Four years ago, I was very excited and honored to become president of the Mayo Clinic Alumni Association. It was supposed to be a two-year position ... that turned into four years! The two years after our 2019 Biennial Meeting in Rochester, Minnesota, were marked by restrictions from the pandemic. Alumni Association board meetings were virtual, and the 2020 international meeting in Portugal was postponed to 2022. The new board members did not have the full experience of being able to meet and interact with each other for those two years. Hence, the decision was made to extend board member terms for an additional two years.

Although the pandemic eliminated in-person alumni events for two years, it did not dampen the spirit of our alumni. We made up for this historic event by coming back even stronger with the Biennial Meeting in Scottsdale, Arizona, in October 2021 and the international meeting in Cascais, Portugal, in September 2022. Both were fantastic events.

I am excited about the Biennial Meeting in Rochester, September 28–30. This meeting also recognizes the 50th anniversary of Mayo Clinic Alix School of Medicine. As a proud graduate from 1980, I am really looking forward to this event. The combination of the Biennial Meeting and medical school anniversary should be a historic occasion.

It has been an honor and a privilege for me to serve as president of the Mayo Clinic Alumni Association for the past four years. I have loved working with a truly extraordinary group of individuals, all of whom exemplify Mayo Clinic values. I want to thank the Alumni Association officers, Executive Committee, Board of Directors and Alumni Center staff. In particular, I want to thank Judith Anderson and Dr. Dawn Davis (PD ’03, DERM ’06), executive director and medical director of the Alumni Center, respectively. Their guidance and enthusiasm have been a great source of inspiration. I am confident that the Alumni Association is in good hands as I pass the gavel to Dr. Theresa Emory (PATH ’94) from Williamsburg, Virginia.

Mayo Clinic’s influence, with the core value that the needs of the patient come first, has been the single most important guiding principle of my career. I will continue to “Connect Mayo Clinic alumni and bring Mayo Clinic values to the world.”

Carl Backer, M.D. (MED ’80)
President, Mayo Clinic Alumni Association
Chief, Section of Pediatric Cardiothoracic Surgery
UK Healthcare Kentucky Children’s Hospital
Lexington, Kentucky
Professor of Surgery
Cincinnati Children’s Hospital Medical Center
Cincinnati, Ohio

About the cover: The kaleidoscope illustration was created from images of heart muscle and stem cells and DNA.
Correction: In the last issue, we listed incorrect credentials for Stephen Burkhart, M.D. (OR ’81), as a speaker at the Alumni Association Biennial Meeting. Dr. Burkhart is a clinical associate professor, Department of Orthopedic Surgery, University of Texas Health Science Center at San Antonio, Baylor College of Medicine, San Antonio, Texas.

Photography, Florian Sommet (pages 4–5, 8–9, 16–17, 24–25); illustrations, Karen Hochman Brown (cover), Jason Schneider (page 22), Yeni Kim (pages 34–35, 42–43)
Research update

NO STONE LEFT UNTURNED
The needs of the patient drive everything at Mayo Clinic. Mayo Clinic researchers relentlessly pursue discoveries that deliver hope and healing to people today and for generations to come.

In several of the stories that follow, Mayo Clinic Alumni magazine highlights notable research advances:

• A single-center first-in-human phase 1 clinical trial of cell-based therapy to rebuild heart tissue for adult patients with hypoplastic left heart syndrome. Via a bioengineering process, a Mayo Clinic team is returning cells to their embryonic state, reprogramming them to become induced pluripotent stem cells, training them to become heart cells and engrafting them into the recipient’s heart muscle.

• A multicenter phase 2 clinical trial of a bioabsorbable scaffolding to deliver cells to the perianal fistula tract to augment the body’s ability to heal itself in patients who have Crohn’s disease. The data from the phase 1 trial is striking, and this treatment stands to be a paradigm shift in wound repair for nonhealing fistulas.

• The Mayo Clinic Program for Rare and Undiagnosed Diseases. This team offers genomics services to find
genetic causes for patients on a quest for definitive diagnoses. Last year, the team pursued more than 600 cases and provided a genetic cause for almost one-third of them. The team also developed an automated system to review new knowledge in the field as it occurs and compare it to patients in Mayo’s genomics database — often long after the patients are in person at a Mayo Clinic location.

“These are just a few examples of the many innovations happening across Mayo Clinic, thanks to our dedicated researchers, physician-scientists, physicians, and laboratory and administrative colleagues,” says Gregory Gores, M.D. (’83, GI ’86), The Mr. and Mrs. Ronald F. Kinney Executive Dean of Research Honoring Ronald F. Kinney, Jr., and the Reuben R. Eisenberg Professor. “Every member of our Mayo Clinic research community leaves no stone unturned in the pursuit of scientific advancements for unmet patient needs.”

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<th>2022 research funding</th>
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<td>$1,075.4m</td>
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<td>$654.2m from external sources</td>
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<td>$421.2m from Mayo Clinic</td>
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<td>$169m from industry</td>
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297 scientific faculty
423k+ square feet of research lab space
10k active IRB-approved human research studies
1,184 new IRB-approved human research studies in 2022
10,600+ Mayo Clinic research advances reported in peer-reviewed publications in 2022
5,881 active grants and contracts
Rebuilding bigger, stronger hearts

FIRST-IN-HUMAN TRIAL OF BIOENGINEERED HEART PRODUCT
“I’m confident that in the decade ahead, we will be able to rebuild hearts and cure congenital heart disease with this technology. It’s laborious work but a labor of love for our patients and their families.”

– Timothy Nelson, M.D., Ph.D.
Timothy Nelson, M.D., Ph.D. (I ’08, CV ’10, CI ’10), intended to be a cardiothoracic surgeon. “As a student in the Medical Scientist Training Program at the Medical College of Wisconsin, I observed a lot of cases and remember the joys of giving families hope that we could repair defects,” he says. “I also remember seeing those patients in clinic years later and the outcomes not being what we’d thought they’d be. I was motivated to find a better way.

“I learned about the promise of stem cells — and the possibility of cures with regenerative medicine — during that time. I wanted to be part of a team that could make that happen. Mayo Clinic was a leader in stem cells and regenerative medicine, which led me there. When induced pluripotent stem cells were discovered in 2006, I thought they could change medicine. It’s looking like that may be the case.”

Dr. Nelson’s regenerative medicine work of the last 12 years has reached a milestone — a first-in-human clinical trial. The phase 1 trial focuses on cell-based therapy to rebuild heart tissue for adult patients with hypoplastic left heart syndrome.

**ROLLING BACK THE CLOCK**

The bioengineering process involves returning cells to their embryonic state. This begins with a biopsy about the size of a pencil eraser taken from a patient’s skin. Cells are extracted from the specimen and

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**About HLHS**

- 10k people in the U.S. have hypoplastic left heart syndrome, a rare, complex condition in people born with an underdeveloped left heart chamber.
- Surgery to reposition arteries and enable a single ventricle to pump blood to the lungs and the rest of the body restores only a portion of circulatory function.
- Heart transplantation is a less than ideal treatment for this condition.
- Only a minority of patients with HLHS live past 30 years.

Human bioengineered heart cells viewed through a microscope.
reprogrammed to become induced pluripotent stem cells. In essence, this turns back the hands of time to when the cells first formed in the womb. The cells divide and become capable of transforming into any type of cell in the body. In this case, for congenital heart defects, they’re trained to become heart cells (cardiomyocytes) — beating, contracting heart muscle cells.

The manufacturing process, from extracting to creating hundreds of millions of cells from an individual’s specimen, takes nine months. In preclinical models in the lab, the cells were engrafted into the recipient’s heart muscle, where they grew, divided and expanded.

Depending on the outcome of the three-year single-center trial, it still could take years before engineered heart tissue is approved for use in clinical care for congenital heart disease.

“We hope the data from our trial shows that this process is safe and can refurbish the heart, making it bigger and stronger,” says Dr. Nelson, director of the Todd and Karen Wanek Family Program for Hypoplastic Left Heart Syndrome at Mayo Clinic. “Patients with single
Timothy Nelson, M.D., Ph.D., observes the regenerative medicine bioengineering process that involves returning patients' cells to their embryonic state and transforming them into cardiomyocytes.
“Stem cell therapy is the best pathway to the future
treatment of heart failure associated with many
congenital heart defects, and the lessons learned from
hypoplastic left heart syndrome will help lead the way.”
– Joseph Dearani, M.D.

ventricle congenital heart defects
like HLHS have very few options,
and this could represent a viable
therapeutic option.”

BABYSITTING CELLS
Dr. Nelson is quick to give credit to
his team. “I’m the spokesperson for
a team of 60 people who work seven
days a week. The team has taken care
of cells in various stages for more
than 4,000 days at this point.”

Dr. Nelson recognizes his surgical
colleagues present and past, including
Mayo’s Joseph Dearani, M.D. (TS ’96),
“Dr. Nelson should be commended for establishing and leading this multidisciplinary group of scientists and caregivers focused on discovering new treatment options for congenital heart disease.”

– Harold Burkhart, M.D., University of Oklahoma College of Medicine

The trial

The Autologous Induced Pluripotent Stem Cells of Cardiac Lineage for Congenital Heart Disease trial may be appropriate for patients who:

• Have univentricular congenital heart disease
• Have end-stage systolic heart failure without transplantation options

Alumni whose patients fit these criteria may refer them to the recruiting trial sites by scanning the QR code or emailing hlhs@mayo.edu.

https://clinicaltrials.gov/ct2/show/NCT05647213?cond=heart+and+iPSC&draw=2&rank=2d

The Sheikh Zayed Professor of Cardiovascular Diseases Honoring George M. Gura, M.D.; and Harold Burkhart, M.D. (TS ’02). Dr. Burkhart, the CHF Brandon Weeden Chair of Pediatric Cardiovascular Surgery at Oklahoma Children’s Hospital and the Paul H. and Doris Eaton Travis Chair in Thoracic Surgery at the University of Oklahoma College of Medicine, completed a cardiothoracic surgery fellowship at Mayo Clinic and was the original cardiac surgery partner in Dr. Nelson’s work.

“We wouldn’t be where we are without Dr. Burkhart’s early contributions at Mayo Clinic,” says Dr. Nelson. “Mayo Clinic takes pride in innovation and transformative medicine — it’s in our cultural DNA. Because we put the needs of patients first, when we need to do something better, we innovate. We’ve had the commitment and support of our departmental and institutional leadership. I’m confident that in the decade ahead, we will be able to rebuild hearts and cure congenital heart disease with this technology. It’s laborious work but a labor of love for our patients and their families.”
The plug and tools used to condition it with patients’ stem cells.
Paradigm shift in fistula care

FIXING A HOLE
It started with a chance encounter in the Gonda Building on Mayo Clinic’s Rochester campus in 2013. Colorectal surgeon Eric Dozois, M.D. (S ’00, CRS ’01), chair, Division of Colon and Rectal Surgery, ran into gastroenterologist William Faubion Jr., M.D. (PDGI ’98, GI ’02), Division of Gastroenterology and Hepatology, and shared an idea. A fellow in colorectal surgery from Spain, Maria Herreros Marcos, M.D., Ph.D. (CRS ’10), had told Dr. Dozois about research she was part of that involved injecting stem cells around perianal fistulas. Drs. Dozois and Faubion wondered if they could incorporate stem cell therapy into their fistula treatment. To learn more, Dr. Dozois spent a week at La Paz University Hospital in Spain, where Dr. Herreros Marcos had returned. That hospital was an early leader in using stem cells to treat patients with perianal Crohn’s disease.

“Dr. Faubion and I had worked together clinically for many years, shared patients and struggled to help those with Crohn’s disease,” says Dr. Dozois. “Dr. Herreros planted the seed of using stem cells to help those patients. The visit to her hospital in Spain furthered the possibility, and I was excited to discuss with my Mayo colleagues what might be possible.”

Those colleagues included Dr. Faubion and Allan Dietz, Ph.D. (ONCL ’02), Division of Transfusion Medicine and former director of Mayo’s IMPACT (Immune, Progenitor, and Cell Therapeutics) Lab. Putting their heads together, the trio built on the promise of stem cell therapy by embedding the cells into a material that would be surgically implanted in the patient.
Allan Dietz, Ph.D., and Eric Dozois, M.D., are outside the IMPACT Lab, where tissue from patients enrolled in a clinical trial for perianal Crohn’s disease is prepared for stem cell therapy.
“The data from our phase 1 trial is the best we’ve seen in any intervention for perianal Crohn’s disease from any institution in the last 100 years.”

– Eric Dozois, M.D.

THE EARLY RESULTS

The current standard of care for perianal fistulas is medical therapy, with setons for drainage used for recurrent infection. Results of closing fistulas with this approach are poor (20%–30% at one year). Using plugs with patients’ own mesenchymal stem cells could be a game-changer. A phase 1 trial, called STOMP (STem cells On Matrix Plug) and led by Mayo Clinic, showed a 76% healing rate in a cohort of patients who were highly refractory to conventional approaches.

“The data from our phase 1 trial is the best we’ve seen in any intervention for perianal Crohn’s disease from any institution in the last 100 years,” says Dr. Dozois, noting that Mayo Clinic is the only institution in the world that is putting cells on material to implant in the patient for this condition. “We’ve created technology that augments the body’s ability to heal itself. Patients, who have been desperate for help, have been very pleased with their results in the phase 1 trial.”
THE PROCESS
It started with a piece of fat. When a patient was enrolled in the trial, they provided a sample of fat from their abdomen. The fat was treated with enzymes to release the stem cells, which were kept in a body-temperature incubator in the IMPACT Lab and fed every three days with a soup-like mixture of carbohydrates, sugars and proteins. The stem cells are fast-growing, doubling in quantity every 24 hours. When Mayo Clinic laboratory staff determined by microscopic review that there were enough cells for the plug, the cells were combined with the plug material for several days. The finished therapy was packaged and transported to the surgeon’s location for implantation.

THE POTENTIAL
“This approach could be a real paradigm shift in wound repair for fistulas that won’t heal,” says Dr. Dozois. “If we succeed in healing perianal fistulas, it’s logical that we could heal other indications with difficult-to-heal wounds, including from GI surgeries, diabetic ulcers and traumas that normally require skin grafts. And the profile of this treatment is incredibly safe — patients get their own cells.”

Dr. Dietz, who oversaw the regulatory and manufacturing processes of the treatment, describes the reliability of this process as outstanding and says he expects to see it in clinical practice within a decade, pending results of subsequent trials.

About fistulas
Approximately 26% of patients who have Crohn’s disease develop perianal fistulas. These occur when an infection in the anal gland progresses into an abscess that can require surgery. Left untreated, these fistulas leak fecal material and can lead to a permanent colostomy and, in some cases, cancer. Perianal fistulas can negatively affect quality of life — recurring infections, antibiotic and narcotic use, drainage, discomfort, odor and social retreat. Even when the fistulas are surgically repaired, they often reoccur. Most of the treatment options have a low success rate.
A Mayo Clinic team conceived of embedding autologous mesenchymal stem cells into a material to be surgically implanted in patients who have perianal Crohn’s disease. A phase 1 trial produced data that team members describe as the best from any intervention for this condition in the last 100 years. They also describe this approach as a potential paradigm shift in wound repair for nonhealing fistulas.

**The process**

**STEP 1**

*Fat collection* Through a small incision, a sample of fat tissue is collected from the patient.

**STEP 2**

*Tissue transport* The tissue is transported overnight from external hospitals participating in the trial to the lab to begin manufacturing.

**STEP 3**

*Cell isolation and plating* Stem cells are isolated from tissue and expanded in the lab in a 2-week period.

**STEP 4**

*Stem cells release testing #1* When sufficient cell numbers have been achieved to assure final product manufacturing, cells are tested for purity, potency and sterility and stored in liquid nitrogen until ready for final product manufacturing.

**STEP 5**

*Plug seeding* In preparation for treatment, the cells are thawed and combined with growth media and fistula plug.

**STEP 6**

*Plug culture* Cells are allowed time to recover and adhere to the matrix.

**STEP 7**

*Release testing #2* The final product is tested again for purity, potency and sterility in preparation for clinical use.

**STEP 8**

*Plug transport* The product is transported back to the hospital.

**STEP 9**

*Plug implant into patient* A surgeon implants the cells/matrix combination.
“Homer’s ‘Iliad,’ one of the oldest pieces of existing Western literature, describes a battle where a soldier is injured, is carried off the field, and his wound is cleaned and stitched together,” says Dr. Dietz. “Although this epic dates back to the 8th century, the way we treat wounds has remained relatively the same. We still stitch together two edges of tissue and let them fix themselves. Our new approach, with a cell-seeded plug, is a paradigm shift in how to treat nonhealing wounds. We take cells from your body and give them back to you to flip the repair switch. The body is capable of fixing itself, and we’re giving it the signal to do so.”

Dr. Dozois says the median duration of the disease prior to treatment in the trial was four years. Those who responded to the trial responded within six months. “We believe this approach will help alleviate this chronic condition in many patients who haven’t had hope, moving them from needing repeated treatment to being healed.

“This is what Mayo Clinic does best — take a significant problem that seemingly has no solution and think about it across disciplines, with colleagues in medicine, surgery and the lab. Individually, we wouldn’t have come up with this solution. Our union of forces led to this landmark work.”

— Eric Dozois, M.D.

The future

Favorable results from Mayo Clinic’s STOMP-I trial led to the creation of Avobis Bio, LLC, a joint venture between W.L. Gore & Associates and Mayo Clinic. The STOMP-II trial, sponsored by Avobis Bio, plans to enroll 60 patients who have Crohn’s disease and a single-tract perianal fistula that has failed to respond to biologic or conventional therapy.

Trial locations include all three Mayo Clinic campuses and several other institutions.

The trial may be appropriate for patients who:

- Are age 18 to 70
- Have Crohn’s disease diagnosed at least 6 months prior to screening visit
- Have a single fistula tract with one internal opening and one external opening, including a previously performed conversion of a branching fistula tract to a single fistula tract where the branching occurred outside the sphincter complex
- Have perianal fistula(s) that were previously treated with either biologic or conventional therapy and demonstrated a failed response or have documented medication intolerance

Alumni whose patients fit these criteria may refer them to the recruiting trial sites by scanning the QR code or emailing the physicians below.

- https://clinicaltrials.gov/study/NCT04847739
- Eric Dozois, M.D., dozois.eric@mayo.edu
- Erin Kammer, study coordinator, kammer.erin@mayo.edu
Genomics detectives on the case
Konstantinos Lazaridis, M.D., is the Carlson and Nelson Endowed Executive Director of the Mayo Clinic Center for Individualized Medicine, which includes the Program for Rare and Undiagnosed Diseases — established in 2018.

He spent three years as a Mayo Foundation Scholar in Genomics at the National Human Genome Research Institute at the NIH in Bethesda, Maryland.
“Through the collaborative efforts of our Department of Clinical Genomics and Center for Individualized Medicine, we’re a leader in providing answers and bringing healing to patients and families who have been on yearslong diagnostic odysseys or have a rare disease.”

– Konstantinos Lazaridis, M.D.
Rare diseases

• Affect approximately 30 million people in the U.S. and 300 million worldwide.
• Number 10,000+ and can strike at any age.
• Approximately 80% caused by genetic defects.
• Almost 50% of rare diseases diagnosed during adulthood.
• 90%+ have no therapy.
• Have an economic burden: 379 of the most frequent rare diseases cost $966 billion in the U.S. annually (2019), including direct medical costs, productivity loss, and nonmedical and uncovered healthcare costs.
• Can affect any organ or system or a combination of congenital and chromosomal abnormalities, neurological, musculoskeletal, neoplasms, eyes, circulatory, immunodeficiency, digestive, endocrine and others.
• At least 16 previously undiagnosed diseases and syndromes have been named for Mayo Clinic physicians, including Plummer-Vinson syndrome, Stickler syndrome and Carney’s complex.
Approximately 15% of patients who go to Mayo Clinic seek evaluation and care for a rare disease.

individualized therapy because of genetic testing results.

“Mayo Clinic’s name and history are synonymous with rare, unusual diseases,” says Dr. Lazaridis. “We not only offer unique testing that addresses the specific needs of the patient with rare disease, but we also are able to organize and connect all the dots for patients and providers. Many patients comment about Mayo Clinic running like a well-oiled machine. Never is the coordination of efforts more important than in helping our patients who have been on exhaustive diagnostic odysseys.”

SYSTEMATIC & INTEGRATED
The approach to rare and undiagnosed diseases at Mayo Clinic is systematic and integrated. An investigation begins with a multigene panel that analyzes a set of genes to look for variations and mutations. The inquiry may include comparing genetic data to other cases with similar symptoms and variants.

The team meets with the patient’s Mayo Clinic providers to discuss the data and propose next steps. Genetics counselors meet with the patient to explain tests and findings. On some occasions, patients may require exome or genome sequencing studies.

A diagnosis can be life-changing ... and lifesaving, including for the patient’s family members who have the same genetic variant. A diagnosis also paves the way for potential specific treatment.

“Providing access to genetic testing and counseling can increase our diagnostic yield,” says Dr. Lazaridis. “Mayo Clinic is in a unique position to improve diagnoses and therapies and fuel discoveries in the care of patients with rare diseases. Through the collaborative efforts of our Department of Clinical Genomics and Center for Individualized Medicine, we’re a leader in providing answers and bringing healing to patients and families who have been on yearslong diagnostic odysseys or have a rare disease.”
Out of sight, never out of mind

RENEW helps to end diagnostic odysseys

New information about gene–disease relationships is identified and published continually around the world, resulting in a steep linear increase in the knowledge about which genes and gene variants cause diseases. If a patient was seen at Mayo Clinic five or 10 years ago and left without a diagnosis, they may be in luck. Just because they’re no longer at Mayo Clinic doesn’t mean they’re not on the minds of physicians and scientists.

AUTOMATING NEW KNOWLEDGE REVIEW

Several years ago, Mayo Clinic developed RENEW (REanalysis of NEGative Whole-Exome/Genome Data), an automated system to scour knowledge in the field and use it to review a cohort of approximately 2,000 patients with rare and undiagnosed diseases whose genomic sequencing results are in Mayo’s omics database. Public databases report thousands of new genetic variants each month. From RENEW, Mayo Clinic produces a new report from the published discoveries twice a year. To date, this system has yielded new diagnoses for 1%–2% of the patients.

“We’ve had patients go through genome sequencing and not get a diagnosis and then six weeks later a new paper is published and we get a ‘hit’ from our expert variant curators who assess this information,” says Eric Klee, Ph.D. (QHS ’05), the Everett J. and Jane M. Hauck Midwest Associate Director, Research and Innovation, Center for Individualized Medicine. “We reach out to the patient’s physician and the lab where the patient was tested to inform them of this new information and that we believe we’ve identified a pathogenic relationship. By some estimates, reanalysis of unsolved cases can increase diagnoses by as much as 10%. We believe our group is alone in systematically reanalyzing cases over time to help patients get answers to their genetic diseases.”

Usually, reanalyzing a patient’s case takes researchers and clinicians...
“We’re in a transformative time in understanding the genetics of disease and creating opportunities for patients. Whether patients are currently at Mayo Clinic or were seen months or years ago, we continue to seek answers for them.”

– Eric Klee, Ph.D.
many hours and days to sift through published papers. RENEW streamlines the manual process of reviewing the new information. Scheduling regular review of diagnostic odyssey patient genomic data using RENEW ensures all cases get regular attention. According to Dr. Klee, there’s no correlation between time from clinical testing to finding a genetic diagnosis. Patients could be in Mayo’s omics database for months or years, and then a critical new finding is published and provides the necessary data to provide a patient with a genetic diagnosis of their disease.

ENDING DIAGNOSTIC ODYSSEYS
Dr. Klee shares the case of Emery Diffendorfer, who presented at age 6 months in 2008 with developmental delays, recurrent upper respiratory infections and macroglossia, possibly related to Beckwith-Wiedemann syndrome. Emery had extensive biochemical and targeted genetic testing. He and his brother, Aiden, who had milder developmental delays, had exome sequencing, which didn’t identify a genetic cause. Nothing significant turned up in RENEW reports until 2022, when a novel variant was identified as a possible genetic cause.

“Mayo Clinic did every test under the sun, and everything came back negative,” says Cheryl Diffendorfer, the boys’ adoptive parent. “But the physicians told us that somewhere down the road, we’d get a phone call to let us know they’d identified Emery and Aiden’s disorder. Twelve years later, out of the blue, they called and said they’d found a diagnosis. They didn’t forget about our kids. They didn’t give up.”

Dr. Klee says the boys’ disease-causing genetic mutation variant was discovered by researchers in Norway. Emery and Aiden Diffendorfer are among 15 people in the world who have a genetic mutation that was discovered in 2021 by researchers in Norway. Mayo Clinic’s RENEW program had been searching for clues to the children’s disease since 2008.
Patients could be in Mayo’s omics database for months or years, and then a critical new finding is published and provides the necessary data to provide a patient with a genetic diagnosis of their disease.

in 2021. The boys are among 15 people worldwide who have been diagnosed with the rare genetic disorder.

The diagnosis hasn’t yet resulted in a targeted therapy, but providing patients with an answer to the cause of their disease is the most important step toward finding a treatment, according to Dr. Klee. “RENEW has helped us identify causal variants and end some patients’ diagnostic odysseys. My hope is that someday down the road, maybe in another few years, we’ll be able to call the Diffendorfer family to say we’ve identified a therapeutic.”

Dr. Klee says there’s been a significant increase in the understanding of the genetics of diseases in the last decade. “There’s movement toward a more open and collaborative environment worldwide to help us identify patients with similar phenotypes and interesting gene variants. You can share genetic changes of interest and get an alert when someone else has the same finding. This collaborative network has allowed us to identify new gene-to-disease relationships, publish about these findings, and get the information in public genetics databases so that labs and tools such as RENEW can benefit from the findings.

“We’re in a transformative time in understanding the genetics of disease and creating opportunities for patients. Whether patients are currently at Mayo Clinic or were seen months or years ago, we continue to seek answers for them.”

33
Thirty years ago, Mayo Clinic in Florida introduced its first residency program — cementing the site’s strength in all three shields and paving the way for today’s more than 66 training programs that have served more than 2,100 residents and fellows.

**ORIGINS**

In 1990, residents from Mayo Clinic in Rochester began rotating to four-year-old Mayo Clinic in Florida for four-month stints. In 1991, Leo Black, M.D. (‘65, died 2020), CEO at Mayo Clinic in Florida, decided to pursue Florida-based residency programs. He believed that strength in all three shields was critical for Mayo Clinic in Florida to be successful, and residency programs were necessary to attract academic-minded physicians to the staff.

The thinking at the time was to develop Mayo Clinic Graduate School of Medicine programs on all three campuses, allowing for three-way movement of residents — moving throughout the system in whichever direction would provide them with the greatest strengths.

A transitional year residency commenced on the Florida campus in 1993, with an internal medicine residency the following year.
Mayo Clinic didn’t have its own hospital in Jacksonville and used St. Luke’s Hospital, about 10 miles from the clinic. Because St. Luke’s wasn’t built for residency training, it lacked space for call rooms, conferences and rounds. Morning report and noon conference took place in a trailer with a leaky roof located between the hospital and medical office building.

Joseph “West” Paul, M.D., Ph.D. (TY ’94, I ’96), was in the first transitional year residency class. He’d completed an M.D.–Ph.D. program at East Carolina University School of Medicine. “My mentor knew Dr. Elliott Richelson (PHAR ’75, Mayo Clinic Emeriti Staff), who told me about the new transitional year program and said I could do research during training.

“I expected some chaos in a new program, but it ran incredibly well as a result of careful planning. We slept in patient beds at St. Luke’s because there was no dedicated respite or sleep space for residents. St. Luke’s hadn’t been a teaching hospital, so the nurses were very apologetic when they woke up sleeping residents. We didn’t usually experience that! We got to eat in the hospital’s medical staff dining room, which helped us get to know more of the staff. I remember the good food and chocolate chip cookies every afternoon.”

Dr. Paul describes the teaching from attending physicians as extraordinary. “Personal, knowledgeable...”

“Any challenges of having our own program were outweighed by our unilateral enthusiasm.”

– Gary Lee, M.D.
Leo Black, M.D., former CEO of Mayo Clinic in Florida, was instrumental in pursuing residency programs for the campus in Jacksonville. © Stan Badz – USA TODAY NETWORK

and high standards. The physicians knew the product they needed to establish to meet the criteria for a Mayo Clinic residency, and they overachieved in creating it. Everyone was fully invested in the program's success and growth."

Having intended to stay at Mayo Clinic for only one year, Dr. Paul changed course and stayed to be part of the new internal medicine residency program. “We did medical and surgical ICU coverage — more than most internal medicine residents because we were the only hands there. We had
a very heavy call schedule, but we learned a lot. We were young, and we were very tired.”

After training, Dr. Paul left Mayo Clinic for another academic medical institution for a couple of years and then returned to Mayo for 17 years, serving as associate program director of the internal medicine residency program for 13 years. Today, he’s founding partner and chief transformation officer at Pamlico Associates Healthcare Consulting in Charlotte, North Carolina.

“I can’t think of a better milieu to have trained in,” he says. “Your Mayo training never leaves you — it’s the basis of your being a physician. I still bleed Mayo blue.”

James “Jim” Johnson, M.D. (TY ’94, FM ’00), also was in the first transitional year residency class. He attended Vanderbilt University on an Air Force scholarship and needed to complete a one-year program before returning to the Air Force. A competitive swimmer and swim coach, he was excited to find a program in Florida.

“It was a dream to be among the first six residents — a huge advantage,” he says. “We got to work directly with attendings who were among the best in their fields in the world. I wouldn’t have had that kind of access anywhere else. Most transitional year and family medicine residencies take place in community-based hospitals. At Mayo, I saw unusual diseases, severe illnesses and high-end surgical procedures early in my career, which led to my having a broader perspective for differential diagnoses. With no other residents or fellows between us and the attendings, we developed close relationships. The core group of physicians who were the first at Mayo Clinic in Florida
gave their all to make sure the residency programs were rigorous and regarded as equal to those in Rochester.”

Dr. Johnson recalls the close bonds among those initial residents. “We did everything together that year. We had regular Tuesday nights at my apartment, watching TV and eating dinner.”

After returning to the Air Force for flight surgeon training, Dr. Johnson came back to Mayo Clinic in Florida as a second-year resident in the new family medicine program. He then went to Stanford University for a primary care sports medicine fellowship and served as a team physician for swimming and other sports at the university and as an Olympic swim team physician. He moved to Nashville, Tennessee, where he has a private sports medicine practice with residents and fellows rotating with him. “I’m among the Mayo Clinic alumni who continue to teach those values to other physicians, residents and students we interact with.”

Teresa Welsh, M.D., (TY ’95, I ’97, CMR ’98), was in the second class of transitional year residents. She’d attended Loyola University Chicago Stritch School of Medicine. “I had no hesitancy about the newness of Mayo’s program. On the contrary, there was excitement around the program, and I thought I’d have the opportunity to be more involved.”

Dr. Welsh planned to be at Mayo Clinic for a year and return to Loyola to pursue anesthesiology residency. She fell in love with internal medicine and Mayo’s approach to education, stayed for that residency and served as chief resident.

“From day one of residency, we were respected as physicians,” she says. “The hospital was our entire life except for one day off a week. We sometimes were on call overnight, rounded the entire next day and had to complete documentation before we went home after 36 hours. We literally resided at the hospital. I look back on it as a joyous time in my life.”

After training, Dr. Welsh moved to Denver, Colorado, where she worked as an internal medicine physician at Kaiser Permanente until retiring in April.

Dr. Lee says the transitional year residency program proved that Mayo Clinic in Florida could attract top-notch residents, train them with excellent outcomes and succeed in the education realm. It was a stepping stone to the internal medicine residency program and others to come.

**INTERNAL MEDICINE**

Joseph Kaplan, M.D., (THDCC ’87), now Mayo Clinic Emeriti Staff, was asked in 1991 to develop the internal medicine residency on the Florida campus. He didn’t have experience in a Mayo Clinic education program, having attended medical school in Illinois and completed residency at Ohio State University and fellowships at Johns Hopkins Medicine. He was in private practice in Davenport, Iowa, for six years before joining the staff at Mayo Clinic in Florida in 1987.
He’d been an assistant professor at Johns Hopkins and taught internal medicine residents. He enjoyed teaching, knew how to conduct and publish research, had faculty experience and was considered to be young enough to have the energy to run the program. He was “it.”

Dr. Kaplan visited the Rochester campus to study its internal medicine residency program and began building Florida’s program in 1992 with help from associate program directors Kenneth Nix, M.D. (CIM ’89), now Mayo Clinic Emeriti Staff, Gerardo Colon-Otero, M.D. (I ’82, HEM ’84), Division of Hematology and Medical Oncology, and Marc Cohen, M.D. (RHEU ’83), now Mayo Clinic Emeriti Staff. The program launched in 1994 for six first-year and four second-year residents. Two of the residents had been in the transitional year program.

“There are physicians at Mayo Clinic in Florida who came from Mayo Clinic in Rochester and understood what a Mayo Clinic training program should look like,” says Dr. Kaplan. “Physicians lined up to contribute their time to teaching in our new residency program. It was a huge boon to morale and the cause of tremendous excitement.”

Dr. Kaplan says the program was different from Rochester’s — lower resident–faculty ratio, more
outpatient time and graduated autonomy, and a larger metropolitan area to draw patients from. “We also recruited more diverse trainees than did Rochester,” he says. Dr. Kaplan served as program director for nine years and, like Dr. Lee, was named a Mayo Clinic Distinguished Educator.

Without question, the early residents on the Florida campus were treated to individual attention — lots of attention. Dr. Kaplan picked up each resident at their hotel to begin the introduction to Mayo and Jacksonville.

Anna Miller, M.D. (I ‘97), was in the first internal medicine residency class. She’d attended the Uniformed Services University of the Health Sciences in Bethesda, Maryland, aiming to practice medicine with an underserved population. “I thought I’d have closer interaction with attendings because there were fewer residents and no fellows in Mayo’s program,” she says. “I had face-to-face daily contact with some of the best and brightest physicians in the world, and we spent time talking about patients, diseases, underlying pathology and treatment options. We had the best of both worlds, training in a community-based hospital and then seeing patients from all over the world with exotic diseases in the clinic.”

After residency, Dr. Miller went to Oklahoma to work for the Indian Health Service as a medical officer. She retired from active duty in 2016 and now works for the Cherokee Nation in Tahlequah, Oklahoma. “My residency training at Mayo Clinic in Florida has been the foundation of this interesting and diverse career,” she says.

The success of the internal medicine program spurred a flurry of other residencies on the Florida campus. Family medicine started in 1995 and general surgery in 1997. When Mayo Clinic in Arizona embarked on an internal medicine program in 1996, Dr. Kaplan and Henry Schultz, M.D. (CIM ’79), internal medicine residency program director at Mayo Clinic in Rochester, assisted Philip Lyng, M.D. (I ’84, THD ’86, CCMI ’87), Division of Pulmonary Medicine, then program director on the Arizona campus.

“My residency training at Mayo Clinic in Florida has been the foundation of this interesting and diverse career.”

Anna Miller, M.D.
One national medical school, three campuses
Visiting medical students from other institutions have been welcomed on Mayo Clinic’s campuses, including Arizona and Florida, for decades. And Mayo’s own medical students have rotated to its other campuses for unique experiences, including neurosciences and pediatric hospital rotations, among others. Since 2017, in addition to the four-year program in Rochester, Minnesota, Mayo Clinic Alix School of Medicine has had a four-year program on the Arizona campus and a two-year program on the Florida campus for students in the clerkship years, making it a national medical school with three campuses.

THE GRAND CANYON STATE

After several years of discussion and planning, Mayo Clinic Alix School of Medicine expanded to the Arizona campus. Three classes of 50 students each have graduated. The Arizona campus, like the Rochester campus, includes M.D.–Ph.D. students.

Integral to the school’s expansion to Arizona were Keith Lindor, M.D. (MED ’79, GI ’86), dean of the medical school’s Rochester campus from 2005 to 2012; and Victor Trastek, M.D. (S ’82, TS ’84), CEO of Mayo Clinic in Arizona from 2002 to 2011 — both now members of the Mayo Clinic Emeriti Staff; and Lois Krahm, M.D. (MED ’89, P ’93, PCON ’94), former dean of the Education Committee at Mayo Clinic in Arizona.

According to Michele Halyard, M.D. (RADO ’89), the former Suzanne Hanson Poole Dean of Mayo Clinic Alix School of Medicine – Arizona campus and vice dean of Mayo Clinic Alix School of Medicine, having a medical school on the Arizona campus helped to cement Mayo Clinic in Arizona as an academic medical center. Dr. Halyard retired in June. “Medical education creates the workforce of the future, and our highly talented medical students will be my future physicians. Being in a leadership role with the medical school as the founding campus dean in Arizona has been one of the most satisfying parts of my career. I’ll be the loudest cheerleader on the sidelines as the school continues its excellent track record on the Arizona campus.”

Dr. Halyard says the medical school’s biggest challenge has been making sure sufficient resources are available, including people, to help the school succeed. “Dr. Fred Meyer (NS ’88, the Juanita Kious Waugh Executive Dean of Education and the Alfred Uihlein Family Professor of Neurologic Surgery) has walked the talk in terms of diversity and provided resources to remove hurdles for people from different backgrounds to apply for, be accepted to and thrive in our medical school. On the Arizona campus, we’ve succeeded in getting medical students who demonstrate grit, excel despite adversity and come from diverse backgrounds including those who have switched from another career. I’m proud of the diversity of the classes the school has attracted.”
“On the Arizona campus, we’ve succeeded in getting medical students who demonstrate grit, excel despite adversity and come from diverse backgrounds including those who have switched from another career.”

– Michele Halyard, M.D.

Victor Trastek, M.D., former CEO, Mayo Clinic in Arizona
Lois Krahn, M.D., former dean of Education Committee, Mayo Clinic in Arizona
Fredric Meyer, M.D., Juanita Kious Waugh Executive Dean of Education, Mayo Clinic College of Medicine and Science, and dean, Mayo Clinic Alix School of Medicine
THE SUNSHINE STATE

Applicants to Mayo Clinic Alix School of Medicine can choose a third program besides four years at the Rochester or Arizona campuses. They complete 18 or so months of preclerkship training in Minnesota or Arizona and then complete their final two years on the Florida campus. Students interested in that option apply to the Florida program and are selected by a committee on the Florida campus. Typically, 700 students apply for 12 spots. Those students go through residency match and commencement on the Florida campus.

“This summer we graduated our second class of the Florida program and recently welcomed our sixth class,” says Gerardo Colon-Otero, M.D. (I ‘82, HEM ‘84), vice dean, Mayo Clinic Alix School of Medicine – Florida campus. “Although our applicants come from all over the country, we particularly attract students who are interested in neurosciences, regenerative medicine, cancer, global health and health disparities or who have family in the Southeast or are interested in practicing on the East Coast. Because we have only 12 students per class, they get significant personalized attention and hands-on experience.”

Dr. Colon-Otero says the energy of having an official medical school program on the Florida campus created palpable excitement. “Many of our faculty volunteered to teach and mentor students, and we helped create local chapters of national medical societies, such as Gold Humanism Honor Society, Student National Medical Association and American Medical Women’s Association. Our residents also were excited to work with medical students. Having a medical school program has added to the already great reputation of Mayo Clinic in Florida.”

“Having a medical school program has added to the already great reputation of Mayo Clinic in Florida.”

~ Gerardo Colon-Otero, M.D.
In 2021, Mayo Clinic Alix School of Medicine launched a highly flexible, customizable curriculum that facilitates individualized learning, encourages innovation and cultivates the talents of the next generation of physicians. This new model allows students to personalize their curriculum to their individual goals as they advance through Mayo’s world-class core educational program.

The new curriculum features:

Active learning with engaging activities including case-based discussion, laboratory exercises, simulation and clinical experiences. This is a move from traditional passive lectures whenever possible.

Longitudinal clinic integration, with a new outpatient clinic for first- and second-year students. By bringing students into the clinical environment and engaging them in direct patient care early in their education, opportunities exist to enhance their clinical skills, demonstrate the relevance of learning through real-world applications and allow students to experience the joy of service to patients.

Individualized pathways that allow students to design almost a year of their educational program to meet their individual goals. Pathways can emphasize research and discovery, global health or underserved care. Students can integrate master’s degrees into their medical school education and can pursue their interests, develop their talents and find their passions in medicine.

Longitudinal coaching in which advisers assist students as they design their pathways, explore careers, and progress through residency match and graduation.
The Mayo Clinic Alix School of Medicine — Arizona campus class of 2021 and administrators wore headbands in recognition of Mayo’s first class of trailblazing medical students — the class of 1976, which was known to have hippie tendencies.

Gerardo Colon-Otero, M.D., vice dean, Mayo Clinic Alix School of Medicine — Florida campus, with medical students Dane Markham (MED ’24), Diana Hla (MED ’24), Scott Anderson (MED ’24) and Katherine Wang (MED ’25).
CODA

Dr. Meyer provides perspective about the significance of the medical school expansion. “Doubling the number of our incoming medical students from 50 to 100 per year put our annual enrollment on a par with other medical schools that are typically ranked in the top 10. Before we expanded, we were considered a boutique medical school and may have been overlooked by applicants, particularly those from diverse backgrounds. Despite our growth, we still have the lowest faculty-to-student ratio in the U.S., which our students love.

“I appreciate the efforts of everyone involved in the medical school to get us to this position. We’ve come a long way in only six years. We will continue to evolve our curriculum and distinguish Mayo Clinic Alix School of Medicine to provide an unparalleled medical education experience steeped in Mayo Clinic values from world-class experts. This is our mission — to compassionately train the next generation of physicians who will contribute to the health and well-being of patients by putting the needs of the patient first.” •
One of Jacob Orme, M.D., Ph.D.’s mentors at the University of Texas Southwestern Medical Center told him to go to Mayo Clinic to learn how to be a good doctor and then go somewhere else to do great science and research. The implication was that Mayo excels only in clinical care.

Dr. Orme (l ’19, HEMO ’22) arrived at Mayo Clinic in 2016 for internal medicine residency and stayed for a hematology/oncology fellowship. He joined the staff in the Division of Medical Oncology last year. Despite his mentor’s admonition, Dr. Orme has been a highly productive researcher at Mayo Clinic, including original discoveries and first- and second-author publications in Cancer Cell and OncoImmunology and groundbreaking clinical trials published in Clinical Cancer Research and the Journal for Immunotherapy of Cancer. He has several granted and pending patents, and his work has been commercialized through Mayo Clinic Ventures.

Dr. Orme’s research as a trainee led to his receiving the 2023 Mayo Clinic Alumni Association Donald C. Balfour Award for Meritorious Research.

Given his experiences at Mayo Clinic, Dr. Orme’s response to his early mentor would be that Mayo Clinic indeed excels at research — research that is laser focused on the needs of the patient.

Jacob Orme, M.D., Ph.D.
Division of Medical Oncology
Mayo Clinic in Rochester

Fellowship: Hematology/oncology, Mayo Clinic
Residency: Internal medicine, Mayo Clinic
Medical school: M.D.–Ph.D., University of Texas Southwestern Medical Center, Dallas
Undergraduate: Brigham Young University, Provo, Utah
Hometown: Provo, Utah
“Everything we do is for the benefit of the patient. When I see patients, my focus is sharpened about what I need to do in the lab. When I’m in the lab, I think about what will help my patients in the future, and my research revolves around that.”

– Jacob Orme, M.D., Ph.D.
“At Mayo, it’s as if the patient is at the bench,” he says. “The patient comes first in the clinic, in the lab, in the classroom. Everything we do is for the benefit of the patient. When I see patients, my focus is sharpened about what I need to do in the lab. When I’m in the lab, I think about what will help my patients in the future, and my research revolves around that.”

**DISCOVERIES & SIGNIFICANT CONTRIBUTIONS TO THE FIELD**

Dr. Orme specializes in genitourinary oncology. “Prostate, bladder and kidney cancers don’t have great outcomes for metastatic disease, so our work is cut out for us,” he says. “All of my research collaborators are working toward the same goal — to help patients live longer and better.”

To help others understand his research, Dr. Orme describes cancers as kidnappers. The cancer cells secrete factors that, in turn, signal and reprogram otherwise normal cells to become co-conspirators. Normally, the immune system combats abnormal cells. However, cancer cells can turn off that immunity. Immunotherapy involves interrupting cancer cell communication with normal cells to prevent their ability to signal other cells to join them.

As a resident in the laboratory of Haidong Dong, M.D., Ph.D. (IMM ’01), Department of Immunology and the Iris and Winston Clement Professor of Research, Dr. Orme discovered a mechanism for how cancer cells spread anti-immunity and a way to interrupt it. He led a clinical trial to test plasma exchange in resensitizing tumors to immunotherapy. He discovered additional resistance mechanisms in prostate cancer and is in discovery of more ways to prevent cancer cells’ ability to create an environment that permits their spread.

For those schooled in more technical terms, Dr. Orme found the origin and consequence of soluble PD-L1 in immunotherapy-resistant cancer, discovered a novel prostate cancer resistance mechanism and biomarker, and elucidated critical crosstalk mediators between healthy and malignant cells. Each of those discoveries is original and a significant contribution to the field, with direct application to patient care, according to Timothy Hobday, M.D. (MED ’94, I ’97, HEMO ’01), program director of the Mayo Clinic Hematology-Oncology Fellowship Program.

Dr. Orme has received recognition including the Mayo Clinic Innovator Accelerator Award, Top Performing Provider Patient Experience Award, 2021 Minnesota Society of Clinical Oncology Outstanding Fellow award, NIH LRP fellowship award and Prostate Cancer Foundation 2022 Young Investigator Award.

**NEW AVENUES IN THE FIGHT AGAINST CANCER**

According to Sean Park, M.D., Ph.D. (RADO ’11), Department of Radiation Oncology at Mayo Clinic in Rochester, Dr. Orme’s laboratory discoveries have opened entirely new avenues in the fight against cancer. “He has the talent to develop into an independent translational research investigator who studies new strategies to overcome cancer resistance in patients to improve their survival. He is in the top 1% of my mentees in a decade of serving as a mentor.”

Alan Bryce, M.D. (I ’06, HEMO ’09), chair, Division of Hematology and Medical Oncology at Mayo Clinic
in Arizona, says Dr. Orme was highly sought after by multiple institutions after completing his training. “We were delighted when he chose to join our staff at Mayo Clinic. It is truly remarkable that Dr. Orme, while he was still a fellow, discovered the resistance mechanism in the laboratory, proposed multiple clinical interventions to overcome it, obtained the needed funding and approvals for a clinical trial, and opened the trial. I know of no other clinical fellow who has accomplished this, and Dr. Orme did so twice during his training at Mayo Clinic.”

Dr. Orme says he’s had the best mentors at Mayo Clinic that anyone could ask for, and they had great mentors before them. “All of the science and discovery of new treatments for patients goes back to the methods and ideas and tools that were developed long before I was born. I look forward to being in a position to clear my shoulders to make a good platform for others to stand on to reach the next treatment for the next patient.

“Mayo Clinic is the only place I interviewed where the patient truly comes first in all aspects. This is where I’d want to get care, where I’d want my family to get care and where I want to give care. I’m glad I discovered not only the rich clinical training Mayo Clinic provides but also the priceless research training.”

Balfour Award nominees are residents or fellows on any Mayo Clinic campus who have a clinical appointment — or have completed an appointment in the past year — in medical and laboratory specialties, surgery and surgical specialties, or internal medicine and medical specialties.
Rolling toward improved wheelchair biomechanics

Omid Jahanian, Ph.D.
(QHS ’19), has conducted research at Mayo Clinic in using MRI to evaluate upper limb secondary pathology and using wearable sensors to measure real-world biomechanics in manual wheelchair users who have spinal cord injury. He is studying the risk factors for the incidence and progression of rotator cuff pathology in manual wheelchair users with spinal cord injury. His work will define how the shoulder responds to manual wheelchair use and determine how altered shoulder function contributes to shoulder health decline in this population.

WHEELY MATTERS
He’s long had an interest in wheely matters. In early adulthood, Dr. Jahanian immersed himself in robotics, winning top prizes in competitions. He served as chief expert for Iran’s team in mobile robotics at WorldSkills competitions for four years, culminating in a silver
medal in mobile robotics at the 42nd World Skills Competition in Germany in 2013. Prior to that, he worked as a research and development engineer for two automotive companies in Iran, developing testing machines for industrial automation.

Going from wheeled robots in robotics competitions and car factories to wheelchairs wasn’t a big leap. “The mathematics behind what I did in wheeled robots is similar to that of wheelchairs,” says Dr. Jahanian. “In the general population, people rely on their lower limbs for mobility. Manual wheelchair users with spinal cord injury rely on their upper extremities for mobility and activities of daily living. Our upper limbs, especially shoulders, weren’t designed for mobility. Manual wheelchair propulsion may contribute to an accelerated rate of pathology and injury in individuals with spinal cord injury, compared to the general population. There’s limited research on the role of upper limbs in mobility and the effects on the body. I want to advance the science to better understand the effects of using upper limbs for mobility.”

“Dr. Jahanian is one of the most talented, promising postdoctoral researchers we’ve encountered.”

~ Melissa “Missy” Morrow, Ph.D.
limbs for mobility on overall health and shoulder pathology specifically. The outcomes of this research could help prevent secondary injury. Ultimately, I want to use my expertise in rehabilitation engineering, biomechanics, robotics and statistics to help this population be as active and independent as possible and preserve their upper limb function by decreasing the risk of overuse injury.

**FIRST OF ITS KIND RESEARCH**

Dr. Jahanian’s postdoctoral research study of manual wheelchair users with spinal cord injury was the first of its kind in spinal cord injury rehabilitation to apply an epidemiological approach to document shoulder health decline on MRI and link the pathology to shoulder function measured in the real world with wearable sensors. He used longitudinal MRI data to define the early phase of shoulder health decline specific to manual wheelchair users and compared it with sex- and age-matched people in the general population. He led the development of a novel tendon pathology scoring system to detect small changes in shoulder health over a short time. This research was funded by the NIH’s Eunice Kennedy Shriver National Institute of Child and Human Development, and the results were published in the Journal of Spinal Cord Medicine. Dr. Jahanian received the Ernest Bors Award for Scientific Development, which recognizes young investigators in the field of spinal cord injury and is presented by the Journal of Spinal Cord Medicine and Academy of Spinal Cord Injury Professionals.

As a research associate, Dr. Jahanian has continued his postdoctoral work, focusing on daily arm use and progression of shoulder pathology in manual wheelchair users who have spinal cord injury. He hopes to develop feedback tools for wheelchair users to help preserve their upper arm function and prevent injuries — to allow them to be active without risk of injury. In addition to this research, Dr. Jahanian is collaborating with Emma Fortune Ngufor, Ph.D. (OR ’14), Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, on a study of remote monitoring for physical activity in aging women with premenopausal bilateral oophorectomy. In another project supported by the Mayo Clinic Kern Center, he is collaborating with a team of experts at Mayo Clinic in Rochester and Florida on quantification of daily physical function, using wearable sensors, in patients who have chronic pain.

Dr. Jahanian says his career focus is to advance rehabilitation technologies and their implementation into practice to improve the health and function of people who have disabilities. His postdoctoral research mentor Melissa “Missy” Morrow, Ph.D. (BME ’09, CTSA ’13), a research collaborator in the Mayo Clinic Kern Center and associate director of the Center for Recovery, Physical Activity, and Nutrition at the School of Health Professions at the University of Texas Medical Branch, says Dr. Jahanian has potential to be a leader in the study of spinal cord injury health and rehabilitation. “Dr. Jahanian is one of the most talented, promising postdoctoral researchers we’ve encountered.”

Dr. Jahanian has 11 peer-reviewed manuscripts — seven as first author. Two of his first-author manuscripts
are cited as the most read and accessed on the respective journal websites. His presentation on shoulder MRI and daily arm use at the American Society of Biomechanics was recognized as a finalist for the Clinical Biomechanics Award, and he was a featured speaker on wheelchair technology at the 2022 Design of Medical Devices Conference. He was a major contributor to the renewal of Dr. Morrow’s R01 grant, and his research led to Dr. Jahanian receiving the Mayo Clinic Alumni Association Edward C. Kendall Award for Meritorious Research.

“I am extremely grateful for being honored with the Mayo Clinic Alumni Association Edward C. Kendall Award,” he says. “Receiving this award not only acknowledges my contributions but also motivates me to continue pushing the boundaries of my field.

“I’ve learned a lot from Dr. Morrow, our team, and colleagues here at Mayo Clinic and at other universities. I came to Mayo Clinic because it’s a leader in physical medicine and rehabilitation and a good fit with my interest in applying robotics and novel technologies to healthcare and rehabilitation.”

Dr. Jahanian had another significant influence on his career path. His father, now deceased, was a biomedical engineer who used a wheelchair for several years due to health problems. “While a wheelchair wasn’t his primary mobility device, it improved his function,” says Dr. Jahanian. “That may play a role in my desire to improve the function and quality of life for people who use wheelchairs. I’ve long known I wanted to work in rehabilitation engineering.”

Kendall Award nominees are M.D.s or Ph.D.s on any Mayo Clinic campus who received a doctoral degree in the past five years and have a postdoctoral research training appointment (includes research fellows and research associates but not fellows eligible for the Balfour Award or visiting scientists) approved by the Mayo Clinic Research Committee or have completed the appointment in the past year.
Mayo Clinic School of Graduate Medical Education gives awards

Each year, Mayo Clinic School of Graduate Medical Education recognizes excellence among residents and fellows. This year’s awards include the following.

**MAYO BROTHERS DISTINGUISHED FELLOWSHIP AWARD**
Recognizes qualities associated with William J. Mayo, M.D., and Charles H. Mayo, M.D. Each year since 1997, Mayo Clinic School of Graduate Medical Education has selected six trainees from Arizona, Florida and Rochester/Midwest to receive the award based on outstanding clinical performance, humanitarianism and scholarly activity.

- **Allison Bock, M.D.**
  (HEMO ’23)
  Division of Hematology
  Mayo Clinic in Rochester

- **Elliott Campbell, M.D.**
  (DERM ’23)
  Department of Dermatology
  Mayo Clinic in Rochester

- **Wiaam Elkhatib, M.D.**
  (I ’23)
  Department of Internal Medicine
  Mayo Clinic in Florida

- **Peace Eneh, M.D.**
  (I ’19, ANES ’22, ANPD ’23)
  Division of Pediatric Anesthesiology
  Mayo Clinic in Rochester

- **Jacob Hammond, M.D.**
  (S ’23)
  Department of Surgery
  Mayo Clinic in Arizona

- **Omair Shariq, M.B.B.S.**
  (S ’24)
  Department of Surgery
  Mayo Clinic in Rochester
BARBARA BUSH DISTINGUISHED FELLOWSHIP AWARD
Recognizes outstanding clinical performance and scholarly activity with a particular emphasis on humanitarianism. The award is named to honor the contributions of Barbara Bush, former U.S. first lady and former Mayo Clinic trustee.

Tiffany Wu, M.D.
(CTSA ’23, GI ’23)
Division of Gastroenterology and Hepatology
Mayo Clinic in Rochester

PATIENT SAFETY AWARD
Recognizes an outstanding patient safety project.

Elaine Griffeth, M.D.
(S ’26, TS ’28)
Department of Surgery
Mayo Clinic in Rochester

DIVERSITY AWARD
Recognizes individuals or projects that have significantly contributed to greater MCGSME diversity and support recruitment or retention of diverse learners.

Shanterian King, D.O.
(PMR ’23)
Department of Physical Medicine and Rehabilitation
Mayo Clinic in Rochester

QUALITY IMPROVEMENT AWARD
Recognizes an outstanding clinical or nonclinical quality improvement project.

Elaine Griffeth, M.D.
(S ’26, TS ’28)
Department of Surgery
Mayo Clinic in Rochester

HEALTHCARE DISPARITIES AWARD
Recognizes an outstanding healthcare disparities project.

Nirosha Perera, M.D.
(I ’23)
Department of Internal Medicine
Mayo Clinic in Rochester

WELL-BEING AWARD
Recognizes individuals or projects that have significantly contributed to greater MCGSME or overall clinical care team well-being.

Sawyer Berrett, D.O.
(P ’23, CAP ’24)
Division of Child and Adolescent Psychiatry and Psychology
Mayo Clinic in Rochester
Mayo Clinic leads $41 million federal grant to advance multiethnic Alzheimer’s research

Armed with $41 million in new federal funding, Mayo Clinic researchers and colleagues from 13 other institutions around the country are pursuing three multiethnic projects to identify targets for treatment.

The new research program seeks to identify the next generation of precision medicine biomarkers and potential novel therapeutic targets of Alzheimer’s disease and related dementias in multiethnic populations. The program, called Centrally-Linked Longitudinal Peripheral Biomarkers of AD in Multiethnic Populations (CLEAR-AD), will be funded by a five-year grant from the National Institute on Aging.

Nilüfer Ertekin-Taner, M.D., Ph.D. (NSCI ’03, IL ’04, N ’07, NBN ’08), will lead the program with co-principal investigator Minerva Carrasquillo, Ph.D. (NSCI ’11) — both in the Department of Neuroscience at Mayo Clinic in Florida — and two others from the Indiana University School of Medicine.

“We know that Alzheimer’s disease affects patients from African American backgrounds at a rate twice as high as that in white populations. For Latino Americans, the risk is one-and-a-half times greater than that in white populations,” says Dr. Ertekin-Taner, who leads the Genetics of Alzheimer’s Disease and Endophenotypes Laboratory at Mayo Clinic in Florida. “These populations have traditionally been understudied for Alzheimer’s disease, leading to a major knowledge gap. When we try to understand the molecular underpinnings, the disease fingerprints, we need to understand it for all of us to identify biomarkers and therapies.”

The research projects aim to:

• Analyze blood and donated brain tissue samples from patients of African American, Latino American and non-Hispanic white backgrounds to identify molecular signatures that will serve as precision medicine biomarkers and therapeutic targets.
• Analyze blood and brain tissue samples from deceased patients with and without Alzheimer’s who have donated their samples for research to identify molecular signatures linked between the brain and the blood.
• Analyze blood samples over time from patients with Alzheimer’s disease and unaffected individuals using large-scale cohorts collected from the Mayo Clinic Study of Aging, Alzheimer’s Disease Neuroimaging Initiative, Alzheimer’s Disease Research Center at Mayo Clinic and five other Alzheimer’s Disease Research Centers across the country.

“We hope to find biomarkers that will enable us to predict whether somebody is going to develop Alzheimer’s disease and how fast their disease may progress and, eventually, find precision medicine cures for this complex condition,” says Dr. Ertekin-Taner.
Paul Friedman, M.D., receives 2022 Mayo Clinic Distinguished Inventor award

Paul Friedman, M.D. (CV ’96, CVEP ’97), the Norman Blane and Billie Jean Harty Chair, Mayo Clinic Department of Cardiovascular Medicine Honoring Robert L. Frye, M.D., and the Edward W. and Betty Knight Scripps Professor of Cardiovascular Medicine in Honor of George M. Gura, Jr., M.D., received the 2022 Mayo Clinic Distinguished Inventor award.

The Mayo Clinic Distinguished Inventor award recognizes innovative inventors at Mayo Clinic. The award is presented to a member of the Mayo Clinic voting staff whose career demonstrates great distinction in innovative and impactful contributions to improving people’s health.

Dr. Friedman’s visionary approach to medical care is reflected in almost 60 issued biomedical patents. He has received funding as principal investigator on awards from the National Institute on Aging and National Science Foundation. His honors and awards include being named a Minnesota Top Inventor, receiving the Bright Idea Award for Innovation.

Mayo study lays foundation to predict antidepressant response in people with suicide attempts

Mayo Clinic researchers have discovered that people with major depressive disorder and a history of attempted suicide have distinct biomarkers that correlate with their response to antidepressant therapy. The findings are key to individualized treatment strategies and early identification of patients who are at the highest risk for suicide.

The researchers used multi-omics technologies — metabolomics and genomics — to analyze samples from patients with major depressive disorder. They compared samples of patients with and without a history of suicide attempt and found distinct blood-based multi-omics signatures between the two groups, despite all patients having the same diagnosis of major depressive disorder. A prior suicide attempt is the highest risk factor for suicide in the general population.

“Evaluating suicidal patients can be challenging because clinical risk assessments are inherently subjective and major depressive disorder has high degrees of variability,” says Paul Croarkin, D.O. (P ’11), Department of Psychiatry and Psychology at Mayo Clinic in Rochester; the Ervin A. and Margaret C. Mueller Director, Mayo Clinic Children’s Research Center; and senior investigator of the study. “Our study lays a foundation for advancing the prognostic potential of this disease and enhancing patient outcomes that use both biological and digital biomarkers.”

The team found that variations in the genes CLOCK and ARNTL differentiate in patients with and without a prior suicide attempt. Both genes are related to the circadian rhythm, which regulates critical functions including behavior, metabolism, hormone levels and sleep. These specific gene variations also are associated with lower antidepressant response and remission rates.

By simultaneously evaluating the genome and metabolome, the researchers discovered biological signatures that could not be found by the genome or metabolome alone. The study is part of ongoing efforts at Mayo Clinic to understand the biology of suicidality to improve diagnostic approaches, treatments, and outcomes for patients with depression and other mood disorders.
A history of cancer, coronary artery disease may reduce risk of dementia

The risks of dementia, cancer and vascular disease increase with age, but the connection among the conditions is not fully understood. Mayo Clinic researchers report an intriguing finding — having a history of cancer or coronary artery disease may reduce the risk of dementia.

The researchers set out to determine how a history of cancer or vascular disease in individuals may influence a future risk of dementia. They analyzed data from 1998 to 2020 from a unique group of Mayo Clinic study participants who died at age 95 or older, had undergone an autopsy and had donated their brains to the Mayo Clinic Brain Bank for research. Researchers evaluated medical records for a documented history of cancer or vascular disease, such as coronary artery disease and diabetes.

The study found that a history of cancer reduced the risk of dementia and was associated with a lower amount of Alzheimer’s disease brain changes, such as buildup of the toxic tau protein, a hallmark of the disease. “It may be the result of underlying molecular changes that oppose each other,” says Melissa Murray, Ph.D. (NSCI ’12), Department of Neuroscience and senior author of the study. “Cancer wants to proliferate whereas molecular changes associated with Alzheimer’s disease want to kill cells. It could be a tug of war.” Dr. Murray leads the Translational Neuropathology Laboratory at Mayo Clinic in Florida.

Researchers say it is possible that common genes and mechanisms normally involved in cell growth and maintenance may be regulated in opposite directions. They speculate that increased pro-growth mechanisms may increase cancer risk, while increased cell death mechanisms may increase dementia risk. Although the topic was not studied in this paper, researchers note that treatments for cancer, such as chemotherapy, also may affect brain cells and prevent the formation and spread of proteins associated with age-related neurodegenerative diseases. They say a better understanding of what is happening inside the brains of patients before, during and after cancer treatment would be beneficial in identifying factors that promote or prevent dementia.

The research team also studied vascular risk factors, such as smoking, hypertension and diabetes, in calculating the odds of developing dementia. While all these conditions increased risk, the researchers found that diabetes was the strongest contributing risk factor. Surprisingly, the researchers found that a history of coronary artery disease was found to decrease the risk of dementia. They hypothesize that this could be associated with the benefits of treatment over many years for known disease. Medications that treat coronary artery disease are designed to reduce dangerous plaques in the coronary arteries and promote the health of blood vessels in the brain.

The researchers recognize that controlling vascular risk factors is a promising strategy for lowering the risk of dementia and say their study results support living a healthy lifestyle overall.

“I think it really does point to a need to emphasize the importance of avoiding diabetes and the potential importance of being treated for coronary artery disease,” Dr. Murray says.
Mayo Clinic to lead new radiotracer trial for detecting pancreatic cancer

In an academic-industrial collaboration, Mayo Clinic is assessing a new radiotracer in pancreatic cancer imaging.

As part of a clinical trial, the new agent, 68Ga-Fibroblast-Activation-Protein-Inhibitors (FAPI)-46 (68Ga-FAPI-46), will be compared with 18-fluorodeoxyglucose (FDG), which is the current standard-of-care radiotracer in PET imaging of pancreatic cancer.

“The research will focus on pancreatic cancer and evaluate whether this radiotracer does what it’s supposed to do, and whether it provides incremental information above and beyond the standard of care,” says Ajit Goenka, M.D. (RD ’15), Department of Radiology at Mayo Clinic in Rochester and principal investigator. “Seeing is saving. In addition to providing novel insights into the biology of the cancer and identifying subtle sites of metastasis, we are particularly excited about our potential ability to see the disease and target it with precision and minimally invasive therapeutics.”

Mark Truty, M.D. (S ’04, CI ’06, S ’09), Division of Hepatobiliary and Pancreas Surgery at Mayo Clinic in Rochester, says that in view of the dismal prognosis of pancreatic cancer, novel treatment strategies are urgently needed to improve outcomes. “FAPI PET could lead to peptide receptor radionuclide therapy for pancreatic cancer, which will be very exciting.”

Dr. Goenka says the wide and evolving role of fibroblast-activating protein-targeted imaging and therapeutics has the potential to scale its impact beyond pancreatic cancer to other applications.

Fibroblast activation protein-expressing cancer-associated fibroblasts play a central role in pancreatic cancer’s aggressiveness. This radiotracer has emerged as a PET radiotracer potentially suited to fibroblast activation protein-targeted imaging and therapy in pancreatic cancer. In this investigator-initiated trial, the team seeks to address the unmet clinical needs in pancreatic cancer and improve understanding of disease biology.

According to Dr. Goenka, Mayo Clinic is uniquely positioned for head-to-head comparisons of 68Ga-FAPI-46 and FDG PET.

In a strategic alliance, Mayo Clinic and Sofie Biosciences investigators will work to identify and translate a technological solution for mitigation of a cancer problem.

“Traditionally, long regulatory and reimbursement approval pathways coupled with high costs of comparative studies have delayed clinical access to promising precision tools,” says Dr. Goenka. “For the clinical translation of therapeutic-diagnostic radiotracers, an academic-industrial partnership based on complementary strengths and a coherent clinical development strategy is needed to reduce the risks and raise the likelihood of meeting FDA standards and consumer expectations.”
Mayo Clinic awards named professorships

Mayo Clinic awarded named professorships — the highest academic distinction at Mayo Clinic.

**Roberto Cattaneo, Ph.D. (MMED ’99)**
Richard O. Jacobson Professor of Molecular Medicine
- Department of Molecular Medicine
- Department of Biochemistry and Molecular Biology
- Department of Immunology
- Mayo Clinic in Rochester

**David Knopman, M.D. (N ’00)**
Robert H. and Susan M. Rewoldt Professor of Neurology Honoring Bradley F. Boeve, M.D.
- Division of Behavioral Neurology, Department of Neurology
- Mayo Clinic in Rochester

**Sean Pittock, M.D.**
(N ’02, I1 ’03, NMS ’04)
Applebaum Family Professor of Neurosciences
- Marilyn A. Park and Moon S. Park, M.D., Director of the Center for Multiple Sclerosis and Autoimmune Neurology
- Department of Neurology
- Division of Clinical Biochemistry and Immunology, Department of Laboratory Medicine and Pathology
- Mayo Clinic in Rochester

**Heidi Connolly, M.D. (I ’89, CV ’93)**
Judd and Mary Morris Leighton Professor of Cardiovascular Diseases and Hypertension in Honor of Dr. Alex Schirger
- Division of Structural Heart Disease, Department of Cardiovascular Medicine
- Mayo Clinic in Rochester

**Aaron Krych, M.D. (MED ’05, OR ’10)**
John and Posy Krehbiel Professor of Orthopedics Honoring Bernard F. Morrey, M.D.
- Division of Orthopedic Trauma Surgery; co-chair, Division of Sports Medicine, Department of Orthopedic Surgery
- Mayo Clinic in Rochester

**Cheryl Willman, M.D.**
(MED ’81, PATH ’81)
David A. Ahlquist, M.D., Professor of Cancer Research
- Stephen and Barbara Slaugie Executive Director, Mayo Clinic Cancer Programs, and Director, Mayo Clinic Comprehensive Cancer Center
- Department of Laboratory Medicine and Pathology
- Mayo Clinic in Rochester

**Paul Friedman, M.D.**
(CV ’96, CVEP ’97)
Edward W. and Betty Knight Scripps Professor of Cardiovascular Medicine in Honor of George M. Gura, Jr., M.D.
- Norman Blane and Billie Jean Harty Chair, Mayo Clinic Department of Cardiovascular Medicine Honoring Robert L. Frye, M.D.
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- Department of Physiology and Biomedical Engineering
- Mayo Clinic in Rochester

**Aleksey Matveyenko, Ph.D. (PHYS ’14)**
J.W. Kieckhefer Professor of Regenerative Medicine to Support Research in Type 1 Diabetes
- Department of Physiology and Biomedical Engineering
- Division of Endocrinology, Diabetes, Metabolism, and Nutrition, Department of Internal Medicine
- Mayo Clinic in Rochester

**Victor Montori, M.D. (I ’99, CMR ’00, CLRSH ’01, ENDO ’02)**
Robert H. and Susan M. Rewoldt Professor of Endocrinology Honoring Daniel L. Hurley, M.D.
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- Mayo Clinic in Rochester

**Thomas Witzig, M.D.**
(HEM ’86)
Barbara Woodward Lips Professor
- Division of Hematology, Department of Internal Medicine
- Department of Laboratory Medicine and Pathology
- Mayo Clinic in Rochester

**Thomas Habermann, M.D.**
(I ’82, HEM ’85)
Purvis and Roberta Tabor Professor
- Division of Hematology, Department of Internal Medicine
- Mayo Clinic in Rochester
Obituaries

Donn Crilly, M.D. (S ’59), died June 16, 2023.
Guoqian Jiang, M.D., Ph.D. (All ’06), died July 15, 2023.
Nolan Karstaedt, M.D. (RD ’89), died May 1, 2023.
Neil Thomford, M.D., Ph.D. (S ’63), died April 25, 2023.

Juliana Kling, M.D., is dean, Mayo Clinic Alix School of Medicine – Arizona Campus

Juliana “Jewel” Kling, M.D. (I ’13, CMR ’14), is the new vice dean of Mayo Clinic Alix School of Medicine and the Suzanne Hanson Poole Dean of Mayo Clinic Alix School of Medicine – Arizona Campus. She is responsible for undergraduate medical education activities on the Arizona campus and is a facilitator and coordinator of the academic, curricular, and administrative activities and programs in Arizona.

Dr. Kling is chair of the Division of Women’s Health Internal Medicine at Mayo Clinic in Arizona, assistant director of the Center for Women’s Health, and associate chair of Equity, Inclusion and Diversity for the Department of Internal Medicine at the Arizona campus. She joined the staff of Mayo Clinic in 2014 and is a professor of medicine in the Mayo Clinic College of Medicine and Science.

Dr. Kling completed internal medicine residency at Mayo Clinic School of Graduate Medical Education in Arizona, followed by appointment as chief resident in internal medicine. She completed medical school and a master’s in public health at the University of Arizona – Tucson.

Dr. Kling succeeds Michele Halyard, M.D. (RADO ’89), who served in the role for 13 years including overseeing the opening of the Arizona campus of the medical school. Dr. Halyard retired in June.

Juliana “Jewel” Kling, M.D.
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Mayo Clinic is committed to creating and sustaining an environment that respects and supports diversity in staff and patient populations.

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‘WE’LL DO IT’

William Worrall Mayo, M.D., and his wife, Louise, mortgaged their home to purchase a microscope. Dr. Mayo had used a microscope while training at Indiana Medical College. After he opened a medical practice in Rochester, Minnesota, in 1864, Dr. Mayo made frequent educational trips to the East Coast. After one of those visits, he told his family he’d seen a new microscope that would benefit his patients but would require him to mortgage the family home. Louise said, “Well, William, if you could do better by the people with this microscope and you really think we need it, we’ll do it.”
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