAUSE WE DON'T KNOW ENOUGH ABOUT WHICH CHARACTERISTICS OF INDIVIDUAL PATIENTS' TUMORS DETERMINE WHETHER THEY ARE LIKELY TO BENEFIT FROM THESE NEW TREATMENTS BEFORE CLINICAL TRIALS ARE INITIATED.
>
> –Jennifer Carew, PhD

pathways that drive disease progression or drug resistance. In turn, Dr. Phillips, a medicinal chemist, designs drug compounds around those specs.

The team currently is working to develop drugs that inhibit autophagy, a process that plays an important role in cancer progression and drug resistance.

"Autophagy is literally 'self-eating,' " Dr. Carew says. "It's a process where cells — when they're under certain stress conditions and they don't have access to nutrients through normal metabolic pathways — eat different pieces of themselves to generate alternative sources of energy that keep them alive."

In patients undergoing chemotherapy or radiation therapy, cancer cells may activate autophagy as a stress response to help tumors resist cell death. The team's research has shown that a number of classes of anti-cancer therapies become more effective when autophagy is inhibited.

However, translating this discovery into direct benefit for patients has been hindered, in part, by the lack of available drugs. So Dr. Carew and Dr. Phillips are working on developing new agents that effectively and safely inhibit autophagy.

They also seek to answer a critical question: Which types of cancer are most dependent on autophagy to survive? The answer may help them identify specific subsets of patients who are more likely to benefit from these new drugs.

"A lot of investigational drugs ultimately fail to earn FDA approval because we don't know enough about which characteristics of individual patients' tumors determine whether they are likely to benefit from these new treatments before clinical trials are initiated," Dr. Carew says. "We hope that the increasing availability of tumor profiling technology will enable us to design smarter clinical trials that yield greater patient benefit during earlier stages of clinical testing."

The goal, as with much of the research and clinical work in the field, is precision. ■

Jennifer Carew, PhD, and James Phillips, PhD

A Well-Rounded Approach

Physician-scientists are tackling precision medicine from multiple angles.

• Androgen hormones are one of the unsolved mysteries of prostate cancer research. Even after patients have treatment that causes the body to stop producing the hormones, prostate tumors somehow continue to make their own androgens to fuel themselves. **Nima Sharifi, MD**, who holds the Kendrick Family Chair for Prostate Cancer Research, heads a laboratory that is studying this phenomenon. His team identified a mutation in an enzyme responsible for the production of androgens that leads to a form of prostate cancer that is resistant to drugs and now is studying the effect of a newly discovered molecule on the enzyme.

• A new imaging technology that takes clearer pictures of breast tissue than current mammograms may help reduce the number of unnecessary breast biopsies. **Stephen Grobmyer, MD**, leads Cleveland Clinic's participation in PIONEER-01, a trial of the technology sponsored by a San Antonio–based medical imaging company.

• **Charis Eng, MD, PhD**, Chair and founding Director of Lerner Research Institute's Genomic Medicine Institute, who holds the Sondra J. and Stephen R. Hardis Endowed Chair in Cancer Genomic Medicine, and colleagues are working on a project to "teach" the IBM Watson supercomputer to evaluate cancer genomics datasets against the world's known public databases and literature to suggest diagnoses and treatments. There are not enough geneticists and genetic counselors in the U.S. to meet the growing demand for their services. Therefore, using technology to gather and interpret data may conserve time for those specialists and make genomic-based treatment accessible to more patients.

Return to Table of Contents

PREVENTING FEMALE PELVIC DISORDERS

By Margot Damaser, PhD

FOR MANY WOMEN, pregnancy and giving birth to a healthy baby are among life's most joyful times, though they do come with their own anxieties. Most mothers-to-be are concerned about their current health and that of their unborn child. They are less likely to worry about adverse effects of childbirth that might show up decades later.

Yet, beginning around age 50, up to half of these women will develop debilitating conditions collectively known as pelvic floor dysfunction. These include incontinence and pelvic prolapse, in which the pelvic organs drop down from their normal positions, all of which can necessitate corrective surgery.

What if we could prevent these disorders during a woman's childbearing years? And what if we could do it without surgery? Our research into the use of adult stem cell technology may provide the answer.

To understand how pelvic floor damage occurs, think about the average size of a newborn: 7 to 8 pounds. Also consider the intensity of childbirth, which stresses muscles and connective tissue holding the mother's organs in place. During the "pushing" stage of labor, the baby's head is only 1 millimeter away from the mother's pelvic bone. When this stage is prolonged, or when a baby is unusually large, severe damage to pelvic structures may occur.

Sometimes, the damage caused by childbirth may not be evident until the mother reaches middle age. Other times, it may occur and resolve itself immediately after she gives birth, only to reappear later in life.

Surgery can treat the symptoms, but it doesn't address the cause of this complex disorder. We are focusing on the bigger picture. As both a biomedical engineer at Cleveland Clinic and a scientist with the Louis Stokes Cleveland Veterans Administration Medical Center, I have a unique perspective on this research.

As we have learned by treating wounded soldiers, adult stem cells have homing factors that direct them to the site of injuries, such as those sustained in battle. Depending on the type of injury, the cells regenerate to form new, healthy cells. They replace dead or dying tissue and secrete growth factors to help injured tissue heal. These cells aren't just smart — they also are responsive.

We are exploring this same technology for women who give birth. Our investigations lead us to believe that if we could treat women with stem cells in the year after they have a baby, we could promote pelvic healing and even prevent problems.

Our results in the lab are promising, but to know for certain that this approach works, we will have to conduct human clinical trials. We need philanthropic support now to take our research to this next critical step. Clinical trials then could lead to a fast, inexpensive treatment for — or prevention of — these debilitating disorders.

Margot Damaser, PhD, is in the Department of Biomedical Engineering at Cleveland Clinic's Lerner Research Institute and holds a joint appointment in Cleveland Clinic's Glickman Urological & Kidney Institute.

"As we have learned by treating wounded soldiers, adult stem cells have homing factors that direct them to the site of injuries, such as those sustained in battle."

Photo: Courtesy Cleveland Clinic; Illustration: Glenn Pierce

Music and the Mind

Neuroscientist Damir Janigro, PhD, was raised in a family of musicians: His father was renowned Italian cellist Antonio Janigro. Passionate about both music and science, Dr. Janigro, of the Department of Biomedical Engineering in Cleveland Clinic's Lerner Research Institute, now studies the ways in which music is therapeutic for the brain.

His investigation centers on the brain's reaction to music. When exposed to music, the brain's electrical activity is altered, and patients become calm. This is true even during hours-long deep brain surgeries, for which patients remain conscious to communicate with their surgeons about whether their symptoms improve as electrodes are placed in their brains to treat tremor, Parkinson's and other disorders.

"Patients need to be conscious — but no one said they have to be upset or bored," he says.

Dr. Janigro was inspired by dentists who give their patients headphones to listen to music to relieve their anxiety. "Then the procedure is easier," he says. He hopes to find new ways of using music in hospitals to promote healing.

"Music is a tool to maintain brain health," Dr. Janigro says.

Girl: Elisabeth Schmitt/Getty Images; flowing lines: Duncan Walker/Getty Images

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Return to Table of Contents

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