Medical Bulletin

UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

FALL 2017

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In sync

How a precisely orchestrated medical team at the U of M separated conjoined twins

PHOTO: BRADY WILLETTE

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Cover photo of twins Paisleigh and Paislyn Martinez by Jim Bovin

Medical Bulletin

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Tolar named Medical School dean

Jakub Tolar, M.D., Ph.D.

UNIVERSITY OF MINNESOTA President Eric Kaler, Ph.D., has appointed Jakub Tolar, M.D., Ph.D., dean of the Medical School, pending approval by the Board of Regents. He succeeds Brooks Jackson, M.D., M.B.A., who has accepted the position of vice president for medical affairs and dean of medicine at the University of Iowa.

A Distinguished McKnight Professor of Pediatrics and holder of the Edmund Wallace Tulloch and Anna Marie Tulloch Chair in Stem Cell Biology, Genetics, and Genomics, Tolar is a longtime member of the Medical School's Faculty, most recently serving as the school's executive vice dean.

He is an internationally recognized leader in regenerative medicine and has directed the University's Stem Cell Institute since 2013.

"Dr. Tolar is known for his dedication to patients and for his collaborative approach to working with elected officials, citizens, health care partners, and colleagues," Kaler said in announcing the new appointment. "I am confident that he will continue our positive momentum through his energetic commitment to advancing discovery, educating the next generation of health care leaders, and leading in high-quality clinical care."

A renowned specialist in epidermolysis bullosa, Tolar sees patients from around the world, including Canadian Jonathan Pitre.

An expert in pediatric blood and marrow transplantation, Tolar sees pediatric patients and conducts research aimed at finding new ways to treat lethal childhood diseases – such as cancer, metabolism errors, and genetic disorders – using stem cell transplantation, gene therapy, and gene editing.

Kaler also named Tolar interim vice president for health sciences "while the University determines an ideal structure for the continued success of our health sciences." Besides the Medical School, the health sciences include the schools or colleges of dentistry, pharmacy, nursing, public health, and veterinary medicine. MB

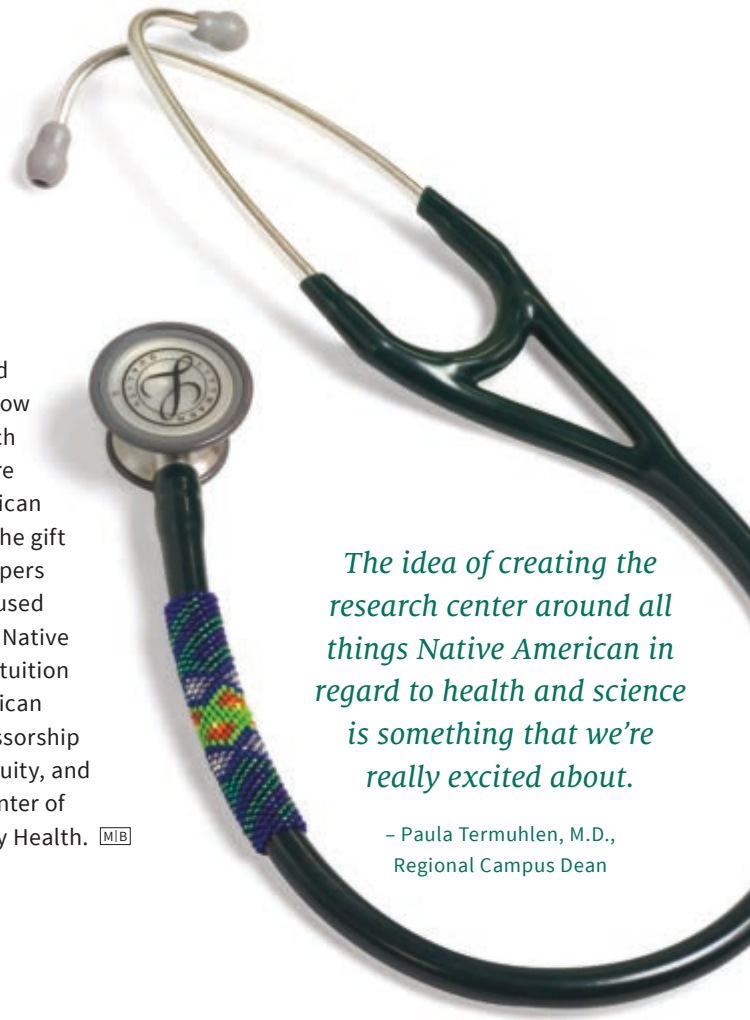
$10 million gift boosts Medical School, Duluth's Native American health initiatives

A $10 million gift from an anonymous donor will establish a Native American Research Center of Excellence at the University of Minnesota Medical School, Duluth campus. The gift – the largest ever to the Medical School's Duluth campus – will support collaboration with American Indian and Alaska Native communities to improve their health through research, leadership, and education.

The Duluth campus is nationally renowned for its efforts to improve health care access and outcomes in rural Minnesota and in American Indian and Alaska Native communities.

"Minnesota has some of the best health outcomes, and yet we know that we have some of the largest health disparities," says Regional Campus Dean Paula Termuhlen, M.D. "The idea of creating the research center around all things Native American in regard to health and science is something that we're really excited about."

Medical School faculty and staff will help to determine how the gift will be used and which topics in health disparities are most critical for Native American communities in Minnesota. The gift will support the Memory Keepers Medical Discovery Team (focused on dementia and diabetes in Native American communities), full-tuition scholarships for Native American students, an endowed professorship in Native American health equity, and pipeline programs for the Center of American Indian and Minority Health. MB



The idea of creating the research center around all things Native American in regard to health and science is something that we're really excited about.

– Paula Termuhlen, M.D., Regional Campus Dean

PHOTO: JOEL MOREHOUSE

WANTED: THE ADVENTUROUS AND THE GENEROUS

The University of Minnesota has transformed the lives of generations of Minnesotans, kept the state's economy strong, fueled creativity, and become a source of answers for people around the world. Few other public universities even come close to the breadth of the U's expertise.

The extraordinary institutional capacity of the state's land-grant university, combined with quintessential Minnesota values—resourcefulness, resilience, and a shared belief in the value of opportunity—creates a powerful force for change.

Driven.
The University of Minnesota Campaign

On September 8, the University announced that it is embarking on the largest philanthropic initiative in its history, *Driven: The University of Minnesota Campaign*, with a $4 billion goal. M|B

Learn more and watch a video about the campaign's priorities at driven.umn.edu.

Honoring a legacy of innovation and healing

Two mold-breaking University of Minnesota centers now bear the name of a pioneering alumnus. In recognition of his support of the University and his field-shaping legacy, the interdisciplinary centers are now known as the Earl E. Bakken Medical Devices Center and the Earl E. Bakken Center for Spirituality and Healing.

Shortly after he graduated from the U in 1948, Bakken founded Medtronic Inc., which later became one of the world's largest medical device development companies. Bakken worked closely with U scientists, engineers, and health care providers over the course of his career.

He also has a unique appreciation for both the art and science of health care, as demonstrated by his longstanding support for the Center for Spirituality and Healing, which is focused on research, outreach, and education related to integrative health and well-being.

Bakken has received honorary degrees from several universities, including the first and only M.D. Honorary Causa from the U's Medical School, in 2007.

University President Eric Kaler and Earl Bakken celebrate the renaming of the centers.

"Renaming these centers is our way of honoring the spirit of discovery and innovation that Earl Bakken has instilled in everyone he has encountered through his work at the University," says University of Minnesota President Eric Kaler, Ph.D. "His efforts have helped us become leaders in finding new ways to promote health and healing in the communities we serve." M|B

PHOTO: SARAH ANDERSON PHOTOGRAPHY

PHOTOS: TODD BAUER, TMB IMAGES

ABOVE Sam Waldron, 17, rode 180 miles over two days to celebrate 15 years as a cancer survivor.

WEB EXTRA

See more photos and watch for information on next year's event at chainbreakerride.org.

Chasing down cancer

THEY RODE IN HONOR of family members whose lives cancer has claimed. They rode to fight back against a disease that upended their lives. They rode for the doctors and scientists who combat cancer on the front lines.

In total, 1,021 cyclists – ranging from age 14 to 81 – and more than 400 volunteers took part in the first-ever Chainbreaker ride for hundreds of reasons. The riders raised $1.3 million for the event, held August 11–13 across the metro area and southern Minnesota, supports collaborative, lifesaving cancer research at the Masonic Cancer Center, University of Minnesota – one of only 49 National Cancer Institute–designated Comprehensive Cancer Centers in the country. MB

GIVE TO THE MAX DAY
16 NOVEMBER 2017

Make your gift to the University of Minnesota Medical School at givingday.umn.edu.

U Medical School ranked among the world's best

The Academic Ranking of World Universities (ARWU) has rated the University of Minnesota Medical School 25th in its latest list of the world's top medical schools.

The ARWU's ranking indicators include alumni and staff who are Nobel Laureates, Fields Medalists, or highly cited researchers. Major universities in every country with a significant number of articles indexed by the Science Citation Index–Expanded and Social Science Citation Index are also included.

In total, more than 1,200 institutions have been ranked in each of the ARWU's five broad subject fields: clinical medicine and pharmacy (the category into which the medical school rankings fall), natural sciences and mathematics, engineering/technology and computer sciences, life and agriculture sciences, and social sciences. Institutions are ranked according to their academic or research performance in each field. MB

U brain scientist receives American Legion's top award

Renowned neuroscience researcher Apostolos Georgopoulos, M.D., Ph.D., was awarded the American Legion Distinguished Service Medal in August. The award recognizes "outstanding service to the nation," according to the American Legion, and Georgopoulos was selected for his decades of research into Gulf War Illness and traumatic brain injuries common among veterans.

The American Legion honor comes just months after the American Immigration Lawyers Association awarded Georgopoulos its 2017 Immigrant of Distinction Award for his significant contributions to medicine.

Georgopoulos, who also holds the American Legion Brain Sciences Chair, is director of the Brain Sciences Center at the Minneapolis Veterans Affairs Health Care System and a professor of neuroscience, neurology, and psychiatry in the Medical School. He also directs the University's Center for Cognitive Sciences and is a leading authority on neural mechanisms underlying movement. MB

PHOTO: BRADY WILLETTE

Apostolos Georgopoulos, M.D., Ph.D., is well known for his research on posttraumatic stress disorder in military veterans.

New grant supports FASD research

A common preventable birth defect, fetal alcohol spectrum disorder (FASD) describes a number of cognitive impairments and physical abnormalities that can occur in children born to mothers who drink alcohol during their pregnancies. An estimated 2 to 4 percent of the population is affected by FASD.

With a new $1.7 million grant from the National Institute for Alcohol Abuse and Alcoholism, Jeffrey Wozniak, Ph.D., associate professor of psychiatry at the University of Minnesota Medical School, aims to better understand how prenatal alcohol exposure changes brain networks over time.

"This area of research is relatively young, so there is a lot to learn," says Wozniak. "We really have no way to predict how the disorder will progress in an individual or what happens to specific parts of the brain as normal development occurs."

Wozniak will scan the brains of about 90 children ages 8 to 16 who are affected by FASD. Then, a year and half later, he'll perform another round of brain scans in the same group. He will analyze the changes in the scans to determine how the brain organizes its networks, how those networks differ from those in healthy brains, and which specific brain circuits appear to be most affected.

"Sometimes FASD presents with physical symptoms—like smaller eyes, changes to the lip and mid-face, ear abnormalities, and other telltale signs—but in most cases, it impacts a child in ways we cannot immediately see," Wozniak says. "If we know how and where FASD affects the brain, we can provide a more accurate early diagnosis."

In doing so, Wozniak adds, physicians will be able to improve the quality of life for children with FASD. MB

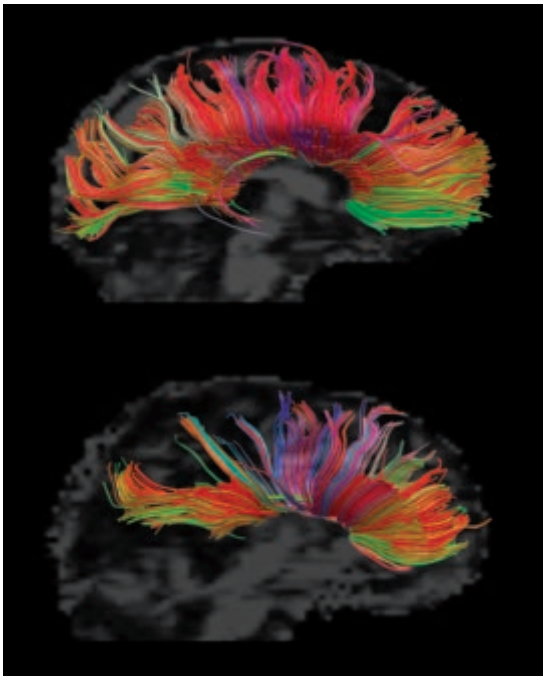


IMAGE COURTESY OF JEFFREY WOZNIAK, PH.D.

Tractography shows typical brain white matter development (top) and abnormalities from prenatal alcohol exposure (bottom).

LOCATION: Chiang Mai, Thailand **MISSION:** Understanding the intersection of human, animal, and environmental health

Interconnected

ONE OF NICHOLAS COOK-ROSTIE'S REVELATIONS from his two weeks in Thailand last winter came courtesy of a rural village elder, a traditional healer who explained that he diagnoses diabetes by watching how long a person's wounds take to heal.

"They don't have access to the technology and textbooks that we do, and the nearest hospital is miles away," says Cook-Rostie of the Thai healers he encountered. "But they have keen observation, and they're so connected with their environment.

"They go out, they find medicinal plants, different herbal remedies, to treat common ailments. The community depends on each other to stay healthy," adds the first-year U of M medical student.

The trip was part of a Learning Abroad Center course called Global Health in Thailand: Humans, Elephants, and Disease. Roughly 25 students from a wide range of disciplines spent time in and near Chiang Mai probing the interconnectedness of human, animal, and environmental health—an approach known as One Health.

The course includes a visit to Woody's Elephant Camp, a sanctuary outside the city. The transmission of tuberculosis from elephants to humans and vice versa offers a vivid example of the One Health concept, says course coleader Karin Hamilton, D.V.M., M.P.H., an assistant professor in the U's College of Veterinary Medicine. Students also examine how disruptions in environmental conditions can foster disease in both humans and animals.

Students participated in small-group "scavenger hunts" during which they observed social determinants of health in Chiang Mai. They found conditions that promote better health and those that compromise it, Hamilton explains.

SUBMIT YOUR WORK

The *Medical Bulletin* is seeking compelling global health photos and stories by or about U of M Medical School students, alumni, or faculty members. Selected submissions will be published in future issues of the *Medical Bulletin*.

For more information or to submit your photo or story, email managing editor Nicole Endres at nendres@umn.edu.

PHOTO: COURTESY OF NICHOLAS COOK-ROSTIE

After the trip, the group met for seven more weeks to debrief. The multidisciplinary mix of students led to rich discussion, Cook-Rostie says.

"It was awesome to be with students studying law, business, all these other fields, and see what they notice—how their experience of health and health care is different from mine, because they are my future patients."

By Susan Maas, a freelance writer and frequent contributor to the *Medical Bulletin*

WEB EXTRA

Read more about Nicholas Cook-Rostie's unlikely path to medical school at z.umn.edu/cook-rostie.

Synchrony

Born conjoined, twins Paisleigh and Paislyn Martinez have grown stronger every day since a 44-person medical team performed their precisely orchestrated separation

BY KRYSTLE BARBOUR

PHOTO: BRIAN CARNELL

Sunlight is peeking through the window on the third floor of University of Minnesota Masonic Children's Hospital, where twin sisters Paisleigh and Paislyn Martinez are lying face to face, holding one another in an embrace. As they stir, they kick their feet — one twin with toenails painted pink, the other blue. ** It's mid-May, and the 3-month-old twins, who were born conjoined, are quickly approaching the big day: separation. ** The rare surgery will be complex: Identified medically as thoraco-omphalopagus conjoined twins, Paisleigh and Paislyn are connected from their chests to their belly buttons, their livers fused in the middle and their hearts entwined. ** "There have been so many 'what ifs' and situations where we were told they might not make it," says the girls' mom, Paris Bryan. "They've overcome so much already at such a young age." ** "I still get emotional thinking of it," says their dad, Ernesto Martinez.

PHOTO: JIM BOVIN

PHOTO: BRIAN CARNELL

ABOVE A 3-D model of the twins' hearts showed for the first time a tiny bridge connecting them – a critical finding that altered their surgical team's plan for separation.

OPPOSITE TOP With Paisleigh and Paislyn having such different care needs, parents Ernesto Martinez and Paris Bryan cherish the moments they can spend with the girls together.

OPPOSITE BOTTOM Paisleigh is being weaned off oxygen therapy and is taking all of her nutrition by mouth.

On May 25, 2017, more than 40 surgeons, nurses, and other medical experts filled the University of Minnesota Masonic Children's Hospital operating room. Each baby had her own color-coded medical team that matched her toenail polish: blue surgical caps for Paislyn's team and red caps for Paisleigh's team. The teams had spent months preparing for this moment—discussing, conducting simulations, and drawing upon the expertise of their hospital and University of Minnesota Medical School colleagues.

"Being in that operating room was pretty climactic. There were 44 people, I think. And everyone had a job. There were no bystanders," says pediatric cardiologist Matthew Ambrose, M.D., who cared for the twins before and after their delivery.

As three anesthesiologists completed their work, four general surgeons, two cardiac surgeons, three cardiologists, four nurse anesthetists, four surgical techs, two heart pump techs, four operating room nurses, and two nurse managers stood at the ready. Then, it was their turn.

Several hours into the procedure, Anthony Azakie, M.D., chief of pediatric heart surgery at Masonic Children's Hospital and a professor of surgery in the Medical School, opened the babies' shared chest wall and divided their ribs. He then separated the "bridge" that connected their hearts.

"We had watched them connected for so many weeks, and now that the final separation had occurred, there was something surreal about it," Azakie says. "The fact that using modern technology and using current surgical strategies and medical care means you can separate them and separate them safely is awe inspiring."

An uncommon event

Conjoined twins are rare, about one in every 200,000 live births. Most surgeons won't see a case in their lifetimes.

"The girls were an embodiment of a kind of physiology none of us had ever seen before," says Ambrose. "The uniqueness of their situation forced us to start basic and build from there."

The team—which included specialists in critical care, neonatology, nephrology, cardiology, and surgery—connected through weekly meetings that started before the twins were born.

"We had to come out of our silos and literally and figuratively get everyone in the same room at the same time," says first-year pediatric resident Timothy Rauschke, M.D., who participated as a member of the consulting pediatric kidney team.

"It was the only way to accomplish the kind of care these babies needed," adds Ambrose. "Having a team-oriented approach filled with sharing, humbleness, and true collaboration is what allowed us to have success."

Advanced technology developed at the U's Earl E. Bakken Medical Devices Center came into play, too. Three-dimensional modeling and virtual imaging developed by graduate students at the center allowed Azakie and his colleagues to take a virtual tour of the girls' organs before the surgery. The model revealed a previously unseen bridge connecting the two hearts—a critical finding that altered the surgical plan.

"The moment we recognized that physical connection between the two hearts was scary," recalls Ambrose. "There were multiple reports of other babies with a similar connection who did not survive surgery, but I suspect that was because it wasn't recognized before the surgery."

The team met numerous times in the operating room to walk through the separation, planning for just about every possible scenario.

PHOTOS: BRADY WILLETTE

UNCHARTED TERRITORY

BEFORE SEPARATING 3-month-old conjoined twins Paisleigh and Paislyn Martinez last May, U of M doctors discovered they had to perform a medical first.

Paislyn had become very ill. Her doctors knew already that she had serious heart conditions, tricuspid atresia with transposition of the great vessels and a ventricular septal defect. When they noticed a drop in her blood pressure and changes in her urine output, they called in pediatric cardiologist and Medical School assistant professor Gurumurthy Hiremath, M.D.

Because of Paislyn's form of congenital heart disease, she needed to have a hole between the two upper chambers of her heart if she was to survive the separation surgery. But the hole in the septum of her heart had become too small and needed to be enlarged through cardiac catheterization.

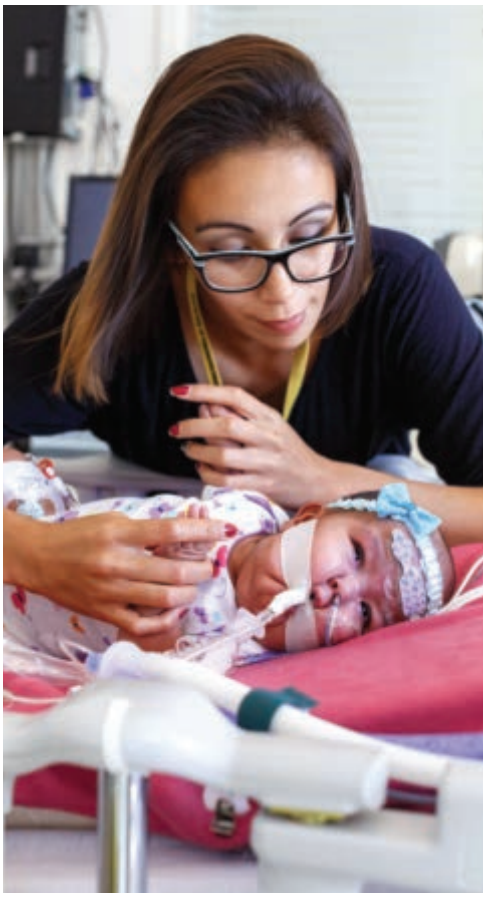
"We were in uncharted territory," says Hiremath. "There had been no report of a transcatheter intervention of any kind being performed in conjoined twins before separation."

Despite several challenges, Hiremath was able to complete the procedure. He inserted balloon catheters into Paislyn's heart through the femoral vein (a major blood vessel in the leg) and expanded the balloons across her septum, enlarging the hole and stabilizing her heart for surgery.

"We all worked so smoothly, effectively, and efficiently. It did not feel like it was our first time," says Hiremath. "The whole experience was planned and executed to perfection."

WEB EXTRA

Watch a video about how the care team meticulously prepared for the separation surgery at z.umn.edu/martineztwins.



PHOTOS: BRADY WILLETTE

Paisleigh's more of the chill person and just loves to watch people and see what everyone is doing. Paislyn can be shy sometimes, but she loves attention! She is really sassy.

– Paris Bryan, the twins' mother

Paisleigh occasionally takes a wagon ride to visit her sister in the cardiovascular intensive care unit, as "play dates" are an important part of their recovery.

After studying the 3-D models, Azakie determined that the entire layout of the operating room needed to change.

All the preparation paid off.

"The separation surgery took approximately nine hours and was orchestrated like a spectacular philharmonic score," says Daniel Saltzman, M.D., Ph.D., chief of pediatric surgery and overall lead for the separation surgery. "Nothing was left to chance, and every contingency was planned for. There were no surprises."

Recovery

For Paislyn and Paisleigh, the surgery opened a new chapter—recovery. Paislyn, who was born with serious heart conditions, tricuspid atresia with transposition of the great vessels and a ventricular septal defect, underwent a procedure called pulmonary artery banding of the heart immediately after separation—one of several operations she will undergo in her lifetime.

Before their separation, Paisleigh was helping to keep Paislyn alive, her body essentially acting as a heart, lung, and dialysis machine for her sister. Although she was born with a stronger "normal" heart, Paisleigh struggled after the separation surgery.

"Because her heart had been used to doing so much work for so long, she didn't tolerate changes in her lung function very well," says Caroline George, M.D., a critical care physician in the hospital's intensive care unit. Fortunately, once Paisleigh's heart got used to functioning on its own and recovered from the separation, her health improved rapidly, George says.

For both girls, growth and development are now priorities. Because of how they were connected, facing each other, their ribcages are misshapen, and their chest walls will eventually have to be reconstructed, possibly as late as a year from now.

"I've never personally taken care of conjoined twins before, but I have definitely taken care of babies born with chest wall deformities or deformities of their abdominal wall," says George, who is also an associate professor of pediatrics in the Medical School. "It's not exactly the same, but they have common problems."

A reconfigured team—which includes such specialists as a nutritionist, a pharmacist, nurses, and surgeons—still meets regularly to discuss the girls' progress. Meanwhile, as the twins' bodies recover and develop, their personalities have started to emerge.

"Paisleigh's more of the chill person and just loves to watch people and see what everyone is doing," says her mom. "Paislyn can be shy sometimes, but she loves attention! She is really sassy."

After spending their early months entwined, Paislyn and Paisleigh are now recovering in separate rooms. During her frequent visits, their mother usually stops first at Paislyn's room in the cardiovascular intensive care unit, where specialists are managing her heart condition. Paislyn is working hard on getting off the breathing tube. Although she's growing bigger and stronger, doctors expect her to remain in the hospital for several more months.

Paisleigh's room is a couple of floors up, on the general floor, where her care team is weaning her off oxygen. If her health stays on track, her doctors say, she may be able to go home next month.

"Play dates" are an important element of the twins' recovery, too, and as often as they can, nurses take Paisleigh out of her crib and put her in a little wagon to visit her sister.

"It's a blessing to see my girls getting bigger every day," says Bryan. "We can't wait for when they come home." MB

Krystle Barbour is a public relations coordinator for the Academic Health Center at the University of Minnesota.

SPECIAL DELIVERY

UNIVERSITY OF MINNESOTA Masonic Children's Hospital became home for Paislyn and Paisleigh Martinez before they were born. A routine ultrasound revealed that the twins were conjoined, and their mother, Paris Bryan, was quickly referred to the University of Minnesota Health Maternal-Fetal Medicine Center, which cares for women experiencing complex pregnancies.

Bryan put her trust in The Birthplace care team and Katherine Jacobs, D.O., who specializes in high-risk pregnancies. The collection of sonographers, nurses, care coordinators, surgeons, and physicians cared for Bryan and closely monitored the girls' growth and development.

They also outlined every detail of the delivery, and then practiced during an obstetric simulation on February 10. Delivery was slated for a month later, but Paisleigh and Paislyn had other plans and were born that same day at 34 weeks exactly.

"It worked out perfectly to have run through the birth scenario just prior to the real event," says Jacobs.

Opportunity knocks

State-funded Medical Discovery Teams are helping Medical School researchers find the keys to solving Minnesota's toughest health problems

BY BARBARA KNOX

Make no mistake: A strong medical school makes for a strong Minnesota. The University of Minnesota Medical School and its partners contributed more than $2.5 billion to the state's economy in 2010, according to a 2015 report by Minnesota Gov. Mark Dayton's blue ribbon commission on the Medical School. Its doctors and students care for more than 1 million people annually—spanning every county in Minnesota.

"The University belongs to Minnesotans, and its primary responsibility is to improve their quality of life," says Medical School Dean Jakub Tolar, M.D., Ph.D. "One of our most critical contributions is our medical and scientific research, through which we are able to improve health outcomes, stimulate new business development, create jobs, and help make Minnesota a better place to live."

So when Dayton signed the higher education funding bill in 2015, a groundswell of excitement began building at the University. Dayton had signed off on an unprecedented $30 million investment in the Medical School—$15 million annually for two years—that would allow the U to hire as many as 50 top-ranked scientists dedicated to addressing some of Minnesota's most pressing health care priorities.

"The ability to focus on problems that are of significant concern to Minnesotans is incredible," says Tolar, who also serves as the U's interim vice president for health sciences. "With this committed funding, we are able to attract the best and brightest researchers and position them for success."

Getting from better to best

The idea of building dedicated research cohorts comprising investigators who are at the forefront of their fields—the new Medical Discovery Teams (MDTs)—grew out of Dayton's blue ribbon commission on the Medical School. The commission recommended this investment strategy as one of the best ways to both strengthen the Medical School and benefit the state.

To make the most of the dollars, the Medical School's first step was to do a kind of in-house triage, an evaluation of which already strong research cadres could be jump-started from strong to world-renowned. After the vetting process, the Medical School identified four areas of focus: addiction, the biology of aging, rural and American Indian health disparities, and optical imaging and brain science.

"We identified these areas because they significantly affect quality of life in Minnesota," explains Tolar, "but also because we had a strong foundation already in place to build from. We can have maximum impact in these areas now and be in a position to lead these fields in the future. That is an exciting place to be."

A neuroscience solution

More than 30 University faculty, working in eight different departments from neuroscience to pharmacy, are already focused on studying addiction, a brain disease considered to be the No. 1 preventable cause of death in the United States. Drug overdose deaths in Minnesota alone rose 11 percent from 2014 to 2015, according to the Minnesota Department of Health.

"We all know there's a crisis with drug addiction in the U.S.," says Timothy Ebner, M.D., Ph.D., head of the Medical School's Department of Neuroscience and holder of the Max E. and Mary LaDue Pickworth Endowed Chair in Neuroscience. "But the strong argument we're making is that the law-enforcement approach, which has so far cost $1.5 trillion, is not working. Addiction is a biomedical problem, requiring science-based solutions."

Ebner, interim director of the Addiction MDT, has already hired four new faculty members who will be headed to the U by year's end; a new Center for Addiction Neuroscience has also been established to unite the addiction research community.

"The future looks very bright here for our work

With this committed funding, we are able to attract the best and brightest researchers and position them for success.

– Jakub Tolar, M.D., Ph.D., Medical School Dean

on addiction," says neuroscience professor George Wilcox, Ph.D., a longtime U of M researcher whose team recently identified a pair of analgesics that, when given together, provide pain relief but aren't addictive—an exciting discovery now in preclinical development. "We're looking forward to the arrival of our new colleagues and even more collaboration in tackling this tough issue."

Mapping brain circuits

Part of the MDT strategy was to increase synergy between related research groups, so it made sense to develop an Optical Imaging and Brain Science MDT, a group of researchers who can interact with the Addiction MDT.

Prakash Kara, Ph.D., the first hire in the Optical Imaging and Brain Science MDT, is working closely with established U faculty and the new MDT recruits to produce a dynamic picture of the functioning brain by developing and applying improved methods of optical imaging.

"In many diseases—like Alzheimer's, vascular dementia, addiction, schizophrenia—the wiring of the brain is disrupted," says Kara. "As we revolutionize our understanding of the human brain, we'll ultimately make progress in our ability to intervene and impact those diseases."

As he explains, the state funding for the Optical Imaging and Brain Science MDT creates an almost unparalleled opportunity for researchers.

"To people outside the academic world, this might sound like just a restructuring of faculty," he says. "But getting legislative support that allows us to bring in new researchers that complement existing faculty at the U … this will create a very exciting, cohesive team of optical researchers. I haven't seen this kind of opportunity at any other institution in the U.S."

Kara's first MDT colleague, Gordon Smith, Ph.D., assistant professor in the Department of Neuroscience, is hard at work, too. As he explains, increasing our understanding of how the brain is wired first requires improving the optical imaging technologies that allow scientists to measure neuronal activity in the brain.

"Existing functional magnetic resonance imaging techniques pool neural activity across thousands of cells," Smith says. "But optical techniques have a resolution of individual neurons or better. And we can manipulate those neurons, turning them on or off. So developing this constellation of optical techniques is key to being able to understand and ultimately treat neurological disorders."

The health equity quest

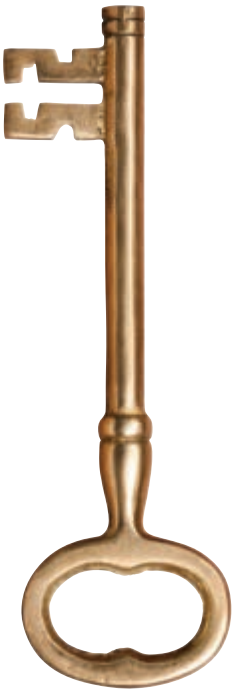
J. Neil Henderson, Ph.D., executive director of the MDT on rural and Native American health disparities, says his new team, dubbed Memory Keepers, will be working to free Minnesota's American Indians and rural populations from the disproportionate rates of dementia and diabetes they face.

"Minnesota has huge health disparities between white and American Indian populations, with similar disparities seen in rural communities," he says. "Dementia and diabetes are two of the worst conditions seen at much higher rates in these groups."

The team's name, Memory Keepers, is particularly apt: According to Henderson, it's common practice in tribes to assign particular members the role of "memory keeper" to help preserve tribal medicines, songs, and stories. "Ultimately, our mission to reduce rates of dementia will help American Indian elders remain lucid as they age," he says, "enabling them to preserve Native culture by passing along tribal stories to younger generations."

Like the newly hired faculty working on addiction and optical imaging, Henderson came into an already strong program on the Medical School's Duluth campus, renowned for its innovative approach to supporting American Indian health professional students and recruiting and training family medicine doctors who go on to work in rural Minnesota. But Henderson's vision, honed in his native Oklahoma, where he's a member of the Choctaw Nation of Oklahoma, calls for strengthening those rural community connections even further. He has already recruited six new

Creating and nurturing these teams will strengthen the Medical School's ability to generate solutions for years to come.



doctoral-prepared researchers, all of whom will join the faculty by the end of 2017.

Kristen Jacklin, Ph.D., the new associate director of Memory Keepers and a professor in the Department of Biobehavioral Health and Population Sciences on the Medical School's Duluth campus, has spent recent years looking at dementia and diabetes in indigenous populations in her native Canada.

"Dr. Henderson's vision is exciting because diabetes and dementia are absolutely connected," says Jacklin, "and with the team he's building, we have so many possibilities for innovation and discovery."

So why is Jacklin, who's leaving a place she "loves dearly," pulling up stakes (along with her husband, Wayne Warry, Ph.D., also a newly recruited member of Memory Keepers) and moving her family to Minnesota?

"This is a truly rare opportunity," she says. "The funding commitment from the state is so significant—it's a real signal that they're behind this effort to make an impact on the health of indigenous Minnesotans."

Improving the 'healthspan'

The fourth MDT addresses a topic that affects us all: the biology of aging.

"What makes an organism age? What are the major genes and proteins involved with the aging process? These are the kinds of questions our researchers are tackling," explains David Bernlohr, Ph.D., Distinguished McKnight Professor and Cargill Chair in Systems Biology of Human Metabolism, who is leading the effort to recruit new faculty to the Biology of Aging MDT. "It's about *healthspan* versus *lifespan*. What we want to do is live more vibrantly, longer. So can we identify the key factors driving those cellular decisions?"

The U already has a strong cohort of scientists who study aging and, as with the other MDTs, new faculty will fill in the gaps to strengthen the research and move as quickly as possible to translate lab breakthroughs into clinical treatments.

But as Bernlohr notes, medical schools across the country are creating aging-themed institutes, making this a highly competitive field; top researchers are in hot demand. So having the legislative commitment has given the U a much-needed competitive edge.

"We couldn't be building this aging program, which includes a new Institute on the Biology of Aging and Metabolism, without this legislative support," says Bernlohr.

For Minnesota's health and well-being

While Minnesota faces many specific health care challenges—primary care physician shortages, growing health disparities, an aging population—creating and nurturing these MDTs will strengthen the Medical School's ability to generate solutions for years to come.

"Having great research teams in these four key areas provides more opportunities for collaboration and innovation," Tolar says, "allowing success in one area to move other areas forward at the same time. In this way, we hope to move quickly to improve Minnesotans' health and quality of life." MB

Barbara Knox is a freelance writer and editor and a frequent contributor to the *Medical Bulletin*.

WEB EXTRA

Watch a video about the Memory Keepers Medical Discovery team at z.umn.edu/memorykeepersmdt, and learn more about all of the teams at z.umn.edu/mdt.

Can stem cells mend our

Regenerative medicine is the physiological equivalent of turning back the clock—by replacing diseased or damaged organs and tissues with healthy, proliferating cells that can restore normal function.

At the core of many approaches to regenerative medicine are stem cells, which have the ability, depending on environment and chemical stimuli, to turn into any kind of specialized cell. Some researchers are working to direct stem cells to take root at the site of an injury and repair or replace damaged tissue. Others are trying to induce specialized cells, such as heart muscle cells, to behave more like stem cells, by dividing and proliferating to replace dead tissue.

For the first time, we are able to deploy cells as medications. Cells can replace and repair and restore function in the body in a way that drugs and biologicals cannot.

– Jakub Tolar, M.D., Ph.D., dean of the Medical School and director of the University's Stem Cell Institute

Regenerative medicine received a jump-start in Minnesota in 2014 when the Legislature created Regenerative Medicine Minnesota, providing about $4.5 million a year for 10 years for stem cell research and education throughout the state.

Here are a few ways state, federal, and private support has boosted the work of University of Minnesota scientists who aim to enhance stem cells' ability to heal the body, including our mightiest muscle—the heart.

mightiest muscle?

BY GREG BREINING

University researchers are turning to stem cells to regenerate diseased or damaged tissues and organs, including the heart

Patching a broken heart

When scientists discovered they could turn pluripotent (reprogrammable) stem cells into cardiac muscle cells in the laboratory with nearly 100 percent success, they started searching for ways to use these muscle "progenitor" cells to repair heart damage from an injury such as a myocardial infarction.

Initially, they tried growing suitable progenitor cells in the lab and injecting them into the heart near the site of the dead muscle tissue, but they soon discovered that few of these cells took hold to produce living, beating tissue.

Brenda Ogle, Ph.D., an associate professor in the University's Department of Biomedical Engineering, tried something different. She printed a mesh 3-D heart "patch" of natural collagen and other protein and seeded it with heart cells derived from human stem cells, a technology she describes in a paper published early this year in *Circulation Research*.

"The impetus comes from our desire to organize the cells before putting them into the heart—that was the idea," says Ogle, who is a member of the University's Stem Cell Institute and Lillehei Heart Institute. "If we can organize them and they can propagate a signal from one side of the patch to the other, they should be able to bypass the scar or the injured area."

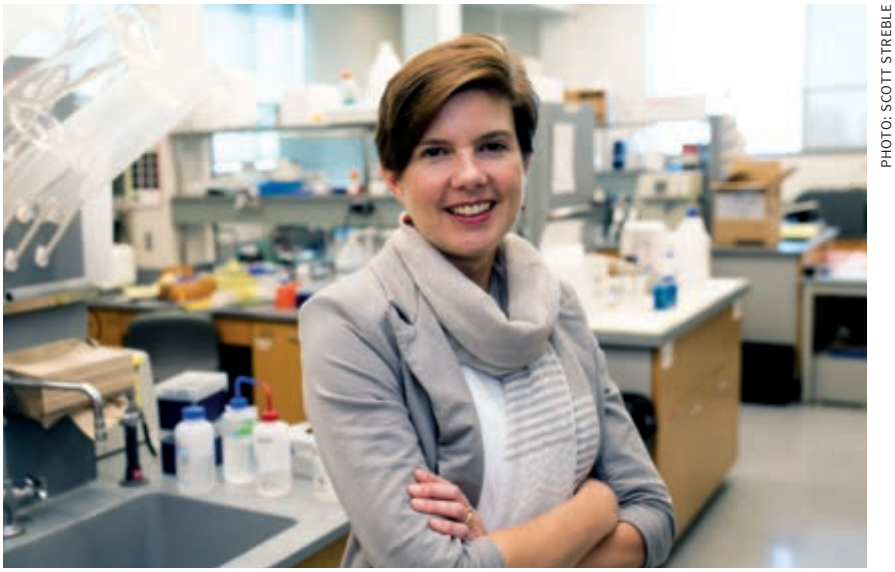


PHOTO: SCOTT STREBLE

Brenda Ogle, Ph.D., and colleagues created a 3-D-bioprinted patch that improved function in mouse hearts damaged by heart attacks.

But not just any mesh will do. Conventional 3-D bioprinting produces a mesh that's too coarse; the stem cells don't settle in and interact with the matrix around them.

Working with colleagues at the University of Wisconsin, Ogle used a printing technique known as multiphoton fabrication to lay down a protein mesh with gaps as small as a single micron (one-millionth of a meter), about 100 times finer than most 3-D bioprinters can produce. "That was the critical part," says Ogle.

The team implanted the mesh with about 50,000 heart muscle cells, smooth muscle

TIME FOR 4-D BIOPRINTING

Three-dimensional printing of complex shapes has become an important new medical technology, allowing researchers to quickly and precisely manufacture items as disparate as custom medical prostheses and collagen scaffolds to implant into the body.

Now medical engineers have added a fourth dimension to printing—time. The University's Michael McAlpine, Ph.D., Benjamin Mayhugh Associate Professor of Mechanical Engineering, is using this 4-D printing to create nanocapsules that can release molecules on cue, much as a cell would, to initiate a biological or other chemical response.

McAlpine and colleague Brenda Ogle, Ph.D., have printed a fine-grained hydrogel mesh embedded with pluripotent stem cells and McAlpine's tiny capsules. The capsules contain signaling molecules. Some direct the stem cells to turn into cardiac muscle cells; others cause them to differentiate into cardiac blood vessels.

The signaling molecules are trapped in their tiny capsules until McAlpine triggers their release. Inside the polymer coatings of the capsules are gold nanorods. Focusing laser light on the capsules heats the rods, rupturing the coating and releasing the molecules. Nanorods of different lengths respond to different laser wavelengths.

"You can trigger the release of multiple molecules and get sort of this orchestrated series of differentiation events happening," says McAlpine. "You could use it in the heart to differentiate some cells into muscle tissue versus other cells into a vascular network."

In March, McAlpine received a two-year, $250,000 grant from Regenerative Medicine Minnesota backing the work. Though the results have yet to be published, he says, "I can tell you that it worked."

WEB EXTRA

See the 4-D printing process in action at z.umn.edu/mightiestmuscle.

IMAGE COURTESY OF BRENDA OGLE, PH.D.

PHOTO: JIM BOVIN

cells, and endothelial cells (which line blood vessels) derived from human pluripotent stem cells. The cells settled into the mesh, spontaneously aligned with one another, and began to contract and relax like normal heart muscle cells—"a very promising outcome," says Ogle. "When we found that, we knew that here was something we should try to transplant in an attempt to improve function of a failing heart."

Ogle's group transplanted patches into mice, placing the sequin-sized mesh over a portion of the heart damaged by a myocardial infarction. After four weeks, more than 11 percent of the transplanted cells had survived and merged with the mice's heart tissues. Though the hearts did not beat as strongly as normal mouse hearts, the team found a significant increase in function, Ogle says.

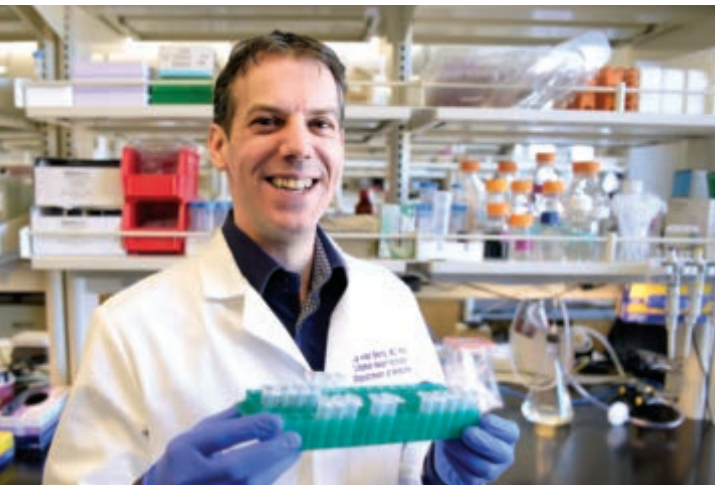
Now Ogle is working on a National Institutes of Health grant to perform similar transplants in pigs. She envisions a day, perhaps within just a few years, when the mesh patch is seeded with human pluripotent cells from a stem cell "bank" and implanted in a patient within hours of a heart attack—truly mending a broken heart.

Unlocking heart muscle repair

If only humans were more like zebrafish. Then our heart muscle cells could simply generate new cells to repair heart damage.

"It would be really handy, but for unknown reasons it doesn't happen in our bodies," says the Medical School's Jop van Berlo, M.D., Ph.D., who holds the Lois and Richard King Assistant Professorship in Medicine and is a member of the Lillehei Heart Institute and Stem Cell Institute. "As a consequence, we can't really regenerate from an injury, like myocardial infarction."

Van Berlo is trying to unlock the genetic pathways that might allow humans to respond more like zebrafish—creating more heart muscle cells to restore a strong, reliable heartbeat. "If we



If only humans were more like zebrafish. Then our heart muscle cells could simply generate new cells to repair heart damage.

could entice these cells to generate more cardiomyocytes [heart muscle cells] in a relatively short time span, we might be able to regenerate our hearts better after such an injury," he says.

Among van Berlo's collaborators is Yasuhiko Kawakami, Ph.D., associate professor in the Department of Genetics, Cell Biology, and Development, who studies the ability of zebrafish to regenerate heart cells. "It's interesting for me to work with him so that we can see why zebrafish have this ability and mice and humans don't," says van Berlo.

Van Berlo recently received a $300,000 award from The Hartwell Foundation to fund exploration of a new treatment for hypoplastic left heart syndrome (HLHS). Children with the congenital defect have underdeveloped hearts with too few muscle cells to pump blood effectively throughout the body—and their bodies are unable to generate more heart muscle cells to take up the slack.

The Hartwell funds will help him test a new approach to adding muscle cells to the heart by unlocking its ability to form new cells—ultimately improving its function. Using computerized high-throughput analysis, van Berlo has identified a number of genes that appear to play a role in regulating heart muscle cell division. He found that switching off these genes stimulated heart muscle cells in culture to begin to divide and multiply. Now he wants to identify which of these genes might be tweaked—either in culture or in the body—to stimulate new heart muscle cell development and help repair the HLHS defect.

There are two ways the body might recruit more heart muscle cells: by signaling resident stem cells to turn into new heart muscle cells, or by stimulating existing muscle cells to divide and multiply. "I'm looking at both of these approaches," says van Berlo.

"My ultimate goal would be to have this happen inside the body so that you wouldn't have to take cells out," he says. "You would essentially just take a pill that would stimulate the progenitor cells to become contractile cells."

Finding such a drug would unlock the potential to treat many types of heart conditions, from congenital defects to the ravages of a heart attack, by helping the body heal one of its most vital organs. MB

Greg Breining is a journalist and author based in St. Paul.

ABOVE LEFT The heart patch for mice is about the size of a sequin. Now the team is working on a larger patch for pig hearts, which are more similar to human hearts.

ABOVE RIGHT Jop van Berlo, M.D., Ph.D., is looking for ways to stimulate new heart muscle cell development to repair an injury or defect.

CORRECTING THE MUSCLES THAT MAKE US MOVE

The Medical School's Rita Perlingeiro, Ph.D., a professor of cardiovascular medicine, is developing stem cell technology to treat muscle-wasting diseases of the body. She and her team have used stem cells to restore muscle function in mice modeling Duchenne muscular dystrophy. The scientists also showed that the same process could work in people, putting the research on the path to clinical safety trials for humans who have Duchenne.

Read the full story at z.umn.edu/mightiestmuscle.

A cunning opponent

BY SUZY FRISCH

Brain tumors are an aggressive and wily form of cancer. They can develop tentacles and spread into different regions of the brain. Adding to the complexity, each cancer cell within one tumor mass is unique from its neighbor, thanks to a multitude of mutations. Plus, the blood-brain barrier prevents many therapies from even reaching the tumors.

These are a few of the reasons why brain tumors are difficult to treat and why there is currently no cure. Brain cancer is the leading cause of cancer-related deaths in children. For glioblastoma, the most aggressive brain tumor, survival is typically just more than a year.

These sobering facts motivate a team of University of Minnesota Medical School researchers to find new ways to attack brain tumors. Michael Olin, Ph.D., one member of that team, also has a very personal motivation for his work: his mother died from cancer that metastasized to the brain, an experience that sparked his interest in developing new strategies to outsmart the disease.

A neuro-immunologist and assistant professor of pediatric hematology-oncology, Olin works with his U of M and Masonic Cancer Center colleagues Christopher Moertel, M.D., and Elizabeth Neil, M.D., to develop treatments that train a person's own immune system to fend off brain tumors.

Try, try again

A 2012 clinical trial of a University of Minnesota–developed immunotherapy made from brain cancer cells showed initial successes. It performed admirably to prolong adults' and children's lives by preventing their tumors from returning. But the progress was short-lived, and the tumors eventually came roaring back.

Olin was determined to find out why this therapy succeeded initially, then failed. He painstakingly compared blood samples taken weekly from study participants. He was evaluating a long list of blood proteins one by one when he noticed slight changes in levels of the protein CD200, also known as OX2.

Patients who didn't respond to the immunotherapy at all had sky-high CD200 levels. Those who responded well had low CD200 levels initially but high levels when the tumors returned.

This observation led to an important revelation about the little-known protein: it plays a starring role in suppressing the immune system and perpetuating brain cancer.

"It was our theory that CD200 was the reason the tumors returned," says Moertel, a pediatric neuro-oncologist at University of Minnesota Masonic Children's Hospital and holder of the Kenneth and Betty Jayne Dahlberg Endowed Professorship in Pediatric Brain Tumor Research. "It turns out that CD200 is an important immunosuppressant agent that tumors make to escape discovery by the immune system."

A University research team designs an immunotherapy to outsmart a challenging adversary—brain cancer

Proving it

Previous scientific inquiry into CD200's role in the immune system hadn't made much progress. However, it was established that CD200 acts as an immune checkpoint that prevents the immune system from attacking tumors. When the U of M team began doing experiments, they found that using the immunotherapy in mice while blocking CD200 made the rodents' brain tumors disappear.

Encouraged by the results, Olin began analyzing CD200 more closely and got even better news: not only does blocking CD200 keep

GREAT MINDS THINK TOGETHER

IN THE QUEST to cure the incurable—brain cancer, Parkinson's disease, Alzheimer's disease, and other devastating neurologic diseases—Clark C. Chen, M.D., Ph.D., believes that the key to success lies in the synergy that results from multidisciplinary collaborations. He recently took the helm of the University of Minnesota Medical School's Neurosurgery Department, attracted by its legacy and the faculty's passion for discovery through team-based science.

"For ideas to thrive and blossom, they need to be shared, scrutinized, and fostered among thinkers who approach these ideas from different perspectives and utilizing distinct frameworks," says Chen, who holds the Lyle French Chair in Neurosurgery. "The University of Minnesota has a group of like-minded people who are genuinely interconnected in mission and in intellect, who are committed to translating ideas into measurable human benefits."

PHOTO: BRADY WILLETTE

Clark Chen, M.D., Ph.D.

A renowned brain tumor neurosurgeon and researcher, Chen came to the University from the University of California, San Diego. A native of Taiwan, he moved to California when he was 12. He earned a bachelor's degree from Stanford University, a master's in epidemiology from the Columbia University School of Public Health, and medical and doctoral degrees from Harvard Medical School.

Chen investigates glioblastomas and how they become resistant to radiation and chemotherapy. He was the principal investigator on multiple clinical studies involving the use of next-generation tools such as high thermal energy lasers and focused ultrasound, as well as oncolytic viruses, to destroy brain cancer cells.

"With malignant brain cancer, the treatment paradigm has been cure rarely and comfort always. Frankly, the effect of these treatments is modest at best," Chen says. "The cure that we seek requires innovation beyond the currently available treatment options. To genuinely make a difference in the trajectory of our brain tumor patients, we will need to throw away the preconception of yesteryear and reframe the problem in ways that we had not previously conceptualized."

Chen says he's intrigued by a U of M research effort that combines a brain tumor immunotherapy with an agent that blocks an immune protein called CD200 (see main story). He sees this therapeutic approach as a refreshingly new way of attacking brain cancers and has already identified opportunities for synergy between this approach and his own work.

"The opportunity to do 'good' as a leader of the Neurosurgery Department is real," Chen says. "It is a once-in-a-lifetime chance. I am deeply grateful for this opportunity, and I look forward to engaging and connecting with the extraordinary minds of this campus."

tumors at bay, it also prompts its transformation from bad cop to good cop. Olin found that chains of amino acids called peptides turn on the CD200's unique activation receptors, switching the protein from perpetuating cancer to fighting it. Using the CD200 peptides turns off the CD200 checkpoint, allowing the immune system to do its job and fight the cancer.

Moertel and Olin then partnered with Liz Pluhar, D.V.M., Ph.D., a professor in the U's College of Veterinary Medicine, to test their CD200 hypothesis on dogs with naturally occurring brain tumors. Canine and human brain tumors are very similar, as are the canine and human immune systems. The team extended dogs' lives by as many as 214 days with their immunotherapy alone, well beyond the typical 30 to 60 days after diagnosis.

The new protocol is even more effective. Using the immunotherapy paired with the CD200 inhibitor has extended the dogs' lives well beyond the survival of those that had received the vaccine only. Today, 25 percent of the dogs involved in the newer studies are still alive, after as many as 730 days—and counting.

"We've seen some fantastic results," Olin says.

Back to the clinic

The success with canines has paved the way for evaluating the new immunotherapy— with the CD200 inhibitor—in humans possibly this winter. The clinical trial will start with 10 to 14 adult glioblastoma patients who have experienced a first or second recurrence of their tumor, says Neil, who joined the U faculty about a year ago and will lead the study. If it is successful, the team hopes to enroll children who have brain tumors as well.

WEB EXTRA

Hear Clark Chen, M.D., Ph.D., discuss his vision for the Neurosurgery Department at z.umn.edu/meetchen.

Neil is hopeful about the new protocol for several reasons. "We know that the vaccine with the CD200 inhibitor allows one's own immune system to kill cancer cells. This immunotherapy approach allows for this natural process to happen without the cancer interfering, impeding the demise of the immune system."

Philanthropic support has helped fuel the team's immunotherapy research. Key donors include the Dahlberg Family Foundation, Bob and Corinne Ferris, Children's Cancer Research Fund (CCRF), CCRF's Dr. Daniel G. Carey Brain Tumor Research Fund, the American Brain Tumor Association, Randy Shaver Cancer Research and Community Fund, Humor to Fight the Tumor, and Love Your Melon.

"We have a long list of people who have made significant contributions to this work and helped us move the research along," says Moertel. "Before we were taking baby steps. This work is a big leap."

Because these investigations are inherently expensive, Olin and Moertel started a company called OX2 Therapeutics to create an avenue for venture capital investment. They see the promise of their work in fighting brain cancer and want to help patients as quickly as possible while also expanding the anti-CD200 immunotherapy model to other cancers.

"This will be a rock star for breast cancer and melanoma as well," Olin predicts. "If we give the inhibitor to mice modeling human breast cancer, they have an 80 percent survival rate."

It's part of the team's shared vision to stop cancer in its tracks.

"We want to cure brain tumors. That's why I do my job," says Moertel, who has worked in pediatric oncology for nearly 30 years. "When I look at kids every single day who don't have a cure for their disease, it's heartbreaking. I want to find an answer." MB

Suzy Frisch is a Twin Cities–based freelance writer who writes frequently about health care and medicine.

PHOTO: BRADY WILLETTE

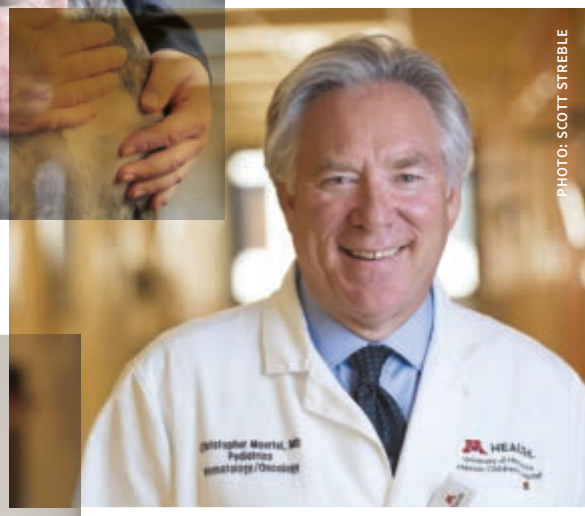


PHOTO: SCOTT STREBLE

PHOTO: COURTESY OF UNIVERSITY OF MINNESOTA HEALTH

TOP Michael Olin, Ph.D., with canine study participant Gidgett, is working with Christopher Moertel, M.D. (middle), to perfect a human brain tumor immunotherapy for a clinical trial that could open as soon as this winter.

LEFT Elizabeth Neil, M.D., will lead the study.

The right fit

Globetrotting helps a surgeon-turned-entrepreneur see the potential in an innovative design for prosthetic sockets

THE ROAD LESS TRAVELED has always been Andrew Pedtke's preferred route. The Minnesota native's path from Minnetonka, where he grew up, to the University of Minnesota Medical School was both winding and years long: He studied in Denmark, rode a bicycle from Brussels to Istanbul, and lived briefly in Ecuador.

"Most of the medical schools I applied to took a look at my application and said, 'Who is this guy? He can't be serious,'" Pedtke jokes.

But Pedtke, who graduated from the Medical School in 2008 and cofounded a San Francisco–based prosthetics company in 2012, sees travel as way to gain new perspectives and glimpse opportunities. He has worked and studied in Brazil, Tanzania, and Nicaragua, among other places.

"Global travel, especially if you're working in another country, opens your eyes to different things," Pedtke says. "It illuminates gaps, inconsistencies, and areas where there are problems—as well as the potential for improvements."

A DIFFERENT APPROACH TO DESIGN

In fact, it was on a surfing-and-work trip in Nicaragua that Pedtke and a friend, Garrett Hurley, hatched a plan to launch LIM Innovations, a prosthetics company. At the time, Pedtke was finishing an internship and residency in orthopaedic surgery at the University of California, San Francisco, and he was intrigued when Hurley, a prosthetist, showed him some sketches for an innovative socket design. Pedtke saw the potential. If they could turn the drawings into a product, he believed, they could make a real difference for people who use prosthetics.

Prosthetics have improved greatly in recent years. Innovations like carbon-fiber cheetah blades and computer-controlled electronic knees have changed the marketplace and improved the lives of many people. But the prosthetic socket, usually made of hard-shell plastic that has to be reworked, adjusted, or replaced as the user's residual limb changes over time, hasn't progressed much. Pedtke likens it to a wooden shoe that might fit fine on the day it's produced but becomes uncomfortable or loose over time.

Hurley's design was different. For starters, it could be made using a 3-D scan of the amputee's leg, rather than the traditional handcrafted plaster-cast method that remains the industry practice for fitting sockets to individual users. What's more, the design could be adjusted—allowing people to add tension, creating a tighter fit when the user was running, for example, or lessen the grip when relaxing.

A NATURAL ENTREPRENEUR

In 2012, Pedtke and Hurley launched LIM, an obvious play on the word *limb*. The company, which employs 40 people, has raised $3 million from friends and family and $20 million from corporate investors. Pedtke now serves as

California-based LIM Innovations, cofounded by Medical School alumnus Andrew Pedtke, M.D. (upper left), and prosthetist Garrett Hurley (above, far left), produces two adjustable, custom leg prosthetics for amputees.

Global travel opens your eyes to different things. It illuminates gaps, inconsistencies, and areas where there are problems – as well as the potential for improvements.

– Andrew Pedtke, M.D.

CEO, honing the company's mission, raising capital, building the workforce, driving sales.

In some ways, he says, being CEO is not unlike being the chief resident of a trauma surgery team: "You're leading a team of med students, interns, and residents while reporting to senior staff to handle complex operations and making major decisions on behalf of critically injured patients. Oftentimes in the middle of the night with little to no resources. If you can do this, you can start a company. It's leadership. The tasks are just different."

For Pedtke, transitioning from medicine to business has come as naturally as hopping a flight from Africa to South America. He also sees his work at LIM as contributing to global health. Amputees who have lost limbs due to poor circulation, land mines, and numerous other causes exist in every country – so an affordable, easy-to-fit socket could improve lives around the world.

"I've always liked the idea of doing something that had impact," Pedtke says. "It just turns out that it's not being a full-time surgeon." MB

By Joel Hoekstra, a Minneapolis freelance writer and editor

PHOTOS: COURTESY OF LIM INNOVATIONS

PHOTO: COURTESY OF IVY VAINIO

Perseverance pays off

After a challenging childhood, Arne Vainio, M.D., Class of 1994, found his path and his passion in medicine. Now a family medicine practitioner at the Min-No-Aya-Win Human Services Clinic on the Fond du Lac reservation in Cloquet, Minn., Vainio was recently named Physician of the Year by the Association of American Indian Physicians. The organization aims "to pursue excellence in Native American health care by promoting education in the medical disciplines, honoring traditional healing principles, and restoring the balance of mind, body, and spirit."

The celebrated Mille Lacs Ojibwe doctor – who also has received the Virginia McKnight Binger Unsung Hero Award and the Early Distinguished Career Alumni Award from the U's Medical Alumni Society – traversed a rough road to success. When Vainio's father committed suicide, his mother often had to leave the 4-year-old Vainio and three siblings in the care of their eldest sister, who was 6. During one of these times, the five youngsters accidentally burned down their home in Sturgeon, Minn., while playing with matches.

Despite the hardships, Vainio managed to enroll as an undergraduate at the University of Minnesota Duluth after finishing high school. The transition to college was difficult, however, and after a few semesters of achieving low grades, he dropped out and started working construction. Vainio was in and out of college from 1976 to the mid-1980s, working a variety of jobs.

After witnessing a neighbor's sudden death, he enrolled in an emergency medical technician training program, which led to a three-year stint as a paramedic in Virginia, Minn. Vainio then returned to Duluth – this time to finish college and pursue a medical degree. Having achieved top marks in medical school, he headed west for his residency at the Seattle Indian Health Board.

From there, Vainio moved back to Duluth and started working on the Fond du Lac reservation in 1997 and has served the Ojibwe community's medical needs ever since.

"All I ever wanted to do was Indian health," he told *Indian Country Today*. "There are future doctors among us; some of them are only 4 years old now. I want to find them before they choose a different path." MB

By Carolyn Bernhardt, communications coordinator at the University of Minnesota Foundation

A true game changer

IT'S OVERSIMPLIFYING TO SAY that hockey is responsible for steering Mickey (Michelle) Moran toward a career in medicine. But it might be fair to credit the sport with an assist.

The second-year student at the Medical School, Duluth campus grew up in a family that lives and breathes hockey. The Morans—who moved from the state of Virginia to Sartell, Minnesota, in 2007—love playing, watching, and officiating the sport.

A freak injury her mother sustained on the rink when Moran was just 7, and the ingenuity with which a Cleveland Clinic medical team diagnosed the puzzling condition it caused, inspired the young athlete to see herself as a future physician.

Moran's mother, Kris, was training for the 2002 Salt Lake City Olympics near the family's D.C.-area home, playing in a men's pickup league, when a former NHL player on the opposing team checked her hard, throwing her some 15 feet across the ice.

At first, her mother seemed fine, Moran remembers. But something wasn't quite right.

"Then these symptoms started happening; whenever she'd work out, she'd get dizzy and pass out," Moran says. "As she trained harder and harder, the symptoms got worse; she'd be taking three naps a day. Her heart rate and her blood pressure would plummet with exercise." Her doctors were baffled.

"At one point, they told her she probably had about six months to live," Moran says. Her mother was also coaching a 19U hockey team at the time, frequently traveling to tournaments across the East Coast and Midwest, and young Mickey began accompanying her. "My job was to explain to others what was going on. I sort of understood [how dire the situation was], but not really."

The Olympics were out of the question.

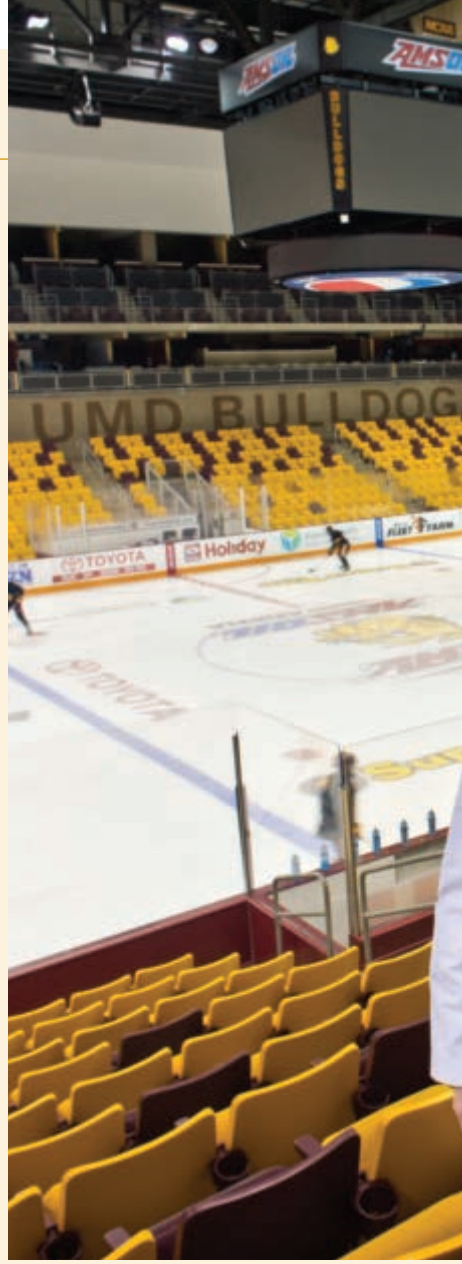
FINDING ANSWERS—AND A CAREER PATH

Seeking answers, Moran's parents contacted the Cleveland Clinic. "We went without a referral—just called, made an appointment, and drove up there from Virginia," Moran recalls.

"[The medical team] came back with a diagnosis of a vagus nerve injury. It's the cranial nerve that controls blood pressure and heart rate," Moran explains. There was no fixing the injury itself, but the Cleveland cardiologist proposed treating its effects with a combination of medication and a pacemaker—an approach that has proven successful.

The way the doctor involved students and residents in the consultation impressed Moran. "To have so many people bouncing ideas off each other … I think it was extremely helpful in this case," she says. "To see how much he included [the students], to see this group of people care for my mom, I was like, 'I want to do this.'"

Today, Moran pictures herself in primary care, ideally as a sports medicine specialist at a rural family clinic. Interested in making youth hockey safer, she has launched a project of her own design, a database to track youth concussions and, eventually, shape policy to reduce them. Her mother, a software engineer for Minnesota State (formerly MnSCU), is helping her with the technical aspects.



Moran is a grateful recipient of the 2017 Peter and Virginia Torreano Scholarship, which allows her to devote time to both the database project and her medical studies.

"It's huge. You're not worrying about, 'Could I get a side job?'" The confidence boost was big, too. "Honestly, when I read the letter, I couldn't believe it. You start to second-guess yourself. 'Did I really do the right thing? Can I handle this?' [The scholarship] was just so reassuring. Someone else thinks I can do this!"

Moran grew up in a family that lives and breathes hockey. A freak injury her mother sustained on the rink when Moran was just 7, and the ingenuity of the medical team that treated her, inspired the young athlete to see herself as a future physician.

PHOTO: BRETT GROEHLER

Second-year medical student Mickey Moran pictures herself one day working in a rural family clinic as a sports medicine specialist.

Of course, Moran still plans to find time for sports, too. Come winter, you might find her on the ice, wielding a broom instead of a hockey stick as she pursues a new interest—in curling, naturally. MB

By Susan Maas, a freelance writer from Minneapolis and a frequent contributor to the *Medical Bulletin*

Hackathon puts the 'flash' in flashcards

PHOTO: TODD FREDERICKS FOR ELSEVIER

Third-year medical student Nathan Ratner estimates that he has made more than 15,000 flashcards over the course of his 17 years in the education system. And this is not unusual.

A problem-solver, Ratner had the chance to curb flashcard overload this summer as one of 16 medical students from around the globe chosen to participate in the Elsevier Hacks Hackathon in Helsinki, Finland.

At the hackathon, Elsevier—an information analytics business specializing in science and health—gave students 48 hours to design and build an application that improves some aspect of medical education. After mingling and sharing ideas, Ratner formed a team with another medical student from India, user experience designers from the Philippines and Finland, and developers from Poland and Hungary.

Together, the teammates came up with an online application that simplifies and automates the cumbersome process of building flashcards and other study devices.

"Every medical student's dream is to leave a lecture with study materials already assembled," says Ratner. "With our app, students can go straight into studying without having to construct—they can get their tools together while sitting in class."

Among the other hackathon projects developed were applications that taught anatomy interactively or enabled medical students to apply theoretical knowledge to real-world scenarios. Ratner's team took third place, receiving a $1,500 prize to invest in launching their new app.

The real reward, says Ratner, was the network of international friendships he forged at the Hackathon—and the prospect of making a difference. "Innovation comes from bringing together groups of people from different backgrounds and perspectives. Through events like the hackathon, medical students are creating networks that lead to a better world." MB

IMAGES: COURTESY OF PERKINS + WILL AND SLAM

When construction is complete in early 2020, the University's Health Sciences Education Center is expected to be one of the most comprehensive interprofessional education facilities in the country.

Success at the Capitol

YOUR ADVOCACY PAID OFF.

By the close of the 2017 legislative session in May, the Minnesota Legislature had appropriated $1.3 billion to the University of Minnesota for FY18–19, providing $54.62 million in new funding for the biennium that includes $14 million for health training restoration and $4 million for MnDRIVE cancer research.

The health training allocation restored funding for two U of M health programs formerly funded by UCare: family medicine and community health residencies, which educate future family physicians and provide care to underserved communities, and the Mobile Dental Clinic, which provides preventive and primary dental care in underserved communities statewide.

Letters in support of state funding were published in 24 different Minnesota newspapers. Thank you to all who gave their time and energy to advocating on the University's behalf.

The MnDRIVE funding improves statewide access to cancer prevention and treatment clinical trials.

In addition, the Legislature signed into law a capital investment bill that includes funding for a new Health Sciences Education Center on the U of M's East Bank campus to replace more than 100,000 square feet of outdated facilities. It will incorporate active-learning classrooms, simulation centers, a technology-rich health sciences library and learning commons, and spaces for student services and amenities—providing opportunities for interdisciplinary learning across all health science professional schools at the U.

The state funds 10 percent of the Medical School's budget, and without that support, the University could not adequately provide needed health care services, train our medical professionals, or help the state flourish and innovate. Many people—including cancer survivors, physicians, students, researchers, alumni, chancellors, and regents—wrote more than 30 op-eds and letters that were published in 24 different Minnesota newspapers in support of state funding for the University. To all those who gave their time and energy to advocating on the University's behalf, thank you! MB

WEB EXTRA

See more renderings of the new Health Sciences Education Center and view the construction timeline at z.umn.edu/hsec.

RPAP and MetroPAP get a new director

The Medical School recently appointed Kirby Clark, M.D., Class of 2001, as the new director of its Rural Physician Associate Program (RPAP) and Metropolitan Physician Associate Program (MetroPAP)—both clerkships.

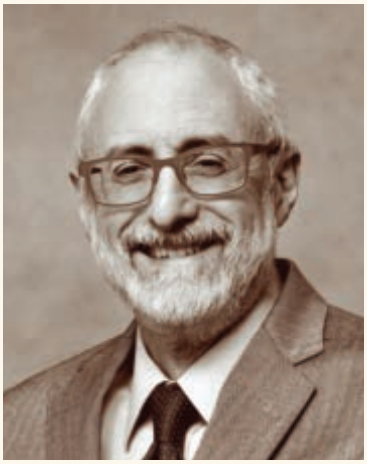
Launched in 1971, RPAP places third-year medical students in rural communities for nine-month longitudinal training experiences across multiple medical specialties. So far, it has helped train more than 1,500 aspiring physicians, many of whom eventually chose to practice primary care in rural areas.

The RPAP-inspired MetroPAP trains medical students in urban, medically underserved communities for nine months, with a focus on resource stewardship, community outreach, and advocacy.

Clark, an assistant professor in the Department of Family Medicine and Community Health, has been a master tutor and instructor in the Medical School. He was most recently associate program director of the family medicine residency program at St. John's Hospital in St. Paul, where he completed his own residency and served as director of medical student education.

"I am grateful for the robust and passionate RPAP/MetroPAP community," says Clark, who started in his new role on August 1. "Serving patients in hard-to-reach rural and urban communities is what drives and connects us."

Clark took the reins from Nancy Baker, M.D., who stepped in as interim director when Kathleen Brooks, M.D., M.B.A., retired in November 2016 after having led the programs since 2008. MB



U mourns loss of a thought leader on preventing heart attacks and strokes

The Medical School lost a beloved professor, colleague, mentor, and friend—Alan Hirsch, M.D., of Minneapolis—on April 14. A longtime faculty member, Hirsch, 62, was a professor of medicine and director of the U of M's Vascular Medicine Program at the Lillehei Heart Institute. While at the U of M, Hirsch established a new standard of care for treating vascular disease, as his research named exercise as a form of prevention. He was a thought leader in promoting the use of daily low-dose aspirin as a way to prevent heart attacks and strokes. Hirsch also was a founder of the Society of Vascular Medicine. He is survived by his wife, Sue Duval; and 3 children. MB

Medical Alumni Society honors eight distinguished graduates

EIGHT UNIVERSITY of Minnesota Medical School alumni were honored for their contributions to the medical profession at the Medical School Alumni Awards Banquet on October 12 at the McNamara Alumni Center on the University of Minnesota's East Bank campus.

The University of Minnesota Medical Alumni Society has presented these alumni with the following awards:

*The **Harold S. Diehl Award** is granted to individuals who have made outstanding contributions to the University of Minnesota Medical School, the University as a whole, and the community. It was established in honor of the Medical School's fifth dean, Harold Sheely Diehl, M.D.*

ROBERT J. BACHE, M.D.

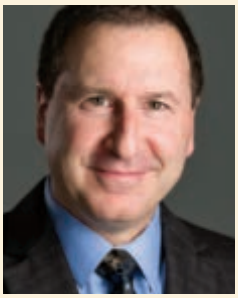
Bache is one of the world's premier investigators of coronary artery physiology and cardiac metabolism. He completed his residency in internal medicine at the University in 1967 and later established a robust research program involving cardiac physiology and nuclear magnetic resonance laboratories at the University—highly innovative at the time. Quiet and calm in nature and a favorite educator among medical students, Bache is recognized by colleagues for his intellectual integrity, problem-solving prowess, and generous mentorship.

RICHARD L. LINDSTROM, M.D.

Considered one of the foremost ophthalmologists in the world, Lindstrom holds more than 40 patents and has developed corneal preservation solutions, intraocular lenses, and ophthalmic instruments that are used today in clinical practices around the globe. Though Lindstrom left academic medicine for private practice in 2003, the Class of 1972 Medical School alumnus and 1978 resident alumnus speaks like a proud parent about the fellows he has trained over the years and their accomplishments.

MARTIN J. STILLMAN, M.D., J.D.

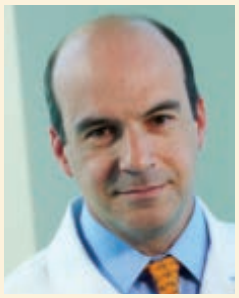
A 1997 Medical School and 1993 Law School alumnus, Stillman remains an active and compassionate clinician as well as an award-winning teacher of law and medicine. Since 2005, he has given generously of his time and talents as president of the Medical Alumni Society. Along with being a national educator on mediating conflict within health care, Stillman employs his leadership and mediation skills as Hennepin County Medical Center's Mediation and Conflict Resolution Officer.



*The **Distinguished Alumni Award** recognizes University of Minnesota Medical School alumni who have made outstanding contributions to their communities—at the local, regional, or national level—through medical practice, teaching, research, or other humanitarian activities.*

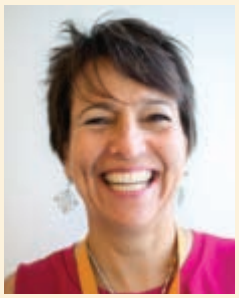
PETER B. BACH, M.D.

Bach is recognized for his renowned body of research on health care delivery and economics, including racial disparities, screening imaging studies, and skyrocketing drug costs. A member of the Medical School Class of 1992 and a sought-out expert source for the media, Bach has played a major role in shaping national public debate on these topics. His new research compares drug prices with their "value," determined by clinical efficacy, and has shown a weak correlation between the two.



JOIA S. MUKHERJEE, M.D., M.P.H.

Mukherjee is an international force for good as she works to strengthen health systems in resource-poor settings, focusing on those facing AIDS and tuberculosis epidemics. An alumna of the Medical School Class of 1992 and chief medical officer for Partners in Health, Mukherjee has helped to develop delivery systems that provide care to those who otherwise would



not have access to it. She also has helped to develop approaches to education that allow societies to populate, maintain, and adapt their own systems more independently.

PAUL A. VOLBERDING, M.D.

One of the world's foremost experts on HIV/AIDS, Volberding cocreated the "San Francisco model" of patient care in the earliest days of the epidemic—a model that has been widely replicated worldwide. A 1975 Medical School alumnus known for his wisdom and grace, Volberding also founded the world's first dedicated AIDS clinic and inpatient ward and has been at the forefront of establishing and advocating for HIV/AIDS policy at the local, national, and international levels. He now directs the AIDS Research Institute at the University of California, San Francisco.

*The **Early Distinguished Career Alumni Award** is given to a physician for exceptional accomplishments within 15 years of graduating from or completing his or her residency at the University of Minnesota Medical School.*

ERIN E. KREBS, M.D., M.P.H.

A member of the Medical School Class of 2000 and residency class of 2003, Krebs leads high-stakes research on treating chronic pain with opioid medications versus nonopioid alternatives. She is a core investigator at the Center for Chronic Disease Outcomes Research and medical director of women's health for the Minneapolis VA Health Care System and has served on several national panels addressing chronic pain management. Colleagues know Krebs for her enthusiasm, open-mindedness, and willingness to help find solutions.

MICHAEL D. MIEDEMA, M.D., M.P.H.

Miedema, a 2005 Medical School alumnus, already has earned international recognition for his work in the field of preventive cardiology. A senior consulting cardiologist at the Minneapolis Heart Institute and a clinical investigator at the Minneapolis Heart Institute Foundation, Miedema demonstrates his passion by speaking to community groups about heart disease prevention and heart-healthy habits on his personal time. Colleagues describe him as humble, knowledgeable, and compassionate toward his patients.

PHOTO: CHILDREN'S HOSPITAL OF PHILADELPHIA

Expert in pediatric neuropathology to receive OAA

Lucy Balian Rorke-Adams, M.D., Medical School Class of 1957, has been named a recipient of the Outstanding Achievement Award by the University of Minnesota Board of Regents.

A pioneer in pediatric neuropathology and an early expert in shaken baby syndrome, Rorke-Adams is internationally recognized for her research on children's neurological disorders, infant brain development, and non-accidental trauma in children. She is an influential teacher and role model who inspired a generation of physicians, scientists, and educators to seek better treatments and cures for children suffering from devastating neurological diseases.

Rorke-Adams will receive the award, among the University's highest honors, on November 1 in Philadelphia. MB

WEB EXTRA

Learn more about her career and achievements at z.umn.edu/rorke-adams.

In Memoriam

CURTIS F. AHRENS, M.D., Class of 1944, Duluth, Minn., died March 20 at age 99. Dr. Ahrens was head of radiology at St. Luke's Hospital in Duluth. He is predeceased by his first wife, Jane, and survived by his second wife, Patricia; 3 children; 2 stepchildren; 7 grandchildren; and 8 great-grandchildren.

DARYL J. BATALDEN, M.D., Class of 1970, Dayton, Minn., died May 19 at age 73. Dr. Batalden was a clinical instructor for the Department of Surgery at the U of M. He is survived by his wife, Carla; 4 children; and 6 grandchildren.

JEAN E. CARLIN, M.D., Ph.D., Class of 1954, Seal Beach, Calif., died June 6 at age 86. Dr. Carlin was dean of the Medical School at University of California, Irvine and a forensic psychiatrist. She is survived by her sister, Joan Wallin.

DENNIS P. CLIFFORD. M.D., Class of 1978, Wheat Ridge, Colo., died May 20 at age 65. Dr. Clifford was president of the medical staff at Lutheran Medical Center, near Denver. He is survived by his wife, Pam; and 2 sons.

ROBERT E. DOAN, M.D., Class of 1952, Plymouth, Minn., died on July 11 at age 90. Dr. Doan founded Wayzata Internal Medicine, now part of the Park Nicollet system, in 1956. He later served as medical director of Hillcrest Nursing Home in Wayzata. He is survived by his wife, Pat; 5 children; and 10 grandchildren.

JAMES D. ELKJER, M.D., Class of 1970, Bakersfield, Calif., died May 5 at age 72. Dr. Elkjer practiced emergency and family medicine. He is survived by 4 children and 2 grandchildren.

RICHARD L. ENGWALL, M.D., Class of 1956, Hopkins, Minn., died Feb. 5 at age 85. Dr. Engwall was an anesthesiologist. He is survived by his wife, Vianne; 3 children; 4 grandchildren; and 2 great-grandchildren.

AARON G. FINGERHUT, M.D., Class of 1954, Bend, Ore., died July 2 at age 87. Dr. Fingerhut was a radiation oncologist and a pioneer in mammography research and early detection methods for breast cancer. He is survived by his wife, Neill; 3 children; and 4 grandchildren.

DAVID W. GRANDE, M.D., Class of 1962, Mankato, Minn., died Feb. 23 at age 81. Dr. Grande was a dermatologist. He is survived by his wife, Gayle; 2 children; 6 grandchildren; and 1 great-grandson.

STEFAN P. GUTTORMSSON, M.D., Class of 1973, Duluth, Minn., died May 24 at age 69. Dr. Guttormsson practiced obstetrics and gynecology. He was also chief of staff at St. Luke's Hospital in Duluth. He is survived by his wife, Rosemary; 3 sons; and 3 grandchildren.

KENNETH HALVERSON, M.D., Class of 1959, Yankton, S.D., died March 13 at age 88. Dr. Halverson was a family medicine practitioner. He is survived by his wife, Mary Alice; 4 children; 8 grandchildren; and 1 great-grandchild.

LEONORE A. HERRERA, M.D., Class of 1978, Clovis, N.M., died June 11 at age 64. Dr. Herrera practiced emergency medicine. She is survived by her husband, Gary; 3 children; and 2 grandchildren.

THOMAS W. HOLM, M.D., Class of 1968, Duluth, Minn., died May 31 at age 74. Dr. Holm was a dermatologist. He is survived by his wife, Karen; 3 sons; and 3 grandchildren.

ALAN R. HOPEMAN, M.D., Class of 1950, Minneapolis, died April 12 at age 96. Dr. Hopeman was a military surgeon and professor of thoracic surgery at the universities of Missouri, Nebraska, and Colorado. He is predeceased by his wife, Dorothy. He is survived by 5 children, grandchildren, and great-grandchildren.

GERALD E. HOWE, M.D., Class of 1950, San Diego, died March 5 at age 95. Dr. Howe was a clinical professor of surgery and urology at the University of California, San Diego. Dr. Howe is predeceased by his wife, Elsie, and survived by 2 children and 3 grandchildren.

PAUL E. JOHNSON, M.D., Class of 1955, Jonesborough, Tenn., died June 8 at age 88. Dr. Johnson was a general practitioner and radiologist. He is predeceased by his wife, Lois, and survived by 3 children and 3 grandchildren.

RICHARD S. JOHNSON, M.D., Class of 1946, Eden Prairie, Minn., died Feb. 8 at age 93. Dr. Johnson was a founding partner of Consulting Radiologists Ltd. and was head of radiology at Methodist Hospital. He is predeceased by his wife, Ruth, and survived by 4 children and 6 grandchildren.

JOHN T. KELLY, M.D., Class of 1956, Wayzata, Minn., died May 10 at age 90. Dr. Kelly was a family physician. He cofounded Northeast Medical Clinic in Minneapolis and later became associate head of the U of M's Department of Family Medicine. Dr. Kelly is survived by his wife, Leah; 1 daughter; 2 grandchildren; and 2 great-grandchildren.

GENE F. KISHEL, M.D., Class of 1970, Virginia, Minn., died March 7 at age 79. Dr. Kishel was a pediatrician. He is survived by his wife, Brynhild; 4 children; and 9 grandchildren.

WILLAM R. KUEFFNER, M.D., Class of 1943, Southport, Conn., died on Feb. 10 at age 96. Dr. Kueffner was a pediatrician. He is predeceased by his first wife, Elizabeth, and his second wife, Nancy. He is survived by 6 sons, 8 grandchildren, and 3 great-grandchildren.

BRADLEY W. KUSSKE, M.D., Class of 1944, West Des Moines, Iowa, died May 31 at age 96. Dr. Kusske was an otolaryngologist. He is predeceased by his wife, Jean, and survived by 1 daughter, 3 granddaughters, and 2 great-grandchildren.

DONALD M. LARSON, M.D., Class of 1946, Minneapolis, died March 2 at age 94. Dr. Larson was an obstetric and gynecologic surgeon. He is predeceased by 1 daughter and 1 granddaughter. He is survived by his wife, Florence; 1 son; and 2 grandchildren.

THOMAS A. LINCOLN, M.D., Class of 1949, Battle Lake, Minn., died May 28 at age 92. Dr. Lincoln practiced preventive medicine.

RAYMOND M. MARTINSON, M.D., Class of 1959, Eveleth, Minn., died March 20 at age 91. Dr. Martinson was the deputy coroner for St. Louis County and served as chief of staff at Eveleth Fitzgerald Hospital. He is survived by 1 sister.

MARY K. MCCULLOCH, M.D., Class of 1986, Hopkins, Minn., died June 27 at age 66. Dr. McCulloch was an internist. She is survived by her husband, Joseph; 3 children; and 5 grandchildren.

LEO J. MORAN, M.D., Class of 1954, Dunedin, Fla., died June 8 at age 88. Dr. Moran was a family physician. He is predeceased by his wife, Jane, and survived by 4 children and 3 grandchildren.

JOHN B. MOYER, M.D., Class of 1943, Duluth, Minn., died April 14 at age 99. Dr. Moyer was an oncologist. He is survived by his wife, Charlotte; 5 children; 13 grandchildren; and 14 great-grandchildren.

KENNETH H. NELDNER, M.D., Class of 1955, Lubbock, Texas, died July 15 at age 90. Dr. Neldner was a dermatologist. He is survived by 3 daughters, 3 grandchildren, and 1 great-grandson.

RODGER K. NELSON, M.D., Class of 1959, Berlin, Conn., died Feb. 25 at age 85. Dr. Nelson was a pediatrician. He is survived by his wife, Rose; 3 children; and 6 grandchildren.

BERNERD L. O'NEIL, M.D., Class of 1966, Prior Lake, Minn., died June 22 at age 82. Dr. O'Neil was an associate professor of family medicine at the U of M Medical School. He is survived by his wife, Nancy; and 2 children.

GEORGE L. OSLAND, M.D., Class of 1970, Minnetonka, Minn., died March 20 at age 73. Dr. Osland was an orthopaedic surgeon. He is survived by his wife, Heather; 7 children; and 6 grandchildren.

EDWARD A. PASEK, M.D., Class of 1948, Sioux Falls, S.D., died May 7 at age 93. Dr. Pasek was an ophthalmologist. He is survived by his wife, Marjorie; 9 children; 20 grandchildren; and 12 great-grandchildren.

ROBERT F. PREMER, M.D., Class of 1950, St. Paul, Minn., died April 13 at age 90. Dr. Premer was chief of orthopaedics at the Minneapolis VA Hospital and was a 2010 Harold S. Diehl Award recipient. He is survived by his wife, Ruth; 2 daughters; and 7 grandchildren.

CYNTHIA A. RASK, M.D., Class of 1980, San Francisco, died July 27 at age 63. Dr. Rask was a renowned epileptologist and drug development expert at the Food and Drug Administration. She is survived by her sister, Pamela.

HAROLD G. RAVITS, M.D., Class of 1941, St. Paul, Minn., died March 27 at age 99. Dr. Ravits was a clinical professor of dermatology at the U of M. He is survived by his wife, Cissy; 3 children; 9 grandchildren; and 3 great-grandchildren.

JOHN P. REED JR., M.D., Class of 1948, Bellevue, Wash., died July 14 at age 93. Dr. Reed was an anesthesiologist. He is survived by his wife, Janet; 2 daughters; 4 grandchildren; and 1 great-grandson.

ROBERT L. SADOFF, M.D., Class of 1959, Abington, Pa., died April 17 at age 81. Dr. Sadoff was a founder of modern forensic psychiatry, and director of the Center for Studies in Socio-Legal Psychiatry at the University of Pennsylvania. He is survived by his wife, Joan; 4 children; and 10 grandchildren.

TERENCE J. SCALLEN, M.D., Ph.D., Class of 1961, Silver Bay, Minn., died March 24 at age 82. Dr. Scallen was a professor of biochemistry at the University of New Mexico School of Medicine and a pioneer in lipid research. He is survived by his wife, Joan; 4 children; and 4 grandchildren.

AIVARS SLUCIS, M.D., Class of 1972, Rancho Palos Verdes, Calif., died March 1 at age 78. Dr. Slucis was a radiologist. He is survived by his sister, Maija.

DAVID W. SONTAG, M.D., Class of 1953, Lake City, Minn., died May 9 at age 90. Dr. Sontag was a general practitioner. He is survived by his wife, Lucy; 5 children; 10 grandchildren; and 4 great-grandchildren.

SHERIDAN S.H. STEVENS, M.D., Class of 1964, New York, died April 3 at age 77. Dr. Stevens was a plastic surgeon. He is predeceased by his wife, Margaret, and survived by 2 daughters.

LESLIE A. SYVERSON, M.D., Class of 1955, Fergus Falls, Minn., died June 29 at age 90. Dr. Syverson was a general practitioner. He is survived by his wife, Lee; 3 daughters; 8 grandchildren; and 1 great-grandchild.

GEORGE TANBARA, M.D., Class of 1951, Tacoma, Wash., died July 1 at age 95. Dr. Tanbara was a pediatrician and a survivor of Japanese internment. He is predeceased by his wife, Kimi, and survived by 4 children.

WESLEY G. TOMHAVE, M.D., Class of 1949, Lincoln, Neb., died July 8 at age 97. Dr. Tomhave was head of the department of metabolism at Northwestern University. He is survived by his wife, Ann; 5 children; 10 grandchildren; and 5 great-grandchildren.

NAIP TUNA, M.D., Ph.D., Edina, Minn., died June 23 at age 95. A 1958 Ph.D. alumnus, Dr. Tuna was an important contributor in building the Medical School's national renown in cardiovascular surgery. He is predeceased by his wife, Türkân, and survived by 2 children and 4 grandchildren.

FORREST H. ADAMS, M.D., Class of 1943, Rancho Santa Fe, Calif., died June 13 at age 97. Dr. Adams was a trailblazer in pediatric cardiology. He performed the first heart catheterization on a newborn, discovered the role of lung surfactant in respiratory distress syndrome, and made key strides in advancing the understanding of congenital heart disease and pulmonary function during fetal life. Dr. Adams also published *Heart Disease in Infants, Children and Adolescents*, considered the gold standard in pediatric cardiology textbooks. Dr. Adams' many awards include the American Academy of Pediatrics' Founders Award in 2000, the Medical Alumni Society's Harold S. Diehl Award in 2009, and the University of Minnesota's Outstanding Achievement Award in 2017. He is survived by his wife, Joan; and 8 children.

ARNOLD S. ANDERSON JR., M.D., Class of 1944, Minneapolis, died May 8 at age 99. Dr. Anderson was a practicing pediatrician and clinical professor at the Medical School. In 1950, he helped start the St. Louis Park Medical Center, which later became the Park Nicollet Medical Center. Dr. Anderson also established the Foundation for Research and Education at the St. Louis Park Medical Center, as well as Minneapolis' Teenage Medical Service and Children's Health Center in Minneapolis, where he acted as the hospital's first CEO and chief medical director. He received the Harold S. Diehl Award from the Medical Alumni Society in 1984, the Gold-Headed Cane Award from the Medical School's Department of Pediatrics in 1990, and the Outstanding Achievement Award from the U of M's Board of Regents in 1993. He was predeceased by his wife, Rusk; and 1 son. He is survived by 9 children, 17 grandchildren, and 8 great-grandchildren.

Copavin: A 'cure' for the common cold

Although the public takes more medications for colds than for the treatment of any other illness, little of real significance has been written concerning their treatment … The reason for this study was the consistently good results I obtained in the treatment of my own colds with morphine.

– Harold S. Diehl, M.D., in the *Journal of the American Medical Association*, 1933

Harold S. Diehl, M.D., then head of the Student Health Service at the University of Minnesota, was in the process of patenting a drug to aid in the respite of the common cold. Licensed to Eli Lilly & Co. for production, Copavin, a name coined by Diehl, was a combination of two "practically harmless" opium derivatives – codeine and papaverine.

In Diehl's 1933 *JAMA* article and in his patent application, he asserted that this combination was "highly effective in the treatment of certain diseases, especially in the treatment of coryza [some typical cold symptoms]."

The 1934 University of Minnesota President's Report highlighted the success of the mixture, noting that 72 percent of nearly 1,500 students treated showed "definite improvement."

In October 1935, *Minnesota Alumni Weekly*, the U of M alumni magazine at the time, noted that more than 2,000 students had requested the medicine in the past year, while during "the cold weather in January 1934, as many as 75 students a day asked for Copavin." Later in 1935, Diehl became dean of the College of Medical Sciences, serving until 1958.

As part of the agreement with Eli Lilly & Co., the University received an 80 percent share of 5 percent of the royalties. Diehl received the remaining 20 percent. The Board of Regents designated the royalties be used for one or more of the following purposes: for the use of the Health Service, but restricted to uses not provided for in the regular budget; for medical research; to supplement for retention of distinguished members of the staff; for financing or endowment of fellowships in public health; or for a building or endowment fund for the Campus Club.

The Copavin Fund received its first payment, of $1,466.74, in 1934 and continued to grow over the next few decades. A portion of the funds helped to complete the Variety Club Heart Hospital in 1950. But the single largest use of the Copavin Fund came with the planning and construction of the Bio-Medical Library and scientific laboratories building in 1959.

Cost estimates for the library topped $1 million, including $832,000 appropriated by the Legislature; $108,000 from the Copavin Fund was the next largest contribution. The Honors Committee recommended naming the new building in honor of Diehl, who had just left his position as dean. It is unclear whether the naming of Diehl Hall also recognized the contributions made through his patented therapeutic mixture.

The Diehl-Copavin Fund is last documented in the University's 1971 annual financial report. With a balance of $45,000 and no new royalties, it likely helped to pave the way for the construction of Units A, B/C, today's Moos Tower, and the Phillips-Wangensteen Building.

Now, as planning and construction of the new Health Sciences Education Center begins (see page 30) and the Bio-Medical Library moves into the new space, know that in the building next door there is a time capsule containing a bottle of Copavin – certainly an elixir, if not a cure, for the common cold. MB

By Erik Moore, head of University Archives at the University of Minnesota Libraries

PHOTO: COURTESY OF UNIVERSITY ARCHIVES

Harold S. Diehl, M.D., was head of the U's Student Health Service when he filed a patent application for the often-requested Copavin.

Side 2P
Patent
Diehl Copavin

No. 2027722

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

Whereas HAROLD SHEELY DIEHL, of Minneapolis, Minnesota, assignor to BOARD OF REGENTS OF UNIVERSITY OF MINNESOTA, of Minneapolis, Minnesota, a corporation of Minnesota,

PRESENTED TO THE Commissioner of Patents A PETITION PRAYING FOR THE GRANT OF LETTERS PATENT FOR AN ALLEGED NEW AND USEFUL IMPROVEMENT IN

THERAPEUTIC AGENTS,

A DESCRIPTION OF WHICH INVENTION IS CONTAINED IN THE SPECIFICATION OF WHICH A COPY IS HEREUNTO ANNEXED AND MADE A PART HEREOF, AND COMPLIED WITH THE VARIOUS REQUIREMENTS OF LAW IN SUCH CASES MADE AND PROVIDED, AND

Whereas UPON DUE EXAMINATION MADE THE SAID CLAIMANT is ADJUDGED TO BE JUSTLY ENTITLED TO A PATENT UNDER THE LAW.

NOW THEREFORE THESE Letters Patent ARE TO GRANT UNTO THE SAID

Board of Regents of University of Minnesota, its successors OR ASSIGNS

FOR THE TERM OF SEVENTEEN YEARS FROM THE DATE OF THIS GRANT

THE EXCLUSIVE RIGHT TO MAKE, USE AND VEND THE SAID INVENTION THROUGHOUT THE UNITED STATES AND THE TERRITORIES THEREOF.

In testimony whereof I have hereunto set my hand, and caused the seal of the Patent Office to be affixed at the City of Washington this fourteenth day of January,

IMAGE: COURTESY OF UNIVERSITY ARCHIVES

PHOTO: COURTESY OF THE HERB MUSEUM, WWW.HERBMUSEUM.CA/

Copavin, a name coined by Diehl, was a combination of two "practically harmless" opium derivatives – codeine and papaverine.

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Editor
Meredith McNab

Managing Editor
Nicole Endres

For more information or to update your address, please contact:

Meredith McNab, editor

612-625-0657 or 800-775-2187
mmcnab@umn.edu

University of
Minnesota Foundation
200 Oak Street SE, Suite 500
Minneapolis, MN 55455–2010

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PAGE 8

Synchrony

“Play dates” are a part of once-conjoined twins Paisleigh (left) and Paislyn Martinez’s recovery.

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