Outlook

Washington University in St. Louis
School of Medicine

WINTER 2023–24

Neuroscience quest

change the world

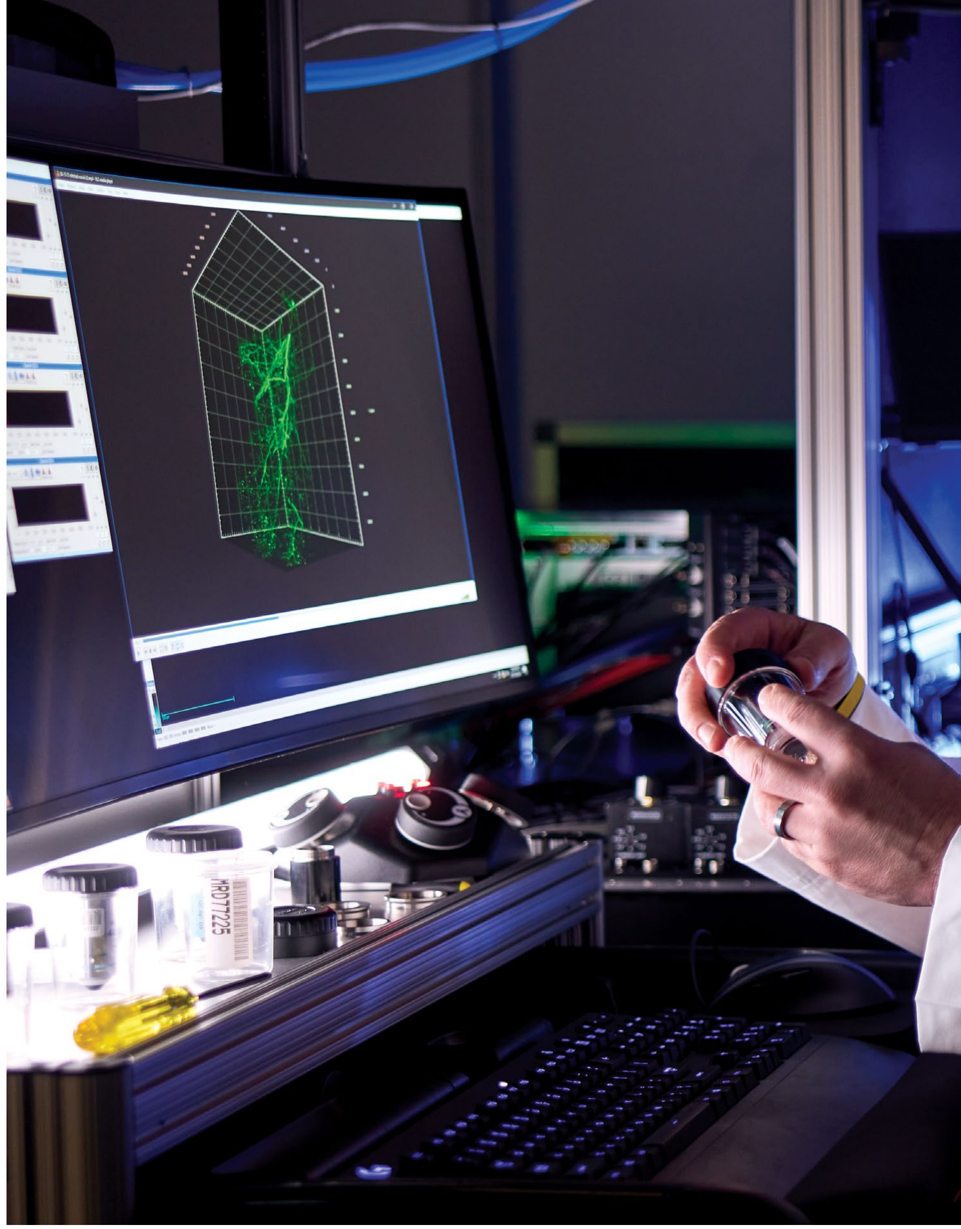
Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU   WINTER 2023–24

SARA MOSER

COVER **Understanding the brain is key to addressing devastating neurological and psychiatric diseases that affect mankind. To accelerate progress in this area, WashU Medicine — already one of the world's premier institutions in neuroscience research — is deepening its investment. A new 11-story building is creating a central home for more than 120 research teams focused on solving the many mysteries of the brain and the body's nervous system.**



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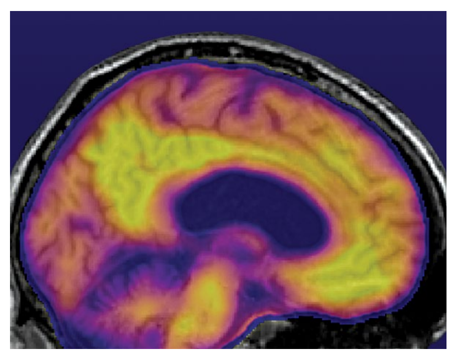
FEATURES

BRIAN GORDON



For decades, visionary benefactors have channeled millions of dollars to Washington University for brain and nervous system research, helping the institution rise to preeminence. (Above) Yellow areas on this brain scan reveal the presence of toxic Alzheimer's proteins — research funded by Charles and Joanne Knight and the Knight family. Read more about gifts from donors, starting on page 31.

Peter Bayguinov, PhD, assistant director of the Washington University Center for Cellular Imaging, sets up a two-photon microscope inside the Neuroscience Research Building. Learn more about neuroscience initiatives on page 4.

MATT MILLER

DEPARTMENTS

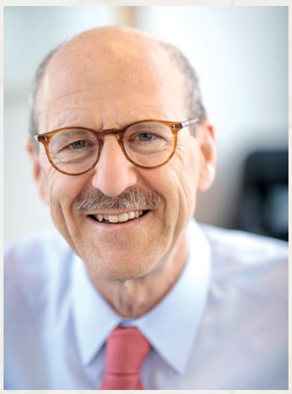
Special credit to Tamara Schneider, PhD, science writer in WashU Medicine Marketing & Communications, for researching and writing the majority of neuroscience content in this issue.

MATT MILLER

Bhooma Aravamuthan, MD, DPhil, a movement disorders specialist, treats children with cerebral palsy. She is one of more than 1,000 investigators working to tackle neurological and psychiatric diseases. See page 14.

A ‘unique, indelible impact’

Talent, technologies coalesce to drive revolutionary therapies



COMPILED BY SARA FREDMAN

Through the power of science and discovery, WashU Medicine is dedicated to unlocking mysteries of the brain, tackling some of the most intractable problems confronting us today and alleviating human suffering.

The new Neuroscience Research Building, which opened in August, is the latest signal of this commitment, providing advanced, collaborative spaces where researchers will probe the frontiers of brain function and develop innovative therapies for a spectrum of neurological disorders.

Here, David H. Perlmutter, MD, executive vice chancellor for medical affairs, the George and Carol Bauer Dean of the School of Medicine and the Spencer T. and Ann W. Olin Distinguished Professor, outlines his vision for neurosciences at the school.

‘A virtuous cycle’

Perlmutter begins by explaining the “virtuous cycle of academic medicine” as a paradigm for how the school’s missions of patient care, education and research are inextricably linked. In this cycle, the school invests in education and research to improve clinical care, patient outcomes and community health. In turn, its clinicians care for patients, identify important areas for study and bring innovations into clinical trials. Ultimately, this cycle strengthens care delivery, helping patients live longer, healthier lives.

PERKINS+WILL / CANNONDESIGN

Glass, three-story lobby on the north side of the Neuroscience Research Building.

Q&A

Dean Perlmutter explains how WashU Medicine is working to translate science into treatments that will help those who are suffering from neurological or psychiatric conditions.

What was the impetus for dedicating an entire building to the neurosciences?

We are the third-largest research-intensive medical school in the U.S., and we are No. 1 in National Institutes of Health (NIH) funding for neurology research. When I think about where Washington University can have a unique, indelible impact on human health, it is in the area of the neurosciences. This is the next frontier of science, in which new technologies and a coalescence of great talent at this university can help us address human suffering.

Much of the world's most cutting-edge neurology research is done in our labs, and so it made sense to build a hub where our brilliant scientists would have all they need to continue that work and break new ground. The building will house over 120 labs. But there's another piece to this that's just as critical — not just having the space to do the work, but also enabling the kind of proximity that encourages and nurtures collaboration.

Collaboration always has been, and will continue to be, a core value at WashU. We believe that the best science and the greatest improvements to human health can't come if you're working in silos but instead flow from conversation and collaboration between scientists and across fields and institutions. This building is going to bring together so many incredible scientists and their world-changing work into one space; conversation and cross-pollination and new ideas will be unavoidable. I'm just giddy at the thought of what will now be possible.

What kind of collaboration do you envision being made possible by this new facility?

Truly, the sky is the limit, but I'll give you an example. Drs. (David) Holtzman, (Jeff) Gordon and (Jonathan) Kipnis recently published a paper in Science that is one of my favorites of all time. The study showed that experimental perturbations of the intestinal microbiome had an impact on tau deposition and progression of Alzheimer's disease.

Think about that, the idea that the gut has an impact on the brain. It has enormous practical implications for new preventative approaches to the disease, and we are looking forward to how the three of them are going to build further on this framework for multiple shots on the target of Alzheimer's. This is the kind of collaborative work that we're hoping to foster.

How will the building's proximity to the Cortex Innovation Community boost innovation?

One of our most important institutional initiatives over the next few years will be commercializing our discoveries, and so there is synergy in situating the building next to this 200-acre district of entrepreneurs and startup companies. We are focusing on starting more companies, licensing more technologies and developing strategic partnerships with pharmaceutical companies to identify emerging research from our labs that can lead to new therapeutics.

> *"Much of the world's most cutting-edge neurology research is done in our labs, and so it made sense to build a hub where our brilliant scientists would have all they need to continue that work and break new ground."*
>
> *— David H. Perlmutter, MD*

Our goal is to shepherd more of our science through the drug development process and translate it into real treatments that will help people who are suffering. The opportunities for serious impact in solving the problems of the brain and neurological function are enormous with the maturation of technology in genomic engineering, cellular reprogramming, imaging tools and computational analysis of large datasets.

This building and the labs within it are a way for WashU Medicine to deepen its impact and, through the "virtuous cycle of academic medicine," elevate everything we are doing for our communities — locally, regionally and globally.

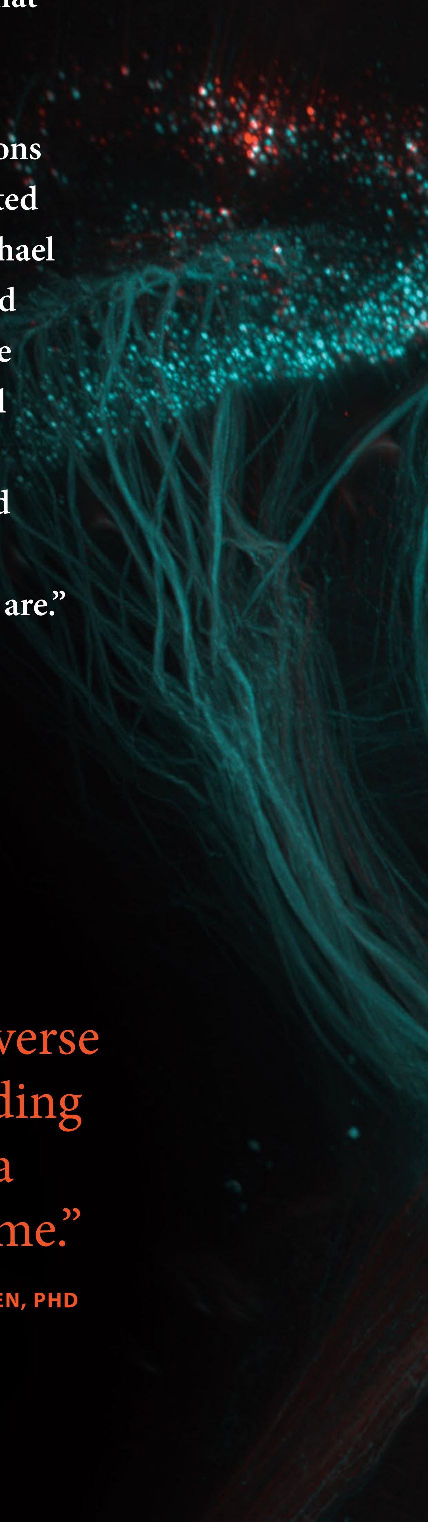
Neurosciences on the rise

Launching a new era of progress

BY TAMARA SCHNEIDER AND DEB PARKER

Inside our heads sits the remarkable human brain, a frontier of biology that still holds many secrets. This incredible organ consists of 86 billion neurons connected by a staggering 100 trillion synapses, numbers so vast that they surpass the number of stars in the Milky Way.

"All of our thoughts and the motivations underlying all of our actions are generated by our amazing human brain," said Michael S. Avidan, MBBCh, the Dr. Seymour and Rose T. Brown Professor and head of the Department of Anesthesiology. "We will never fully understand ourselves until we understand how our minds work and how our brains work. Because those are questions that are at the core of who we are."



> "The human brain is a universe within us, and understanding its complex geography is a grand adventure of our time."
>
> — DAVID C. VAN ESSEN, PHD

KERAN YANG, KEPECS LAB

The long, slender axons of neurons that terminate in the mouse superior colliculus — a part of the brain involved in sensation — glow blue and red after infection with fluorescent tracing viruses.

Valeria Cavalli, PhD (left), the Robert E. and Louise F. Dunn Professor of Biomedical Research, collaborates with staff in her neuroscience lab, which studies neural injury and repair.

Understanding the brain — when it functions normally and when it doesn't — is one of the most pressing challenges in the fields of neuroscience and medicine today, with profound implications for our well-being and scientific advancement.

"If we can unravel the mysteries of the brain, even partially, we could help millions of people who are suffering today from neurological disease and mental illness," said Eric J. Lenze, MD, the Wallace and Lucille K. Renard Professor and head of the Department of Psychiatry.

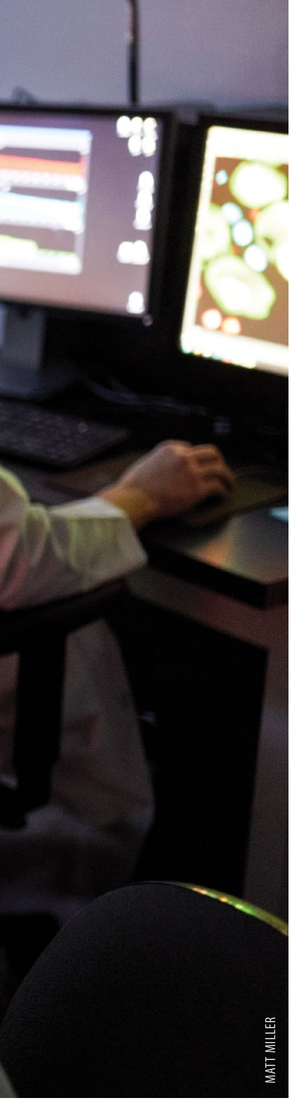
In the U.S., about 6 million struggle with Alzheimer's disease, the top cause of dementia, and over 11 million serve as their unpaid caregivers. These numbers will double as our population ages. Also, one in five adults is living with serious mental illnesses, such as major depressive disorder. Meanwhile, another million people grapple with movement disorders, such as Parkinson's disease, losing bodily control over time.

The challenges in treating neurodegenerative disorders and mental illnesses are immense. Their causes and mechanisms often are elusive, and they manifest differently in each individual. However, decades of meticulous research and technological advancements are yielding promising results. Washington University School of Medicine is at the forefront of this groundbreaking research.

Among other advancements, WashU Medicine researchers are: visualizing brain activity and connections via neuroimaging; mapping the brain's network of connections; applying machine learning to analyze complex data and predict cognitive outcomes; understanding the brain's neuroplasticity and ability to adapt; uncovering genetic factors underlying neurological and psychiatric disorders; creating brain-computer interfaces and neuromodulation devices; using regenerative stem cell therapies to treat brain diseases and injuries; and focusing on the neurobiology of mental health conditions.

In recent years, two breakthrough discoveries pioneered here — a brain-computer interface to aid stroke patients in regaining hand and arm function and a blood test for early Alzheimer's disease diagnosis — have entered the market.

In this moment of promise, the institution is rallying its strengths to combat neurological and psychiatric diseases. "Washington University



MATT MILLER

School of Medicine wants to change the world," Avidan said. "We want to change the world in fundamental ways that alter our understanding, create fresh insights, and enable people to live better and more fulfilling lives.

"And the key to that is neuroscience. Your brain is fundamental to your health, to your identity, and to your reason for living. By addressing the profound mysteries underlying the functions of the brain and the emergence of the mind, we'll be able to transform the way people live," he added.

Building momentum

To accelerate this progress, WashU Medicine recently opened the Neuroscience Research Building (NRB) — a 609,000-square-foot, 11-story facility — at 4370 Duncan Ave. The university invested $616 million to construct the building, the largest and most expensive in the medical school's history. The investment was driven by leaders' belief that the building will become one of the nation's premier neuroscience research hubs.

"This is an enormous investment, even by Washington University's standards," said Andrew M. Bursky, chair of the university's Board of Trustees. "But we believe there is no field in medical science with greater opportunity than brain science and no place in the world with greater capability or vision to pursue these opportunities than Washington University. Yes, this is a venture of immense proportions, and yes, it carries risk. But it is a risk we eagerly embrace."

Bursky added that David H. Perlmutter, MD, executive vice chancellor for medical affairs and the George and Carol Bauer Dean of the School of Medicine, convincingly made the case that this investment in neuroscience can address some of our most critical societal challenges, including atypical childhood development, mental health and the effects of aging.

"I came to WashU because I knew it was home to the most cutting-edge work and the most creative scientific minds," explained Perlmutter, also the Spencer T. and Ann W. Olin Distinguished Professor. "Right now, there is a lot of momentum around neurosciences, one of our areas of considerable strength. It was clear to everyone that we have a fantastic opportunity to strategically leverage our deep bench in this area to bring about a true sea change in our understanding of the brain, the nervous system and the devastating neurological diseases and disorders that touch every family and community across the globe.

"This building represents not only our investment in neuroscience research more broadly but also our urgent commitment to bringing the finest minds and tools together to find groundbreaking treatments and therapies.

"When you talk to any of our faculty, there is real passion for this vision, and there is excitement because we can see real hope for transformation in our lifetime. I want to see WashU remain at the forefront of this transformation," Perlmutter added.

Continued on page 10

MATT MILLER

Neuroscientist Ilya Monosov, PhD (third from left), problem-solves with (left to right) graduate student Yang-Yang Feng, senior scientist Ethan Bromberg-Martin, PhD, and graduate student Julia Pai.

NEUROSCIENCE RESEARCH BUILDING

A hub for collaboration

WashU MEDICINE

ABOUT THE BUILDING

one hub
researchers from 16 campus locations

120
research teams

11 floors

$616M
total cost

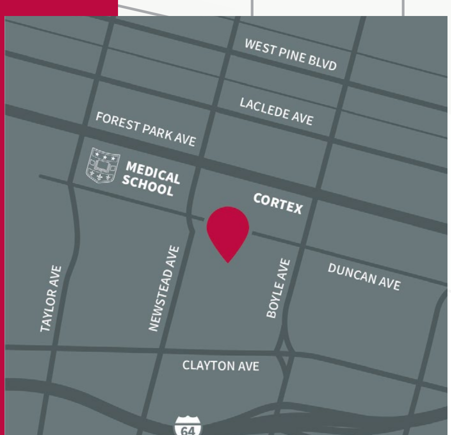
609,000
square feet

1,846
parking spaces

CROSS-LAB COMMUNICATION AND COLLABORATION

ORGANIZED BY RESEARCH AREAS

- Neural Systems & Theory
- Psychiatric Neuroscience & Therapeutics
- Pain & Peripheral Nervous System
- Circuits, Neuroplasticity & Behavior
- Neurodegeneration & Neuroimmunology
- Brain Tumor Biology
- Developmental Brain Disorders & Neurogenomics



CORTEX CONNECTION

The NRB sits between the hospital precinct and the Cortex Innovation District, encouraging entrepreneurial activity to accelerate technology transfer and translation.

MATT MILLER

Gregory Zipfel, MD, head of the Department of Neurosurgery, and Katherine Schwetye, MD, PhD, associate professor of pathology and immunology, discuss their research in Kaldi's Coffee at the Neuroscience Research Building.

The power of convergence

The Neuroscience Research Building (NRB) on the Medical Campus houses one of the world's highest concentrations of neuroscientists — joining together investigators in neurology, psychiatry, anesthesiology, neuroscience, neurosurgery and other areas. With its sleek design, advanced laboratories and collaborative workspaces, the building fosters interdisciplinary research aimed at understanding the brain and nervous system, transforming treatments for neurological and psychiatric diseases.

Researchers from different disciplines work side by side in shared lab space and equipment rooms. Amenities such as a cafe with rooftop terrace and meeting spaces spur cross-collaboration. An event-sized lobby and auditorium enable larger gatherings for research exchange.

FRESH PERSPECTIVES

Equity and inclusion guided all aspects of construction. The core team, including architects, managers and contractors, achieved a 60% male and 40% female balance. Project leaders also actively promoted opportunities for minority-, women- and veteran-owned business subcontractors.

MODEL OF SUSTAINABILITY

The space offers energy-efficient research freezers, sophisticated airflow systems, all-LED lighting, electric vehicle charging stations, a bicycle fix-it station, and native landscaping.

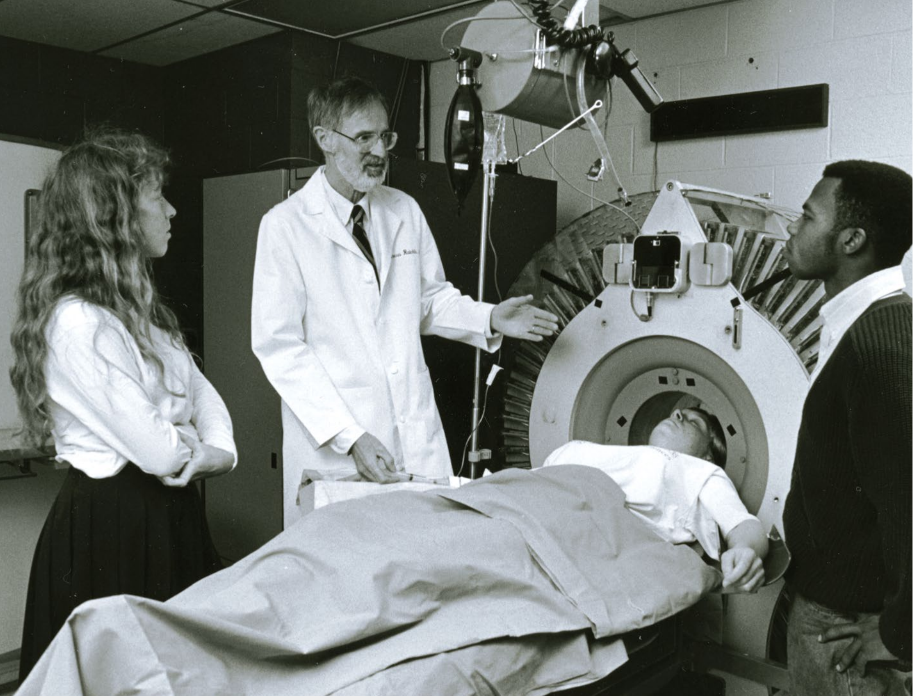
EXTENDED LINK

A pedestrian link for employees and badged visitors connects the NRB to St. Louis Children's Hospital garage, creating an east-west walkway from the Cortex Innovation District to the Medical Campus core.

Multiplying strengths

The NRB also houses specialized equipment and capabilities, including:

- **A mass spectrometry center to discover neurodegenerative biomarkers in Alzheimer's disease and related disorders.**
- **The most advanced microscopes — able to view tiny synapses, to whole-brain connectivity — located in the Washington University Center for Cellular Imaging-Neuro and the Alafi Neuroimaging Lab.**
- **Neurotech Hub with precision laser cutters and high-resolution 3D printers to accelerate in-house ideation, prototyping and one-of-a-kind applications and devices.**
- **One of the world's largest collections of zebrafish. The transparent embryos of zebrafish make them useful for observation. The zebrafish is a promising model for studying age-related changes in cognition and perception.**
- **A viral vector core to design gene-delivery tools based on harmless viruses for research and therapeutic applications.**
- **A flow cytometry core to analyze and sort cells by their physical and chemical properties.**
- **A microanatomy core to visualize the fine structure of the brain and map the patterns of gene activity.**



BERNARD BECKER MEDICAL LIBRARY

Neurologist Marcus Raichle, MD (center), discusses the PET scanner with students in 1993.

Neuroscience research highlights

Washington University researchers:

- Developed screening tests used worldwide to diagnose Alzheimer's disease.
- Created the first positron emission tomography (PET) scanner to show how the brain and other organs function.
- Performed the first nerve transplant using tissue from a cadaver donor.
- Identified the triggers of nerve degeneration involved in conditions, including Parkinson's disease, amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), glaucoma and peripheral neuropathy.

Developing a medical model of psychiatry: professors Samuel Guze, MD (left), and Eli Robins, MD, in 1959.

Through ongoing research, they are:

- Leading a global effort to map major brain circuits and identify their connection to brain disease.
- Exploring the genetic influences at play in alcohol, smoking and drug addiction.
- Developing new ways to diagnose and treat stroke and aneurysm.
- Leading an international collaboration to study inherited forms of Alzheimer's and evaluating ways to prevent or delay onset of the disease.
- Investigating ways to create and improve nonaddictive treatments for chronic pain.

Continued from page 7

The building's design further promotes cross-disciplinary collaboration, something that has long been intrinsic in WashU Medicine culture. More than 1,000 researchers on 120 research teams — previously scattered in 16 Medical Campus locations — now work in the same building. The space unites experts in neurology, neuroscience, neurosurgery, psychiatry, anesthesiology, radiology, genetics and developmental biology, who will leverage their collective expertise to probe the mind, brain and body and heal what is broken.

"With this new building, we are able to offer the neuroscience community a central home and a laboratory environment that can inspire entirely new concepts that allow us to grasp a much deeper understanding of the brain and have a global impact on health and science," said Chancellor Andrew D. Martin.

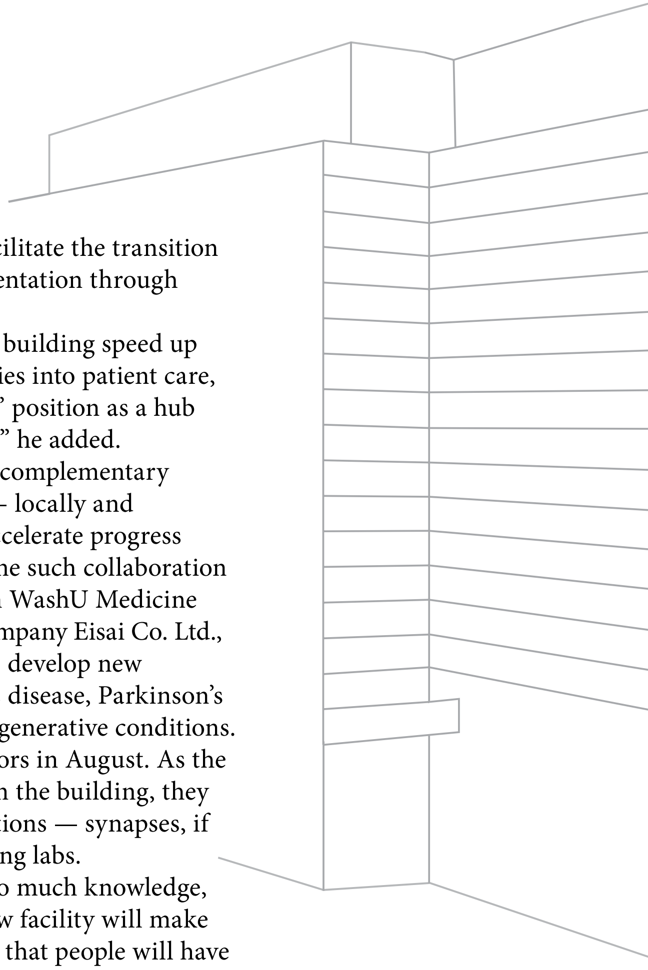
The building is organized by research themes, such as neurodegeneration, brain tumor biology and pain, rather than department affiliation. These themes advance areas of existing strength and holistically address critical challenges. The research building will house one of the world's highest concentrations of neuroscientists. By arranging them strategically to foster collaboration, new synergies will naturally arise.

"The real power is having people with different perspectives and expertise working side by side," said Linda J. Richards, PhD, the Edison Professor of Neurobiology and head of the Department of Neuroscience. "You can't help but generate new ideas and new approaches to solving problems. That is where you get real scientific power," she added.

This expansion also will open doors to collaboration and innovation for graduate students and faculty at all levels and significantly enhance educational opportunities.

Accelerating treatments

The ultimate goal of biomedical neuroscience research, of course, is not just to understand how the nervous system works, but to heal and protect it. And translating WashU Medicine findings into real-life clinical applications will help St. Louis' future economic health, too. Developing commercially viable therapeutics and technologies will play a key role in regional growth.



To facilitate such efforts, WashU Medicine leaders positioned the new building in the 200-acre Cortex Innovation District on the eastern edge of the Medical Campus. Cortex is one of the fastest growing business, innovation and technology hubs in the U.S. and home to numerous biotech startups founded by Washington University faculty, staff and students.

Jeffrey D. Milbrandt, MD, PhD, the James S. McDonnell Professor of Genetics, has a track record of translating basic discoveries into clinical applications. In 2017, he and Aaron DiAntonio, MD, PhD, the Alan A. and Edith L. Wolff Professor of Developmental Biology, co-founded Disarm Therapeutics. Their objective: to create drugs targeting axonal degeneration, a disease process that underlies numerous neurological disorders. Such treatments potentially could help millions of patients with debilitating nerve damage caused by various conditions. Notably, Eli Lilly and Co. acquired Disarm in 2020.

"When Aaron and I started Disarm, we had no real option other than to start it on the coast," Milbrandt said. "But with the rapid growth and transformation of the Cortex Innovation District over the last several years, it's easier for startups to stay here in St. Louis. The location of the NRB in Cortex creates opportunities for WashU Medicine neuroscientists to make connections with people at companies there and facilitate the transition from discovery to implementation through starting companies.

"Not only will this new building speed up the translation of discoveries into patient care, it will strengthen St. Louis' position as a hub for biomedical innovation," he added.

By taking advantage of complementary strengths, such alliances — locally and internationally — could accelerate progress toward new treatments. One such collaboration is already in place between WashU Medicine and the pharmaceutical company Eisai Co. Ltd., headquartered in Japan, to develop new treatments for Alzheimer's disease, Parkinson's disease and other neurodegenerative conditions.

The NRB opened its doors in August. As the labs establish themselves in the building, they will begin to form connections — synapses, if you will — with neighboring labs.

"By bringing together so much knowledge, talent and passion, this new facility will make it considerably more likely that people will have the kinds of water-cooler discussions that lead to interdisciplinary game-changing ideas and projects," said David M. Holtzman, MD, the Barbara Burton and Reuben M. Morriss III Distinguished Professor. "I'm very excited to see what we will do."

MATT MILLER

WashU Medicine neurologists Randall Bateman, MD (right), and David Holtzman, MD (left), talk with Eisai Co. Ltd. leaders Teiji Kimura, PhD (center right), and Kanta Horie, PhD, before a kickoff event to mark their collaboration.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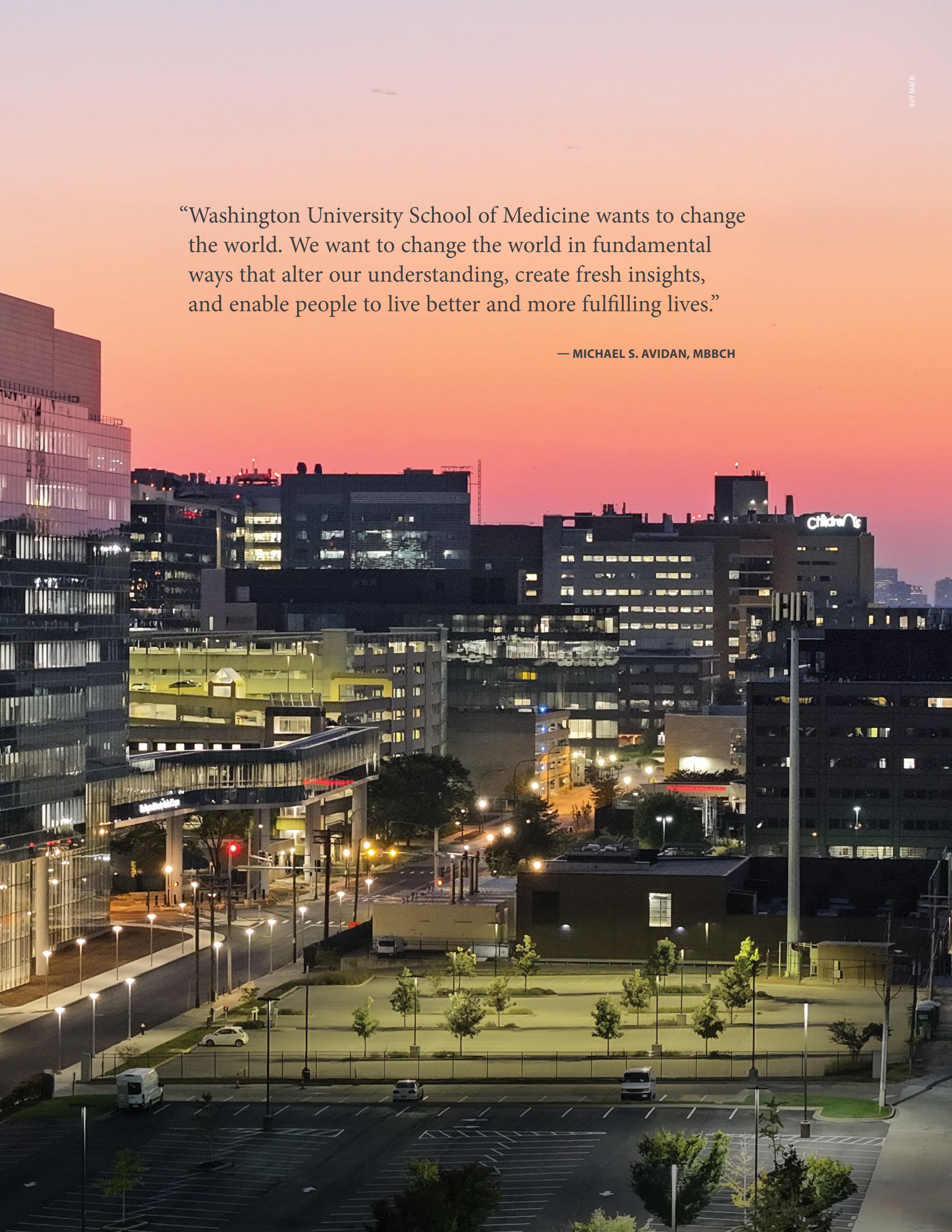


HUY MACH

"Washington University School of Medicine wants to change the world. We want to change the world in fundamental ways that alter our understanding, create fresh insights, and enable people to live better and more fulfilling lives."

— MICHAEL S. AVIDAN, MBBCH

Navigate the neurosciences at WashU Medicine

Explore the extensive scope of neuroscience research conducted at WashU Medicine in the following pages. These examples provide just a glimpse into the ongoing investigations that impact all of us in some way.

- Pain & addiction
- Sleep quality
- Brain tumors
- Human development
- How the mind works
- Neurological injury
- Immune-brain nexus
- Neurodegeneration

GETTY IMAGES

PAIN & ADDICTION

Breaking the grip

Pull on any loop of the Gordian knot that is finding treatments for pain and addiction, and the whole knot just tightens. Powerful painkillers come with a daunting risk of chemical dependency. The persistent sadness, worry and inability to find joy in life that can accompany chronic pain make substance use more appealing.

“Understanding pain and addiction is one of the most pressing needs in health care,” said Michael S. Avidan, MBBCh, the head of the Department of Anesthesiology and anesthesiologist-in-chief at Barnes-Jewish Hospital. “The way we treat pain has exacerbated the opioid epidemic, which is one of the biggest scourges in our society. We’re not going to solve this by waging a war on drugs. We’re going to address this by understanding the mechanisms of pain, why addiction occurs and by translating scientific insights into clinical practice.”

It’s in your genes

There’s a persistent myth that behavioral disorders are less grounded in biology than physical diseases such as diabetes, and therefore less treatable. Psychiatrist Laura Bierut, MD, has helped prove that idea false through her work on the role of genetic factors in smoking, alcoholism and other substance-use disorders. Among other things, she has identified genes that influence a person’s risk of becoming a heavy smoker and of developing lung cancer, and showed that providing smokers with personalized risk information based on their genetics helps them kick the habit.

MATT MILLER

Clinical research coordinator Bulenda Shayo tests a patient at the Washington University Pain Center.

Pain and pleasure

It's hard to be happy when you're always hurting. That's one reason opioids can be so addictive — they dampen both physical and emotional pain, leaving people temporarily pain-free and euphoric. Neuroscientists Meaghan C. Creed, PhD, and Jose A. Moron-Concepcion, PhD, have identified circuitry in the brain that links pain to negative emotions such as sadness, anxiety and an inability to feel joy. The finding suggests that modulating the circuitry could treat both emotional and physical suffering, an approach that could reduce the addictive potential of opioids and improve quality of life for people with chronic pain, even when it's not possible to completely eliminate pain itself.

"By targeting the emotional aspects of pain, we hope to make pain less debilitating so that patients won't crave the emotional high they get from opioids."

— Jose A. Moron-Concepcion, PhD

Nonaddictive pain relief

The devastating and deadly ongoing opioid epidemic highlights the difficulty of balancing the need for pain relief against the dangers of addiction. Pain scientist Robert W. Gereau IV, PhD, studies how pain signals are transmitted from the body to the brain with the aim of finding new ways to alleviate pain. He has created a tiny, flexible LED device that can be implanted in body parts that experience persistent pain to interrupt the transmission of pain signals. In other work, pharmacologist Susruta Majumdar, PhD, is working on improving the safety profile of fentanyl, a powerful opioid pain reliever and the leading cause of opioid overdose deaths. He has created an altered fentanyl molecule that he expects will be less lethal and addictive but still able to alleviate pain.

MATT MILLER

Robert Gereau IV, PhD, holds a pair of tiny microLED implants.

The Centers for Disease Control and Prevention estimates that more than 51 million people — 20% of U.S. adults — have chronic pain.

GETTY IMAGES

SLEEP QUALITY

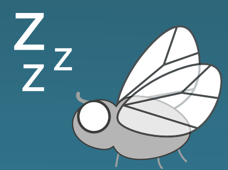
Keeping the brain sharp

There's nothing like a good night's sleep. Apart from the pleasure of waking up refreshed and relaxed, sleep consolidates memories and enhances learning and creativity, which is why people grappling with a thorny problem are well advised to "sleep on it." Sleep allows time for the brain's housekeeping cells to clear away the molecular debris from the day so the brain can start the next day fresh.

And poor sleep doesn't just make people grouchy; it has been linked to diabetes, heart disease, depression, Alzheimer's and many other chronic conditions. WashU Medicine scientists are leaders in exploring sleep, from the fundamental question of why we do it in the first place, to how and why sleep disturbances undermine health and what can be done to address it.

"The fly has so much to offer us. A lot of times we get inspiration for our fly experiments by talking to clinicians. Clinicians see complex problems in their patients and they come up with hypotheses that are difficult to test in people, but we can test in the fly. And more often than not, we succeed. We keep on getting things that match what people are finding in humans."

— Paul J. Shaw, PhD



Why do we sleep?

Step aside, lab rat. The humble fruit fly is sleep scientists' lab animal of choice because its sleep habits are similar to ours, but its brain is just one-millionth the size. Studying fruit flies, neuroscientist Paul J. Shaw, PhD, has figured out the neurological basis of baffling phenomena such as why people sleep more after learning new things, and why it can sometimes be impossible to fall asleep despite tiredness. For flies with memory defects or Alzheimer's-like brain changes, Shaw's team has shown that improving sleep enhances cognitive performance — suggesting that people with certain neurological disorders may also benefit from improved sleep.

Neurologist Yo-El Ju, MD (right), monitors a participant during a sleep study on REM sleep behavior disorder.

MATT MILLER

Do I have a sleep disorder?

- Habitual loud snoring, associated with pauses or snorting noises
- Frequent brief choking, awakening with gasping or shortness of breath
- Awakening with a headache
- Persistent sleepiness when awake or episodes of falling asleep unintentionally
- Persistent fatigue
- Persistent difficulty falling or staying asleep
- An urge to keep moving the legs at bedtime or a rhythmic twitching of the legs after falling asleep
- Unusual behaviors during sleep such as sleepwalking

WashU Medicine sleep experts treat sleep disorders with lifestyle changes, CPAP machines, implantable devices, medication, behavior therapy or surgical management.

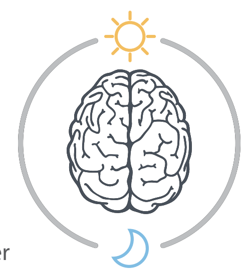
Losing sleep

It's the old chicken-and-egg problem: Does chronic bad sleep injure the brain, or are sleep problems a symptom of damage? To neurologist Yo-El S. Ju, MD, the answer is probably both. A few years ago, she showed that sleep apnea — in which frequent breathing stoppages prevent deep sleep — worsens the signs of early Alzheimer's disease, and that treating the breathing problems improves such signs. Now she co-leads an international study of REM sleep behavior disorder (RBD), a condition that often heralds dementia, Parkinson's disease and other serious conditions. In RBD, the first sign of a neurological problem is a tendency to thrash about and act out dreams.

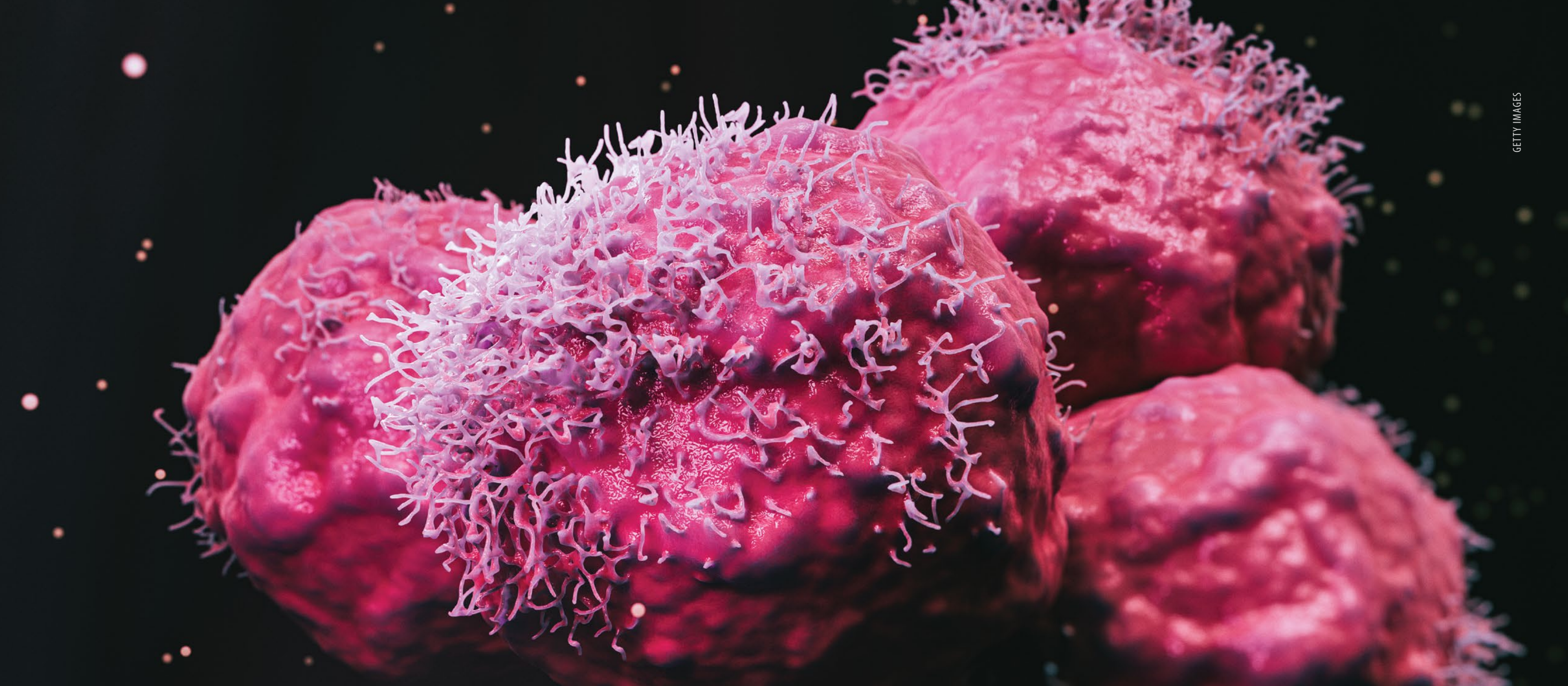
Sleep is the best medicine

To Brendan P. Lucey, MD, director of the Washington University Sleep Medicine Center, the goal is to help people sleep better. After his lab and others showed that poor sleep increases brain levels of two damaging Alzheimer's proteins, he set out to determine whether good sleep could lower the levels of toxic proteins and thereby prevent or delay the onset of cognitive symptoms. He leads an ongoing phase 2 clinical trial of suvorexant, an FDA-approved insomnia drug. Preliminary results have been promising, hinting at the potential of sleep medications to slow or stop the progression of Alzheimer's disease.

Out of sync



Our bodies are designed to follow the sun. Not just sleeping and waking, but digestion, immune responses and many other biological processes exhibit daily cycles of activity. When normal circadian rhythm is disrupted by jet lag, night shifts, odd sleep habits or disease, it can have far-reaching detrimental health effects. Neurologist Erik S. Musiek, MD, PhD, has shown that circadian disruptions accelerate the accumulation of damaging Alzheimer's proteins in the brain. He has identified a gene that may be responsible for the link, pointing the way to a possible new approach to treating Alzheimer's.



GETTY IMAGES

BRAIN TUMORS

Fighting with targeted tools

Whether malignant or benign, a brain tumor is life-altering. Malignant tumors can spread and become deadly. And benign doesn't mean harmless; benign tumors can cause serious problems such as paralysis, seizures and personality changes depending on which parts of the brain they affect.

"Brain tumors affect the fundamental attributes of people — their personality and behavior; their ability to move, speak, see, think — that are just such essential characteristics of a human being," said neurosurgeon Albert H. Kim, MD, PhD, the founding director of the Brain Tumor Center at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. "To understand and treat brain tumors we have to attack them from different angles, and tailor therapy to each person."

Personalized predictions

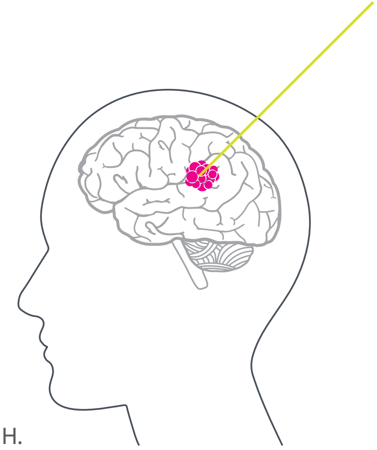
People with the neurofibromatosis type 1 (NF1) genetic disorder can develop tumors on nerves anywhere in the body, including in the brain. David H. Gutmann, MD, PhD, neurologist and director of the Washington University NF Center, discovered that the specific mutation a child is born with, neuronal activity and hormones all play roles in determining whether tumors develop and what problems they will cause. Based on these discoveries, Gutmann and data scientists Philip R.O. Payne, PhD, and Aditi Gupta, PhD, created risk-assessment models using advanced AI methods that can inform personalized approaches to management of each person with NF1.

"One of the biggest challenges in caring for children with NF1 is not being able to predict who might develop a brain tumor."

— David H. Gutmann, MD, PhD

Zika's silver lining

Zika virus made headlines worldwide in 2015 when it caused thousands of babies in Brazil to be born with tiny, misshapen brains. Neuro-oncologist Milan G. Chheda, MD, and virologist Michael S. Diamond, MD, PhD, aim to harness the virus's infamous power to kill brain cells and direct it against brain cancers. They have shown that the virus can activate immune cells to destroy an aggressive brain cancer in mice, giving a powerful boost to an immunotherapy drug and sparking long-lasting immunological memory that can ward off tumor recurrence for at least 18 months.



Laser focus

WashU Medicine neurosurgeons were among the first to use MRI-guided, high-intensity laser interstitial thermal therapy (LITT) to treat inoperable brain tumors. This minimally invasive technique uses lasers to heat and destroy tumors while leaving surrounding brain tissue undamaged. Neurosurgeon Albert H. Kim, MD, PhD, studies how to make laser therapy even more effective. He discovered that LITT temporarily opens the blood-brain barrier, potentially allowing chemotherapy drugs to mop up remaining cancerous cells, and stimulates the immune system, an opportunity to develop add-on immunotherapies. Alexander H. Stegh, PhD, research director of the Brain Tumor Center, targets tumors with a different approach, using nanotechnological platforms to manipulate the tumor's genetic program and to arm the body's immune system to fight brain cancers.

Breaking the barrier

Biomedical engineer Hong Chen, PhD, and neurosurgeon Eric C. Leuthardt, MD, pioneered sonobiopsy, which uses targeted ultrasound and microbubbles to temporarily disrupt the blood-brain barrier that normally shields the brain from harmful substances in the blood. This disruption allows RNA, DNA and proteins to flow from the brain into the blood where they can be detected and analyzed. "Sonobiopsies provide invaluable molecular and genetic information without the risks of brain surgery," Leuthardt said. "It's the third revolution in brain cancer diagnosis, after structural and functional brain imaging."

MATT MILLER

Neurosurgeon Albert Kim, MD, PhD (center), and chief resident Adam Bevan, MD, PhD, perform a right parietal craniotomy to remove a brain tumor.

RYAN J. DEAN, PHD

HUMAN DEVELOPMENT

Starting out strong

The first 1,000 days, from conception to around the second birthday, are a period of exponential brain growth and development. Anything that affects the process — from genetic alterations, to chemicals such as alcohol, to the home environment — can have lifelong consequences. WashU Medicine researchers are leading efforts to understand the factors that influence brain development in order to promote healthy brains and help people live their best lives.

Building the brain

How do billions of neurons organize themselves into structures and networks to form the enormously complex machine that is the brain? The answer could shed light on the roots of conditions such as epilepsy, autism and intellectual disability, but studying the developing brain in utero has proven challenging. Linda J. Richards, PhD, the head of the Department of Neuroscience, has pioneered the study of brain development in marsupials, which are born 16 days after conception. They are born with brains little more than nubs and undergo the bulk of development after birth. Recently, she showed that distinct activity patterns emerge in different brain areas just weeks after conception. “Would alterations to patterned activity disrupt how brain circuits are set up, and if so, could that cause developmental disorders?” she asked.

The human brain:

- has an estimated **86 billion neurons** and **100 trillion synapses**
- **doubles in size** in the first year
- reaches **80%** of its adult size by age 3 and **90%** by age 5

Exposure to stress and trauma can have long-term negative consequences for the child’s brain, whereas talking, reading and playing can stimulate brain growth.

Childhood stress changes the brain

Even preschoolers can get depressed, according to the research of child psychiatrist Joan L. Luby, MD, who studies the biology and treatment of brain and behavior disorders in children as young as 3. Luby has shown that childhood stressors such as poverty and neglect are linked to anatomical changes in the brain, and that these changes can be partially counteracted by nurturing care. Her work has changed the way psychiatry recognizes and addresses mental illness in young children, particularly depression.

“The psychosocial environment is very powerful. A child’s brain doesn’t develop based solely on its genetic infrastructure. It’s influenced by the stressors of poverty, violence, the loss of a parent and other adverse experiences, which together can have serious health consequences that may become evident in early childhood.” — Joan L. Luby, MD

Holding a seat at the table

Child neurologist Christina A. Gurnett, MD, PhD, a co-director of the school’s Intellectual and Developmental Disabilities Research Center (IDDRC), believes the perspectives of patients and families are indispensable to good research. “They are the experts on their own conditions,” she said. “We need to know whether the answers we’re finding in the lab address questions relevant to people living with these conditions. Families must be at the table for the planning of any kind of research.” The IDDRC, one of only 15 such sites in the U.S., works to advance knowledge, prevention and treatment of intellectual and developmental disability.

MATT MILLER

Why prematurity leads to social impairments

Children born in the seventh month of pregnancy or earlier are at risk of developing depression, anxiety, learning disabilities, ADHD and other issues. Child psychiatrist Cynthia E. Rogers, MD, and pediatric neurologist Chris D. Smyser, MD, are imaging the brains of premature infants to learn why. “We want to understand the differences in brain structure and function that underlie elevated rates of social impairment that we see in children born very prematurely,” Rogers said. “Our hope is to find ways to develop interventions that improve outcomes for these children.”

Cynthia Rogers, MD, visits a patient in the NICU at St. Louis Children’s Hospital.

SARA MOSER/GETTY IMAGES

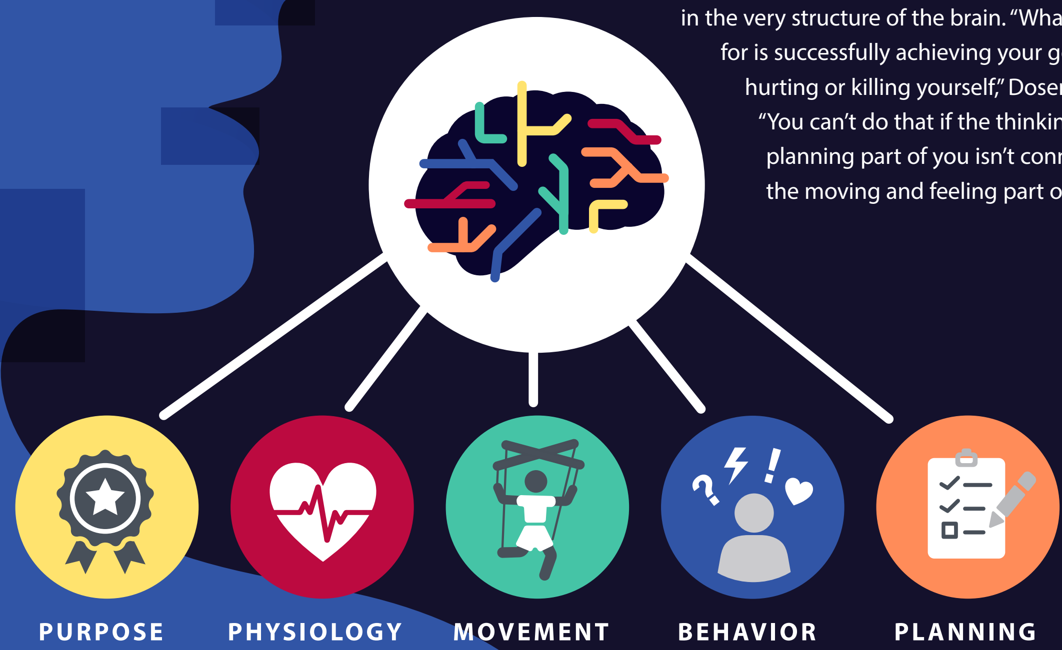
HOW THE MIND WORKS

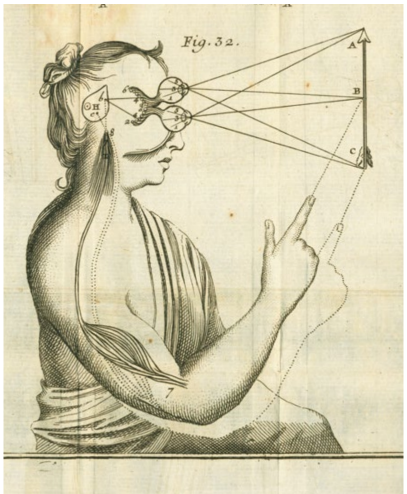
Thinking about thinking

The French philosopher René Descartes believed that body and mind are separate and independent, each capable of existing without the other. Modern neuroscientists would argue the opposite: The mind is what the brain does, they say, just as pumping blood is what the heart does. WashU Medicine neuroscientists are pushing the boundaries of our understanding, investigating how the cells, circuits and structures of the brain give rise to the complex mental functions that make us who we are.

The mind-body connection

Neurologist Nico U. Dosenbach, MD, PhD, believes he has proven Descartes wrong. Dosenbach led a study showing that brain areas controlling movement are plugged into networks involved in thinking, planning and control of involuntary functions such as blood pressure. The findings represent a literal linkage of body and mind in the very structure of the brain. "What the brain is for is successfully achieving your goals without hurting or killing yourself," Dosenbach said. "You can't do that if the thinking and planning part of you isn't connected to the moving and feeling part of you."





French philosopher René Descartes' (1596-1650) illustration of dualism in "Treatise of Man."

Do you really want to know?

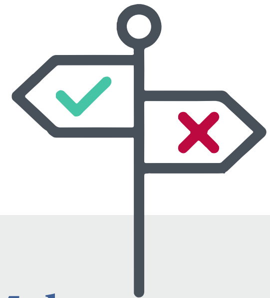
In the information age, we're surrounded by knowledge. When should we seek it out? And when is it better not to know? According to research by neuroscientist Ilya E. Monosov, PhD, your brain has specific neural circuits that measure how uncertain you are about whether to seek knowledge. Different circuits are involved when weighing whether to seek information about good possibilities versus bad. "Our curiosity to know the future is altered in many mental disorders, particularly OCD, anxiety and depression," Monosov said. "Understanding how the brain handles uncertainty could lead to new approaches to mental disorders associated with an inability to tolerate uncertainty."

MATT MILLER

Apoorva Arora, a graduate student in the Roy and Diana Vagelos Division of Biology & Biomedical Sciences, builds mazes for rats in the lab of Adam Kepecs, PhD.

You sure about that?

Have you ever waited in a slow-moving line and wondered if it's worth the wait? In moments like these, our "confidence neurons" are silently assessing our commitment. Neuroscientist Adam Kepecs, PhD, took this idea into the lab, training rats to identify ambiguous sounds and giving them the choice to skip uncertain trials. When faced with challenging decisions, rats often chose to opt out, reflecting their confidence level. Kepecs identified unique neurons that tracked a rat's moment-to-moment confidence and guided its persistence in waiting. By devising quantitative methods to study subjective mental states in animals, his research offers new insights into human disorders rooted in misjudged confidence, such as hallucinations and anxiety.

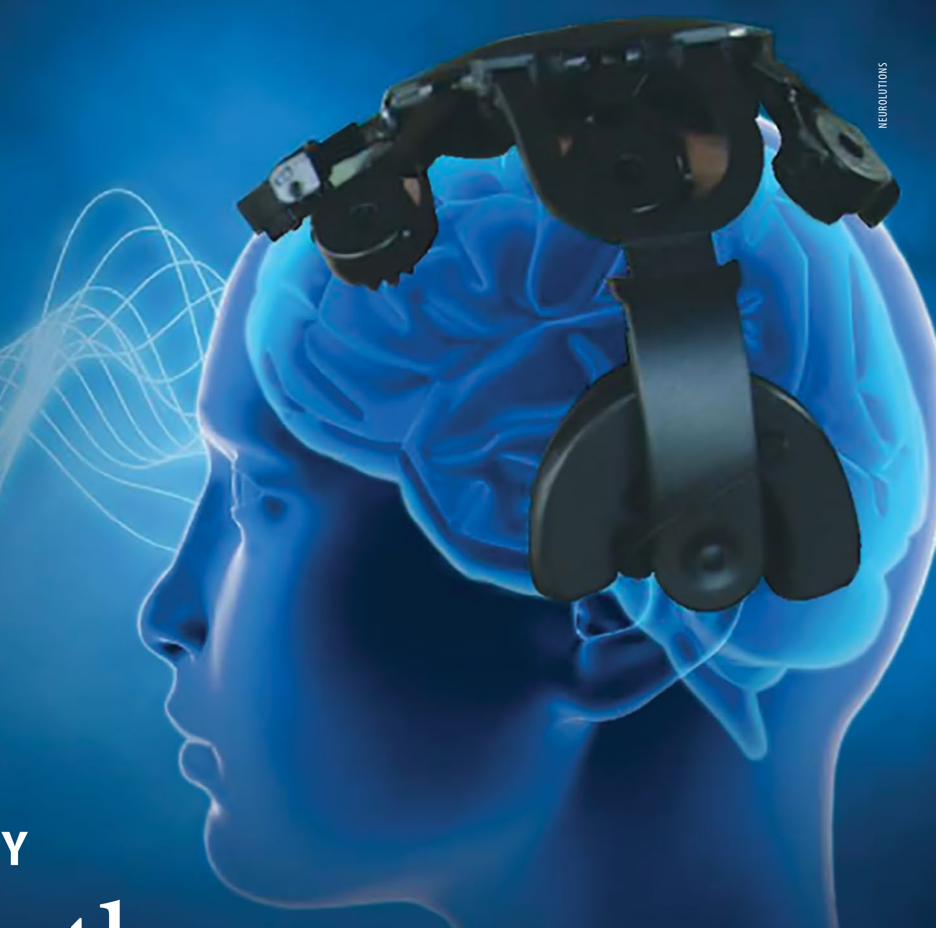


Make your choice

When you are faced with a choice — say, whether to have ice cream or cake — specific sets of brain cells fire as you weigh your options, one set for each option. Since he discovered those cells in the mid-2000s, neuroscientist Camillo Padoa-Schioppa, PhD, has been carefully figuring out the rules that determine exactly how they encode subjective value and interact to determine a final choice.

"In a number of mental disorders, such as addiction and eating disorders, patients consistently make poor choices. We're trying to understand why."

— Camillo Padoa-Schioppa, PhD



NEUROLUTIONS

> “I was walking down the hall and one of the patients excitedly flagged me down and said, ‘I just want to let you know that I can put my pants on for the first time in three years.’ At that moment, I realized my work had changed someone’s life.”
>
> **— Eric C. Leuthardt, MD**

NEUROLOGICAL INJURY

Smoothing the road to recovery

An EEG electrode device in the IpsiHand system measures the patient’s intended motor function.

A car accident, a gunshot, a stroke — in an instant, everything changes. Returning to the way things were tends to be slow and difficult, with no guarantees. WashU Medicine researchers are making crucial discoveries regarding the biology of regeneration and recovery. These discoveries pave the way toward — and in some cases already have achieved — innovative new therapies and devices to help people recover from neurological injury as fully as possible.

A breakthrough device

NEUROLUTIONS

The first FDA-approved device that helps stroke patients retrain their brains is based on research by neurosurgeon Eric C. Leuthardt, MD, and biomedical engineer Daniel W. Moran, PhD. Leuthardt’s insights into motor signaling in the brain led to the development of the IpsiHand, in which patients use a brain-computer interface to control a robotic glove that opens and closes their hands. Repeated use gradually teaches patients’ brains to do it on their own, restoring significant hand function. The FDA designated the IpsiHand a “Breakthrough Device,” which means it meets a critical unmet need, and gave it “de novo” authorization, as there was no similar medical device on the market.


MATT MILLER

Physical therapist Elizabeth "Beth" Hughes, DPT, works with patient Alishia Bean, using speech, occupational and physical therapies to treat hemiparesis following a stroke.

Limiting aneurysm damage

Brain aneurysms — bulges in the walls of brain blood vessels — can burst without warning, triggering a life-threatening medical crisis. The brain has ways to protect itself in the aftermath of a rupture, but those mechanisms can get overwhelmed. Gregory J. Zipfel, MD, the head of the Department of Neurosurgery, has pieced together the molecular pathways underlying the brain's natural resilience and, in the process, found a way to bolster them and minimize brain damage. His discoveries lay the groundwork for new and promising therapies for this unpredictable and often fatal event.

Coaxing cells into regenerating

Unlike nerves elsewhere in our body, the damaged spinal cord has very limited ability to recover. Neuroscientist Valeria Cavalli, PhD, wants to understand how peripheral nerves heal so she can coax the spinal cord into doing the same. She has discovered that support cells surrounding injured peripheral neurons help them regenerate, and identified a drug that activates these cells and enhances regrowth. Cavalli hopes to translate these findings into therapies for spinal cord and peripheral injuries.

New approaches to stroke recovery

What happens in the first hours to weeks after a stroke can be the difference between good recovery and lifelong impairments. Jin-Moo Lee, MD, PhD, head of the Department of Neurology, analyzed the genomes of stroke survivors and identified two genes related to neuronal excitation associated with good recovery in the pivotal first 24 hours. This suggests that calming overexcited neurons may improve outcomes. One of these genes has already been studied in animal models of stroke, and drugs are being developed to target the gene to mitigate brain injury due to stroke.

- Every year in the U.S., more than **795,000 people have a stroke.**
- Stroke is a **leading cause of serious long-term disability.**
- Stroke **reduces mobility in more than half** of stroke survivors age 65 and older.

SANDRO DA MESQUITA

IMMUNE-BRAIN NEXUS

Wielding a double-edged sword

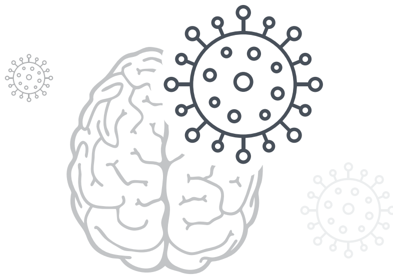
The brain was once thought to be off-limits to the immune system, too sensitive to tolerate immune cells with their sharp weapons. Now, scientists know that immune cells and molecules flow into and out of the central nervous system all the time, supporting normal brain function, fighting infections and tumors and, yes, sometimes causing injury and disease. The nexus between the immune and nervous systems provides new opportunities to intervene to promote health and prevent or treat neuroinfectious, neuroimmune and neurological conditions ranging from COVID-19 to multiple sclerosis to autism.

Immune surveillance

The idea that the immune system surveils and protects the brain is now widely accepted, but until recently it wasn't clear how and where. In 2015, neuroscientist and immunologist Jonathan "Jony" Kipnis, PhD, found a network of vessels in the meninges — the tissues encasing the brain — that drains fluid and small molecules from the brain into the lymph nodes. Subsequent research indicated that immune cells stationed in the meninges inspect fluid as it washes out of the brain. Such cells are prepared to initiate an immune response if they detect signs of infection or injury, Kipnis said.

"The immune cells that sit on the borders of the brain could potentially be a feasible target for treating neurological diseases such as Alzheimer's, once we better understand their role in these complex diseases."

— Jonathan "Jony" Kipnis, PhD



Pandemic brain fog

Before the COVID-19 pandemic made "brain fog" a household term, infectious diseases physician Robyn S. Klein, MD, PhD, grappled with the neurological consequences of another virus: West Nile virus, which can cause memory problems. She found that some West Nile patients' symptoms worsen even after the virus is cleared because persistent immune activation causes ongoing damage. Long COVID-19, she discovered, was similar. The virus doesn't infect the brain, but immune molecules released elsewhere spill over into the brain, injuring tissue and causing brain fog. "The same immune response that saved your life could be damaging your brain," Klein said.

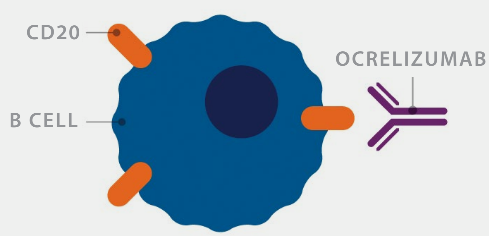
Treating HIV

Before COVID-19 brain fog, there was HAND, or HIV-associated neurocognitive disorder. Since the 1990s, infectious diseases physician David B. Clifford, MD, has led national efforts to understand and treat HAND. Clifford and others have shown that lifesaving antiretroviral therapy reduces but doesn't eliminate the cognitive consequences of HIV infection, which can include confusion, difficulty concentrating and behavioral changes. "About half of HIV patients in care have some cognitive impairment," Clifford said. "That is an unreasonable burden that should be reversed as soon as possible."

Anne Cross, MD, talks with clinical trial participant Brian Phillips, who has multiple sclerosis (MS), as he receives an infusion of rituximab, an experimental drug that depletes B cells. Cross transformed the world of MS research when she discovered that B cells play a critical role in the disease.

When T cells attack

Multiple sclerosis (MS) occurs when T cells attack the nerves' insulating sheath, slowing signal transmission and causing fatigue, numbness and miscoordination. But T cells don't do their damage alone, points out neurologist Anne Cross, MD. Her work has revealed that B cells are essential for turning T cells against nerves, a seminal discovery that led to an FDA-approved MS drug that works by suppressing B cells. Meanwhile, molecular biologist Naresha Saligrama, PhD, is investigating how the T cell populations of healthy people and people with MS differ. "Everyone has some self-reactive T cells, but not everyone has an autoimmune disease. What's different about people who get MS?" he asked.



Targeting B cells in MS

While rituximab was never approved to treat MS, it paved the way for a new class of MS therapeutics. The FDA has approved three antibody-based drugs that deplete B cells by targeting the CD20 molecule, a marker exclusive to B cells. Once targeted, the B cell is marked for destruction. Ocrelizumab (left) was the first such drug approved.

Good or bad?

Scientists are just beginning to grasp how complicated the immune system's role in neurological diseases can be. Take the gene *TREM2,* which helps control the activity of immune cells in the brain. Immunologist Marco Colonna, MD, and colleagues discovered that, in early stages of Alzheimer's disease, immune cells lacking *TREM2* do a poor job of removing toxic proteins. So *TREM2* is good, right? But wait: At later stages, immune cells without *TREM2* cause less neurodegeneration, so maybe *TREM2* is bad? "Figuring out how to use the immune system to treat neurological diseases like Alzheimer's is not simple," Colonna said.

MATT MILLER

NEURODEGENERATION

Preserving function

Beau Ances, MD, PhD, talks with trial participant Adam Kloppenburg, who is on his way to get a PET scan. Ances is studying the intersection of Down syndrome and Alzheimer's disease, as part of the Alzheimer's Biomarkers Consortium-Down Syndrome (ABC-DS).

Neurodegeneration tends to start slowly, almost imperceptibly. For a variety of reasons, neurons gradually stop functioning as well as they used to, and some start dying. In Alzheimer's disease, the most common neurodegenerative disease, signs of decay are detectable long before memory problems arise. This slow start provides an opportunity to intervene while the problem is still manageable. WashU Medicine researchers are working on detecting and healing ailing neurons, opening up paths to new treatments.

Gut feeling

Gut bacteria may play a surprisingly important role in Alzheimer's disease, according to two groundbreaking papers this year. Studying mice, neurologist David M. Holtzman, MD, and microbiome expert Jeffrey I. Gordon, MD, discovered that gut bacteria influence the activity of immune cells that can damage brain tissue. Meanwhile, neurologist Beau M. Ances, MD, PhD, and microbiome expert Gautam Dantas, PhD, reported that the microbiomes of healthy people and people with presymptomatic Alzheimer's differ in significant ways. Taken together, the studies suggest that the gut microbiome might harbor important clues to how Alzheimer's develops, which could lead to new therapeutic approaches.

Frayed nerves

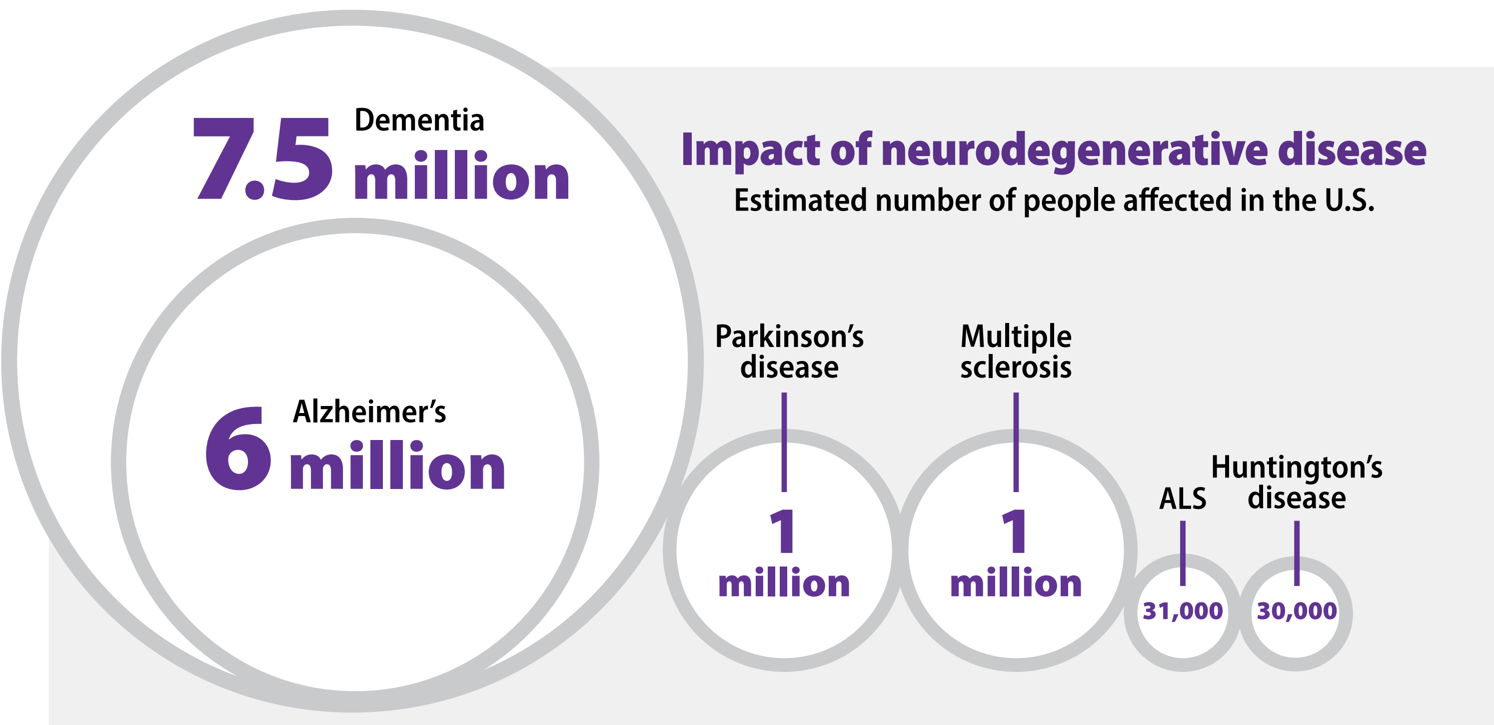
Nerve damage, whether caused by illness or injury, involves deterioration of the axons, the part of neurons that transmits signals and serves as the wiring of the nervous system. Geneticist Jeffrey D. Milbrandt, MD, PhD, and developmental biologist Aaron DiAntonio, MD, PhD, identified a key molecular driver of axonal injury and figured out how to inhibit it. They founded the startup Disarm Therapeutics — since acquired by Eli Lilly and Co.— to develop drugs to help the millions of people living with debilitating nerve damage by blocking or slowing axonal degeneration.

Therapy for few; hope for many

In April, the FDA approved the drug tofersen — based on research by WashU Medicine neurologist Timothy M. Miller, MD, PhD — for an inherited form of amyotrophic lateral sclerosis (ALS), a paralyzing neurological disease. The drug targets a gene called *SOD1*, and clinical trials show that it slows disease progression in the 2% of ALS patients with *SOD1* mutations. The drug's success provides new hope for disease-changing therapies for other forms of ALS, once thought to be untreatable.

"My whole career has been built on the assumption that ALS is a treatable disorder."

— Timothy M. Miller, MD, PhD



MATT MILLER

Chihiro Sato, PhD (left), assistant professor of neurology, and Kanta Horie, PhD, research associate professor, study tau protein using the mass spectrometer at the Tracy Family Stable Isotope Labeling Quantitation Center. The team found a novel tau biomarker for primary tauopathies.

Early diagnosis of Alzheimer's

When the FDA approved the first disease-modifying Alzheimer's drug, lecanemab, earlier this year, it changed the game. Only people with mild or very mild symptoms are eligible for the drug, making early diagnosis critical. Neurologist Randall J. Bateman, MD, whose previous research led to the development of an Alzheimer's blood test, recently discovered a biomarker with the potential to pinpoint the stage of disease and track progression. A clinical test based on this biomarker may help people gain access to next-generation therapeutics.

Ensuring research benefits all

Led by director John C. Morris, MD, the Knight Alzheimer Disease Research Center has become a national leader in health equity with one of the most diverse volunteer cohorts in the country. WashU Medicine researchers have uncovered troubling racial disparities: some Alzheimer's blood tests yield results that differ by race; and African Americans tend to encounter delays in obtaining specialist memory care, putting them at risk of missing the drug treatment eligibility window.

Why symptoms appear with age

Huntington's disease is caused by a genetic error present at birth, though symptoms such as memory lapses and clumsiness don't arise until middle age. Developmental biologist Andrew S. Yoo, PhD, pioneered a technique to transform skin cells from Huntington's patients into neurons that carry each patient's genetic defect. This allowed him to study Huntingon's noninvasively. To better understand aging in Huntington's patients, he obtained skin cells from patients of different ages. He discovered that as patients age, a vital cellular process called autophagy gradually becomes impaired in such neurons, causing them to deteriorate and die, and that boosting autophagy improves neurons' survival.

New tricks for old drugs

People diagnosed with neurodegenerative diseases typically have few treatment options. To expand the formulary, some scientists are looking at repurposing drugs already approved by the FDA for other ailments. Using human genomic data, geneticist Carlos Cruchaga, PhD, identified 15 existing drugs with therapeutic potential for Alzheimer's, as well as seven for Parkinson's, six for stroke and one for amyotrophic lateral sclerosis (ALS). In related work, neurologist David M. Holtzman, MD, discovered that some white blood cells exacerbate brain degeneration. "It's likely that some drugs that act on white blood cells called T cells could be moved into clinical trials for Alzheimer's disease relatively quickly," Holtzman said.

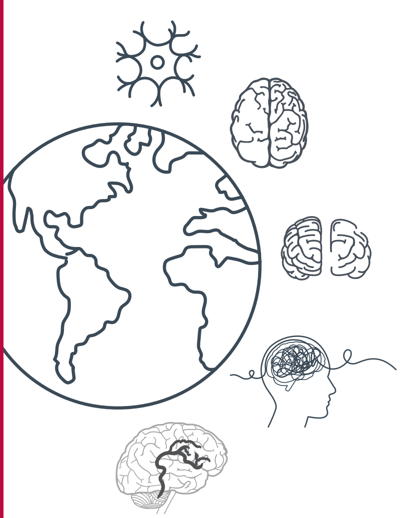
MATT MILLER

A patient undergoes an electroencephalogram (EEG) to measure electrical activity in the brain.

Nurturing neuroscience

Donors play key role in driving discovery

BY MARY LEE

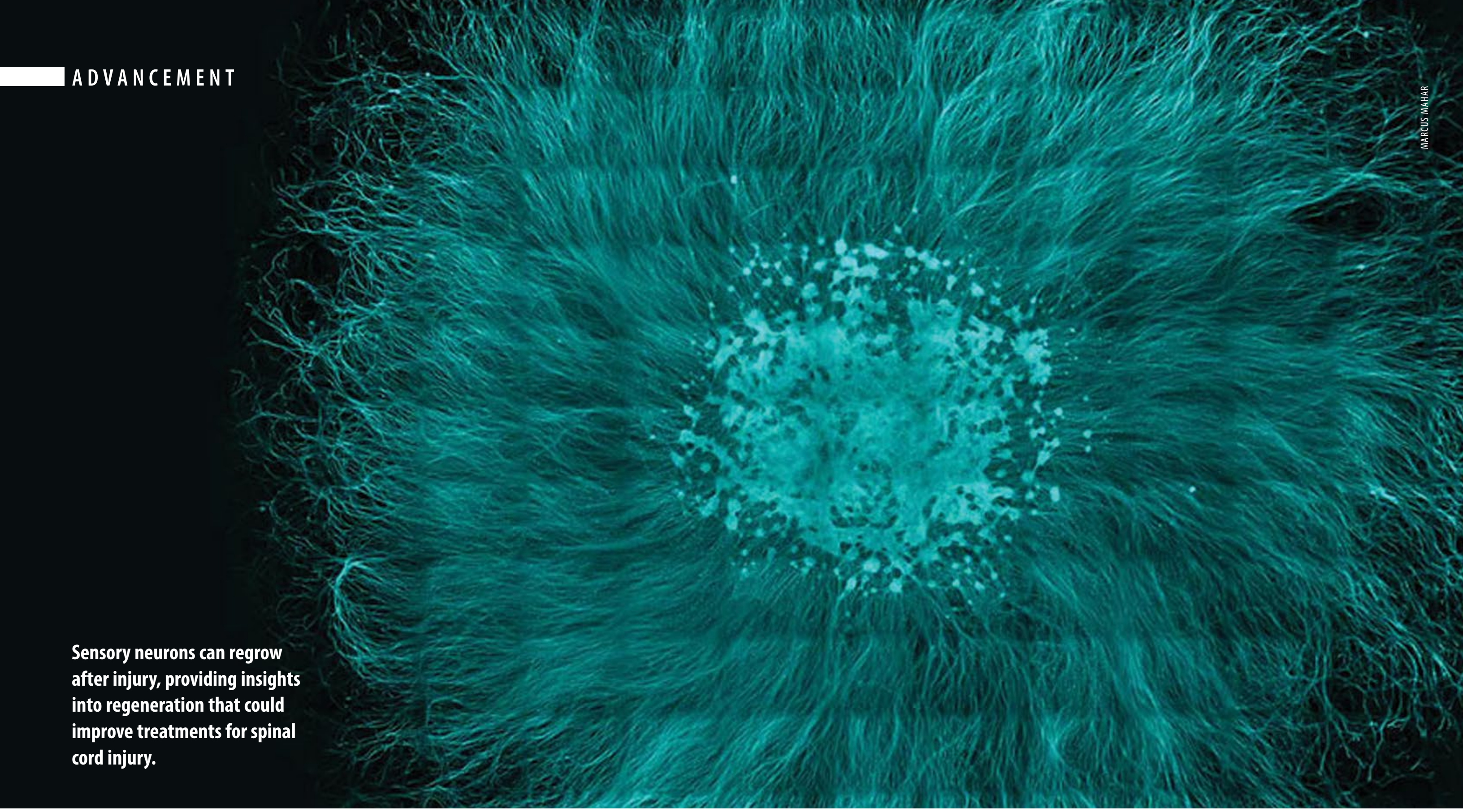


Washington University's renowned neuroscience research enterprise is built on a bedrock of scientific expertise and interdisciplinary collaboration. Not to be overlooked, however, is the critical role private philanthropy plays in cementing these assets.

For decades, visionary benefactors have channeled millions of dollars to the university for brain and nervous system research. This money fills gaps in federal funding, which takes years to secure and is often limited in scope. Gifts from donors provide a flexible source of funding to explore new ideas and support equipment purchases, recruitment and other critical activities.

These investments have a deep impact on faculty members' ability to unravel the brain's mysteries and drive discoveries that benefit patients, from new drugs to prevent Alzheimer's disease and treat psychological disorders, to technology that minimizes damage from aneurysm and stroke.

Learn more about donors who have helped advance neuroscience research.



MARCUS MAHAR

Sensory neurons can regrow after injury, providing insights into regeneration that could improve treatments for spinal cord injury.

Empowering a community

James S. McDonnell Foundation

$5.5 million in 1980
to establish the McDonnell Center for the Study of Higher Brain Function (renamed the McDonnell Center for Systems Neuroscience)

$5 million in 1983
to establish the McDonnell Center for Cellular and Molecular Neurobiology

$11 million total
in subsequent gifts for both centers

McDonnell Aircraft Corp. founder James S. McDonnell had a lifelong fascination with the workings of the brain. His family foundation endowed two centers in the 1980s to explore major issues in brain science — one focused on systems neuroscience and one on cellular and molecular neurobiology. Together, these centers have bolstered WashU's neuroscience research community.

The centers support faculty members in more than a dozen departments across the Medical and Danforth campuses by funding seed grants and proposals for equipment, pilot feasibility data and other resources. The return on investment is significant. In the McDonnell Center for Systems Neuroscience alone, 64 grants and resource proposals backed by $6.12 million from 2016 to 2021 generated four patents and 29 external grants totaling more than $82.64 million.

"Neuroscience is an extremely interdisciplinary field, and the centers reinforce that by providing resources for a broadly defined swath of interrelated study," said Tamara G. Hershey, PhD, director of the systems neuroscience center and the James S. McDonnell Professor of Cognitive Neuroscience. "This lifts all boats and enhances our ability to achieve breakthroughs."

The centers also help recruit and retain talented investigators. From 2016 to 2021, they contributed startup financing for 21 researchers in nine departments. And a revamped fellowship program sponsored by both centers offers incentives that supplement postdoc recruitment packages.

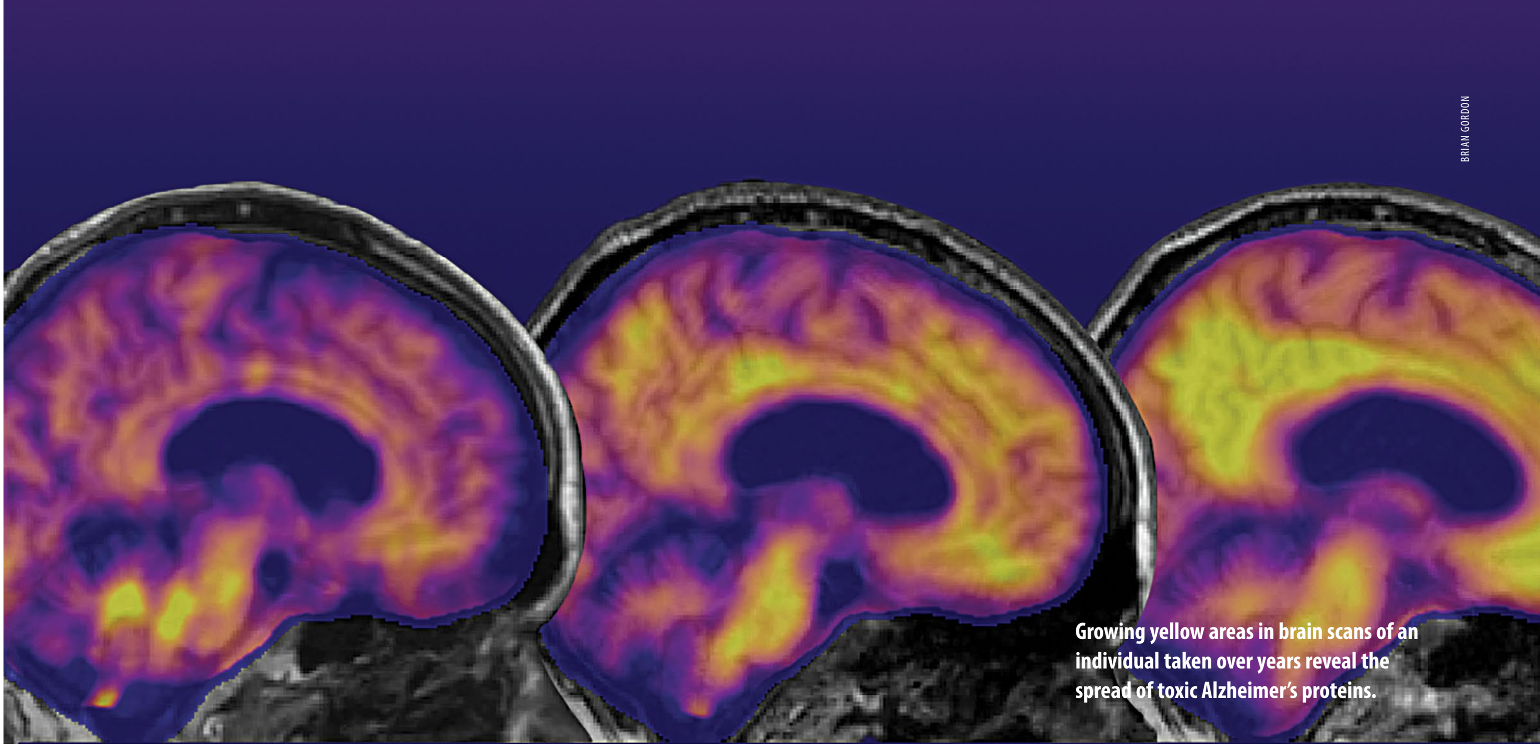
In recent years, studies sponsored by the centers have shown that Zika virus kills brain cancer stem cells, sleep deprivation accelerates Alzheimer's disease, and poverty negatively impacts structural wiring in children's brains.

"The centers help make our neuroscience community one of the best in the world," said Linda J. Richards, PhD, director of the cellular and molecular neurobiology center, head of the Department of Neuroscience and the Edison Professor of Neuroscience. "For 40 years, they have been the glue that binds us together and moves us from good to great."

A new gift from James S. McDonnell III and his wife, Elizabeth, through the JSM Charitable Trust will pave the way for additional advances. Their $25 million pledge to support neuroscience research at the medical school enhances the family's legacy as a catalyst for biomedical discovery.

"This lifts all boats and enhances our ability to achieve breakthroughs."

— Tamara G. Hershey, PhD



BRIAN GORDON

Growing yellow areas in brain scans of an individual taken over years reveal the spread of toxic Alzheimer's proteins.

Preventing Alzheimer's

Former Emerson Electric Co. CEO Charles "Chuck" Knight and his wife, Joanne, made their first gift for Alzheimer's disease research at the School of Medicine in 1997. Over the years, substantial support from the Knight family has helped propel WashU Medicine to the forefront of efforts to understand, detect, treat and ultimately prevent Alzheimer's.

Among the most lauded in the world, Alzheimer's investigators at WashU Medicine have identified genetic mutations and molecular biomarkers associated with the disease, developed novel imaging techniques to reveal brain damage, and created a highly accurate blood test for early diagnosis.

The university's Charles F. and Joanne Knight Alzheimer Disease Research Center (ADRC) serves as the nexus for this work. The center has been funded by the National Institute on Aging since 1985. Knight family gifts made before and after Chuck's death in 2017 have enhanced the center's capacity to coordinate a robust slate of research, training and outreach.

"This philanthropy allows us to dream big and say yes to ideas that fall outside the realm of traditional funding mechanisms," said John C. Morris, MD, the Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology, who directed the ADRC from 1998 until this year and now serves as associate director. "These ideas are often the ones that point us in important new directions."

A recent pledge from the Knights will provide up to $11.5 million for a first-of-its-kind study. The Primary Prevention Clinical Trial conducted by the Knight Family Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) will evaluate whether an experimental drug can stop brain changes before they lead to cognitive decline in young people with an inherited form of the disease.

"It's unusual for private individuals to play a key role in a major clinical research effort," said Randall J. Bateman, MD, director of the Knight Family DIAN-TU and the Charles F. and Joanne Knight Distinguished Professor of Neurology. "But it's fitting they are part of this potentially world-changing trial since they have been seeding the success of Alzheimer's research at the university for years."

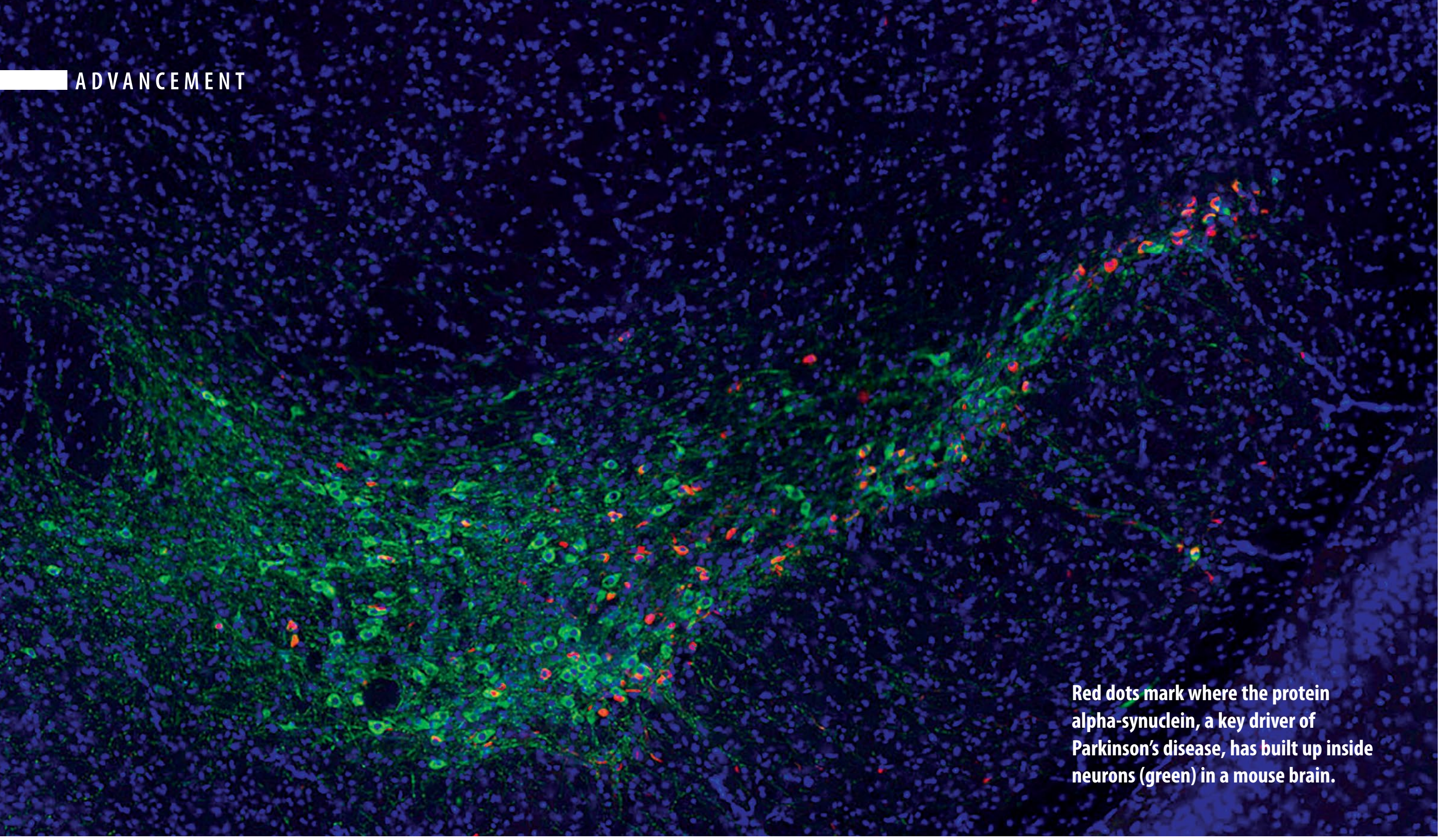
"This philanthropy allows us to dream big and say yes to ideas that fall outside the realm of traditional funding mechanisms."

— John C. Morris, MD

Charles & Joanne Knight & the Knight family

About $20 million
to establish a distinguished professorship in neurology and support the Charles F. and Joanne Knight Alzheimer Disease Research Center

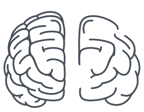
$11.5 million
pledge to help launch an Alzheimer's prevention trial



Z.M. WARGEL AND B.M. FREEBERG

Red dots mark where the protein alpha-synuclein, a key driver of Parkinson's disease, has built up inside neurons (green) in a mouse brain.

Targeting neurodegeneration



Rodger & Paula Riney

$11 million from 2014 to 2019
for Alzheimer's disease research

$7.5 million in 2019 and 2020
for Parkinson's disease research

After watching family members struggle with the effects of Alzheimer's and Parkinson's disease, Scottrade founder Rodger Riney and his wife, Paula, have directed considerable philanthropic support to neurologists exploring these conditions. Their gifts are powering science that crosses disease boundaries.

Parkinson's research funding totaling $7 million for Joel S. Perlmutter, MD, the Elliot H. Stein Family Professor of Neurology, has produced several important findings. Using PET imaging, Perlmutter's team identified new treatment targets associated with brain pathway dysfunction in Parkinson's patients. It also developed PET tracers to evaluate the role of inflammation in brain damage associated with the disease and to assess the efficacy of experimental anti-inflammatory drugs. This work could shed light on other conditions linked to brain inflammation, such as multiple sclerosis and Alzheimer's.

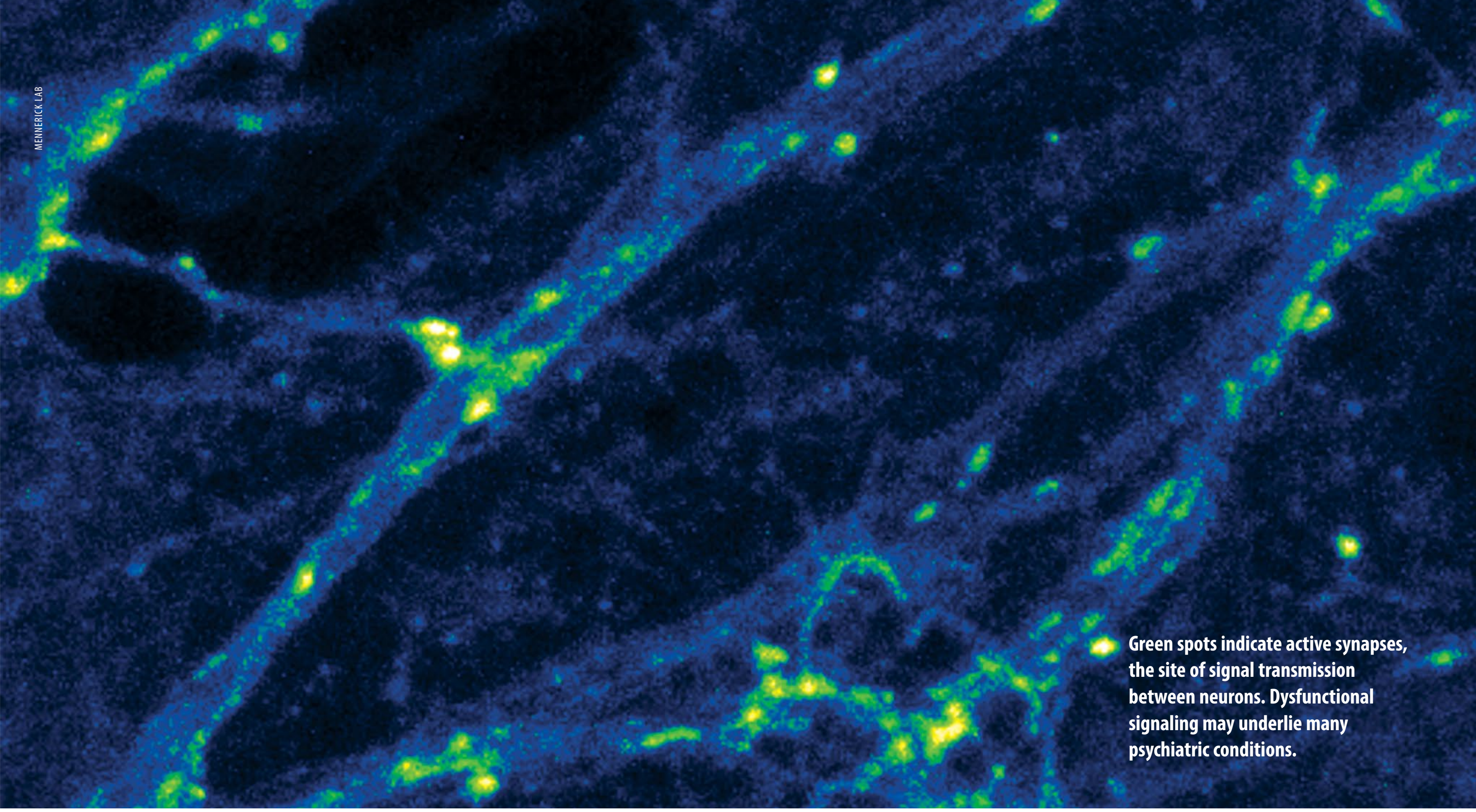
To facilitate this promising line of study, the lab has purchased two high-resolution PET/CT scanners with money from the Rineys, one of which was installed in 2021. "The machine permits measurements in much smaller brain areas that are critical for Parkinson's research," Perlmutter said. "It's truly the best scanner in the world for this type of investigation, and it will accelerate our progress." The second scanner will be installed in the beginning of 2024.

In the Alzheimer's arena, a portion of the Rineys' funding established a clinical trials unit in the Charles F. and Joanne Knight Alzheimer Disease Research Center. The unit, which launched in 2020, has enrolled 50 participants from throughout the St. Louis region in seven trials, including a multicenter trial that led to Food and Drug Administration approval of lecanemab for the treatment of mild Alzheimer's dementia. The Riney funds also have benefited the Knight ADRC in establishing the utility of a new blood test to aid in the diagnosis of Alzheimer's disease.

More than just investors, the Rineys are deeply engaged with researchers, who meet with the couple yearly to share scientific updates. "The relationship builds teamwork and trust," Perlmutter said. "We have the same goals, and we are bringing our resources together to improve lives. It's a powerful formula for success."

"The relationship builds teamwork and trust."

— Joel S. Perlmutter, MD



Green spots indicate active synapses, the site of signal transmission between neurons. Dysfunctional signaling may underlie many psychiatric conditions.

Improving mental health

Since its launch 10 years ago, the Taylor Family Institute for Innovative Psychiatric Research has been laser-focused on advancing new treatments for mental illnesses. Bolstered by gifts from Enterprise Holdings Executive Chairman Andrew Taylor, his wife, Barbara, and the Taylor family's foundation, a universitywide group of researchers has made rapid progress by focusing on neuroactive steroids. The Food and Drug Administration approved two drugs to treat postpartum depression — brexanalone in 2019 and zuranalone in August 2023 — and several other neurosteroids are being evaluated in clinical trials.

"It's almost unheard of to develop new therapies so quickly," said Taylor Family Institute Director Charles F. Zorumski, MD, the Samuel B. Guze Professor of Psychiatry. "And we couldn't have done it without the Taylors. The money they provided has been a godsend."

Payout from the institute's endowment is allocated to more than 10 faculty members each year. They may use the discretionary funds for preliminary data, neuroimaging studies, equipment — whatever drives their work forward. "We want them to take risks, to be able to turn on a dime and pursue a promising concept until they can get external financing," Zorumski said.

The strategy has yielded impressive results: Affiliated scientists have secured 14 patents and $165.5 million in external grants, including $12.2 million from the National Institute of Mental Health to establish a prestigious Silvio O. Conte Center, which focuses on neurosteroids. This has freed the Taylor Family Institute to expand its basic research portfolio and support investigators working to repurpose other types of therapeutic agents, such as ketamine, nitrous oxide and the psychedelic drug psilocybin.

In a field where treatments have remained largely unchanged for decades, the Taylor Family Institute provides a model for expediting progress. "Waiting two or three years for federal funding can kill great ideas," Zorumski said. "Because we have the latitude to make investments in real time, we have shortened the timeline for discovery."

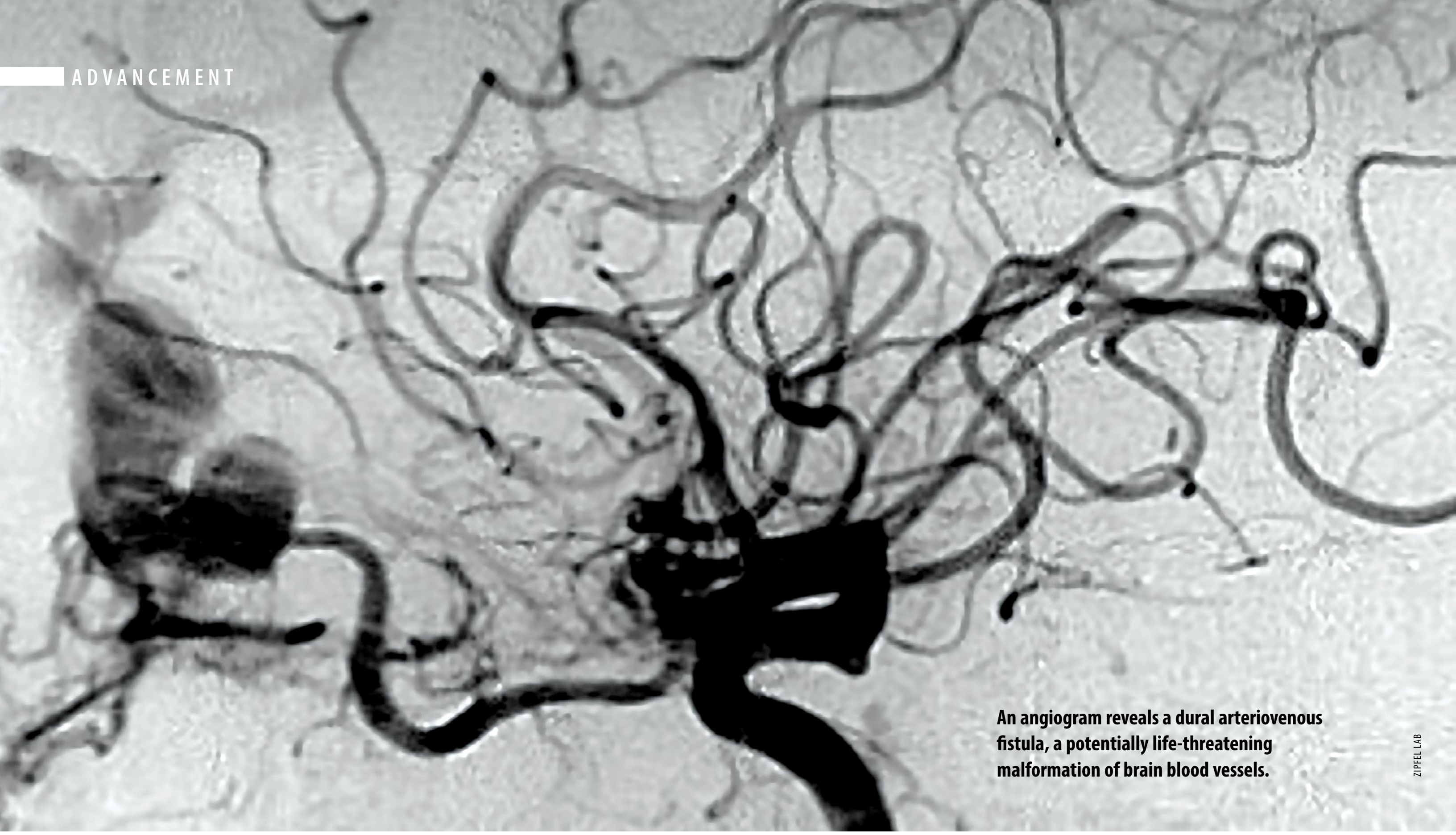
"It's almost unheard of to develop new therapies so quickly. And we couldn't have done it without the Taylors."

— Charles F. Zorumski, MD

Andrew & Barbara Taylor & the Crawford Taylor Foundation

$20 million in 2013
to endow the Taylor Family Institute for Innovative Psychiatric Research

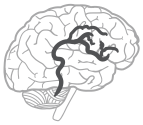
$10 million
in subsequent gifts for research and a distinguished professorship



An angiogram reveals a dural arteriovenous fistula, a potentially life-threatening malformation of brain blood vessels.

ZIPFEL LAB

Fueling neurosurgery innovation



Jeffrey Fort

$5 million in 2019
to establish a professorship in neurosurgery and fund cerebrovascular research

Award-winning videographer and entrepreneur Jeffrey Fort made his gift for cerebrovascular research after WashU Medicine researchers treated him for a dural arteriovenous fistula (dAVF), a blood vessel malformation that threatened his life. Now, neurosurgery faculty members are using his support to drive innovations that will benefit future patients with dAVFs and related conditions, including brain aneurysms and stroke.

Gregory J. Zipfel, MD, head of neurosurgery and the Ralph G. Dacey Distinguished Professor of Neurosurgery, said the money has had a broad impact in a short period of time. It helped his lab set up a multicenter consortium for dAVFs that offers a data registry with a cohort of more than 1,000 patients. The dataset is a boon for investigators across the world seeking insights on a rare condition. It has facilitated more than 10 published studies since 2021.

> *"When individuals and families enter into a collaboration with us, it energizes our efforts and drives us to keep pushing forward."*
>
> *— Gregory J. Zipfel, MD*

The Fort gift also provided funding to launch a basic science research program exploring the immune response to brain injury after aneurysm; develop devices such as specialized catheters that are easier to maneuver in the brain; and recruit a scientist to advance technology that enables stroke patients to recover motor function.

"When it comes to new technology, philanthropy can really help us move the dial," Zipfel said. "It can smooth the way through the development pipeline, from idea to prototype to patent. And from there, you can attract investors who can push you over the finish line."

Beyond the tangible impact of philanthropy, partnerships with donors inspire WashU Medicine researchers, Zipfel said. "When individuals and families enter into a collaboration with us, it energizes our efforts and drives us to keep pushing forward."

Find your friends.

Classnotes are organized first by year of degree/training completion and then in alphabetical order.

How about you?

To share your news, visit alumni.med.wustl.edu/class-note. Submissions will be printed in a subsequent issue of Outlook magazine as space allows. Photos are welcome.

1950s

J. Roger Nelson, LA '49, MD '53, published the book "A Harrowing Journey," which follows freed Israelite slaves as they struggle to follow God and Moses on the Exodus march from Egypt to Canaan.

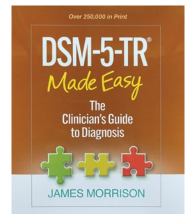
Irving Kushner, MD '54, published two papers this year: "The Constellation of Vitamin D, the Acute-phase Response and Inflammation" in the Cleveland Clinic Journal of Medicine with Maria Antonelli and Murray Epstein; and "C-reactive Protein — My Perspective on its First Half-century, 1930-1982" in Frontiers in Immunology.

Lewis Thomas Jr., MD '57, is proud to share that one of his grandsons, Lewis J. Thomas IV, is an assistant professor in urologic oncology at WashU Medicine. As such, he keeps Thomas Jr. informed about the school's remarkable progress since his retirement 27 years ago.

Hal Kindred, DDS '58, had his right leg amputated two years ago. While he doesn't run marathons anymore, he's doing well and looking forward to another good year.

1960s

Jim Hales, DDS '65, is in his 57th year of practicing dentistry and working full time in Grants Pass, Ore. He still enjoys the work and receiving compliments and feels blessed to be working at age 87. He thinks he is the last in his class "still fixing teeth." He is proud to say he graduated from Washington University in St. Louis.



James Morrison, MD '65, had his book "DSM-5-TR Made Easy: The Clinician's Guide to Diagnosis" published by Guilford Publications. It is a 670-page guide, with case examples, to the new edition of "The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR)," which is the American Psychiatric Association's standard reference for mental health diagnosis. This year, he will have the third edition of "Diagnosis Made Easier: Principles and Techniques for Mental Health Clinicians" published. In it, he has tried to convey everything he's learned from medical school and his career about the science and art of making a mental health diagnosis.

David Bray, MD '66, has retired — well, almost. He helps out in his old office once a week, which keeps him in the ball game. He and his wife, Leeza, have three sons who are college graduates and employed. He was saddened to hear about Anne Pelizzoni's death. The longer he practices head and neck surgery, the more grateful he is for the education he received at WashU.

Ira Kodner, LA '63, MD '67, professor emeritus of surgery and former chief of the Section of Colon and Rectal Surgery in the Department of Surgery, was honored with the establishment of an endowed chair in his name. The Ira Kodner, MD, Chair in Palliative Medicine and Supportive Care was created through a gift to The Foundation for Barnes-Jewish Hospital from philanthropists John and Anne McDonnell. Debra Parker Oliver, PhD, a noted expert in end-of-life caregiving, is the inaugural holder.

Michael Pacin, LA '65, MD '69, is self-employed as an expert witness. He and his bride, Amy Ronner, just celebrated their 20-year anniversary. To celebrate, they are taking a Silversea cruise out of Cape Town, South Africa, and traveling to Mozambique, Comoros, Madagascar and ending in the Seychelles. Afterward, they will spend a month in Miami before going to Aspen, Colo.

1970s

Bruce Brodie, MD '70, and his wife, Dora, have retired in Greensboro, N.C. They look forward to maybe one more great reunion.

Tien Hsin Cheng, MD '76, retired March 31, 2020, after the onset of the COVID-19 pandemic. He no longer has his landline but can be reached on his cell phone at 951-452-6604.

Philip Zazove, MD '78, retired as chair of family medicine at Michigan Medicine July 1, 2022, and joined his wife, and fellow alumna, **Barbara Reed, MD '78,** in retirement. He has been writing novels, running the Louise Tumarkin Zazove Foundation, traveling and seeing grandkids. They'd love to hear from anyone, anytime, and if alumni are in the Ann Arbor, Mich., area, they encourage them to reach out at pzaz@umich.edu or barbr@umich.edu.

1980s

Walter Peters, MD '82, retired from the practice of colon and rectal surgery and, in January, was named chief medical officer for Baylor Scott & White Health, a system of 51 hospitals headquartered in Dallas.

1990s

Linda Peterson, MD '90, was elected president of the Society for Heart and Vascular Metabolism (SHVM) and was installed at the SHVM meeting in Seoul, South Korea, in 2022.

Sara Jo Grethlein, EN '84, HS '91, has been appointed chief medical officer for Providence Swedish's clinical institutes across the Puget Sound region. She lives in West Seattle and loves the Pacific Northwest.

Paul Ruggieri, HS '93, is a general surgeon who trained in general surgery at Barnes-Jewish Hospital and Washington University. He recently published a memoir about his experiences, titled "Confessions of a Surgeon: A Deeper Cut."

John Carico, MD '94, HS '98, is celebrating his sons' accomplishments. His oldest son, Alex, graduated from the Medical College of Georgia in May and matched to Mallinckrodt Institute of Radiology at Barnes-Jewish Hospital for his radiology residency. His other son, Will, is finishing his second year of medical school at the Medical College of Georgia (along with his fiancee, Hannah Dixon). On a sadder note, Carico's wife, **Julia (Julie) Bussom Carico, MSOT '92,** died in November 2022 after a prolonged battle with acute myelogenous leukemia.

Sandeep Jauhar, MD '98, published his latest book, "My Father's Brain: Understanding Life in the Shadow of Alzheimer's," in April. It is a memoir of his relationship with his father as his father succumbed to dementia. The book describes his father's descent into Alzheimer's alongside his own journey toward understanding the disease. Jauhar's previous books include "Intern: A Doctor's Initiation," "Doctored: The Disillusionment of an American Physician" and "Heart: A History." His books are available on Amazon.

2000s

Mark Corriere, MD '00, had his second book, "Winning With Diabetes: Inspiring Stories From Athletes to Help You Thrive," published by Johns Hopkins Press. The book chronicles 16 elite athletes with diabetes and their ability to achieve success at the highest levels, while also managing the disease. Corriere is an adjunct assistant professor of medicine at the Johns Hopkins University School of Medicine and a clinical endocrinologist at Maryland Endocrine.

Hannah Wunsch, MD '02, wrote her first book, "The Autumn Ghost: How the Battle Against a Polio Epidemic Revolutionized Modern Medical Care." She is a critical care physician and researcher at Sunnybrook Health Sciences Centre and professor of anesthesiology and critical care medicine at the University of Toronto, as well as a Canada Research Chair. Wunsch is looking forward to starting a new role as vice chair of research in the Department of Anesthesiology at Weill Cornell Medicine in New York City in September. She lives in Toronto, Ontario, and Woods Hole, Mass.

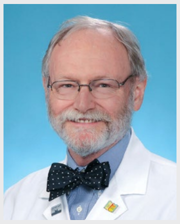
Timothy Loftus, MD '06 (right), and **Adam Froemming, MD '06** (second from left), and **Jennifer (Boland) Froemming, MD '06** (left), caught up after 17 years while visiting Haleiwa, a historic town on Oahu, Hawaii. The Froemmings were vacationing with their three sons, and Loftus was celebrating his mom's 75th birthday.

2010s

Corey (Fine) Woldenberg, DPT '10, is excited to share that she joined the WashU Program in Physical Therapy faculty March 1.

Tassy Hayden, LA '07, MD '11, joined Thermo Fisher Scientific's Clinical Research Group as an investigator for clinical trials in pharmaceutical and medical device development in November 2022. In addition to keeping trial participants safe and healthy, she hopes to bring her skills from caring for LGBT+ populations and people living with HIV into her new position and work toward greater diversity in clinical trial participant populations.

Kelley (Semens) Mantei, MSOT '12, and her husband, Jason, welcomed their second son, Dexter, March 23. He joins big brother, Archer. Mantei shares that everyone is happy and healthy and adjusting to being a family of four.



Richard D. Brasington Jr., MD, professor emeritus of medicine, 71

Richard D. Brasington Jr., MD, ’56, a highly regarded professor emeritus of medicine and former director of the rheumatology fellowship training program at Washington University School of Medicine, drowned Sunday, April 30, 2023, while fishing in the North Fork River in Ozark, Mo. He was 71.

Brasington joined the faculty in 1996 and trained dozens of medical residents and fellows as coursemaster for the second-year rheumatology course. He also mentored the many third-year students who trained in his clinic. He directed the university’s rheumatology clinic and the rheumatology division’s fellowship training program for many years.

With his primary focus on education and patient care, Brasington also pioneered a trainee evaluation tool that was used at many rheumatology centers around the country. Further, he played a key role in developing a curriculum guide for the American College of Rheumatology that was used in fellowship training.

In addition to his work in rheumatology, Brasington and his family cared deeply about mental health and wellness. In 2010, he played a key role in creating the James and Philip Brasington Memorial Endowed Fund in the medical school’s Department of Psychiatry.

“Dr. Brasington was an outstanding clinician, renowned for his ability to diagnose and treat patients with complex rheumatic and autoimmune disorders,” said Victoria J. Fraser, MD, the Adolphus Busch Professor and head of the Department of Medicine. “He was warm, caring and compassionate and deeply loved by his patients. He also was an exceptional teacher with tremendous knowledge and a passion for sharing what he knew with his trainees.”

He is survived by his wife, Kathleen Ferrell; children Ned Brasington, William Bashert and Liz Dueweke; stepdaughter, Melissa Haralson; siblings Evan Brasington and Becky Clark; six grandchildren; and three great grandchildren.

David C. Farrell, former trustee, 89

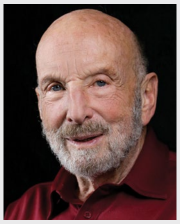
David C. Farrell, a former longtime member of the Washington University Board of Trustees, died Monday, June 5, 2023, at his home in Ladue, Mo. He was 89.

Farrell, former chairman and CEO of the May Department Stores Co., served on the university’s Board of Trustees from 1979 to 2005 and served as an emeritus trustee from 2005 to 2022. Among his service to the university, he was a chairman and life patron of the Danforth Circle Eliot Society and an inaugural member of the William H. Danforth Leadership Society. He also had served on the Alvin J. Siteman Cancer Center community advisory board and on the School of Medicine’s medical finance committee and National Council.

David and his late wife, Betty, provided transformative philanthropic support for Washington University. The Farrells’ support includes the David C. and Betty Farrell Distinguished Professorship in Medicine, the state-of-the-art Farrell Learning and Teaching Center on the Medical Campus and the Farrell Family Medical Research Fund to support research into Alzheimer’s disease.

Farrell is survived by two sons, Mark Farrell, of Dallas, and David Farrell, of St. Louis; a daughter, Lisa Heller, of St. Louis; a sister, Anne Boho, of Illinois; and four grandsons.

Thomas Hornbein, mountaineer and anesthesiologist, 92



Tom Hornbein, MD ’56, one of the team of mountaineers who made the first ascent up Mount Everest’s West Ridge in 1963, died Saturday, May 6, 2023, at his home in Estes Park, Colo., after fighting leukemia. He was 92.

Hornbein, Willi Unsoeld and Dick Emerson made the historic Mount Everest climb, alongside a small team of Nepali porters and guides that helped until the final push. They began their ascent just weeks after Jim Whittaker made headlines as the first American to climb Everest. But Hornbein and his cohort chose a different route, one that no one had conquered in decades: Everest’s treacherous West Ridge.

Born in St. Louis, Hornbein developed his love for climbing while at summer camp in Colorado. He earned a medical degree from Washington University in 1956 and completed an anesthesiology residency at Barnes Hospital. Hornbein joined the faculty at the University of Washington School of Medicine in Seattle and served as chair of the Department of Anesthesiology from 1978 to 1993. He worked as an anesthesiologist and a professor, and he continued climbing regularly into his 80s.

Over the years, Hornbein pursued research on the effects of altitude on the body. This work led him to develop the Maytag mask — a single-valved oxygen mask that was effective for high-altitude climbing — with the help of Fred Maytag, owner of the Maytag washing machine company.

Hornbein, a U.S. Navy veteran, later wrote the book “Everest: The West Ridge” about the team’s experiences. In 2016, he came back to campus and shared his adventures with WashU Medicine students, serving as the MD Commencement speaker.

He is survived by his wife, Kathryn Mikesell Hornbein; his six children, Lia, Lynn (Tom), Cari, Andrea, Bob, Melissa (Aaron); and a granddaughter, Hazel.

Robert M. Senior, MD, professor emeritus of medicine, 86

Robert M. Senior, MD, a highly regarded physician-scientist, died peacefully Thursday, June 8, 2023, at his home in St. Louis. He was 86.

In 1969, the noted pulmonologist joined the School of Medicine faculty, where he served many years as a professor of medicine in the Division of Pulmonary & Critical Care Medicine and a professor of cell biology and physiology.

In recognition of Senior's outstanding contributions to the field of pulmonary medicine, in 1988 he was named the Dorothy R. and Hubert C. Moog Professor of Pulmonary Diseases in Medicine, a position he held until his retirement in 2015.

Originally from White Plains, N.Y., Senior earned an undergraduate degree from Oberlin College in 1957 and a medical degree from George Washington University School of Medicine in 1961. He conducted his internship and first year of medical residency at then-Barnes Hospital and was a senior resident at then-Jewish Hospital of St. Louis. He pursued postdoctoral research as a fellow in cardiorespiratory physiology at the Columbia University College of Physicians and Surgeons.

After completing medical training, Senior became chief of the pulmonary function laboratory at Walter Reed Army Medical Center. From 1966-69, he served in the U.S. Army Medical Corps.

Senior returned to St. Louis to serve as the director of Pulmonary and Critical Care Medicine at Jewish Hospital and also interim physician-in-chief and director of the Department of Medicine from 1989-90. He also served as a consultant at the John Cochran Veterans Administration Medical Center, and was an attending physician at Barnes, Jewish and Barnes-Jewish Hospital for more than 40 years.

He is survived by his wife, Martha Senior; his daughters, Jocelyn and Rebecca Senior and Devra Bram; his son, David Senior; and seven grandchildren.

1940s

Irving A. Koffler, MD '47; March '23

Jeanne (Grigg) Mill, NU '45; April '23

1950s

James W. Barbero, PT '56; February '23

Sue (Langford) Every, PT '58; March '23

Michael Gass, MD '58, HS '68; April '23

Richard C. Hammond Jr., MD '56; March '23

Douglas R. Lilly, MD '56; March '23

Emil Mantini, MD '58; August '23

Eugene F. Martin, DE '58, GD '62; February '23

Wilbur E. Mattison Jr., HS; February '23

Helen (Johns) Ondes, NU '51; February '23

Dorothy Llewellyn Rodgers, MD '50; April '23

Clyde F. Shelton, HS; March '23

Norval R. Smith, DE '53; February '23

Jean (Graham) Whipple, NU '51; April '23

1960s

Mohammad T. Amjad, HS; March '23

Philip Baugh, DE '68; April '23

Robert W. Colman, HS '67; March '23

Robert J. Dreher, HS '67; March '23

Harry L. Ellis, HS '63; March '23

Karl H. Muench, MD '60; March '23

Jerry G. Prisbrey, DE '61; March '23

Charlie W. Shaeffer Jr., MD '64; February '23

Albert F. Wermuth Jr., MD '67, March '23

Gabriel S. Zatlin, MD '60; March '23

1970s

Stephen E. Campbell, MD '70; January '23

Philip H. Fleckman, MD '73; March '23

Mary Lee Holland, MD '71; November '22

Jeffrey W. Mix, DE '72; February '23

Alan J. Tiefenbrunn, LA '70, MD '74; March '23

Stephen R. Waltman, HS '70, EMHS '00; April '23

1980s

Charles R. Lyon, DE '85; March '23

1990s

Dwayne Anderson, HS '98; February '23

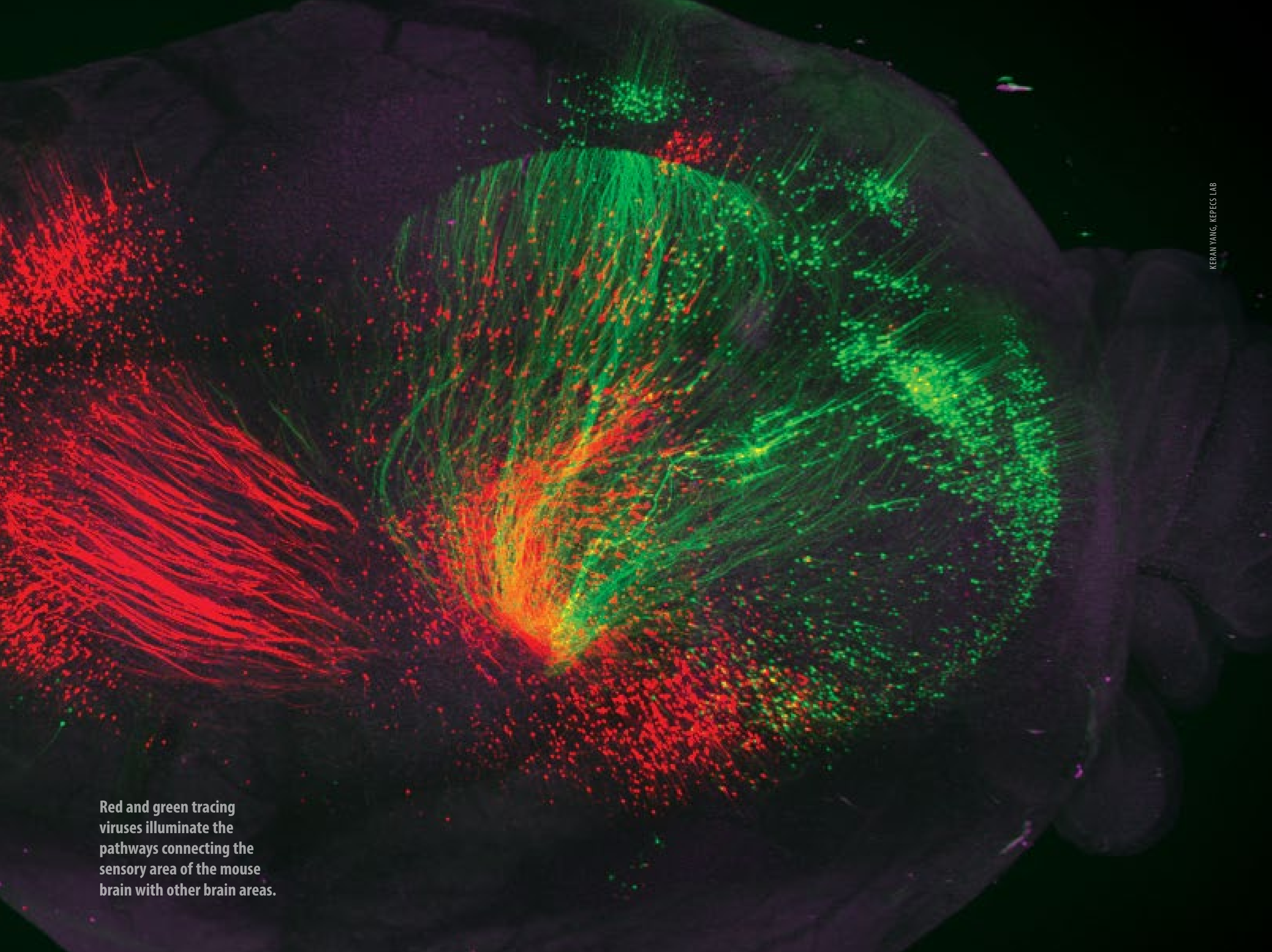
2000s

Emily L. (Engelland) Bannister, LA '96, MD '01; March '23

Jennifer L. Stark, HS; February '23

In Memoriam

To view past In Memoriam listings or to submit an obituary for publication, visit **alumni.med.wustl.edu.**



KERAN YANG, KEPECS LAB

Red and green tracing viruses illuminate the pathways connecting the sensory area of the mouse brain with other brain areas.

"Trying to figure out what's going on in the brain is like space exploration, totally unknown. When I started, we knew nothing, and now we know just a tiny bit.

"I'm a rock collector. Do you know what a geode is? When you break open a geode, you're the first person in the world to see it. That's what these discoveries are like: You're the first person in the world to see and understand what's going on.

"To gain some understanding of what's going on in the brain, to translate that into what's going on with a patient, and then to figure out a better way of treatment?

"What a privilege."

— **JOEL S. PERLMUTTER, MD**

Excerpted with permission from "Neurology at Washington University: Evolution of a Groundbreaking Department."

Washington University School of Medicine
WashU Medicine Marketing & Communications
MSC 8508-29-12700
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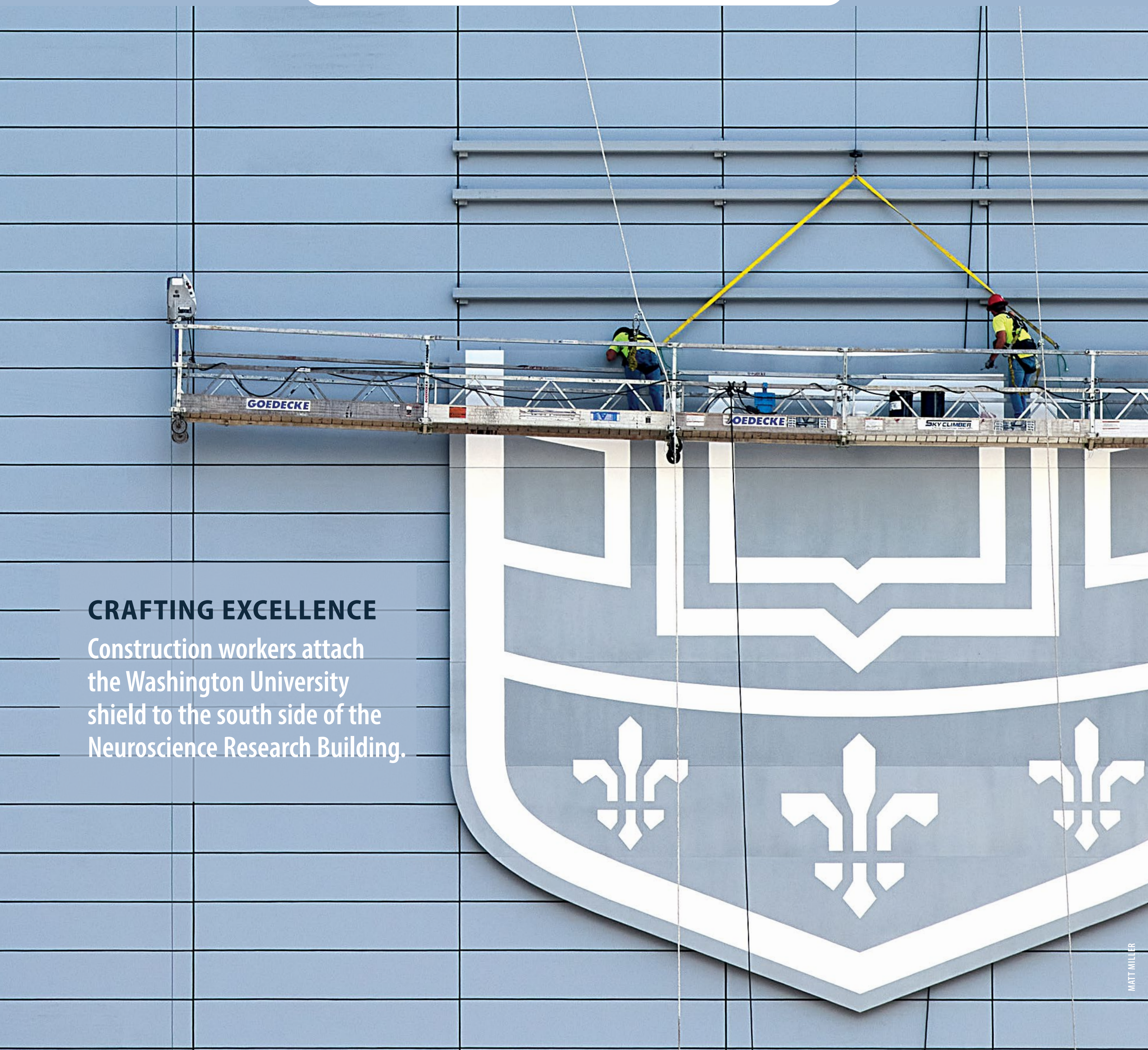
St. Louis, MO 63110-1010



CRAFTING EXCELLENCE

Construction workers attach the Washington University shield to the south side of the Neuroscience Research Building.

MATT MILLER