ISSUE 5, MARCH 2024

Vestigo

VANDERBILT UNIVERSITY **SCHOOL OF MEDICINE BASIC SCIENCES**

Special Sesquicentennial issue:

150 years of biomedical innovations

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New centers for applied AI, excellence in mass spectrometry

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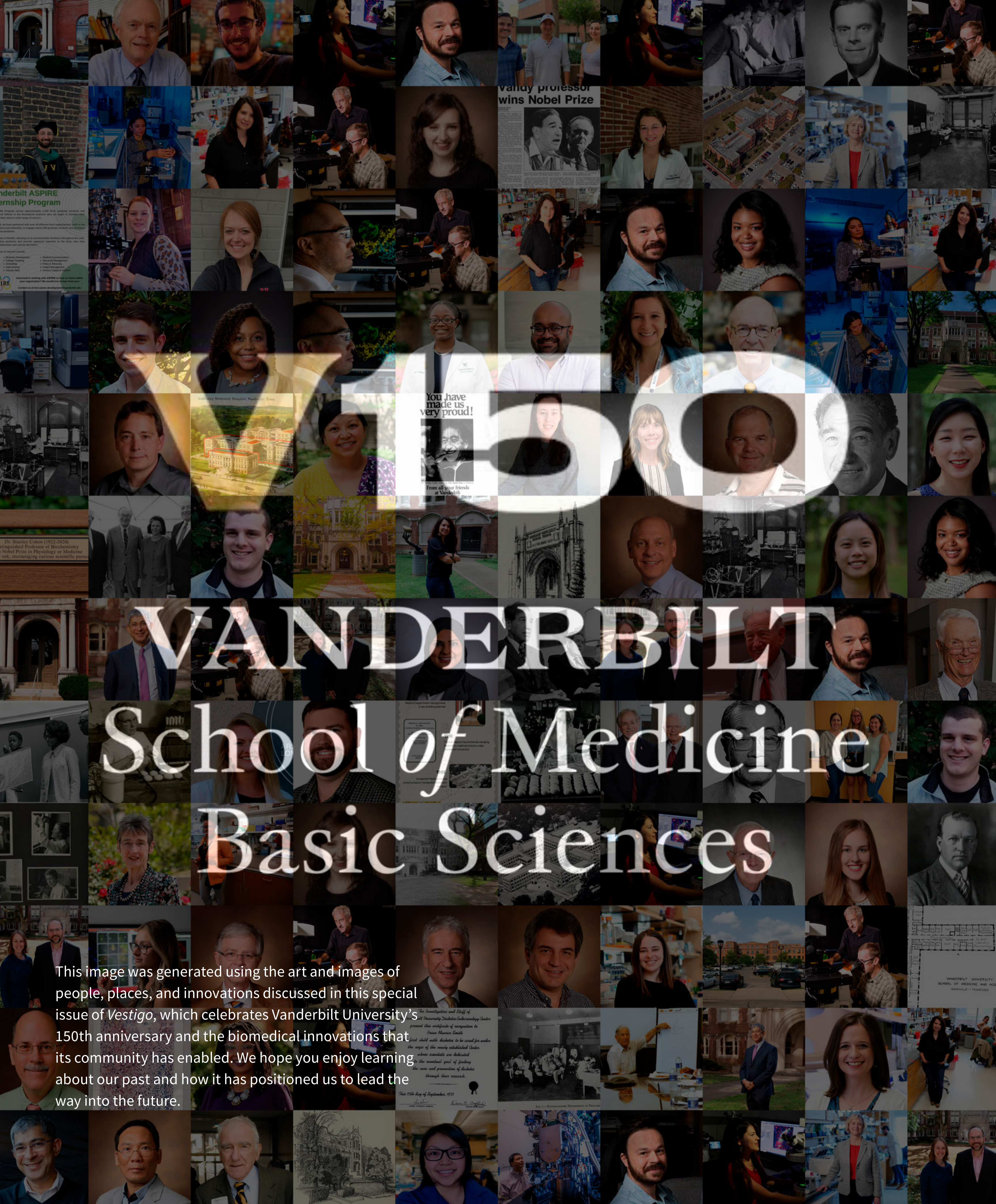
Understanding addiction to destigmatize an illness



This image was generated using the art and images of people, places, and innovations discussed in this special issue of *Vestigo*, which celebrates Vanderbilt University's 150th anniversary and the biomedical innovations that its community has enabled. We hope you enjoy learning about our past and how it has positioned us to lead the way into the future.

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Cover: In a tapestry of scientific endeavor, the cover art weaves a narrative that traverses the evolving landscape of cellular imaging. 1920s medical illustrator Susan Wilkes' masterful strokes join the intricate details revealed by transmission electron microscopy in the research lab of Antentor Hinton Jr. and the vibrant revelations afforded by high-powered light microscopy in the lab of Matthew Tyska. This visual symphony pays homage to the ceaseless march of innovation in scientific instrumentation. It is a nod to the scholarly pursuit of unraveling the enigmatic wonders of the cellular and subcellular realms in the foundational studies of basic sciences. Art by Kendra H. Oliver

IN EVERY ISSUE

SPECIAL SESQUICENTENNIAL ISSUE

Vestigo, (ves-TEE-go) the name of our magazine, comes from the Latin *vestigare*: to discover, search after, seek out, inquire, investigate. It encapsulates the spirit of discovery and dedication to research we strive to embody at Vanderbilt University School of Medicine Basic Sciences.

If you just can't wait for the next issue of *Vestigo* to keep up with Basic Sciences, we can send you news straight to your inbox. We have weekly and monthly newsletters — sign up at vanderbi.lt/BasicSciencesNewsSignUp.

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vubasicsciences

This project was funded in large part by a Vanderbilt Sesquicentennial Grant. We are grateful for this institutional support.

V150

Dear alumni and friends:

As **Larry Marnett** informed you in the last issue of *Vestigo*, he has stepped down from his position as dean of the School of Medicine Basic Sciences and returned to full-time scholarship and his lab. I have had the good fortune to be selected as the new dean.

As the dean emeritus has noted, the school is very well positioned for the future, and I am very grateful that we can all benefit from his excellent stewardship of the school. I am indebted to Larry for his guidance in helping me transition into my new role.

In this issue of *Vestigo*, as Vanderbilt University celebrates 150 years of existence, we glance back at biomedical research that has taken place here with an eye to the future. Celebrating 150 years of scientific progress is an opportunity not just for reflection but also for anticipation. The advancement of human knowledge has been awe inspiring, and with each passing year, we continue to solve new mysteries and confront unprecedented challenges.

Vanderbilt has been a center of groundbreaking discoveries that have had a direct impact on the improved treatment of human disease. In this issue, we discuss the history of biomedical research at Vanderbilt and the founding of School of Medicine Basic Sciences. You'll read about our Nobel Prize connections and histories of our four departments. You'll also learn about the evolution of medical and research illustration: We have come a long way from the hand-drawn images of cells and now can rely on high-powered, million-dollar imaging equipment to give us insights at the molecular level.

Leaving the past, we profile several of Vanderbilt's trailblazing scientists, including award-winning female faculty. You'll learn about the outstanding work of current researchers in the areas of addiction and human genome regulation and read about research being conducted by graduate students and postdocs, which is an appropriate segue to the future.

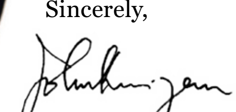
Artificial intelligence presents numerous groundbreaking opportunities in the field of biomedicine. These opportunities can significantly impact research, diagnosis, treatment, and health care delivery. To that end, we introduce you to our newly launched Center for Applied AI in Protein Dynamics, whose aim is to explore the intersection of artificial intelligence, machine learning, and macromolecular mechanisms to understand protein structures and their functions in the human body.

The past 150 years of biomedical research have seen the development of cures, reduced disease mortality rates, and dramatically improved health outcomes for millions. The next 150 years hold the promise of discoveries we can scarcely imagine. Our goal is to harness this potential for the betterment of humankind.

My hope, as the new dean of basic sciences, is to bring you good news of groundbreaking research from our labs in each issue of this magazine.

JOHN RUSSELL

Sincerely,



John Kuriyan
Dean of Basic Sciences
School of Medicine, Vanderbilt University

Could a biomedical Ph.D. graduate student or postdoc help support your organization's initiatives?

Vanderbilt ASPIRE Internship Program

The ASPIRE Program serves approximately 1,100 Ph.D. graduate students and postdoctoral scholars in the biomedical sciences who are eager to broaden their skills and learn about a wide range of careers.

Since 2015, we have partnered with more than 40 different host organizations, both in the Nashville area and nationally, to engage nearly 200 graduate students and postdocs in internship positions.

Our program is flexible, allowing us to accommodate timelines throughout the year. We advertise positions and provide applicant materials to the host, who then conducts interviews and selects the intern.

Career areas of interest include:

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- **Project Management**
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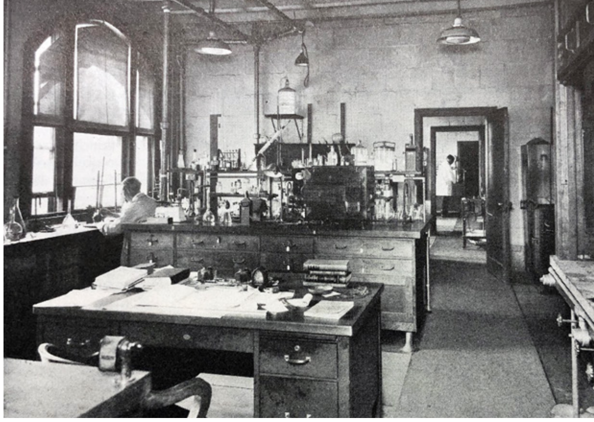
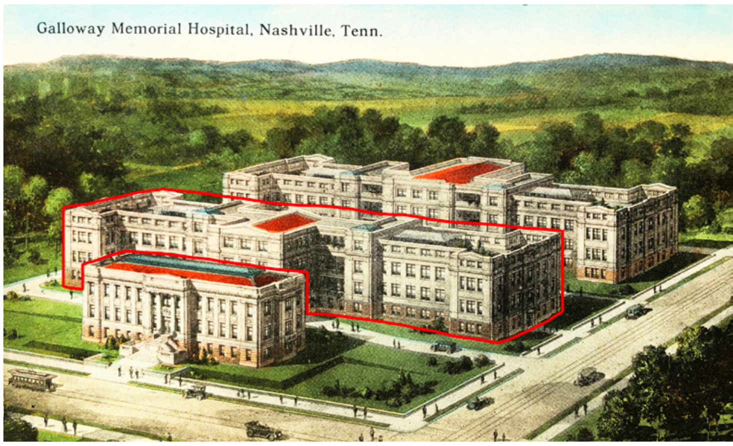
Interested in working with ASPIRE to host an intern within your organization? We would love to hear from you!

Contact us at bret.career.development@vanderbilt.edu

ASPIRE





Established 52 years after the university, the Vanderbilt University School of Medicine has been conducting innovative biomedical research for almost 100 years. It has witnessed social progress, infrastructure development, and expansion alongside the university and Nashville itself.

Welcome to this special issue of *Vestigo*, which celebrates the sesquicentennial of Vanderbilt University. We have crafted a series of articles that highlight some of the discoveries and accomplishments of researchers in our four departments—and their predecessors!

We hope you enjoy the journey as much as we enjoyed the process of making this issue. And we thank the Vanderbilt Sesquicentennial Grant program for the funds that allowed this project to come to life!

-The *Vestigo* editorial team

Basic science at Vanderbilt University: A BRIEF HISTORY

By Larry Marnett and Stephen Doster

The School of Medicine Basic Sciences is a unique entity among schools of medicine in the United States. It bridges Vanderbilt University and Vanderbilt University Medical Center and has a mission to advance discovery science and Ph.D. training in the biomedical sciences. At a time when many schools of medicine are reducing their commitment to basic science, how did our school come about?

In the beginning

In 1849 the Tennessee State Legislature passed a bill establishing the Medical College (owned and controlled by its medical faculty) as part of the University of Nashville. The first session of the Medical College opened in 1851 with 121 matriculants. The campus stood on Rutledge Hill, south of downtown Nashville.

Vanderbilt was established in 1873 on 70 acres west of downtown Nashville. A year later, the Vanderbilt Board of Trust and the Medical College arranged for the creation of a medical department serving both Vanderbilt University and the University of Nashville, which allowed students to choose which school issued their diplomas.

In 1908, the Flexner Report, commissioned by two national organizations with a mission of improving health care in America, recommended a drastic reduction in the number of medical schools and the creation of science-based medical training, and recognized the need to fund a new medical school in Nashville.

Vanderbilt Chancellor **James Kirkland** secured $4 million from the Rockefeller Foundation's General Education Board in 1919 and hired **Dr. Canby Robinson** as dean. Robinson and others lobbied to build a new medical school on Vanderbilt's west campus, along 21st Avenue, as opposed to the Rutledge Hill/south campus location that Kirkland initially wanted. It was designed by Boston architect **Henry R. Shepley** as a structure that, for the first time in this country, would house under one roof all the facilities needed for the laboratory and clinical training of students and the research of their mentors.

Finally, 52 years after its founding, Vanderbilt opened its own medical school in 1925. To support science-based training, the administration established departments of anatomy, biochemistry, pharmacology, and physiology, which evolved over time into our current departments: biochemistry, cell and developmental biology, pharmacology, and molecular physiology and biophysics. Weekly journal clubs kept students and faculty abreast of research literature, departments and clinics collaborated on research projects, and graduate students received their degrees from the university instead of the medical school—as they do today.

Moving the Vanderbilt medical school from downtown Nashville to the university campus resulted in its close integration with the university. As the university grew, the medical center came to occupy the center of the campus, surrounded on three sides by the schools of engineering, arts and science, and education. This unique geography

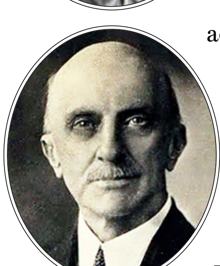
BASIC SCIENCES HAS EMERGED WITH AN INDEPENDENT IDENTITY AND HAS EXCELLED IN FACULTY RECRUITING, GRANT FUNDING, AND FOSTERING OF COLLABORATIONS WITH FACULTY IN THE SCHOOLS OF ENGINEERING, ARTS AND SCIENCE, AND EDUCATION

established a highly effective platform for collaboration across the university. The medical school developed a strong faculty that included members of the National Academy of Science and National Academy of Medicine and two recipients of Nobel Prizes—**Earl Sutherland** and **Stanley Cohen**.

Interdisciplinary centers arose that involved faculty from many different departments and schools and not only served as foci for research but were also the homes for training programs for Ph.D. students, M.D. students, postdocs, and residents. Such centers ingrained collaboration as a distinguishing characteristic of Vanderbilt, which has been leveraged repeatedly over the years.

The VU-VUMC reorganization

Despite having developed into a powerhouse for research and training reinforced by trans-university collaboration, VU and VUMC reorganized into separate entities in 2016. The financial crisis of 2008 drastically changed the economics of health care delivery and put significant pressure on academic medical centers, which complicated their financing and governance when located within a university structure.



Top to bottom: Abraham Flexner, author of the Flexner Report (photo by Vanderbilt University); Canby Robinson (Rockefeller Foundation Archive); James Kirkland (photo by Vanderbilt University)

Within such a structure, the resources for biomedical research and education—both medical and graduate—originate from the financial performance of the medical center. As clinical margins tightened, medical centers struggled to adequately invest in research and training, which was particularly challenging for basic science departments and led in some cases to the elimination of departments or the fusing of multiple departments into single mega-departments.

Consequently, after careful deliberation, on April 30, 2016, the Vanderbilt Board of Trust split Vanderbilt University and Vanderbilt University Medical Center into two separate corporations with two separate governing boards, led by **Nicholas Zeppos** and **Dr. Jeffrey Balser**, respectively.

Zeppos and Balser were strong proponents of basic biomedical research and, to maintain a strong home for basic biomedical research and education, they helped create Basic Sciences concomitant with the VU-VUMC split. **Larry Marnett** was named its first dean.

The School of Medicine Basic Sciences

The new school was incorporated into the governance structure of the university—its dean reporting to the university provost—and ceased to directly rely on the clinical margin of VUMC. This structure provides not only an independent home for basic science research and training, but also predictable resources to help support operations, faculty recruiting, Ph.D. student training, and investments in infrastructure. In addition, the university funding model incentivizes the school to be entrepreneurial in its approach to revenue generation.

Basic Sciences is responsible for all Ph.D. education within the School of Medicine. Students are recruited mainly through two umbrella programs and join one of 11 graduate training programs after their first year. Faculty from across the School of Medicine and other schools participate in Ph.D. training, which represents a major unifying force among the faculty. All training programs are coordinated through the Office of Biomedical Research Education and Training, and all supporting work for the school occurs through administrative pods.

The first year following the separation was challenging because of the absence of existing structures and procedures, which were developed "as the plane rolled down the runway." In the years since, Basic Sciences has overcome challenges ranging from business difficulties related to the university's adoption of a new general ledger to unprecedented trials related to a worldwide pandemic. Faculty and staff have worked tirelessly to develop and accommodate new processes and proved resilient in the face of massive challenges.

Seven years post-separation, Basic Sciences has emerged with an independent identity and has excelled in faculty recruiting, grant funding, and fostering of collaborations with faculty in the schools of engineering, arts and science, and education. Basic Sciences has the second largest budget in the university and accounts for 40 percent of the grant funding at Vanderbilt. The anticipated financial stability has been realized, serving the school well during the financial roller coaster experienced during the COVID-19 pandemic.

To be sure, there are remaining challenges associated with the bifurcated structure of the medical school, and Basic Sciences will confront them as a new post-pandemic normal sets in.

Over the past nearly 100 years, VU and VUMC have leveraged their unique geography and commitment to excellence to become one of the top institutions in the world for biomedical research and training. The reorganization of VU and VUMC, including the creation of Basic Sciences, illustrates Vanderbilt at its best: identifying a problem and formulating a solution even if it requires dramatic change, and thinking outside the box. The current structure highlights Vanderbilt's long-term commitment to excellence in research and education and provides a world-class home for discovery science to drive biomedical innovation and improve human health. ■

VANDERBILT UNIVERSITY

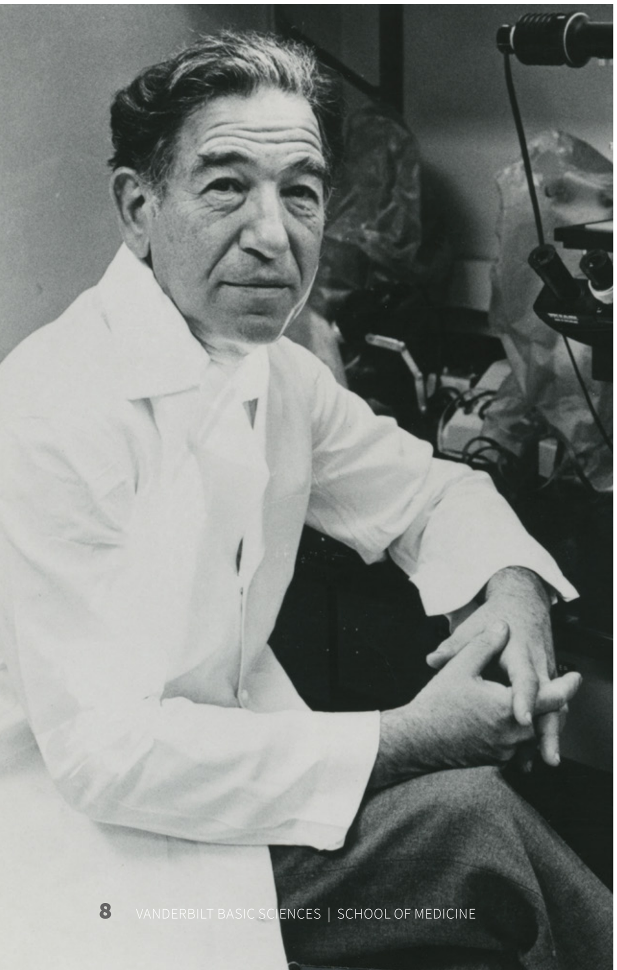
A Nobel-worthy discovery spawns a new field—and new therapies

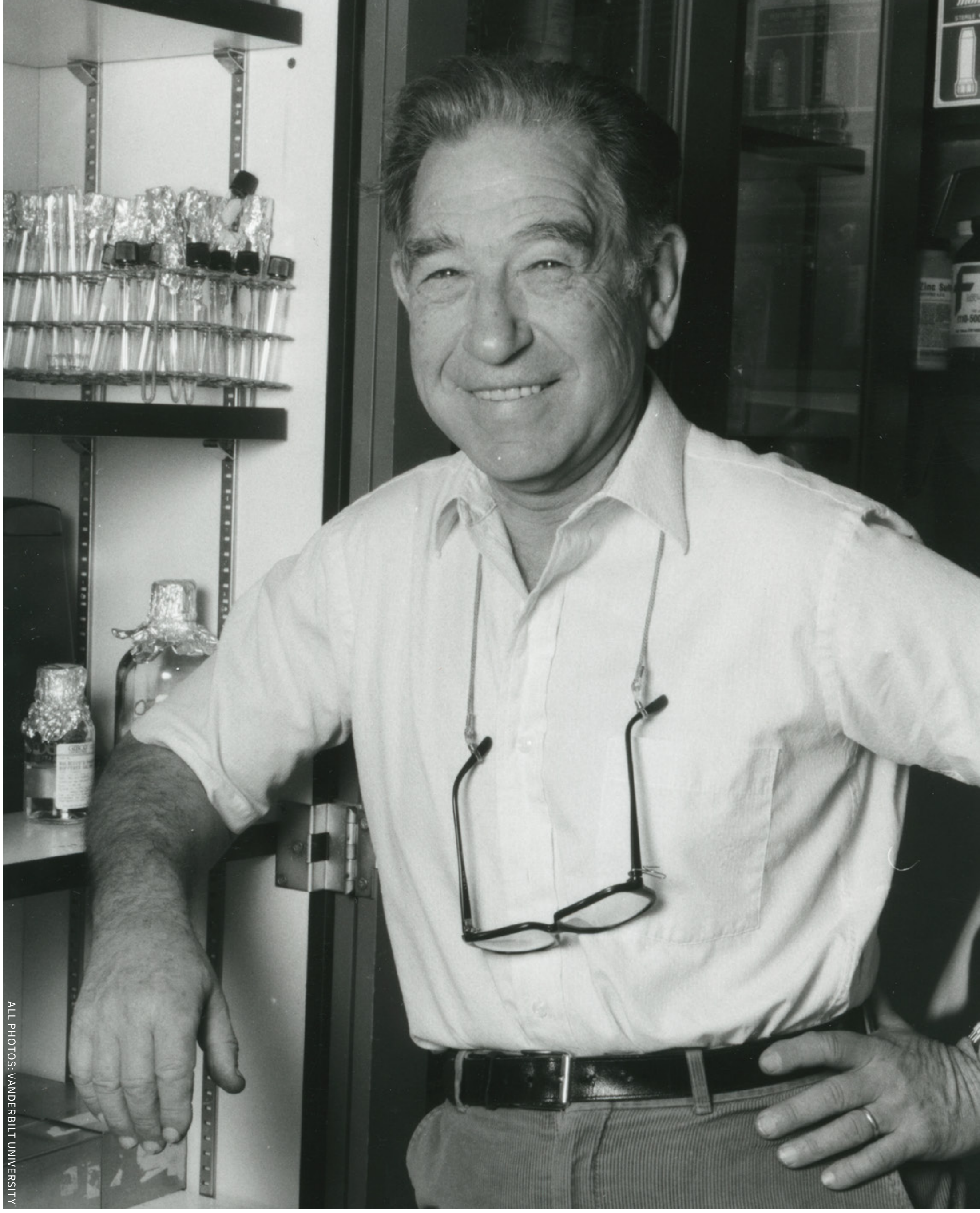
By Stephen Doster

The phone rang in the wee hours of the morning. Fighting dread, **Stanley Cohen**, Distinguished Professor of Biochemistry Emeritus, picked up the phone. "For the first time in my life the middle-of-the-night call was good news," he later said.

The call was to notify Cohen that he'd been awarded the 1986 Nobel Prize in Physiology or Medicine for his discovery of epidermal growth factor, a protein produced in the body that influences the development of nerve and skin tissues by stimulating cell growth and differentiation.

Cohen, who died in 2020, shared the Nobel Prize with **Rita Levi-Montalcini**, an





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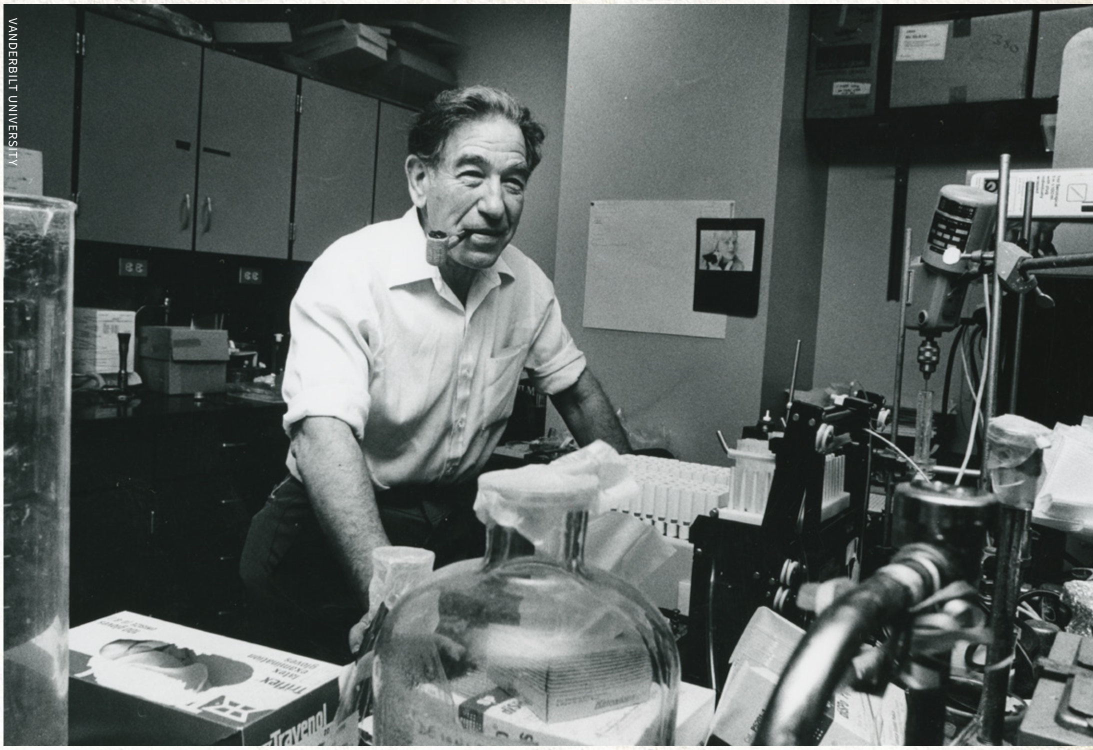
Italian neurobiologist with whom he had collaborated in the 1950s during their time at Washington University in St. Louis.

"The discovery of EGF launched an entire field of research into growth factor signaling and had major impacts on human health," Department of Biochemistry Chair **David Cortez** said.

Although cancer remains a complex and challenging disease, the knowledge gained from Cohen's discovery has paved the way for transformative advancements that have extended lifespan, enhanced symptom management, improved treatment efficacy, and provided greater hope for patients and their families. From early detection and personalized therapies to improved supportive care and survivorship, cancer patient outcomes in 2023 are substantially better compared to outcomes 100 years ago.

"For example, there are more than 10 cancer drugs approved by the U.S. Food and Drug Administration that target EGF receptors and many more that interfere with downstream signaling components," Cortez said. "These drugs help tens of thousands of cancer patients each year." Such targeted therapies, including EGF receptor inhibitors, have shown success in specific diseases such as breast, colorectal, head and neck, non-small cell lung, pancreatic, and thyroid cancers as well as squamous cell (skin) carcinoma.

Additionally, several biological processes, including immune system regulation, have been identified thanks to Cohen and Levi-Montalcini's work. Ongoing clinical studies on the therapeutic properties of nerve growth factor, which they were attempting to isolate when they discovered EGF, focus on neurodegenerative diseases—such as Alzheimer's disease and Parkinson's disease—traumatic brain injury, epithelial diseases and wound healing, and eye disorders such as corneal ulcers, glaucoma, retinitis pigmentosa, macular degeneration, and optic gliomas. Recently, Vanderbilt researchers—led



VANDERBILT UNIVERSITY

"The discovery of EGF launched an entire field of research into growth factor signaling and had major impacts on human health." —David Cortez

by **Dr. Raymond Harris**, professor of medicine and molecular physiology and biophysics, and **Dr. Ming-Zhi Zhang**, professor of medicine—discovered that activation of EGFR is essential for the development of kidney fibrosis, which could lead to the first effective treatment for this condition and may provide insight into the development of fibrosis in other organs.

Being a Nobel laureate gave Cohen a platform to promote the need for basic research. "The road to medical discovery often begins as an unmarked trail," he said to interviewer **Vicki Brown** in 1986. "We're not always smart enough to know when the work is relevant. We must work on applying what we know but continue putting more money into finding out what we don't. It's not possible to think what will be the most important research 100 years from now."

Or even 10 years from now. ■

Stanley Cohen through the years. He is pictured alone and with President Ronald Reagan (left, middle) and Professor of Biochemistry Richard Caprioli (right, bottom).

Cell and Developmental Biology pushes the limits of cancer research

By Leah Mann

If you had visited Vanderbilt nearly a century ago searching for cellular research, you would have found yourself in the Department of Anatomy. Established in 1925, the Department of Anatomy gave way to the Department of Cell Biology before taking on its current moniker—Cell and Developmental Biology—in 2001.

When **Dr. Harold "Hal" Moses**, professor emeritus of cancer biology, accepted the role of chair of the cell biology department in 1985, he was charged with preserving the standard of teaching and furthering research. He hired the internationally recognized **Brigid Hogan**, who became the Hortense B. Ingram Professor of Cell Biology, to help him recruit additional developmental biologists; together they brought an additional 20 faculty members on board. Indeed, the department thrived and ranked "34th in the nation for [National Institutes of Health] funding when I joined and fourth when I stepped down," Moses said.

Earlier in his career, Moses attended the Vanderbilt School of Medicine, was a professor of pathology, and assumed positions at the NIH and the Mayo Foundation. Before his final return to Vanderbilt, Moses made his mark in the early 1980s as a co-discoverer of transforming growth factor-beta, a cytokine that plays significant roles in immune and stem cell regulation. Moses and his colleagues garnered enormous attention when they demonstrated that TGF-β is a growth inhibitor, establishing its clinical relevance to cancer and diseases. They later determined the paradoxical nature of the protein, as TGF-β signals contribute to tumor suppression in early stages of cancer but promote tumor growth in later stages.

Although the impact of Moses' work on TGF-β has been immeasurable, there is no clean-cut implication for TGF-β to improve clinical outcomes. Yet Moses remains hopeful that TGF-β may prove to be clinically significant for pharmaceuticals in light of promising cancer immunotherapies that seek to block its signaling.

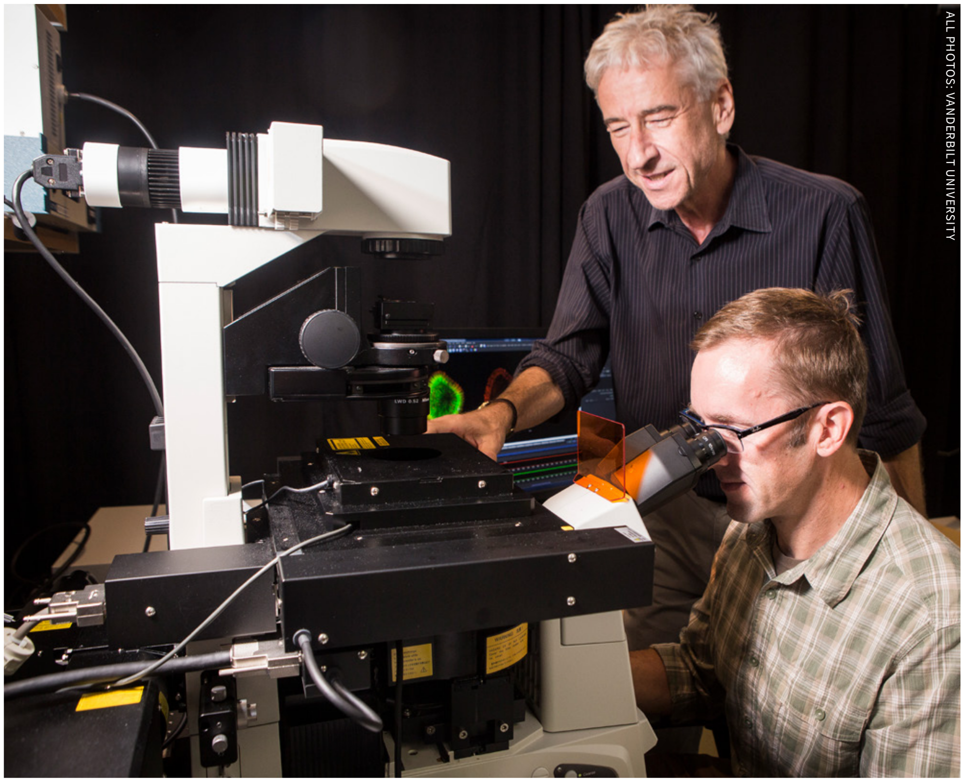
A path to the future

In 1998, Moses was succeeded as chair by **Susan Wente**, former professor of cell and developmental biology who subsequently became provost and then interim chancellor, who was in turn succeeded by **Ian Macara**, Louise B. McGavock Professor and current chair of the department. Since his arrival, Macara has recruited nearly 50 percent of the department's faculty, increased the number of microscopes from three to more than 30, and worked diligently to establish the Nikon Center of Excellence—a key microscopy and imaging resource for scientists across campus.

While the scientists in the department ask "fundamental questions about how cells work and organisms develop," many of these investigations do cross into the realm of clinical research, Macara said.

Building on Moses' findings, **Dr. R. Daniel Beauchamp**, the John Clinton Foshee Distinguished Professor of Surgery and professor of cell and developmental biology who died in November 2022, maintained a strong research program of TGF-β alterations in colorectal cancer. On parallel non-TGF-β cancer tracks, cell and developmental biologists at Vanderbilt are investigating changes in cells that lead to pancreatic cancer, subpopulations of cells responsible for brain tumor growth, and the interactions between oncogenes and other proteins for developing cancer treatments.

With the solid foundation laid by basic science scholars such as Moses, Wente, and Macara, the Department of Cell and Developmental Biology continues to be a highly collaborative department that advances biomedical research and trains future scientists. ■



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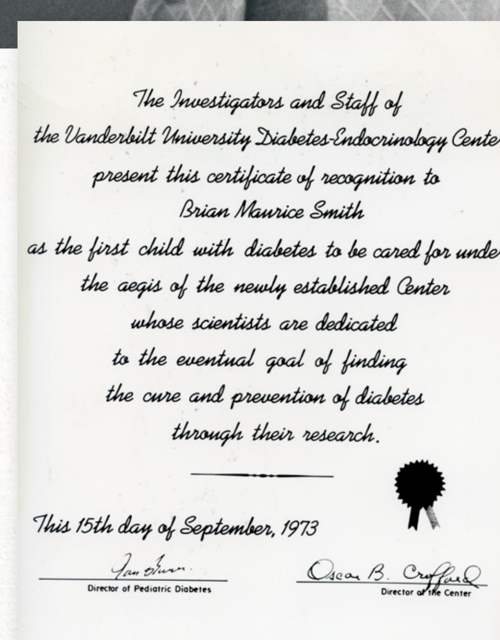
Clockwise from top left: Susan Wente, Matthew Tyska (at the microscope) and Ian Macara, Daniel Beauchamp, Ian Macara, Hal Moses

At the formal opening of the Diabetes Center in 1973, former U.S. Rep. Richard Fulton presented patient Brian Maurice Smith and his mother with a certificate attesting that Smith was the first patient of the center.

VANDERBILT UNIVERSITY



The Investigators and Staff of
the Vanderbilt University Diabetes-Endocrinology Center
present this certificate of recognition to
Brian Maurice Smith
as the first child with diabetes to be cared for under
the aegis of the newly established Center
whose scientists are dedicated
to the eventual goal of finding
the cure and prevention of diabetes
through their research.

This 15th day of September, 1973

Director of Pediatric Diabetes

Oscar B. Crofford
Director of the Center

"I doubt that there is another department of its kind in the world that has had, and continues to make, as much impact in diabetes research and its contribution to patient care."

—**Alan Cherrington**

Diabetes discoveries:

TRANSFORMING UNDERSTANDING AND CARE

By Aaron Conley

Living with diabetes in the early 1900s was filled with adversity. Prior to insulin's introduction to the clinic in 1922, life expectancy after a type 1 diabetes diagnosis was only one to two years. Even after insulin, without the understanding and technology we have today, managing diabetes was a struggle. Extensive research was crucial for physicians and scientists to understand its mechanisms and provide improved patient care.

Established in 1925, the Department of Physiology—now Molecular Physiology and Biophysics—went beyond clinical training and cultivated robust and enduring research in a variety of disciplines, including diabetes research. **Dr. Rollo Park**, who became the department chair in 1952, was the first to prove that insulin could transport glucose into cells. Park recruited and trained dozens of students who themselves went on to impact the field. **Tetsuro Kono**, for example, discovered that glucose transporters cycled between the cytosol and cell membranes.

A pivotal transformation occurred in 1963 with the arrival of **Dr. Earl Sutherland**, a decorated former U.S. Army surgeon under Gen. George S. Patton. Sutherland's lab delved into the role of cyclic AMP in hormone action, unraveling its intricate roles in cellular signaling pathways. Their discoveries laid the groundwork for many therapeutics, exemplified by the use of the hormone glucagon in insulin overdose cases, and earned Sutherland the Nobel Prize in Physiology or Medicine in 1971.

Dr. Oscar Crofford joined the physiology faculty in 1965 and focused on insulin's effects on adipose tissue. This work led to a class of drugs that targets fat cells and helps control metabolism. Crofford chaired the National Commission on Diabetes, which made recommendations to the U.S. Congress and championed the National Diabetes Act of 1973. This act launched diabetes centers across the country, including the Vanderbilt Diabetes Center—the nation's first. Crofford also chaired a groundbreaking, $165 million clinical trial that found that proper use of insulin lessened complications in diabetic patients.

A Sutherland postdoctoral fellow, **Dr. John Exton**, who died in 2023, played a vital role in studying gluconeogenesis and its hormonal control and went beyond cyclic AMP to understand calcium signaling in cells.

Exton nurtured a generation of scientists, including **Alan Cherrington**. Cherrington, who arrived at Vanderbilt in 1975 and is now a professor of molecular physiology and biophysics, solidified our understanding of glucagon as a hormone and showcased the different roles of epinephrine and norepinephrine versus glucagon in the responses to various challenges. Cherrington and his trainees created a one-of-a-kind animal model and partnered with pharmaceutical giants Eli Lily and Novo Nordisk to develop designer insulins. He was also involved in developing a newer class of drugs called GLP1 receptor agonists, which are now widely used to treat type 2 diabetes.

Dr. Daryl Granner, a clinician and researcher, was recruited to chair the department in 1984. He was one of the world's first molecular biologists and changed the name of the department to the current "molecular physiology and biophysics" to showcase this new field. He uncovered the way in which insulin regulates genes important for glucose metabolism and directed the VDC for 16 years. The center, now renamed the Vanderbilt Diabetes Training and Research Center, is to this date one of the top diabetes centers in the nation.

Today, living with diabetes is managed through accurate blood sugar testing, controlled use of insulin, and myriad drugs and treatments. These advances have been made possible through tireless research at Vanderbilt and across the globe.

"Diabetes research in the department has been preeminent for decades," Cherrington said. "There have been many significant discoveries, some of which have been recognized with an array of awards and many of which have played a role in the development of new therapeutic agents. I doubt that there is another department of its kind in the world that has had, and continues to make, as much impact in diabetes research and its contribution to patient care." ■

Pharmacology's tradition of academic excellence and mentorship

By Kendra Oliver and Marissa Shapiro

In the heart of rural Kentucky, on a modest farm surrounded by rolling fields and endless skies, **Elaine Sanders-Bush** began a journey that would lead her to become an icon in the world of science, where she unraveled some of the brain's myriad mysteries.

Sanders-Bush earned a bachelor of science degree in biology and chemistry at Western Kentucky University. Between 196 and 1967, she was part of the graduate program in pharmacology at Vanderbilt University, which became the backdrop of her remarkable scientific career rooted in discovery and mentorship.

Returning to Vanderbilt as a faculty member in 1969 following a brief postdoctoral fellowship, Sanders-Bush's research centered on serotonin and its receptors from a lens of pharmacology, signal transduction, and in vivo brain function. She joined the department during **Allan D. Bass**' two-decade tenure as department chair, during which he grew the department's reputation to what it is today: a nationally recognized program focused on academic excellence and mentorship.

The bulk of her Vanderbilt career was during **Joel Hardman**'s tenure as department chair. Hardman heavily influenced the department's emphasis on trainee mentorship while also fostering rigorous scholarship. His work included the discovery of guanylate cyclase, the enzyme responsible for synthesizing cyclic GMP from GTP, and led scientists to understand that cGMP, like cAMP, can serve as an intracellular second messenger.

Across Sanders-Bush's career, she leveraged advancements in molecular biology, genetics, and new understandings of behavior to unravel the mysteries of the brain. This work would have ripple effects for generations of Vanderbilt trainees and faculty in the years to come.

Beyond her academic research, Sanders-Bush was the driving force behind the development of Vanderbilt's neuroscience research and graduate education programs; thanks in large part to her efforts, Vanderbilt established its Ph.D. program in neuroscience in 1997.

This period also saw another first in the department: the first female chair, **Lee Limbird**. Limbird joined Vanderbilt 10 years after Sanders-Bush in 1979. She was department chair from 1991 until 1998 and became the first associate vice chancellor for research at the Vanderbilt University Medical Center, serving in that role until 2003. Limbird, who went on to hold leadership positions at Meharry Medical College and Fisk University, studied the basis for the actions of epinephrine and norepinephrine via α2-adrenergic receptors and examined trafficking itineraries, the functional relevance of the receptors' structure, and their interface with a variety of signaling pathways.

Limbird and Sanders-Bush joined forces to expand the department's activities together, a task that was facilitated by Sanders-Bush's appointment as the inaugural director of the Vanderbilt Brain Institute in 2002. Like Limbird, she shared a passion for diversity, equity, and inclusion, which she has demonstrated through work designed to enhance minority training programs at Tennessee State University, Meharry Medical College, and Vanderbilt. The impact of her efforts and outstanding mentoring earned her the inaugural Levi Watkins, Jr., Award for Leadership Diversity and the Dr. Dolores C. Shockley Lecture and Partnership Award.

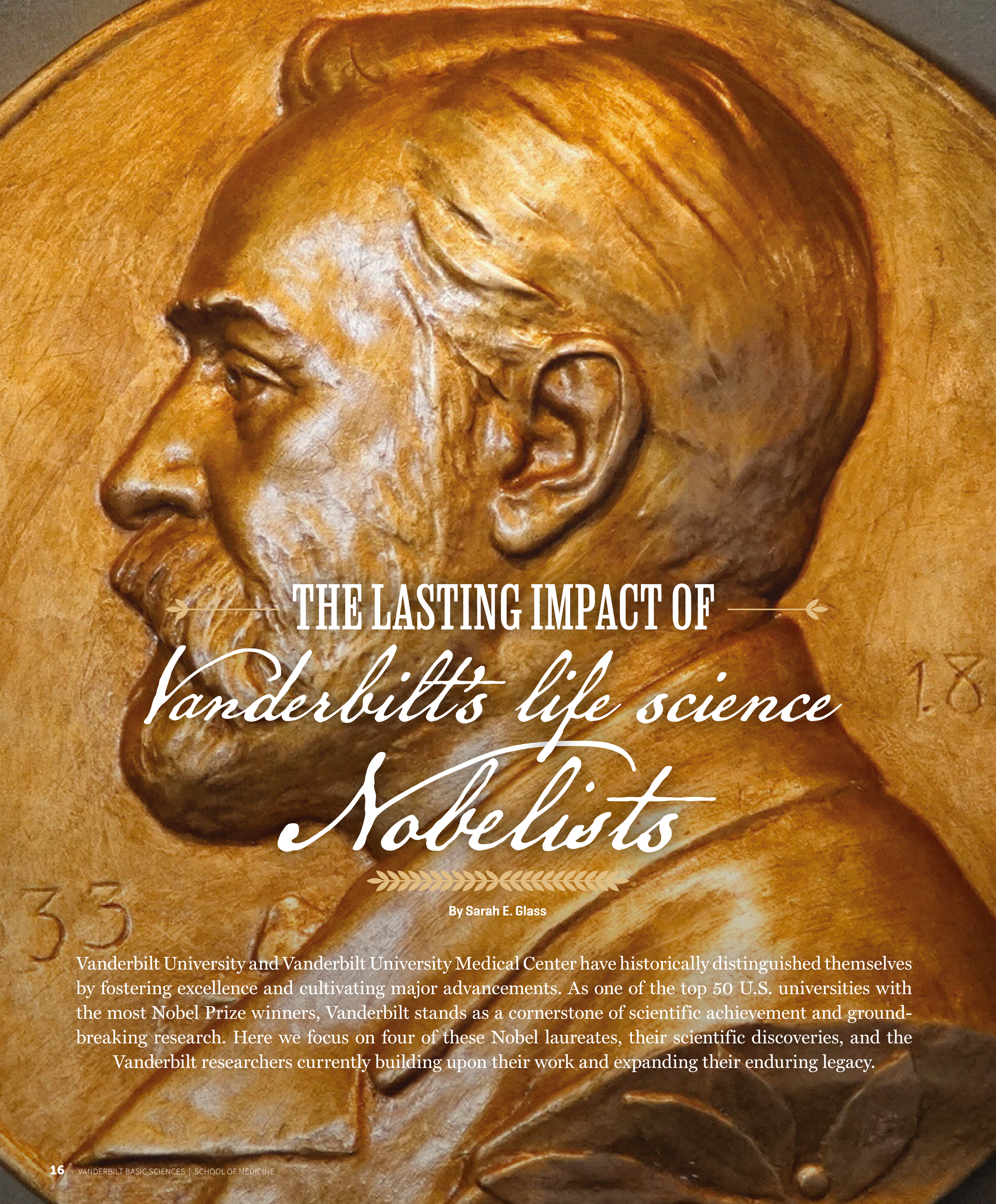
Over her research career, Sanders-Bush received other prestigious awards on national and international stages, including the Bristol-Myers Squibb Award for Neuroscience Research and a MERIT Award from the National Institute of Mental Health. She became interim chair of the Department of Pharmacology in 1999 until **Heidi Hamm** was named chair in 2000.

Sanders-Bush's legacy joins that of others in the Department of Pharmacology and extends far beyond scientific achievements into mentorship and a commitment to widening the gates of the discipline to welcome scientists of all backgrounds. This long tradition of inclusion and rigorous inquiry has known no bounds and has paved the way for the next 150 years. ■

A 1992 article in the Houston Chronicle *featured Sanders-Bush and her research on serotonin. "With a no-strings-attached neuroscience research group from Bristol-Myers Squibb, Dr. Sanders-Bush is working to better understand the various interactions of serotonin—research that may lead to … better drug treatments in depression and other mental disorders."*

HOUSTON CHRONICLE

Sanders-Bush's legacy … extends far beyond scientific achievements into mentorship and a commitment to widening the gates of the discipline to welcome scientists of all backgrounds.



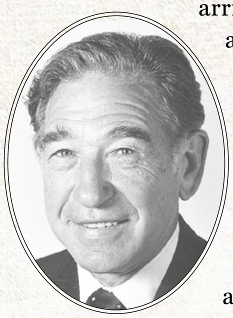
THE LASTING IMPACT OF *Vanderbilt's life science Nobelists*

By Sarah E. Glass

Vanderbilt University and Vanderbilt University Medical Center have historically distinguished themselves by fostering excellence and cultivating major advancements. As one of the top 50 U.S. universities with the most Nobel Prize winners, Vanderbilt stands as a cornerstone of scientific achievement and groundbreaking research. Here we focus on four of these Nobel laureates, their scientific discoveries, and the Vanderbilt researchers currently building upon their work and expanding their enduring legacy.

Stanley Cohen

Cohen, distinguished professor of biochemistry emeritus, was already conducting Nobel Prize–winning research by the time he arrived at Vanderbilt University in 1959. Cohen and Rita Levi-Montalcini are credited with discovering the first growth factor, called nerve growth factor, while at Washington University in St. Louis in 1956. Growth factors are signaling molecules that stimulate cell processes such as proliferation.



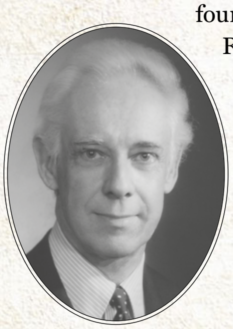
Once at Vanderbilt, Cohen continued this fruitful line of investigation to discover another growth factor, epidermal growth factor. It is now well established that EGF and its receptor, EGFR, are intimately involved in regulating cell growth, differentiation, and survival, which are deregulated in cancer. Cohen and Levi-Montalcini received the Nobel Prize in Physiology or Medicine in 1986 for these discoveries.

Cohen's research on EGF has informed the work of Vanderbilt investigators like **Robert Coffey**, Ingram Professor of Cancer Research and professor of cell and developmental biology, and **Dr. Christine Lovly**, associate professor of medicine and Ingram Associate Professor of Cancer Research, who study the role of EGFR signaling in colon and lung cancer, respectively. Lovly's laboratory and clinical research focus on the role of EGFR and other ErbB family members in the development and treatment of lung cancer.

Countless patients are indebted to the work of Cohen and his colleagues as it has led to a variety of drugs—such as cetuximab—that treat cancer by targeting EGFR.

Stanford Moore

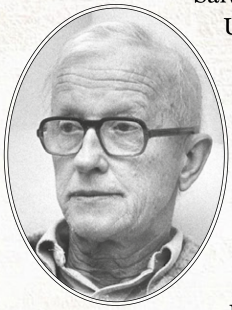
Moore graduated from Vanderbilt University with an undergraduate degree in chemistry in 1935. With this strong scientific foundation, he launched his research career at Rockefeller University by studying enzymes with a chemical approach. There, Moore and colleague William Stein developed an amino acid analyzer to determine the amino acid sequences of enzymes such as ribonuclease, which can cleave RNA. They won the Nobel Prize in Chemistry in 1972 for their work on ribonuclease.



Moore returned to Vanderbilt in 1968 as a visiting professor in health sciences. His discoveries live on in the research studies of **John Karijolich**, associate professor of pathology, microbiology, and immunology, who studies the role of ribonucleases and their interacting partners in diseases such as cancer.

Max Delbrück

Delbrück embodies the strong heritage of interdisciplinary and collaborative excellence widespread at Vanderbilt. Although originally recruited as a physics instructor in 1940, he began conducting research in a biology lab and collaborating with Salvador Luria, a microbiologist at Indiana University. His theoretical physics morphed into practical biology as he determined that a bacteria's resistance to viral infection was dependent upon random mutations. Delbrück was awarded the Nobel Prize in Physiology or Medicine in 1969 for his discoveries, which now inform the work of many researchers.



Hassane Mchaourab, professor of molecular physiology and biophysics, has followed a similar path by applying his physics training to biological questions. His focus on protein dynamics led him to tackle how bacteria and cancer acquire drug resistance phenotypes. More recently, he is leveraging his physics training to embrace the recent revolution in artificial intelligence and machine learning methods within protein science.

Earl Sutherland

Another Vanderbilt Nobel laureate was Earl Sutherland, professor of physiology. While at Case Western Reserve University, Sutherland discovered cyclic AMP, a molecule that works as a second messenger for many signaling pathways. Sutherland moved to Vanderbilt in 1963 and identified cAMP as the second messenger for epinephrine signaling, demonstrating that hormones are not the sole contributors to signaling cascades.

Sutherland was awarded the Nobel Prize in Physiology or Medicine in 1971 while a faculty member at Vanderbilt. He determined that cAMP affects more than thirty physiological processes, although this number has since grown as cAMP is now understood to serve important roles in metabolism, cancer, neurotransmission, and more.

As cAMP is ubiquitous in biological pathways throughout the human body, the research of many Vanderbilt investigators is informed by and builds on Sutherland's discoveries. For example, **Eugenia Gurevich**, associate professor of pharmacology, is investigating long-term, cAMP-dependent and -independent changes in dopaminergic signaling in the brain during disease and in response to drugs. ■

Molluscum bodies.

Left: A hand-drawn illustration of molluscum bodies, a histologically distinctive marker of molluscum contagiosum, also known as water warts. Water warts are caused by a viral infection of the skin. The illustration was created by Elizabeth Hobbs, a staff member of the Department of Illustration, in 1932.

Bottom: A hyper-realistic drawing of an eye by Susan Wilkes. Dr. Canby Robinson made the decision to hire Wilkes after seeing this drawing.

ARTiculating science

By Kendra H. Oliver

Art has always been a part of science—from the first field drawings of prehistoric cave paintings to today's 3D computer-generated protein structures. The Department of Illustration at Vanderbilt University provides a prime example of the power of visualization. Although this department no longer exists, its influence helped to articulate and accelerate Vanderbilt's biomedical research excellence and education.

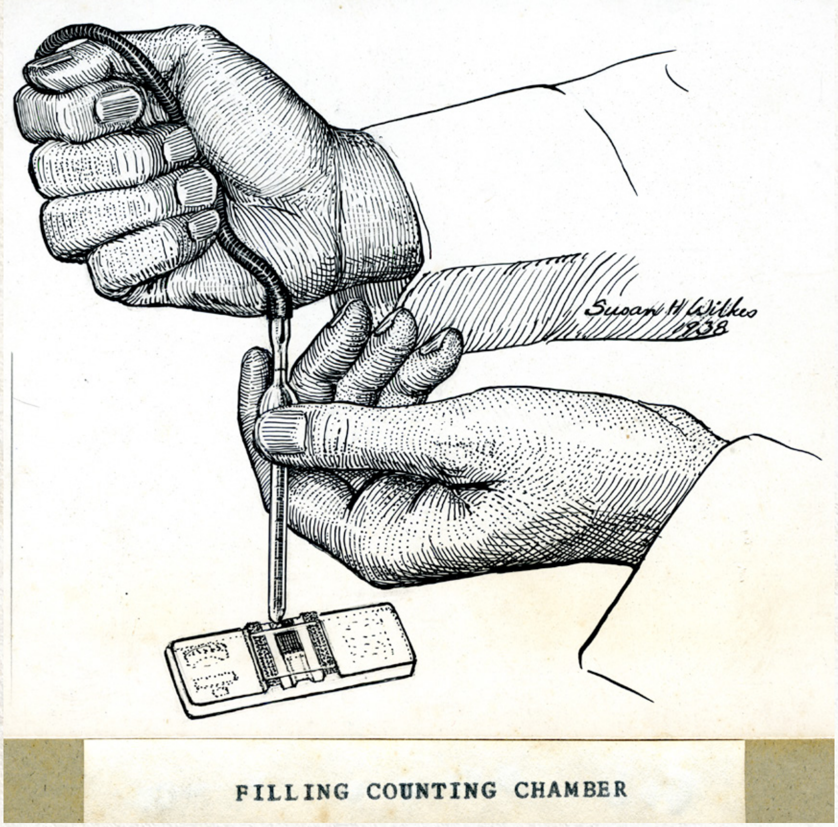
Susan Heiskell Wilkes, trained by the founder of the field of medical illustration, **Max Brodel**, was hired in 1925 by **Dr. Canby Robinson** to head the first medical illustration department at Vanderbilt University Medical Center. Wilkes, in turn, trained **Robert Vantrease** and worked with him to visually represent medical and anatomical subjects with accuracy and detail. As medical illustrators, they employed their artistic skills and anatomical knowledge to create illustrations, diagrams, and visual aids that enhanced comprehension, aided in diagnosis, explained surgical procedures, and facilitated student and patient education.

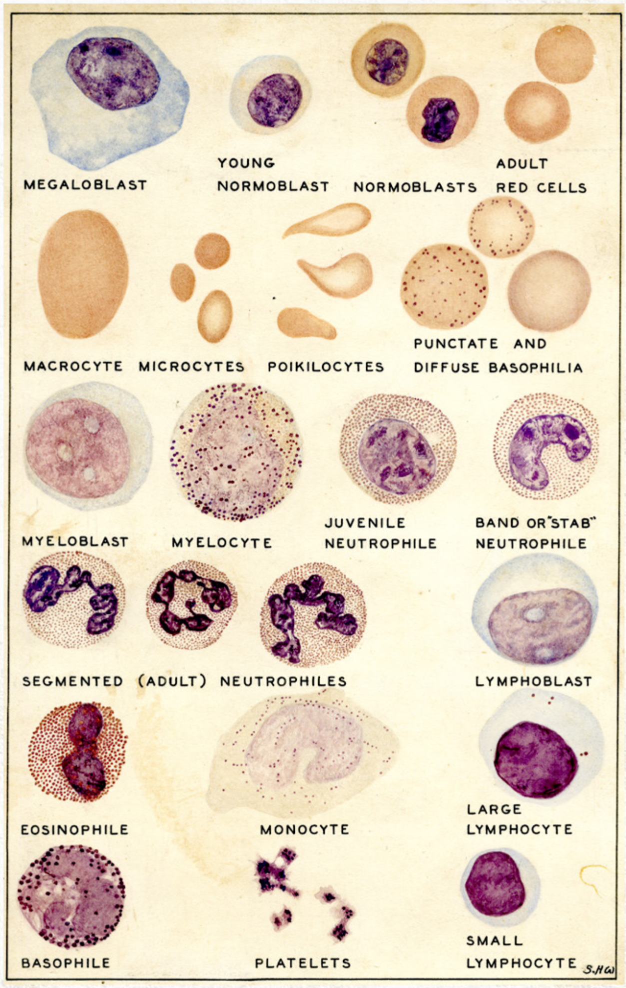
The art of science visualization has been a vital component of the success of biomedical innovation at Vanderbilt. Visuals possess emotional and intellectual power, essential for effective scientific communication across diverse audiences and purposes. Emotionally, visuals can evoke curiosity, empathy, and a sense of wonder, fostering engagement and connection with scientific information. Intellectually, visuals simplify complex concepts, facilitate comprehension, and enhance retention, enabling effective communication of scientific ideas to individuals with varying levels of expertise. These are some of the reasons why the ArtLab and Vanderbilt Institute for Infection, Immunology and Inflammation's Artist-in-Residence program has been so successful.

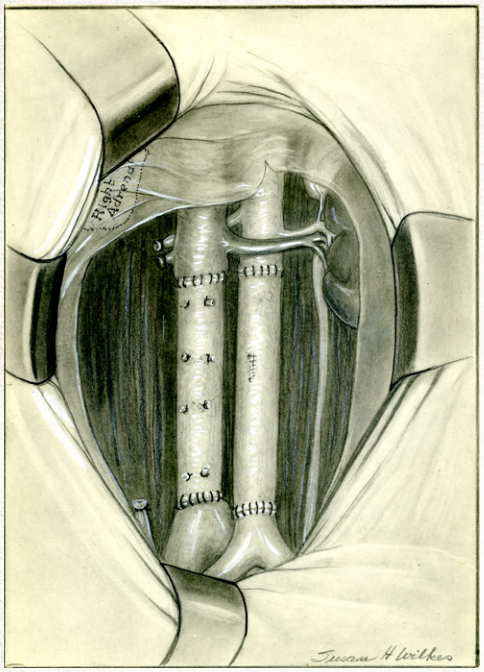
As the Basic Sciences transdisciplinary space, ArtLab, founded and directed by Associate Professor of Pharmacology **Kendra H. Oliver**, has fostered collaboration between art and science since 2017. Serving as an experimental platform where scientists, artists, and researchers come together to explore new ways of understanding and interpreting the world, ArtLab has fomented the creation of multiple transdisciplinary programs. The VI4 Artist-in-Residence program, co-led by **Eric Skaar**, professor of pathology, microbiology and immunology, with internal support and external funding from the Burroughs Wellcome Fund, has brought together artists and scientists to question and discuss the latest research through visual science communication. Art-science collaborations have yielded extraordinary results, contributing to academic discourse, public engagement, and the breakdown of traditional academic silos by encouraging innovative ways of thinking.

Technology integration, new artistic mediums, visualizations, and communication will likely continue to be criteria for success in biomedical innovation. ■

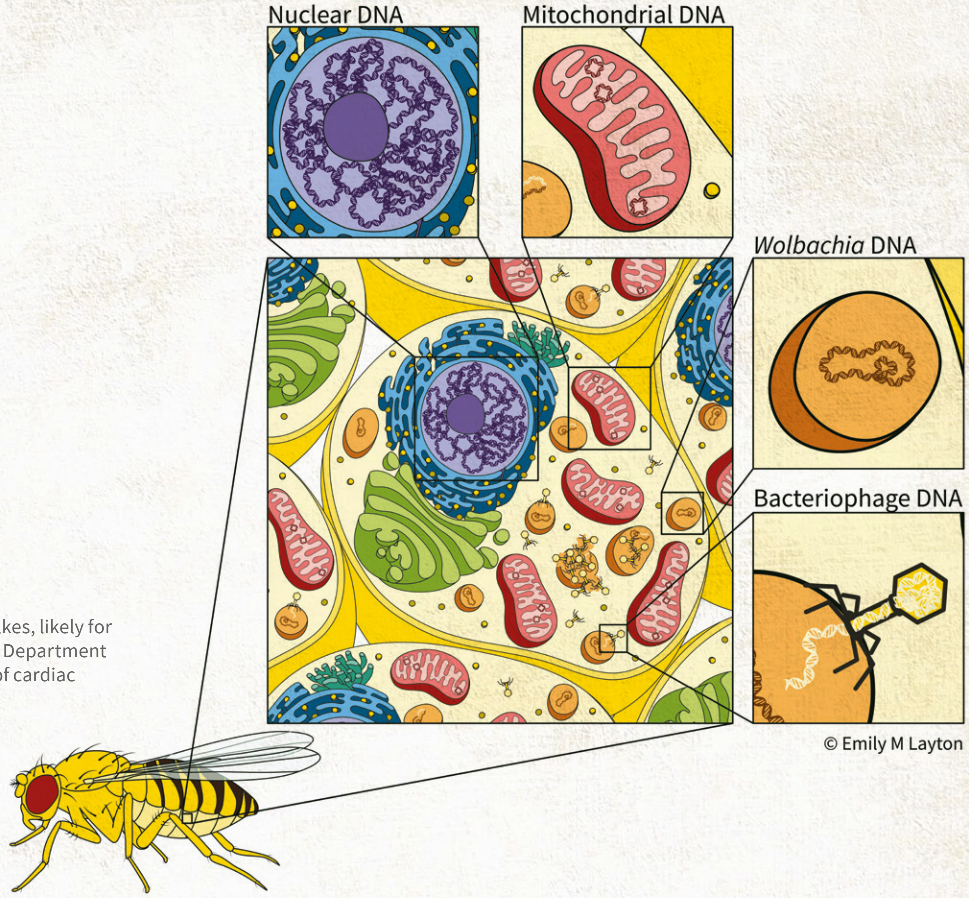
The illustrations below drawn by Susan Wilkes, are part of a series created for John B. Youmans, a Vanderbilt professor and dean of medicine in the 1950s. They were produced for the publication "Essentials of the Diagnostic Examination."







The above image of a surgical procedure was created by Susan Wilkes, likely for a talk or presentation by Dr. H. William Scott, who was chair of the Department of Surgery in the 1950s. According to Dr. Walter Merrill, professor of cardiac medicine and chief of staff of the Vanderbilt University Hospital, "this illustration appears to show that the right adrenal gland and the right kidney have been removed. The stump of the right ureter is just seen towards the bottom of the incision. Both the inferior vena cava and the inferior abdominal aorta appear to have been replaced with some sort of conduit, perhaps an aortic allograft in both cases." An alternative interpretation, by Dr. Ken Sharp, professor of surgery, suggests that this illustration shows a "pretty radical resection for a large right adrenal tumor, including resection of the [vena] cava and aorta!"

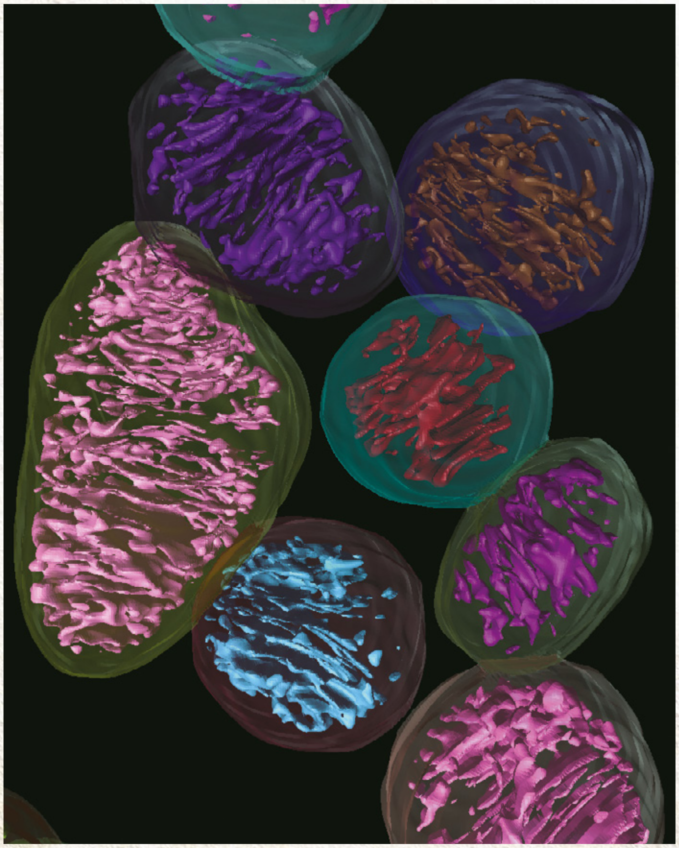


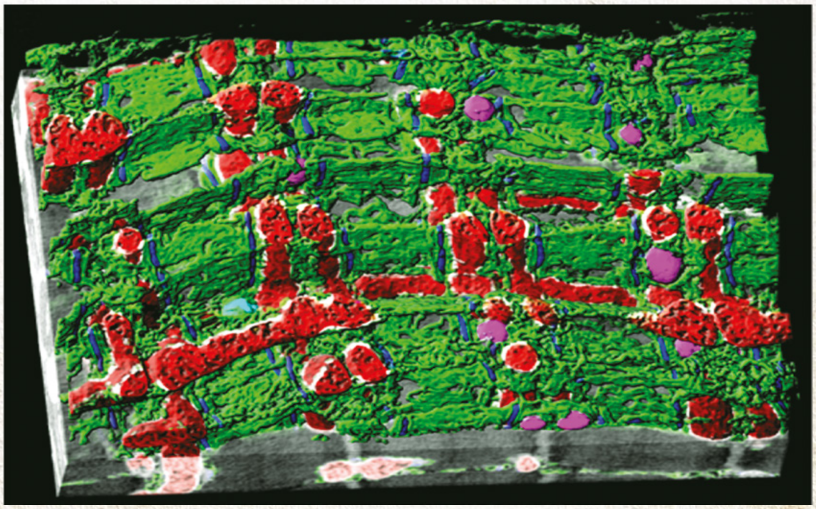
© Emily M Layton

Above: This figure was created by Emily Layton, BS'20, an ArtLab Artist-in-Residence between 2018 and 2022, for the *Wolbachia* Project, an educational outreach initiative designed to give students hands-on research experience. The figure shows a fly and its possible four sources of DNA: 1) its own nuclear DNA, 2) its own mitochondrial DNA, 3) DNA from *Wolbachia*, a widespread bacteria that prevents the replication and transmission of viruses, and 4) DNA from bacteriophages, viruses that infect bacteria such as *Wolbachia*.

Left: Mitochondria have two membranes: a smoother, outer one and an inner one with a lot of folds and creases called cristae. This image, a 3D reconstruction of cristae from brown adipose tissue, was created by the lab of Antentor Hinton Jr., assistant professor of molecular physiology and biophysics.

Below: This image—also generated by the Hinton lab—was created using a variety of techniques, including transmission electron microscopy and focused-ion beam scanning electron microscopy. It shows mitochondria–ER contacts or MERCs, junctions between the mitochondria and another organelle called the endoplasmic reticulum. Mitochondria are shown in red, actin in blue, lysosomes in pink, lipid droplets in teal, MERCs in white, and the ER in green.





Spotlight:

Barrier breakers

By Jennifer Welsh

By putting one foot in front of another, these trailblazers have changed Vanderbilt—and the world—with their dedication to basic research and breaking down barriers for themselves and others.

These 10 scientists have blazed new paths through Vanderbilt's basic sciences departments, even before the establishment of the school itself. Their influence has ricocheted throughout the university, setting a diverse and excellent example for their peers.

Ann Minot

In 1926 Minot joined Vanderbilt as a research assistant in the Department of Pharmacology, but she shifted departments throughout her career. She became the first female full professor in a Vanderbilt basic sciences department—biochemistry—in 1951. Minot directed the Clinical Chemistry Laboratory at Vanderbilt and established and operated the university's first blood bank.

VANDERBILT UNIVERSITY

Her research interests included hookworm, vitamin deficiency in children, muscular dystrophy, and other aspects of the pathophysiology of disease. She was widely respected and was a skillful and highly effective teacher. She died in 1980.

Masakazu Shiota

Shiota joined Vanderbilt in 1994 as a postdoctoral fellow studying the role of glucokinase in the regulation of hepatic glucose metabolism and its deterioration in obesity and diabetes. He led his own lab as an associate professor in the molecular physiology and biophysics department for several decades and now works part time as a research associate professor.

COURTESY OF MASAKAZU SHIOTA

Shiota created crucial surgical techniques and instruments that propelled the Vanderbilt Mouse Metabolic Phenotyping Center to the forefront of metabolism research, leading to almost 1,000 published papers authored with Vanderbilt researchers and worldwide collaborators. A key apparatus he developed is now referred to as "the Masa" in his honor.

Susan Wente

Wente joined Vanderbilt in 2002 as the first female chair of the cell and developmental biology department. She rose in the institutional ranks during her pathbreaking, 19-year career at Vanderbilt, becoming the first woman to lead the university as interim chancellor and the first woman and first life scientist to serve as its provost.

JOHN RUSSELL

During her time at Vanderbilt, Wente worked to advance opportunities for women across the university and advocated for equity and inclusion in academic affairs. She left Vanderbilt in 2021 to become the first female president of Wake Forest University.

Wente's research focuses on the nuclear pores that help move proteins and RNA between the nucleus and cytoplasm. She has personally mentored several dozen predoctoral and postdoctoral trainees.

Linda Sealy

Sealy joined the Vanderbilt faculty in 1986 and attained tenure in 1993. She spent decades highlighting and repairing disparities in Ph.D. attainment and co-directed Vanderbilt's Initiative for Maximizing Student Development (originally "Diversity") with **Roger Chalkley**, the former senior associate dean of biomedical research education and training, since its inception as a postbac program in 2002. In 2017 she became associate dean for diversity, equity, and inclusion for Basic Sciences until she was awarded emerita status in 2020.

JOHN RUSSELL

Sealy mentored more than 150 underrepresented minority students. Under her watch, Vanderbilt became one of the top producers of Black Ph.D.'s in biological and biomedical sciences in the country. Sealy, a citizen of Chickasaw Nation, is herself part of a minority underrepresented in science.

Her research focused, in part, on identifying changes that lead to metastatic breast cancer.

Imogene Phelps Earle

Earle was the first recorded biochemistry program graduate student at Vanderbilt. She got her M.S. and Ph.D. in 1927 and 1929, respectively. She and **Howard West Robinson** made up the first cohort of doctoral biochemistry graduates. As a student, she worked with **Glen Cullen**, the first professor and chairman of the biochemistry department, and studied how pH and carbon dioxide levels vary in the liquid portion of the blood of healthy people. She later

NASHVILLE BANNER

worked for the U.S. Department of Agriculture and developed a lighter formulation of food rations for horses deployed in World War II, helping to maximize cargo space.

Vivien Casagrande

Casagrande's first paper—published when she was a graduate student—landed in *Science*. That paper started a long history of influential research. She joined Vanderbilt in 1975 and became a full professor in 1986.

STEVE GREEN

Casagrande was known internationally for her contributions to visual neuroscience. Her work helped explain the organization and evolution of the brain's sensory systems. She found clues to the evolution of the visual system and added greatly to understanding brain development and plasticity.

Casagrande, who died in 2017, strongly advocated for increasing the representation of women in the Department of Cell and Developmental Biology and was instrumental in bringing key female faculty on board. The Vanderbilt Brain Institute holds an annual Vivien Casagrande Lecture in Systems Neuroscience in her memory.

Michael Fant

Fant graduated from MIT in 1973 with an S.B. in biology followed by an M.D./Ph.D. from Vanderbilt in 1980. He was Vanderbilt's first Black M.D./Ph.D. and first Black Ph.D. in a biomedical science department (biochemistry).

NATIONAL MEDICAL FELLOWSHIPS

During this time, he worked to improve the enrollment and support structure for minority students at the medical school.

After graduating, Fant specialized in clinical neonatology and conducted basic research on placental growth regulation. Fant retired in 2019 as professor emeritus at the University of South Florida-Morsani College of Medicine.

Lee Limbird

Limbird joined the Department of Pharmacology in 1979. By 1991 she was the first female chair of the department and of Basic Sciences. Under her guidance, the department became one of the top pharmacology departments in the country based on funding, graduate training, and research publication impact. She retired from Vanderbilt after 25 years to pursue her passion for mentoring minoritized scientists, first at Meharry Medical College and now at Fisk University.

ANNE RAYNER

She and her trainees have been recognized for their discoveries of how a type of cell receptor for adrenaline in the nervous system controls blood pressure, sedation, pain suppression, and sensitivity to opioid drug action, a prelude to the strategic design of new therapeutic interventions.

Antentor Othrell Hinton Jr.

Hinton's lab uses 3D electron microscopy to reveal mitochondrial structural roles in diabetes and cardiovascular disease. In addition to being a renowned mitochondrial researcher, Hinton is also a national leader in diversity, equity, inclusion, mentoring, and career development in the biomedical sciences. The second Black faculty member in Basic Sciences, he has guided more than 85 mentees directly and shadow-mentored more than 500. He has championed inclusion through more than 160 speeches, *STEM Tea* podcast episodes, mentions and features in articles in popular news outlets such as *Forbes* and CBS News, and articles in leading journals such as *Nature* and *Cell*.

VANDERBILT UNIVERSITY

Jennifer Pietenpol

Pietenpol was in the first graduate class of the cell biology department (now cell and developmental biology), earning her Ph.D. in 1990. She returned to Vanderbilt to the Department of Biochemistry in 1994, achieving the rank of full professor in 2002.

VANDERBILT UNIVERSITY

Throughout her career, she has been appointed to top researcher and administrator roles, including director of the Vanderbilt-Ingram Cancer Center, member of the National Cancer Advisory Board, a chief scientific advisor for the nonprofit breast cancer organization Susan G. Komen, and chief scientific and strategy officer at the Vanderbilt University Medical Center.

Her primary research interests include triple-negative breast cancer and the p53 gene. During her tenure at Vanderbilt, she has trained more than 60 scientists and students, including more than 25 early-career faculty members.

We are so glad you joined us on our journey through Basic Sciences history.
Read on to learn more about the latest work and developments from our community!

WHAT'S NEW IN SCIENCE?

ADOBE STOCK

DNA replication discovery opens pathways to understanding and treating cancer, aging, and degenerative disease

A team of international researchers, led by **David Cortez**, Richard N. Armstrong, Ph.D. Chair for Innovation in Biochemistry, delved into how cells handle DNA damage and genome instability in a recent paper published in *Science*, unearthing groundbreaking findings with implications for cancer and disease treatments.

When cells divide, they need to copy their DNA so that both resulting cells have a complete set of genetic information. This copying process occurs at a site called the replication fork, where the DNA double helix unwinds.

First author: Wenpeng Liu, postdoctoral fellow

Sometimes, DNA replication encounters obstacles such as damage induced by environmental toxins, which may lead to mutations that can cause cancer. In response to these replication obstacles, cells employ a strategy called "replication fork reversal." During this process, the replication fork pauses and then moves backward, a move that is accompanied by the annealing of the two daughter DNA strands. Fork reversal safeguards the genome by increasing tolerance to the replication obstacles, allowing for accurate DNA repair.

Understanding this process is crucial because it sheds light on how cells can accurately copy their DNA without introducing errors that can lead to diseases like cancer.

Led by **Wenpeng Liu**, a postdoctoral fellow, the team discovered a mechanism that relies on a protein called RAD51. This mechanism allows cells to successfully carry out DNA reversal while dealing with replication stress. The discovery not only completely changes our understanding of how fork reversal works but also solves a mystery that has puzzled researchers for years about how this beneficial process is compatible with the current understanding of replication.

By gaining a deeper understanding of DNA replication, scientists can lay the groundwork for addressing abnormalities that underlie various diseases, and this line of research offers promising avenues for developing more effective therapies.

Other collaborators on the paradigm-shifting research included **Alessandro Vindigni** at Washington University in St. Louis and **Masato Kanemak**i at the National Institute of Genetics in Japan.
— **Marissa Shapiro**

***Liu, W.**, Saito, Y., Jackson, J., Bhowmick, R., Kanemaki, M.T., Vindigni, A., Cortez, D. (2023). RAD51 bypasses the CMG helicase to promote replication fork reversal.* Science*, 380(6643), 382-387. https://doi.org/10.1126/science.add7328.*

New drug type may reduce opioid addiction but keep its pain relief properties

Researchers at the Warren Center for Neuroscience Drug Discovery have found that selective blocking of the M5 muscarinic acetylcholine receptor—referred to as mAChR—can influence behaviors during the opioid addiction process without negative impacts to motor function, motivation, or opioid-mediated analgesia—pain relief—in rats. This recent work, led by **Carrie Jones**, director of in vivo pharmacology and development for the WCNDD and associate professor of pharmacology, and **Laura Teal**, graduate student in the Jones lab, could provide a new solution to the prevalent problems of opioid misuse and opioid use disorder around the world.

Opioids, such as morphine, fentanyl, and oxycodone, are commonly prescribed to patients to treat pain and are one of the most prescribed drug classes around the world. However, opioid analgesics can be extremely addictive, and the drugs' continuous use can lead to OUD, among other health issues, and even death due to overdose. According to the Centers for Disease Control and Prevention, there were almost 70,000 opioid-related overdose deaths in 2020, and the rate of these deaths increased by almost 40 percent from 2019 to 2020.

Jones and her colleague **Craig Lindsley**, executive director of the WCNDD, have been looking for new targets, such as the M5 mAChR, that can diminish the addictive effects of opioid analgesics while still retaining their pain-relieving effects in patients. Together, they have discovered several M5 selective negative allosteric modulators, including VU6008667, the NAM investigated in this study.

In their article, Jones and Teal explored VU6008667 administration in rats to better understand how it affected addiction behaviors, including acquisition, withdrawal, and relapse of oxycodone drug seeking. For the first time, they say, they found that selective blocking of the M5 mAChR subtype lessens oxycodone-seeking behavior in opioid-naive rats over a period of 21 days using M5 NAM VU6008667.

First author: Laura Teal, recent Ph.D. graduate

In addition, the acute and chronic administration of VU6008667 had little to no effect on rats' motivation, motor function, or cognition, and it did not influence withdrawal. Most importantly, VU6008667 did not affect oxycodone-induced analgesia. According to the authors, their results indicate that selective M5 NAMs offer a promising way to prevent opioid misuse and relapse of OUD without unfavorable effects and without altering opioid-induced pain relief. — **Alexandra Scammell**

***Teal, L.B.**, Bubser, M., Duncan, E., Gould. R.W., Lindsley, C.W., Jones, C.K. (2023). Selective M5 muscarinic acetylcholine receptor negative allosteric modulator VU6008667 blocks acquisition of opioid self-administration.* Neuropharmacology. *2023;227:109424. https://doi.org/10.1016/j.*

Using fluorescence endoscopy to detect colonic adenomas

Detecting adenomas by colonoscopy remains one of the main preventative measures for colorectal cancer, with almost 100,000 adenomas identified during first-time screenings per year in the U.S. Unfortunately, using white-light colonoscopy—the clinical standard—without probing for a particular molecular marker of adenomas can lead to 30% of lesions going undetected.

First author: Jashim Uddin, research associate professor

Md. Jashim Uddin, research associate professor of biochemistry, **Larry Marnett**, Mary Geddes Stahlman Professor of Cancer Research and university distinguished professor of biochemistry, and colleagues chose to use cyclooxygenase-2 or COX-2, an enzyme that increases inflammation and that is upregulated in preneoplastic lesions and colorectal cancer, as the marker to target when developing a fluorescent imaging agent to improve adenoma detection.

This work, reported in the *Journal of Biomedical Optics*, signifies an advance in adenoma detection by colonoscopy, which could reduce the number of colorectal cancer cases considering that adenomas, precursor lesions, can be removed during colonoscopies.

In 2010, the researchers discovered a fluorescent inhibitor of COX-2 called fluorocoxib A; it was the first COX-2-targeted molecular imaging agent for the in vivo fluorescence imaging of inflammation and cancer and has since been widely used in research in the U.S. and across the globe. Now, the authors sought to forge a path to the clinic and packaged fluorocoxib A into an FDA-approved polymer to improve delivery to the adenomas.

Uddin and colleagues administered fluorocoxib A to mice before a colonoscopy, which allowed them to clearly identify colonic adenomas in mice containing elevated levels of COX-2 in the lesions. The colon tissues of normal mice were not illuminated with the fluorescent compound, indicative of the lack of lesions. Pre-dosing the mice with a non-fluorescent inhibitor of COX-2 or with a fluorescent molecule that does not inhibit COX-2 led to minimal labeling of adenomas.

Packaging the COX-2 inhibitor in the FDA-approved polymer creates a tractable path for clinical trials that could ultimately impact adenoma detection for the millions who undergo colonoscopies every year across the country. — **By Sarah E. Glass**

***Uddin, M.J.**, Niitsu, H., Coffey, R.J., Marnett, L.J. (2023). Development of Pluronic nanoparticles of fluorocoxib A for endoscopic fluorescence imaging of colonic adenomas.* J Biomed Opt. *2023;28(4):040501. https://doi.org/10.1117/1.*

WHAT'S NEW IN SCIENCE?

ADOBE STOCK

Their new method, called Structured Tracking of Alcohol Reinforcement or STAR, provides a quantitative framework for assessing alcohol drinking behaviors in animals.

A new framework synergizes basic and translational alcohol use research

Consumption of alcohol is popular worldwide due to its euphoric effects. However, the abuse of alcohol is also a global problem, resulting in around three million deaths each year. In the United States alone, nearly 30 million people suffered from alcohol use disorder in 2020, according to the 2021 National Survey on Drug Use and Health.

Cody A. Siciliano, assistant professor of pharmacology, and **Alex R. Brown**, former lab manager of the Siciliano lab, and other members of the Vanderbilt Center for Addiction Research have designed a novel method of tracking alcohol reinforcement that addresses the ongoing difficulty of integrating basic and translational alcohol research. This flexible framework can aid in the eventual development of therapeutic interventions for AUD.

First author: Alex Brown, former lab manager

Significant research effort is devoted to understanding how alcohol acts on the brain and body using nonhuman model species. These efforts span a wide range of disciplines, from biochemistry and toxicology to neuroscience and psychology, and represent both basic and translational research questions. Despite the diversity of alcohol research, little effort is put toward integrating findings from different subfields, even as these lines of research often exist in parallel. For example, basic research into how alcohol binds to certain receptors may use non-overlapping terminology with translational research aimed at testing whether pharmacotherapeutics targeted to certain receptors decrease alcohol consumption. The lack of synergistic frameworks for understanding and reporting alcohol's effects undoubtedly account for a number of missed opportunities and breakthrough discoveries.

In answer to these challenges, the VCAR scientists created a better method to ease collaboration between basic and translational AUD researchers. As explained by the study authors, "basic investigations require flexibility of experimental design as hypotheses are rapidly tested and revised, whereas preclinical [translational] models emphasize standardized protocols and specific outcome measures."

Their new method, called Structured Tracking of Alcohol Reinforcement or STAR, provides a quantitative framework for assessing alcohol drinking behaviors in animals. STAR uses a phenotyping analysis to group subjects into "low drinker," "high drinker," and "compulsive drinker" categories based on differences in alcohol intake and their tendencies to continue to consume alcohol even when drinking was punished with a negative outcome (in this case, the punishment was adding quinine to the alcohol, which gives it a bitter taste and causes most mice, but not all, to reduce their drinking).

Once categorized, STAR imposes minimal constraints on experimental design, allowing for researchers to make alterations as needed for specific questions. Importantly, the authors show that once mice have established their preferences for alcohol, they remain in the same drinking category over several months of repeated testing. Thus, by reporting findings within this framework, researchers can retain conceptual continuity without sacrificing experimental flexibility. By bridging subfields, the STAR framework promises to synergize efforts across diverse areas of alcohol research. — **Alexandra Scammell**

***Brown, A.R.**, Branthwaite, H.E., Farahbakhsh, Z.Z., Mukerjee, S., Melugin, P.R., Song, K., Noamany, H., Siciliano, C.A. (2023). Structured tracking of alcohol reinforcement (STAR) for basic and translational alcohol research.* Molecular Psychiatry, *28, 1585–1598. https://doi.org/10.1038/s41380-023-01994-4.*

Vanderbilt biochemists join international researchers in discovery of the first new antibiotic for urinary tract infections in more than 20 years

By Marissa Shapiro

Neil Osheroff, professor of biochemistry and medicine, is part of an international research collaboration resulting in what is on track to be the first new antibiotic treatment for uncomplicated urinary tract infections or uUTIs in more than 20 years.

"We now have a direct path connecting the work conducted in our lab to improving human health," said Osheroff, who holds the John Coniglio Chair in Biochemistry. "A new antibiotic will come on the market and be used by people who have serious infections, in part because of what we did in this lab. To be able to say we are one of the lead research groups working on this is why I am at Vanderbilt and why I am a biochemist."

The antibiotic, gepotidacin, completed enrollment in phase III trials ahead of schedule based on an analysis of its efficacy and safety.

GSK, the global biopharma company conducting the trials, is working with the Food and Drug Administration on a new drug application for the antibiotic. Gepotidacin inhibits bacterial DNA replication by a distinct mechanism of action determined by Osheroff's lab that is foundational to GSK's FDA application.

"Uncomplicated urinary tract infections are the most common outpatient infection with over half of all women developing a uUTI during their lifetime and more than a quarter of women suffering from recurrent uUTIs," said Chris Corsico, senior vice president and head of development at GSK. "There has been no new class of oral antibiotics for uUTI for over 20 years. With the number of uUTIs caused by [resistant] bacteria increasing, new antibiotic treatments are necessary."

Current antibiotics like Cipro (ciprofloxacin) are within a drug type called fluoroquinolones, some of the most widely prescribed antibacterials in the world.

"The problem with fluoroquinolones is that we're seeing antibacterial resistance, including specific mutations within enzymes, that makes the drug not interact with infection the way we want," Osheroff said.

Fluoroquinolones affect two enzymes, but only one mutation in the bacterial DNA can be enough to cause antibiotic resistance. Gepotidacin targets two enzymes that share responsibility in attacking bacterial DNA. This means that bacteria would have to mutate at two spots at exactly the same time to become resistant to this new antibiotic.

"Antibacterial resistance is significantly more difficult with this approach," Osheroff said.

Osheroff, along with former graduate student and current senior research investigator at Bristol Myers Squibb **Elizabeth Gibson**, and postdoctoral researcher **Alexandria Oviatt**, successfully worked to target the two enzymes that attack bacterial cells.

"Our work in the Osheroff lab becomes even more impactful knowing it can help a new oral antibacterial class come to market," Gibson said. "During my pharmacy training, it wasn't uncommon to see patients come back to the pharmacy week after week to fill a new antibacterial prescription to find one to clear up an infection (especially UTIs). Knowing a part of my graduate school work played a small part in combating antimicrobial resistance, a world-wide problem, continues to motivate my work in drug development to help improve patient quality of life."

The age of aging research

By Eric Butterman


ADOBE STOCK

From age-related diseases to understanding the interventions that extend lifespan, Vanderbilt University scientists grow their focus on aging research to improve quality of life.

Aging is unavoidable. In fact, you just aged while reading that sentence. Although aging is a pillar of life, much about it is unknown. At the Vanderbilt University School of Medicine Basic Sciences, researchers including **Kris Burkewitz**, assistant professor of cell and developmental biology, are taking on the challenge of unraveling one of life's greatest mysteries, focusing on ways to improve quality of life as we get older.

Burkewitz says there are many ways to study the aging process. "Historically, research has focused on the specific diseases that arise primarily in older age. These include problems like neurodegeneration, heart disease, and forms of cancer," he said. "On the other hand, a newer approach called geroscience focuses on the aging process itself: the molecular and cellular events that define the transition from youth to old age, because these are the events that drive all those various age-related diseases." The aim is to learn how to target specific aging processes that result in the increased risk for these broad diseases so a therapeutic can be created to provide broad spectrum protection against several or many of these ailments all at once.

Invertebrate models have become the engines of discovery in the aging field because they allow mapping and manipulation of the genes that impact the aging process. Part of Burkewitz's work focuses on studying the aging process in a species of nematodes known as *C. elegans*. These invertebrates can help determine whether a particular intervention has the potential to extend lifespan or healthspan in an animal system because though they age much more rapidly than humans, they go through many of the same processes.

When looking at how aging occurs, there are many ways to go about it. According to Burkewitz, "one involves mapping out all of the changes that are different between an old animal and a young animal." However, this method comes with challenges because there are an incredibly large number of changes that occur, "and not all of those changes are things that we think are driving the aging process," he said.

Take gray hair, for example.

It correlates with the change from youth to older age, he said. "But our graying hair is not what causes heart disease rates to go up, and reverting it back to its youthful color won't cure our heart disease either." The goal is to go to the roots of age-related disease and identify which molecular and cellular changes are causal to the aging process of the whole animal. "That's the real challenge," he said.

Another part of Burkewitz's research focuses on understanding the interventions we already possess that extend lifespan. Dietary restriction is a key example that he has studied. When dietary intake is reduced to a level that doesn't cause malnutrition, it can extend lifespan and protect against diverse age-related diseases in many models, including primates. But these dietary interventions tend to be rather severe, causing quality of life issues in addition to undesirable physiological side effects. That is why the search is on for ways to "mimic the benefits of dietary restriction, but pharmacologically, without such a profound lifestyle change."

A big focus of the aging field is an organelle known as the mitochondrion. Mitochondria play many roles in the body, including providing much of the energy and molecular building blocks of cells, and they have captured their share of Vanderbilt researchers' attention as they relate to age.

For example, **Jason MacGurn**, associate professor of cell and developmental biology, is looking into mitochondrial roles in aging in yeast. **Antentor Hinton Jr.**, assistant professor of molecular physiology and biophysics, is mapping how mitochondrial structures change in mammalian systems as they age.

Vanderbilt's aging research is aging well, Burkewitz said. He has seen strong growth in this area at the school in the past several years and is enthusiastic when it comes to its future.

"I think it is a really exciting area of biology generally, and also one of the exciting newer areas of biomedical science as we continue to find ways to translate our research into improvements in human health," he said. "It has a chance to become even more of a strength here with our nucleus of researchers."

Understanding and treating addiction—with science

By Ilima Loomis

For years, people thought of dopamine as the “reward molecule,” fueling cravings for drugs and other substances by giving users a hit of pleasure. But recent studies by Vanderbilt Center for Addiction Research investigators, such as **Erin Calipari**, assistant professor of pharmacology and VCAR director, have challenged that assumption.

“What my work has shown is that it’s not really a reward signal,” she said. “It responds to anything important in the environment, and it helps us learn. If you put your hand on a hot stove, that would also increase dopamine.”

The finding has major implications for drug addiction and treatment because it shows how dopamine triggered by drug use helps people learn drug-taking behaviors that become deeply ingrained. Conversely, when people stop taking drugs and dopamine drops, learning to change those behaviors becomes much, much harder.

It’s the kind of research that **Danny Winder**, now chair of the Department of Neurobiology at UMass Chan Medical School, hoped to see when he launched VCAR in 2016. Vanderbilt was already known for its addiction research, he said, and the combination of the surging opioid crisis—which increased public interest in addiction research—and a renaissance in technologies for studying and manipulating the brain made the timing uniquely right. Winder hoped that the center would foster greater collaboration among Vanderbilt researchers, while also attracting new stars—one of the first of which was Calipari.

One approach that sets the center apart is its innovative use of technology, he said. While recent years have seen an explosion of new capabilities for studying the brain in minute detail, those technologies have mainly been applied to studying conditions like Alzheimer’s disease, Parkinson’s, and other neurodegenerative diseases, he said—not addiction.

“We’re known for implementing cutting-edge technology with substance use disorder questions, which is pretty unique,” said Winder, who was the founding director of VCAR.

Another strength of the center is the opportunity it creates for collaborations, he said, especially between animal and human researchers. This allows scientists to take discoveries they make in the lab and fast-track them toward applications that can be used in human medicine.

“There’s always the challenge in preclinical research: You’re climbing up a mountain, but is it the right mountain?” he said. “We have awesome opportunities at Vanderbilt not only to climb the right mountain, but to work with entities like the Warren Center for Neuroscience Drug Discovery to move something forward into actual clinical trials without ever having to leave campus to do that.”

In 2023, VCAR joined the cadre of research centers funded by the Discovery Vanderbilt portfolio, an initiative of the Office of the Provost and one of three pathways in the university’s Dare to Grow campaign, established to support and extend the resources underpinning Vanderbilt’s most innovative research and education.

One area of exciting new research in the center has focused on understanding how abstinence impacts the brain. Researchers already knew that it is common for people in recovery to develop symptoms of anxiety and depression after they stop using substances—and this distress often contributes to relapse.

In a mouse study, Vanderbilt researchers took a closer look at the circuits of the brain involved in anxiety and depression and what happened when animals that had previously been given alcohol had the alcohol removed.

“They found that if we intervene in the first few days of abstinence, we can prevent the development of anxiety- and depression-like symptoms,” Winder said. “It shows that this might be a particularly important treatment window during the recovery process.”

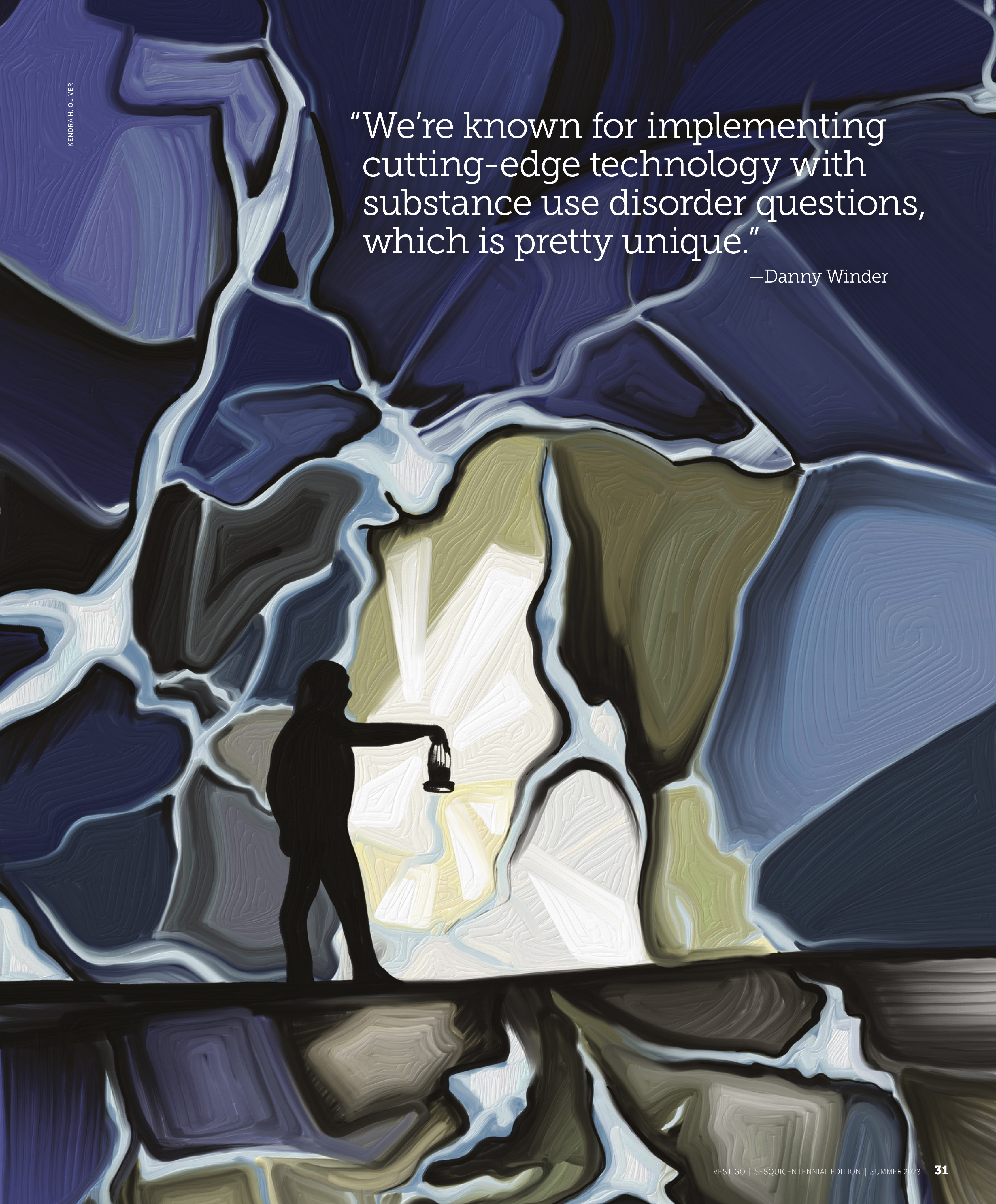
Destigmatizing substance use disorder

In addition to the science, both Winder and Calipari say that destigmatizing substance use disorder motivates their work. Calipari noted that while diseases such as cancer and COVID-19 easily attract resources and public support for study and treatment, addiction medicine has often been left behind.

“With COVID-19, the world recognized so quickly that we needed to solve the problem,” Calipari said. “And the number of deaths it took to get there was a fraction of the addiction deaths each year—it wasn’t even close.”

From nicotine-linked cancers to alcohol-related deaths and the current overdose crisis, addiction is a leading cause of death in the U.S. and results in an enormous public cost. And yet, treating substance use disorder as a moral failing rather than a medical problem has led to the issue being understudied, resulting in a lag in science-based solutions.

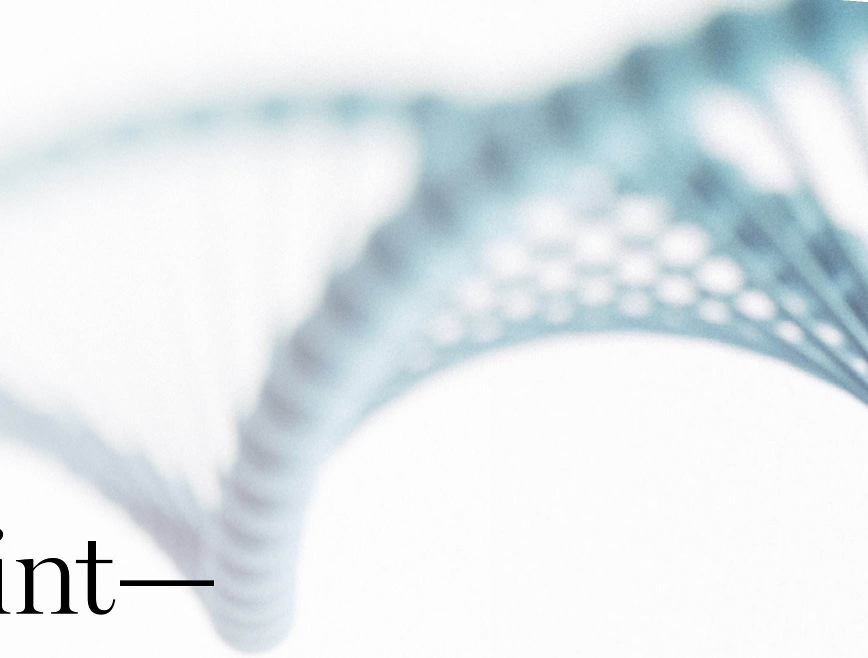
“The problem of addiction leads to a huge public health problem that we walk through on a daily basis, and we don’t really think about it,” Winder said. “We need people to understand that basic science can impact a disease like addiction, just like it can cancer and COVID-19.”



KENDRA H. OLIVER

"We're known for implementing cutting-edge technology with substance use disorder questions, which is pretty unique."

—Danny Winder



DNA is the ultimate blueprint—but epigenetics changes how it's read

By Marissa Shapiro

The human genome is a rich and diverse field of study at which Vanderbilt University and Vanderbilt University Medical Center scientists stand at the forefront. **William Tansey**, professor of cell and developmental biology and biochemistry and co-leader of the Vanderbilt-Ingram Cancer Center Genome Maintenance Program, gives us a bird's-eye view of the field and some of Vanderbilt's research contributions to the space.

What is the discipline of epigenetics and human genome regulation?

In general, the big question that scientists are trying to answer is how genetic information—our DNA and the information encoded in DNA—is used. The basic problem is that every cell in your body has, for the most part, the same DNA content. And we know DNA is the blueprint for life. But we also know that all the cells in our bodies are different: A cell in the iris of our eye is very different from a cell in our liver or a cell from muscle. How can the same blueprint lead to such differences?

For a long time, scientists have been asking questions about how cells achieve such diversity and plasticity even though they're working from the same script. The answer to that question is that cells read different parts of the blueprint depending on what their function is—and the process of reading the blueprint, and different bits of it, is called "gene expression."

The field of gene expression is trying to understand—in very broad terms—the molecular processes that allow the use of the genetic information. Some of the control of gene expression is hard-wired into the DNA sequence. But not all. This is where epigenetics comes in.

Formally speaking, epigenetics—"epi" meaning "above"—is any form of control of gene expression that is above the level of the DNA or that is not encoded directly in the DNA.

It refers to a layer of regulation that has to do with how the genetic material is labeled and packaged. Every cell has about two meters (six feet) of DNA in it, and it exists in huge strands that are folded and wrapped around proteins into structures that layer on top of each other and pack into a sphere that's just a few micrometers in diameter. It's the ultimate storage solution on one hand, but it also means that the cell can control how information is used by packaging or labeling the genetic material in specific ways.

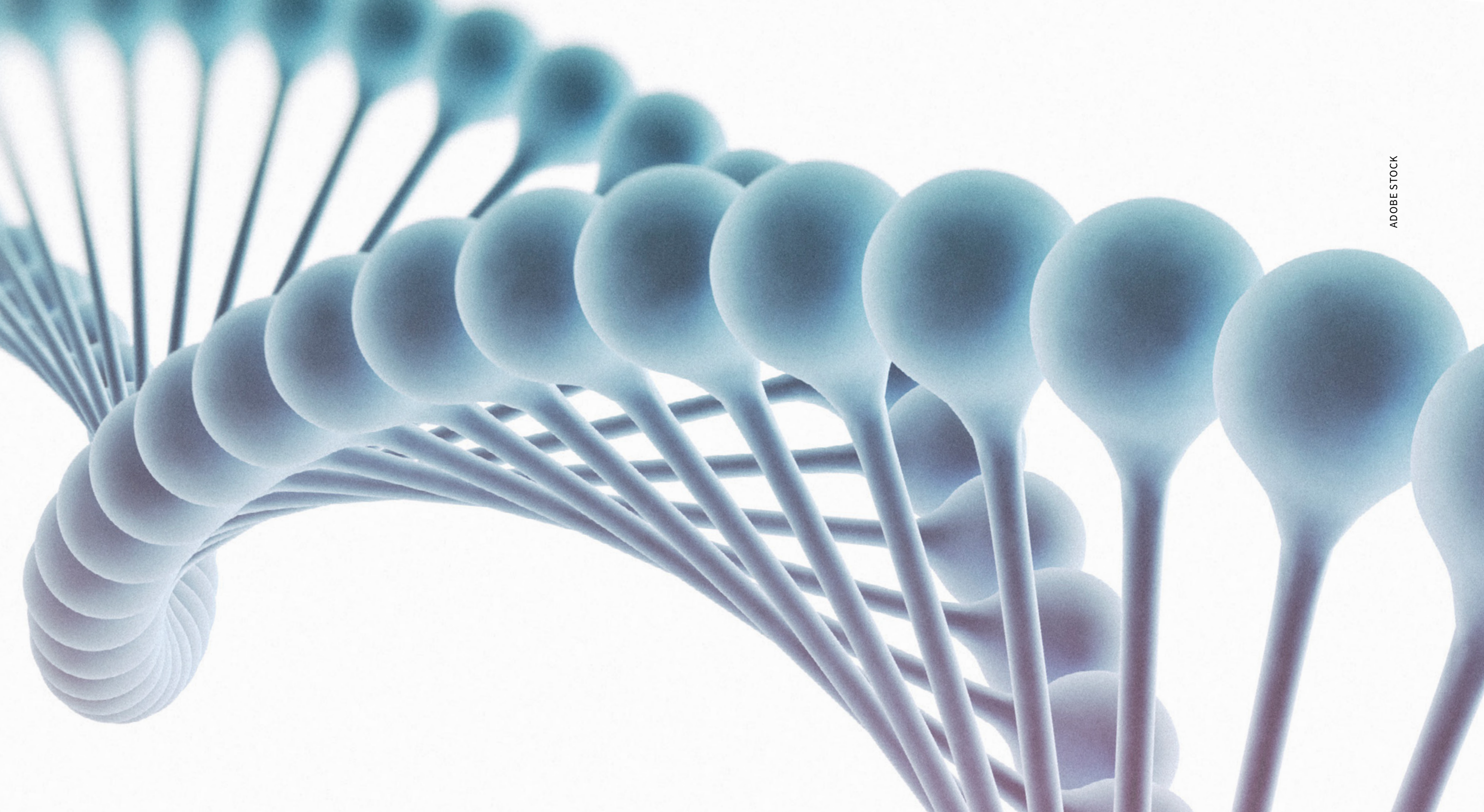
Control of gene expression by this level of packaging and labeling is epigenetics. At a molecular level, it is driven by chemical alterations in the DNA and those proteins it wraps around. Although these chemical alterations don't change the sequence of the DNA, they can very much determine what part of our genome is expressed in a given cell.

How does this fit in the blueprint analogy?

Epigenetics is like someone taking a pencil and crossing something out—or adding something—on a blueprint, saying, "don't make that here, make it over there." And that's a good analogy because, unlike the messages encoded in our DNA sequence, the messages that epigenetics communicate are reversible and changeable. That allows adaptability; genes can be expressed in specific places, at specific times, and in response to specific signals or cues.

How do scientists like yourself work to understand the human genome through epigenetics and gene expression?

The genome, epigenetics, and gene expression are all interconnected because, ultimately, gene expression is all about anything that will impact or control the ability of a cell to express a piece of its genome. Historically, the fields of gene expression and epigenetics were somewhat separate because the mechanisms of epigenetics were not really understood. But in the last two to three decades, that all changed. Now, when we talk about a piece of



ADOBE STOCK

DNA and how that gene is regulated, we have to figure out if it's regulated through DNA sequence, epigenetics, or a combination of both. Usually, it ends up being both.

This field of gene expression is massive—it's one of the oldest fields in molecular biology. Everybody bites off a little piece of the problem. I, for example, study how gene expression goes wrong in cancer by looking at a protein called MYC ("mick"), which alters gene expression and is influenced by epigenetic processes. My interest is in understanding how MYC controls gene expression and using that information to think of ways to stop MYC in cancer. But that's just one sliver of the gene expression and epigenetics fields, and it's just a fraction of gene expression research in Basic Sciences.

How are scientists in Basic Sciences probing gene expression and epigenetics?

We have a number of superb researchers here who work on different aspects of gene expression and epigenetics! My familiarity with our research in this area is mostly from the cancer perspective because I co-lead the Genome Maintenance Research Program, a cancer-focused program made up of 25 investigators working on understanding all aspects of how the genome is packaged, expressed, duplicated, and maintained—and how this can go awry in cancer.

We have amazing strength in this area. And we are attacking the problem from different perspectives. The primary interest of **Emily Hodges**, for example, is understanding DNA methylation, a small chemical modification that can be added to DNA that acts epigenetically to regulate gene activity. **Scott Hiebert** is also interested in gene regulation and epigenetics from the point of view of how aberrant gene expression occurs in leukemias. **Jared Nordman** and **David Cortez**, my GMRP co-leader, work on how epigenetics intersects with DNA replication and repair and maintenance of DNA integrity.

KENDRA H. OLIVER

Vanderbilt launches Center for Applied Artificial Intelligence in Protein Dynamics

By Aaron Conley

JAMIE MCCORMICK

Hassane Mchaourab

"The amazing advances in AI and machine learning that are transforming human communication are also being used to understand and design biological machinery."
—Hassane Mchaourab

The School of Medicine Basic Sciences has launched the Center for Applied Artificial Intelligence in Protein Dynamics, which is focused on the intersection of artificial intelligence, machine learning, and macromolecular mechanism. It is helmed by **Hassane Mchaourab**, who holds the Louise B. McGavock Chair in the Department of Molecular Physiology and Biophysics.

Proteins are one of the most important macromolecules of biology, and they often change shape to carry out their biological functions. To develop therapeutic treatments that work on them, researchers first must understand their three-dimensional structures and how they work in the body. Recent AI algorithms, such as AlphaFold, have revolutionized the field of protein structure prediction and design, representing a first wave of AI-based methods that already are working to provide transformative tools for helping understand protein networks.

"We are living in an exciting time where we have both immense data and computational tools to make discoveries in structural biology at a speed that was inconceivable before," said **John Kuriyan**, dean of Basic Sciences. "Leveraging these emerging tools through the Center of Applied AI in Protein Dynamics, while synergizing with existing expertise across Vanderbilt and Vanderbilt University Medical Center, has the potential for driving breakthroughs that could broadly impact human health."

Recent publications, including some from Mchaourab and **Jens Meiler**, research professor of chemistry, successfully leverage AI methods to capture proteins in the shape-shifting act. These contributions, published in the journals *PNAS, PLOS Computational Biology,* and *eLife*, offer new information on the mechanisms of genetic diseases and expand available approaches to the discovery of therapeutics.

At its outset, the center will recruit experts in AI and machine learning to adapt and create computational approaches to develop an understanding of protein energy landscapes that mediate shape changes; leverage new information to identify new drug candidates more precisely; develop graduate training programs in AI-centric computational protein structure and dynamics; and conduct outreach programs that increase awareness of AI's role in shaping society. The outreach programs will include bringing the latest AI into Nashville schools, especially for students from underrepresented minorities in STEM who may have limited exposure to AI.

The center will include faculty in the protein structure and dynamics subspace of emerging AI technologies. It will train students and postdoctoral fellows affiliated with Basic Sciences, the Data Science Institute, the College of Arts and Science, the School of Engineering, and VUMC.

"We live in a protein-based world. When things go right, they go right because your proteins are working correctly. And when things go wrong, it is usually because something is wrong with one or more of your proteins," said **Charles Sanders**, vice dean of basic sciences, holder of the Aileen M. Lange and Annie Mary Lyle Chair in Cardiovascular Research, and former president of the Protein Society. "This is why 99 percent of all drugs target proteins."

Mchaourab, whose research is focused on illuminating the principles that govern protein dynamics, also founded the Program in the Molecular Basis of Genetic Diseases in collaboration with Meiler and **Tony Capra**, research associate professor of biological sciences. The program, which will be folded into the new center, investigates the links among genetic mutations, protein function, and the way disease itself presents in a patient.

"The amazing advances in AI and machine learning that are transforming human communication are also being used to understand and design biological machinery. We can 'write' with the language of the genetic code," Mchaourab said. "This area of our work in the Center for Applied AI in Protein Dynamics has unlimited possibility to improve human health."

Advancing science and entrepreneurship:

Leasure awarded the second ASPIRE to Innovate Postdoctoral Fellowship

Catherine Leasure, PhD'23, has been awarded the prestigious ASPIRE to Innovate Postdoctoral Fellowship. In her new role, which began on July 1, 2023, she is focusing on forming a start-up company based on technology developed at Vanderbilt University by **Gregor Neuert**, associate professor of molecular physiology and biophysics, that can model the pharmacodynamic profile of drugs.

The ASPIRE to Innovate Postdoctoral Fellowship is a collaborative initiative of the School of Medicine Basic Sciences, the BRET Office of Career Development's ASPIRE Program, and the Center for Technology Transfer and Commercialization that seeks to bridge the gap between academic excellence and entrepreneurial pursuits. Leasure will be supported in her efforts for up to two years, will receive extensive mentorship and supplemental training, and will participate in a variety of networking opportunities. Leasure is the second person to participate in this fellowship, following **Karrie Dudek**, PhD'21, who inaugurated the program in 2021.

"We are thrilled to bring Leasure on this summer as our second ASPIRE to Innovate Postdoctoral Fellow and are excited to watch her learn what it takes to be a founder while advancing entrepreneurial activities in the School of Medicine Basic Sciences," said **Kathy Gould**, senior associate dean for biomedical research education and training. "We have no doubt that she will be successful and will make great strides towards mapping out a commercialization pathway for Dr. Neuert's technology."

Leasure completed her Ph.D. training in Vanderbilt's Microbe-Host Interactions program this past spring, studying heme homeostasis in *Staphylococcus aureus* and host stress sensing in *Bacillus anthracis*. While gaining experience in research and scientific methodology, she has been passionate about applying these skills to projects at the intersection of science and business and is excited about the opportunity to grow her business acumen and strategize how to turn an idea into a company.

"It's an honor to have been selected for this fellowship and to have the opportunity to translate basic science into real-world solutions," Leasure said. "I am excited to have been given this protected time as a postdoc to develop myself as a businesswoman while working to build a viable company."

During her time as a graduate student, Leasure took advantage of numerous opportunities to expand her experiences and understanding of business and entrepreneurship. She finished the ASPIRE Program's Management and Business Principles for Scientists module, served as president of the Graduate Student Association in the Department of Pathology, Microbiology and Immunology, and acquired hands-on experience in the pharmaceutical industry by completing a three-month internship in the Microbial Science division at AstraZeneca.

Leasure hit the ground running, working alongside staff at the CTTC to learn about intellectual property rights, licensing, and market research. She is also spending time with Neuert and his research team to gain familiarity with the technology they want to commercialize. This past fall, Leasure participated in the Ideator program at the Wond'ry and secured microgrant funding after pitching her business idea to a panel of judges. This accomplishment made her eligible to apply for the National Science Foundation's National I-CORPS program, additional entrepreneurial training, and a $50,000 non-dilutive grant to help support further commercialization of the technology. Leasure was accepted into the program and will participate both in I-CORPS and in the Wond'ry's Builder program this spring.

Final deliverables for ASPIRE to Innovate Postdoctoral Fellows include creating a market research and customer discovery presentation, developing a business plan and financial model, building a pitch deck for speaking to investors and delivering it at various business pitch competitions, and submitting applications for a Launch Tennessee microgrant and a Small Business Innovation Research grant from the National Institutes of Health to secure future funding.

"The ASPIRE to Innovate Postdoctoral Fellowship has been an incredible experience and opened more doors than I could have ever thought possible," Dudek said. "I am excited for Catherine to have a similar opportunity and can't wait to see her be successful."

"We all know that starting a company is a high-risk endeavor, but regardless of whether a viable company is ultimately formed, this fellowship is a win-win situation, both for the biomedical postdoctoral fellow, who gets superb entrepreneurial training, and the Vanderbilt research community, which benefits from the dedicated effort of evaluating a potentially commercially viable new technology," Gould said. "We are grateful to Dean **John Kuriyan** of the School of Medicine Basic Sciences for his support in continuing this exciting initiative, as well as the CTTC, the Wond'ry, and Drs. Neuert and **Ethan Lippmann**, Karrie's partner during her fellowship, for their contributions to training and mentoring of the fellows in the program."

"I am excited to have been given this protected time as a postdoc to develop myself as a businesswoman while working to build a viable company."

—Catherine Leasure

Catherine Leasure, left, and Gregor Neuert

STEPHEN DOSTER

Vanderbilt and Bruker establish first-of-its-kind Mass Spectrometry Center of Excellence

By Marissa Shapiro

Vanderbilt University and Bruker Daltonics, a manufacturer of scientific instruments for molecular and materials research, are collaborating to establish a Mass Spectrometry Center of Excellence, the first of its kind established by Bruker, to be housed in the School of Medicine Basic Sciences' Mass Spectrometry Research Center. The MSRC is a university-wide facility serving the university and Vanderbilt University Medical Center and is directed by **Richard Caprioli**, Stanford Moore Chair in Biochemistry.

The center of excellence will acquire four new state-of-the-art Bruker mass spectrometers. Bruker will assist the center with service and software and will collaborate on joint development of instrument protocols and modifications. This collaboration represents a multimillion-dollar endeavor made possible by Caprioli, Dean of Basic Sciences **John Kuriyan**, Dean Emeritus **Larry Marnett**, Provost **C. Cybele Raver**, and overwhelming faculty support across the university and medical center that leverages years of research collaboration with Bruker.

"Vanderbilt's symbiotic relationship with Bruker will directly increase our capabilities in biomedical scholarship and discovery—technology development that will create avenues for international research collaborations, attracting external funding, and exposing graduate students and postdoctoral trainees to state-of-the-art technologies," Kuriyan said. "We are very pleased to broaden our relationship with Bruker for these reasons and beyond."

The MSRC at Vanderbilt is one of the world's largest academic mass spectrometry centers and is a leader in research, technology development, and core capabilities. These capabilities are key to continued pathbreaking discoveries in the "-omics era," where technologies like mass spectrometry are used to study large data sets such as DNA (genomics), RNA (transcriptomics), proteins (proteomics), lipids (lipidomics), and endogenous metabolites (metabolomics).

A mass spectrometer measures the mass-to-charge ratio of an ionized molecule, allowing its exact molecular weight to be calculated. Mass spectrometers are used to identify unknown compounds, quantify known molecular compounds, and determine the structure and chemical properties of molecules. Over the years, mass spectrometry has been used to help diagnose genetic diseases in newborns, detect the use of steroids in athletes, monitor patients' breathing during surgery, locate oil deposits by measuring petroleum content in rocks, and more. Now more than ever, the molecular specificity and sensitivity of this technology is leading to amazing discoveries, advancing the understanding of human health and disease, and developing strategies for disease diagnosis and treatment.

"This fast-moving technology brings phenomenal capabilities to support ground-breaking scientific exploration," Caprioli said. "It is critical in this -omics era that Vanderbilt leads and has state-of-the-art equipment in its cores to support the numerous research activities in the university and medical center."

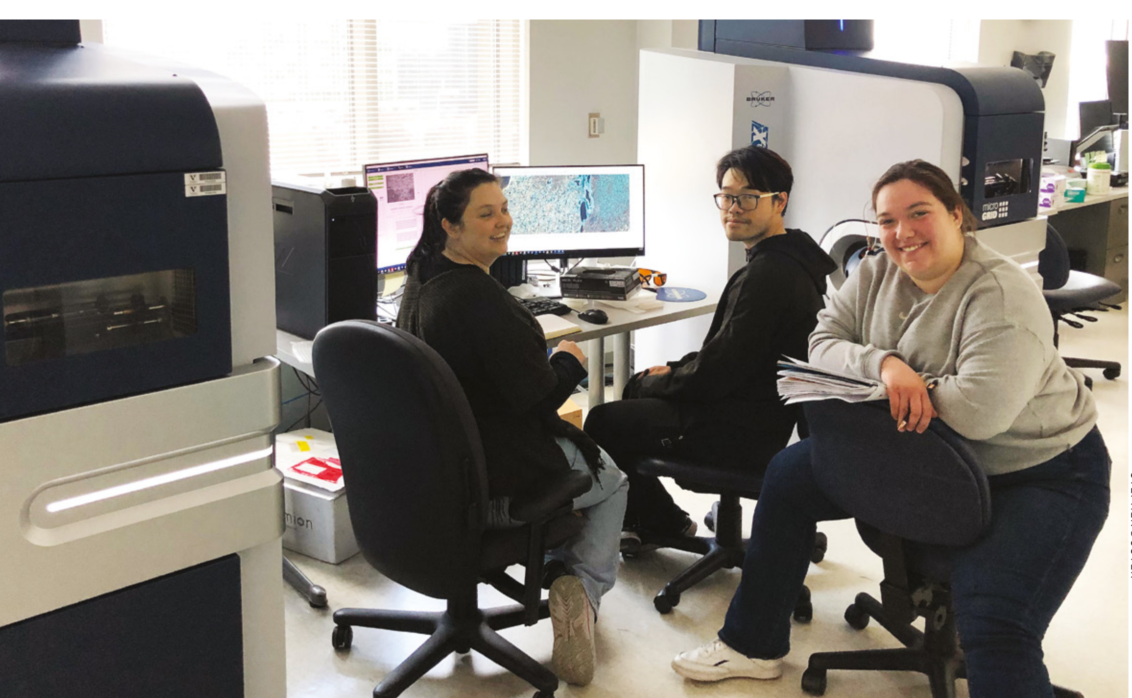
Caprioli developed imaging mass spectrometry with his experiments dating back to 1998. "Biological processes that occur in organs and how drugs interact with them can be difficult to fully understand because they happen in different cells scattered throughout the organ and at different times," Caprioli said. "Multiple techniques can give smaller pieces of this puzzle, but imaging mass spectrometry provides scientists with maps of thousands of molecules in a tissue. It is a technology that has burst open new capabilities for research. It is truly a next-generation molecular microscope."

The MSRC at Vanderbilt is one of the world's largest academic mass spectrometry centers and is a leader in research, technology development, and core capabilities.

The MSRC facilitates pioneering discoveries across the university and medical center. **Jeffrey Spraggins**, associate professor of cell and developmental biology and director of the Biomolecular Multimodal Imaging Center, develops advanced IMS and multimodal molecular imaging technologies. He and Caprioli have received $13.6 million in grants to develop molecular "atlases" of the brain, kidney, eye, and other tissues. **Kevin Schey**, professor of biochemistry and ophthalmology and visual sciences and director of MSRC core facilities, has engaged mass spectrometry to reveal how proteins in the human eye's lens change over time, often leading to formation of cataracts—a condition that affects more than 65 million people worldwide.

"We are thrilled to expand our collaboration with Vanderbilt University in support of the MSRC Center of Excellence. The feedback and exchange we will receive will be incredibly valuable," said Rohan Thakur, president of life science mass spectrometry at Bruker. "In turn, this engagement with Vanderbilt will help ensure that the MSRC Center of Excellence remains at the leading edge of MS technology. It's truly a win-win scenario for advancing Vanderbilt's world-class biomedical research programs."

HARRISON MCCLARY



STEPHEN DOSTER

Opposite page: Hayes McDonald, research assistant professor of biochemistry and associate director of the MSRC

Left: Postdoctoral fellows Madeline Colley, left, and Thai Pham, middle, and graduate student Jacqueline Van Ardenne at the MSRC facility in Medical Research Building III

Vanderbilt to establish new biosafety level 3 lab

By Lorena Infante Lara

ADOBE STOCK

The Vanderbilt University Medical Center has received $8 million in funding from the National Institutes of Health and has allotted an additional $4 million to establish a new biosafety level 3 laboratory on campus. This funding was possible thanks in large part to the efforts of **Eric Skaar**, director of VI4—the Vanderbilt Institute for Infection, Immunology and Inflammation—as well as the VUMC Office of Research.

Biosafety levels in the U.S. are assigned to laboratories based on the type of precautions that researchers must take to safeguard their health from biological agents and range from BSL-1 to BSL-4.

The lowest biosafety level requires just basic hand washing before and after doing laboratory work, for example, while the highest biosafety level demands intense protections such as full-body suits, airlocks, and chemical and personal showers upon exit from the lab.

The new BSL-3 space on campus will allow researchers to work with agents that can cause serious and potentially lethal disease. Vanderbilt currently has two BSL-3 labs that are assigned to the labs of specific faculty members, but the new space will be available—after appropriate approvals and training—to the VI4 community, which includes several primary and secondary Basic Sciences faculty.

A handful of researchers are already lined up to expand their current work at the BSL-3 facility when it opens in the spring of 2025. Their research focuses on a wide array of bacterial and viral pathogens such as fully virulent *Bacillus anthracis* (the bacterium that causes anthrax), *Mycobacterium tuberculosis*, SARS-CoV-2 (the virus that causes COVID-19), and emerging viruses such as Zika, hantavirus, Marburg virus, and Ebola.

"This is a big win for VI4, Vanderbilt, and our region," Skaar said. "The lab won't just be a research facility; it has the potential to serve as an emergency-use facility in Nashville in the event that there is some sort of outbreak, pandemic, or even a biological attack somewhere in the region."

Although some labs on campus provided diagnostic development and therapeutic testing during the onset of the COVID-19 pandemic, those labs are not equipped for certain types of infectious agents. The new facility will provide additional flexibility and capacity for response to COVID-19 and beyond.

A university of courage. Vanderbilt University was created to unite a fractured country through civil discourse, rigorous inquiry, and insightful leadership—values more crucial than ever today.

Now, we're committed to bold new levels of achievement through Dare to Grow, a $3.2 billion campaign—the largest fundraising effort in our history.

Roger Chalkley

At the School of Medicine Basic Sciences, we are harnessing this ambition through new initiatives like the **Roger Chalkley, Ph.D. Critical Need Fund.** Created to support Ph.D. students facing financial challenges, the fund honors longtime faculty member Roger Chalkley, who created the school's nationally recognized Ph.D. training programs in biomedicine and was fiercely committed to his students' success. By alleviating students' emergency expenses, the fund enables talented scholars to focus on their studies and advance life-changing discoveries.

Dare to grow. Giving to the Chalkley fund is one way to join us on our quest to empower our bright and enterprising students. Be a part of Vanderbilt University's courageous future.

Volunteer. Participate. Give.

Visit our website and learn about all the ways you can help propel Vanderbilt University and the School of Medicine Basic Sciences into our next 150 years.

vu.edu/daretogrow

VANDERBILT UNIVERSITY

Educational neuroscience program is epicenter of research

By Leah Mann

Have you ever wondered how your brain learned to read the very words of this article? Or how you comprehend the numbers listed on each page of *Vestigo*?

These questions provide a glimpse into the field of educational neuroscience, a realm of cognitive neuroscience focused on the neural mechanisms of learning. While such inquiries are compelling on their own, it is the answers and inherent application of the findings that truly inspire educational neuroscientists.

It was this hope to understand how the brain changes over development and how this process relates to learning outcomes that inspired the launch of the educational neuroscience Ph.D. program at Vanderbilt nearly 10 years ago.

The interdisciplinary program was established in 2012, bringing together the Vanderbilt Brain Institute and the Peabody College of Education and Human Development. The VBI serves as one of 10 trans-institutional Basic Sciences entities and is devoted to neuroscience research and education. **Lisa Monteggia**, Barlow Family Director of the VBI and professor of pharmacology, credits the "seamless and exceptionally synergistic" collaboration between the VBI and Peabody with "bringing educational neuroscience and related fields to the attention of the broader neuroscience community."

In the decade since its inauguration, seven students have graduated and an additional five are currently enrolled. At present, seven VBI training faculty members serve as educational neuroscience faculty. They are **Laurie Cutting**, professor of special education; **James Booth**, Patricia and Rodes Hart Professor of psychology and human development; **Eric Wilkey**, assistant professor of educational neuroscience; **Sophia Vinci-Booher**, assistant professor of psychology and human development; **Kathryn Humphreys**, associate professor of educational neuroscience; **Mark Wallace**, Louise B. McGavock Chair and professor of psychology; and **Autumn Kujawa**, associate professor of psychology and human development.

According to Cutting, this program is the "nexus of both the powerful, highly [regarded] college of education and the neuroscience expertise." Historically, the majority of educational neuroscience research has been dedicated to the mechanisms, neurobiology, and difficulties associated with reading. For example, **Andrea Burgess**, a fifth-year educational neuroscience Ph.D. candidate, has been working with Cutting on a longitudinal study to determine the way in which features of text may modulate demands during reading and to predict which children will require intervention.

Yet, Cutting has expanded her lab's focus beyond reading and disabilities to broadly address child development and academic outcomes. **Emily Harriott**, a third-year student in the program, has spent time studying the association between neurofibromatosis type 1, a congenital disorder characterized by tumors on nerve cells, and cognitive outcomes.

Wilkey, who was part of the very first cohort of educational neuroscience Ph.D. students at Vanderbilt, conducts math-focused research. As a graduate student, Wilkey worked with **Gavin Price**, former associate professor of psychology and human development at Peabody, to investigate the role of executive function systems, specifically inhibition, in basic number processing. Wilkey determined that processing is "not just about the basic concepts of numbers but also about managing the flow of information and dealing with numbers in the face of conflicting information." Wilkey's lab is continuing down this avenue, exploring other executive functions—the cognitive skills that control behavior, such as working memory—and studying how they are integrated with mathematical thinking.

In his last few months as a postdoctoral fellow, **Andrew Lynn**, working with both Cutting and Wilkey, used functional magnetic resonance imaging, a noninvasive way to measure and map brain activity, to examine the relationship between individual differences in executive functions and symbolic magnitude comprehension—the ability to map digits to quantities and compare numbers. "Each child will enter kindergarten with a different level of understanding, begging the question of how kids are leveraging cognition to learn magnitudes," Lynn said.

Another area of research spearheaded by Vanderbilt is handwriting. Recent hire Vinci-Booher uses handwriting to understand how actions are related to brain function and structure in early reading development. Vinci-Booher designed an MRI-compatible digital tablet that allows her to study brain function during handwriting using neuroimaging. Her work suggests that activities that link vision and action, such as handwriting, may be important for changes in brain function associated with early reading development and that brain structure may underlie individual differences in early learning outcomes.

What ties them together

Vanderbilt's educational neuroscience program offers not only the opportunity to be trained by world leaders in the field, but also to build a community. Although Harriott had set her sights on Vanderbilt so she could work with Cutting, she was pleased to also work with "professors who really care about their research and their students."

Alisha Compton, a third-year student in the program, agrees. "There is something special about the space at Vanderbilt," Compton said. Although she is primarily investigating mechanisms underlying reading skill and anxiety symptoms with her mentor, Booth, she has also collaborated with other faculty members.

These collaborations and interdisciplinary efforts are at the heart of educational neuroscience research at Vanderbilt. According to Wilkey, there are "different tiers of analysis that the research wheel relies on, requiring us to leverage expertise across domains."

The ability to do just that is what makes Vanderbilt a leader in the realm of educational neuroscience. "This program constructs a new dimension within traditional neuroscience studies while addressing a critical societal need in neuroscience-based education initiatives," Monteggia said.

ALL PHOTOS: VANDERBILT UNIVERSITY

Opposite page and above: Laurie Cutting. Bottom left: Eric Wilkey. Right: Children who participate in cognition neuroscience research studies practice performing the experiments in mock MRI machines to get them acclimated to the process of going through a real MRI machine.

Outstanding faculty in the Basic Sciences recognized for high-impact work

By Alexandra Scammell, Bill Snyder, and Kiya Gaskin

The School of Medicine Basic Sciences fosters an environment where curiosity thrives, and its diverse community of scientists is empowered to acquire new knowledge about human biology, health, and disease.

A pillar of this community is the female faculty who are passionate about advancing and making notable impacts on their basic sciences fields. For many, their efforts have been recognized by the highest-caliber professional societies around the world. **Dr. Nancy Carrasco, Lisa Monteggia**, and **Dr. Kimryn Rathmell** are three such Vanderbilt scientists who have received awards and recognition from the National Academy of Medicine, the American Association for Arts and Sciences, and others.

Nancy Carrasco

JOHN RUSSELL

Carrasco, the Joe C. Davis Professor and chair of the Department of Molecular Physiology and Biophysics, received the 2024 Award for the Biophysics of Health and Disease from the Biophysical Society and was named the 2023 SEC Faculty Achievement Award winner.

The BPS recognized Carrasco's "seminal and elegant" biophysical approaches to characterizing the sodium/iodide transporter. The SEC Faculty Achievement Award recognizes faculty members from each of the 14 SEC universities for excellence in research and teaching, particularly at the undergraduate level.

"Dr. Carrasco is renowned for her work in molecular physiology, particularly in understanding iodide ion transport and the structure of the sodium/iodide symporter. Her pioneering contributions to thyroid pathophysiology have impacted research in public health by leading to a clearer understanding of the danger of certain water pollutants, such as the toxic perchlorate ion," said John Kuriyan, dean of the School of Medicine Basic Sciences. "I am pleased to congratulate her on being recognized for [the SEC Faculty Achievement Award]."

Throughout her career, Carrasco has received numerous scientific awards and has served as president of societies such as the Society of Latin American Biophysicists. Carrasco was elected to the National Academy of Sciences in 2015, the National Academy of Medicine in 2020, and the American Academy of Arts and Sciences in 2022. In 2023, she was named a Biophysical Society Fellow.

JOHN RUSSELL

Lisa Monteggia

Monteggia, Barlow Family Director of the Vanderbilt Brain Institute and professor of pharmacology, was elected to membership in the National Academy of Medicine in 2022 for "seminal contributions to the neurobiology of emotion ... [and] transformative contributions to our understanding of synaptic plasticity mechanisms that underlie the therapeutic effects of psychiatric treatments."

Monteggia's laboratory has been investigating the role of neurotrophins—nerve cell growth factors—and the role they play in depressive-like behavior and the efficacy of antidepressants. The NAM cited her "pioneering work identifying a causal link between neurotrophin signaling and antidepressant action" in its decision to offer her membership.

Her work to identify the proteins in the brain that are targeted by the rapid-acting antidepressant action of ketamine has opened the door to new possibilities for the development of drugs that mimic ketamine's antidepressant benefits without its side effects. This aspect of Monteggia's work has resulted in additional recognitions, including from the Anna-Monika Foundation. The AMF recently named Monteggia and collaborator and Department of Pharmacology Chair **Ege Kavalali** as recipients of its Anna-Monika Prize, presented to researchers who have "made significant advances in neurobiology and treatment of depressive disorders."

JOHN RUSSELL

A pillar of this community is the female faculty who are passionate about advancing and making notable impacts on their basic sciences fields.

Kimryn Rathmell

Rathmell is internationally recognized for her molecular biology research in the pathogenesis of kidney cancer, nationally funded large-scale genomic studies of cancer, and clinical investigations that have brought new biomarkers, imaging modalities, and lifesaving therapies to patient care. Formerly the Hugh Jackson Morgan Professor of Medicine, chair of the Department of Medicine, and professor of biochemistry, Rathmell was appointed by President Joe Biden as director of the National Cancer Institute as of December 2023.

In October 2023, she was presented with the Paragon Award for Research Excellence from the Doris Duke Foundation.

"This award means a lot to me," Rathmell said. The Clinical Scientist Development Award she received "allowed our research to really move into the translational space—supporting our first foray into functional imaging with FDG-PET scans as a part of predicting patient response to therapy."

Rathmell was also elected to the American Academy of Arts and Sciences—one of the oldest professional academies in the U.S., which honors excellence from "every field of human endeavor"—and the National Academy of Medicine in 2022.

Her NAM election recognized her basic science investigations of kidney cancer that are "paving the way for new therapeutics" and contributions to the mentorship, recognition, and career advancement of physician-scientists.

Rathmell is known for her advocacy for physician-scientist training, for championing support of kidney cancer research, and for the development of policies that address drug shortages and conflicts of interest in scientific publishing in equitable ways.

Basic Sciences appoints Gama as new associate dean for equity and inclusive mentoring

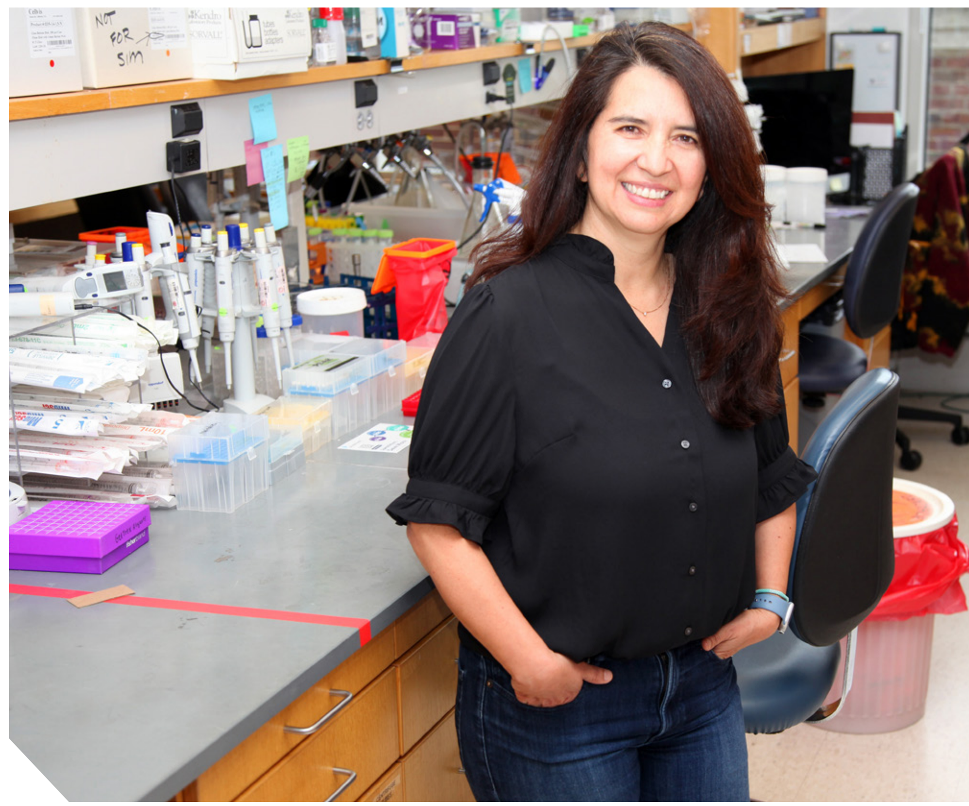
By Aaron Conley

Vivian Gama, associate professor of cell and developmental biology, was named the new associate dean for equity and inclusive mentoring as of Sept. 1, 2023.

"Vivian brings unique and key perspectives as a faculty member, award-winning mentor, and international scholar," said John Kuriyan, dean of basic sciences. "Her leadership will broaden our efforts in a holistic and integrated way and will accelerate our continuing efforts to build equity and inclusion in School of Medicine Basic Sciences."

Basic Sciences has a 20-year history of leadership in equity and inclusion. **Linda Sealy**, associate professor emerita of molecular physiology and biophysics, co-directed what is now known as the Vanderbilt Initiative to Maximize Student Development and served as associate dean for diversity, equity, and inclusion before her retirement. Alongside Sealy, **Larry Marnett**, dean emeritus of Basic Sciences, also focused on expanding faculty diversity. During his tenure, 60 percent of faculty recruits were women or from backgrounds underrepresented in science.

In 2023, **Felysha Jenkins**, who was hired in 2021 as the Basic Sciences diversity, equity, and inclusion program manager, became assistant dean of DEI. Jenkins has expanded strategy, programming, and training around DEI topics. Also in 2023, **Alyssa Hasty**, associate dean for faculty of Basic Sciences, partnered with Vanderbilt University Medical Center to launch a $17 million, multiyear program with support from the National Institutes of Health to accelerate DEI in the biomedical research faculty community.



STEPHEN DOSTER

Gama and her vision

Gama completed her Ph.D. in pharmacology in 2009 from Case Western Reserve University. Before joining Vanderbilt in 2015, she completed her postdoctoral training at the University of North Carolina Chapel Hill in the laboratory of Professor of Cell Biology and Physiology **Mohanish Deshmukh**.

Since joining Vanderbilt, Gama's research has focused on the molecular principles governing organelle remodeling as a driver of cellular transitions during neurogenesis—the process by which neurons develop in the brain.

Gama's experiences, including immigrating to the U.S. from Colombia and being mentored by Deshmukh, played a significant role in her career trajectory. Her background motivates her interactions with trainees and staff, especially when building her laboratory. She considers each laboratory member's background and specific needs for success.

"My main goal is to contribute to empowering and maximizing the talent that we have been fortunate to recruit to Vanderbilt, but also of new trainees and colleagues we are hoping to bring into our laboratories and departments in Basic Sciences," Gama said.

Gama believes that it is imperative to further integrate inclusive policies at every step of the recruitment and training process for students, postdocs, faculty, and staff. "I am inspired by the incredible advances colleagues like Linda Sealy made toward achieving this goal, and I am honored to continue those efforts in this new role," she said. Gama sees the whole Basic Sciences community as key to this effort.

"Vivian's expertise and leadership will undoubtedly enrich our initiatives aimed at cultivating a holistic and integrated approach to equity and inclusion," said **C. Cybele Raver**, provost and vice chancellor for academic affairs. "As we honor our past accomplishments and look towards a future of progress, Vivian's insights and dedication will play a pivotal role in shaping policies that empower all individuals in our academic community."

A winding path to happiness

By Lorena Infante Lara

Karissa Culbreath, PhD'08, is an Albuquerque, New Mexico, native with a successful career as a clinical microbiologist. Culbreath's love of science started from the time she was young and took her from Albuquerque to Nashville to Chapel Hill, North Carolina—and eventually back to Albuquerque.

"Life may be a little squiggly line—nothing is very straight," she said, "but just keep moving."

Join us for our regular alumni interview and learn about Culbreath's past—and learn about a career path you may not have known about.

What degree did you get at Vanderbilt and when did you graduate?
I received my Ph.D. in microbiology and immunology (pathology was a separate department at the time) in 2008.

What kind of research did you do?
I worked in the lab of **Mary Zutter** doing research on the innate immune response to *Listeria* infection in a mouse model.

What brought you to Vanderbilt?
I attended Fisk University, right down the street there in Nashville, and did a summer reads research program at Vanderbilt. It was a wonderful experience, and it was my first exposure to Vanderbilt. And since I was local, I was able to continue some of the work from my summer program into the fall semester and stay connected to Vanderbilt. So, Vanderbilt was at the top of the list when it came time to apply to graduate schools.

What kind of path led you to a career in science?
When people ask me how I got interested in science or when I knew I wanted to have a career in science, the answer for me is that there was never a time in my life in which I didn't want a career in science. I've always been very curious about the world around me; I got dissecting kits for Christmas when I was a kid, so that's just always been me.

But it did take me a while to figure out how I wanted that science to show up in my career. I knew that I was very interested in science and mechanisms and in understanding the world, but I also wanted my work to have a clinical application. **Dr. Charles Stratton**, a faculty member in the Department of Pathology who passed away [in 2022], really helped to open up the world of clinical microbiology to me. He really made a profound impact on me and my career, and I would not be in this career if it weren't for his guidance and support. Finding the career of clinical microbiology truly gave me the perfect intersection of the science and the clinical applicability that I was looking for.

What do you do as a clinical microbiologist?
I'm the section chief and medical director of infectious disease at TriCore Reference Laboratories in Albuquerque, New Mexico. As clinical microbiologists, we are responsible for the diagnosis and support for any infection in clinical samples. I work with hospitals, doctors' offices, and clinics to support the diagnosis of any condition—from strep throat to HIV to sepsis—and help to provide treatment recommendations based on susceptibility testing and other factors.

COURTESY OF KARISSA CULBREATH

When the pandemic first emerged, there weren't very many commercially available diagnostic tests for COVID-19, so, working within regulations, we provided laboratory-developed tests and helped clinicians understand the test and the results. Once the commercially available tests became available, we started providing those.

What general or career advice do you have for current Ph.D. students or postdocs?
Always stay curious. You may not know the entire path that's in front of you, but never stay still. Keep moving forward and take the next best step, and that will often get you to where you want to be.

Staff shoutout:
Special Graduate Student Association edition

By Caroline Cencer

GSAs allow graduate students to fill leadership roles, making them a pivotal part of building their departments' legacy on behalf of all graduate students. Each department GSA is unique, with its own mission statement and events designed to promote an environment that helps trainees thrive.

Graduate students are not staff members, but the leaders of the GSAs put in a lot of hard work behind the scenes to improve their departments' academic and social interactions and increase their sense of community. Get to know current and past GSA leaders and learn about their initiatives and legacies in this issue's special edition staff shoutout.

BIOCHEMISTRY

The Biochemistry Postdoctoral Researcher and Student Association, led last year by Co-Presidents **Kate Clowes** and **Jessica Collins**, strives to uphold a creative, supportive, and inclusive environment with a focus on student mental and physical wellness. As such, the BPSA established a wellness committee last year and began a mentoring program that paired senior graduate students with new trainees to help them build connections within their new department while holding several wellness-focused events. The BPSA also puts on "Social Issues in STEM" discussions in which they explore films or literature, such as *The Immortal Life of Henrietta Lacks*, and talk about how the presented issues have affected scientific research and how they can do better in the future.

Collins said that these discussions have "spurred extensive conversations on sensitive issues that are often overlooked" and that she's appreciative that the department acknowledges these systemic issues in the basic sciences. As a whole, said **David Cortez**, the chair of the Department of Biochemistry, "The BPSA makes the department a better place to learn and discover."

Ronan Bracken and **Vincent Yao** lead the organization this academic year, with **Juan Carvajal García** serving as its postdoc liaison. An additional group of 17 departmental members lead various aspects of BPSA function, including managing a biweekly student/postdoc colloquium, helping second-year students with qualifying exams, and organizing social activities.

This year's BPSA officers, listed from left to right. Back row: Todd Blakely Jr., Juan Carvajal García, Nicky Eleuteri, Vincent Yao, Kevin McCarty, Ronan Bracken, and Menghan Mei. Front row: Jessica Collins, Yelena Perevolova, Lilia Merbouche, Jenny Tran, Gabriela Gonzalez Vasquez, Jordan Stacy, Jill Armenia, and Lily Yu.

The PhGSA enjoys hosting retreats off campus. Shown here are some current and former PhGSA leaders. From left to right, they are Jared Phillips, Vivian Truong, Amy Stark, Christine Konradi, José Zepeda, Emma Webb, and Jade Miller.

PHARMACOLOGY

The Pharmacology GSA, led this year by President **Jared Phillips**, works to bring understanding and appreciation of the pharmacological sciences to campus and the surrounding community by putting on multiple events. In the past, the PhGSA has moderated academic events, such as seminars and career workshops, to highlight the latest trends in pharmacology. They also organize social activities, such as their annual retreat, which also welcomes Meharry Medical College faculty and students, to facilitate connections among all members of the pharmacology department and beyond.

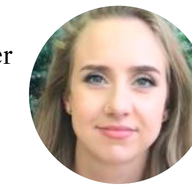
One of the PhGSA's most important events is the Pharmacology Student-Invited Forum, which is held each spring and hosts experts studying a niche topic of interest. The 2023 theme was "Pharmacology in the Wild" and featured experts focused on natural product discoveries in marine environments and researchers from the Vanderbilt community as they delved into advances in pharmacology through a focus on natural products.

Pharmacology Director of Graduate Studies **Christine Konradi** praised the students' recent efforts on the PhGSA and the department's DEI Committee. Konradi also emphasized that, due to COVID-19, "the PhGSA students in the last few years faced a very different structure than previous PhGSA leaders. We are still trying to find a new level of normalcy."

This year's PhGSA leadership also includes **Emma Webb**, **KJ Li**, **Jade Miller**, **José Zepeda**, **Christopher Hansen**, **Montana Young**, and **Tony Ferranti**.

MOLECULAR PHYSIOLOGY AND BIOPHYSICS

The MPB GSA, led by Co-Presidents **Julia Pinette** and **Julie Burkett**, aims to create a supportive community for MPB students, to increase communication between department members, and to foster a productive environment for discovery.



Julia Pinette

A couple of years ago, the department established a Diversity, Equity and Inclusion Committee that is made up of graduate students, postdocs, and faculty. The MPB GSA also recently chronicled the history of Black excellence in physiology. Originally organized by MPB alumna **Slavina Goleva**, PhD'21, this initiative unveiled a poster in 2021 to commemorate Juneteenth and showcased a timeline of Black researchers who have contributed to the field of physiology. The poster is still on display in Light Hall, and, according to Sweet, "It really kickstarted a dialogue between the members of the MPB community about the importance of DEI."

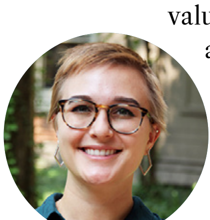
Julie Burkett

Additionally, with in-person gatherings becoming more frequent, the MPB GSA officers are excited to bring back past events, such as the annual Halloween party and costume contest, as well as create new events, such as happy hours and a holiday cookie exchange.

The rest of the MPB GSA leadership is made up of **Serena Sweet**, **Darian Carroll**, **Hannah Waterman**, **Erykah Coe**, **Emily Hawes**, and **Payam Fathi**.

CELL AND DEVELOPMENTAL BIOLOGY

The CDB GSA, led by President **Maggie Fye**, Vice President **Stephanie Medina**, and President Emerita **Megan Stanchfield**, values student interaction and scientific discussion while promoting an inclusive community. To uphold these goals, a new officer position, Community Development Chair, was created in the last couple of years and was filled by former CDB President **James White**. Additionally, the CDB GSA leadership comprises a small events committee and a liaison with the Graduate School.



Maggie Fye

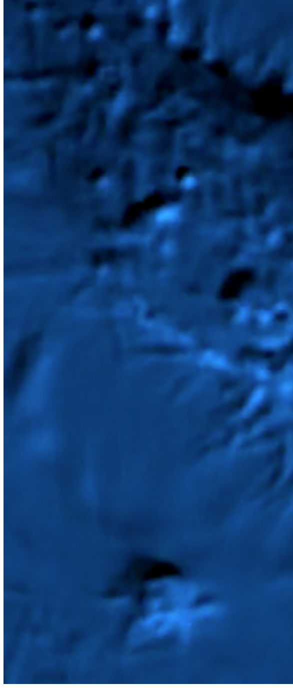
Events for graduate students and postdocs over the past year included monthly lunches as well as coffee and pastry writing hours. These events provided a space for trainees to discuss their research in a relaxed setting while building interdepartmental connections. The CDB GSA also hosts student-invited speakers to enhance their academic training.

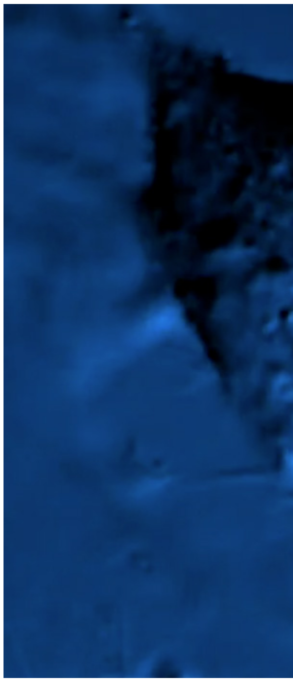
According to White and President Emerita Stanchfield, the "department's trainees have been able to come together and rebuild our sense of community and collaboration post COVID-19 thanks to the CDB GSA."

Stephanie Medina

Through the lens:

Vanderbilt's excellence in microscopy revealed in Nikon Small World awards

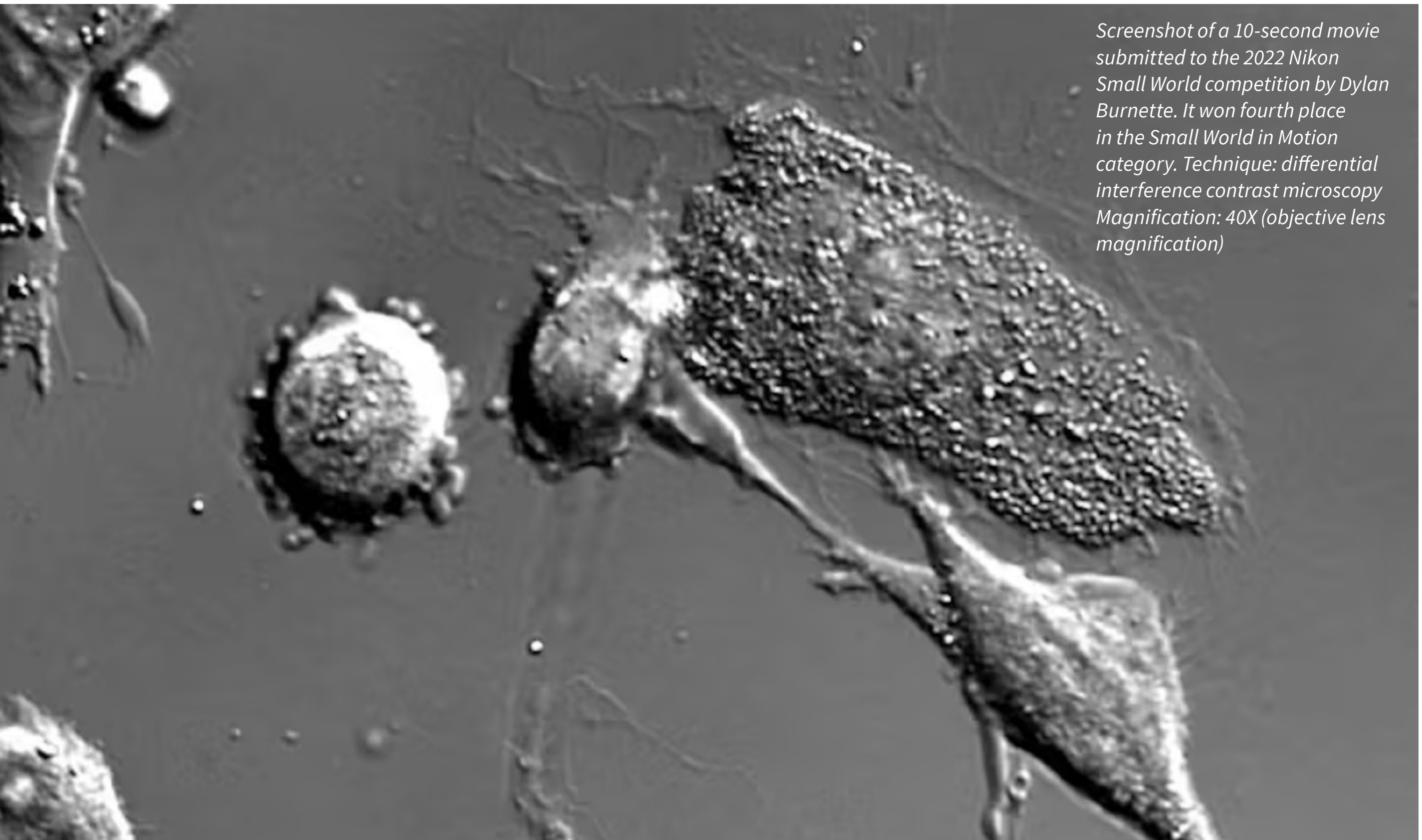




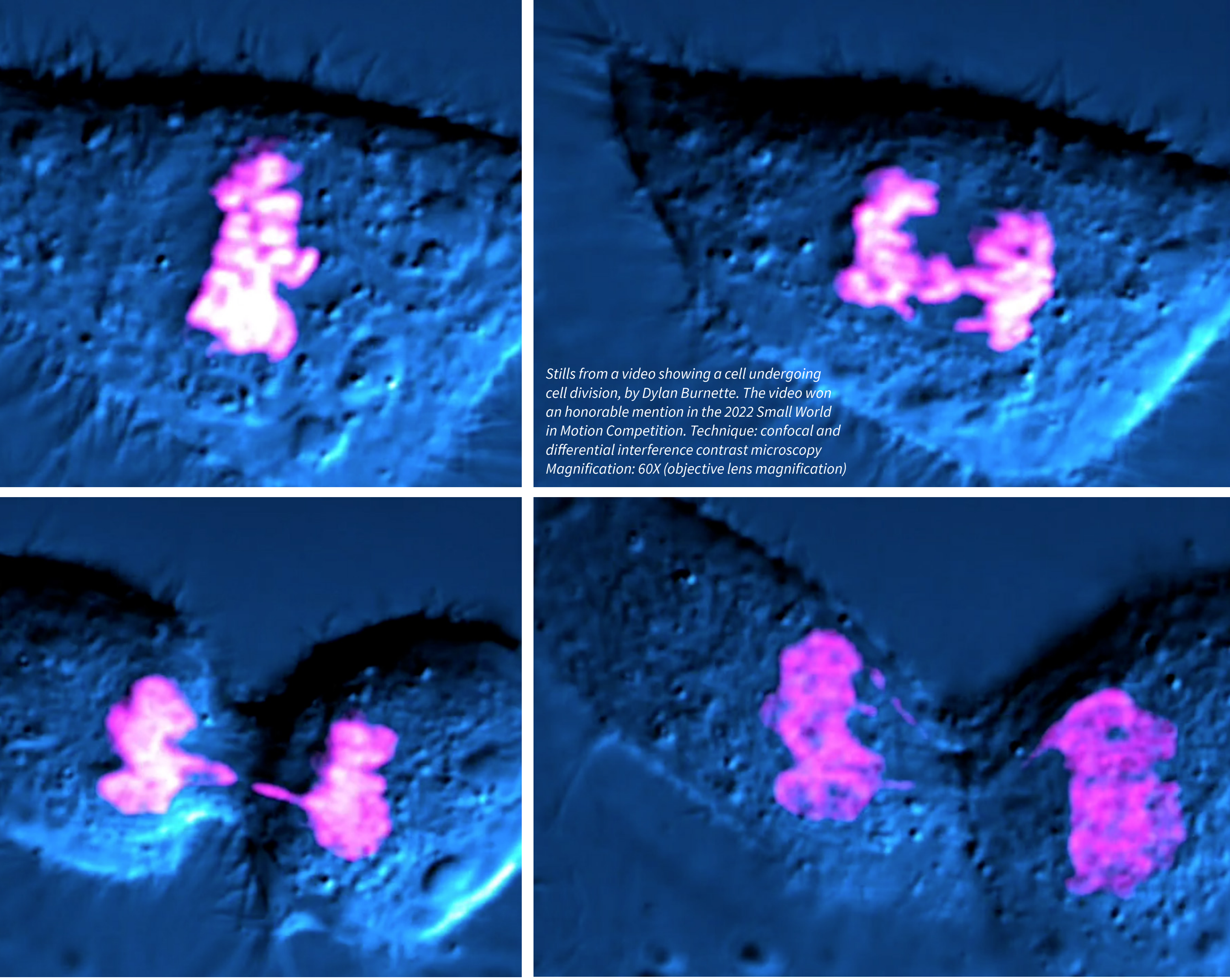
Dylan Burnette, associate professor of cell and developmental biology, and **Olivia Perkins**, a graduate student in the Department of Cell and Developmental Biology, were awarded prizes in the 2022 Nikon Small World and Nikon Small World in Motion competitions.

Founded in 1975, Small World recognizes the top microscope images and movies by annually awarding winning and honorable mention prizes. Aptly summarized by comedian **Stephen Colbert** as "a contest for tiny pictures of tiny things," Small World has become legendary and serves as a visual testament to the advancement of microscopy for nearly 50 years.

Burnette was awarded one honorable mention in the image category, in addition to fourth place and two honorable mentions in the movie category. Perkins was awarded an honorable mention in the movie category.



Screenshot of a 10-second movie submitted to the 2022 Nikon Small World competition by Dylan Burnette. It won fourth place in the Small World in Motion category. Technique: differential interference contrast microscopy Magnification: 40X (objective lens magnification)

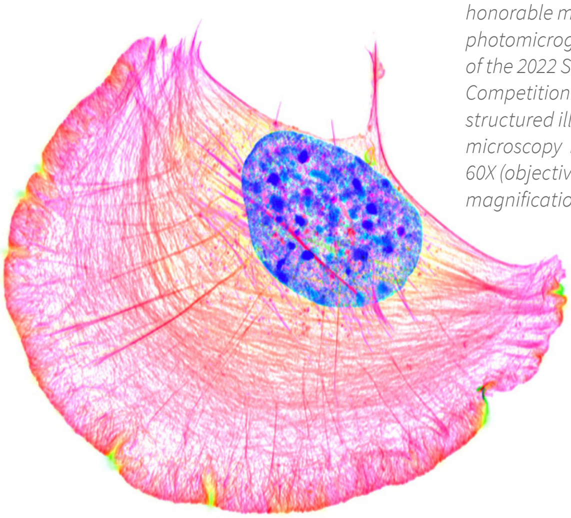


Stills from a video showing a cell undergoing cell division, by Dylan Burnette. The video won an honorable mention in the 2022 Small World in Motion Competition. Technique: confocal and differential interference contrast microscopy Magnification: 60X (objective lens magnification)

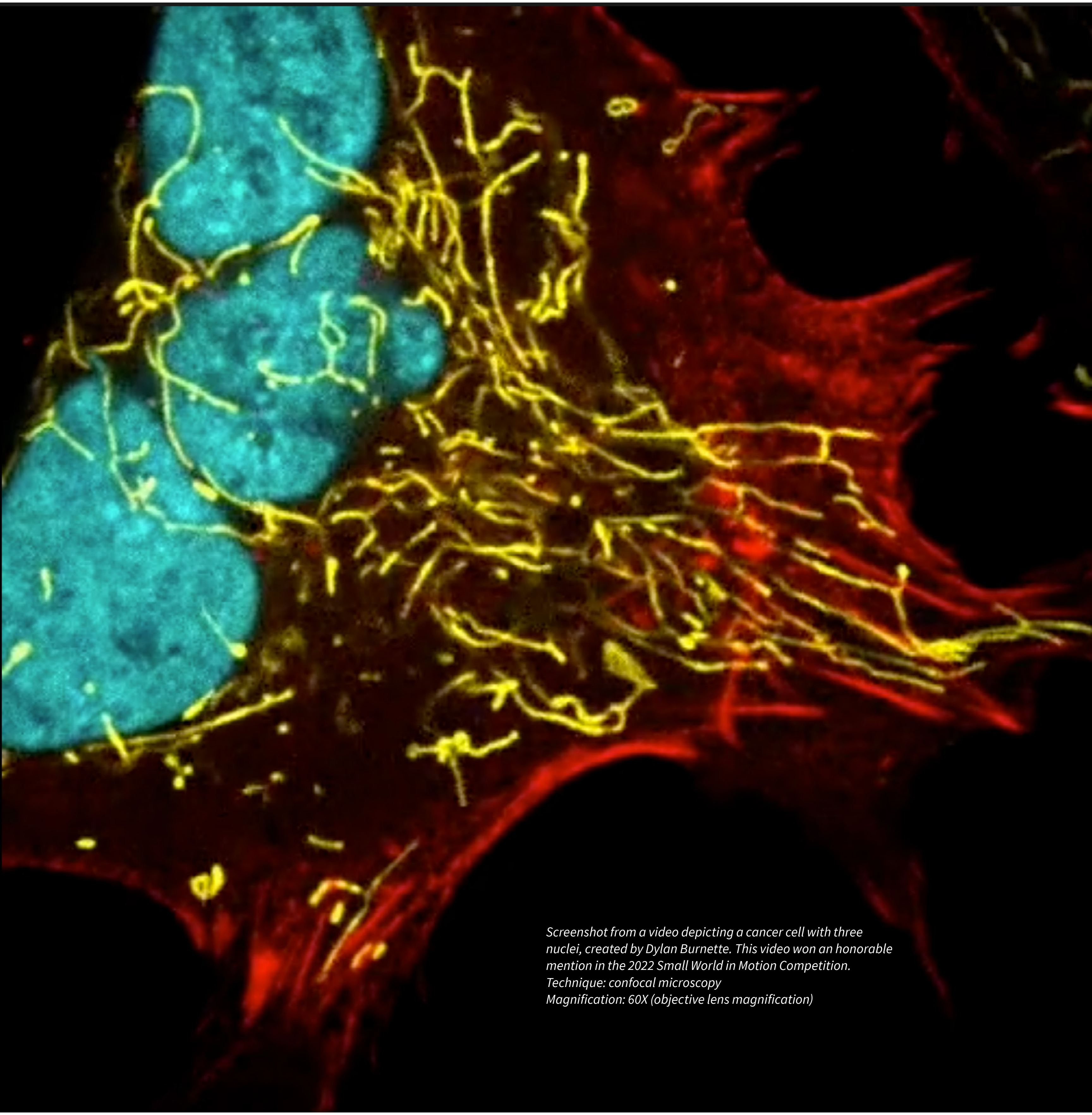
Despite the vast number of submissions to the contest from scientists worldwide each year, Vanderbilt is no stranger to Small World awards. Vanderbilt researchers have amassed a total of 17 recognized images and movies in the past several years, placing Vanderbilt in the top 15 of the most awarded institutions in the history of the competition.

Vanderbilt's success can be attributed in part to the outstanding microscopy core facilities available on campus. Led by Scientific Director **Matthew Tyska**, who holds a Cornelius Vanderbilt Chair and is a professor of cell and developmental biology, and Managing Director **Jenny Schafer**, who is also a research associate professor of cell and developmental biology, the Cell Imaging Shared Resource offers a wide variety of microscopes—including super-resolution and electron microscopes—across campus.

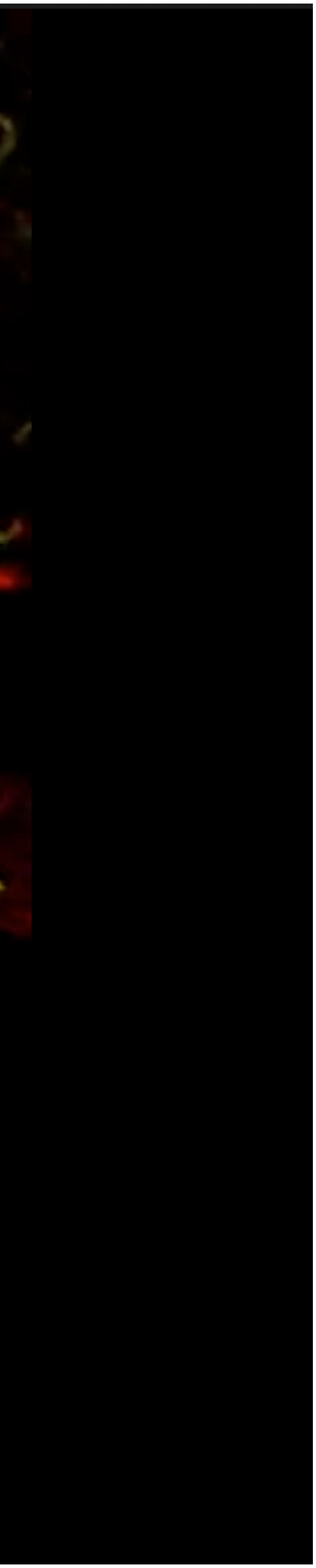
In 2016, CISR opened its state-of-the-art Nikon Center of Excellence facility in partnership with Nikon Instruments. By housing microscopes



This image of a crawling cell won Dylan Burnette an honorable mention in the photomicrography category of the 2022 Small World Competition. Technique: structured illumination microscopy Magnification: 60X (objective lens magnification)



Screenshot from a video depicting a cancer cell with three nuclei, created by Dylan Burnette. This video won an honorable mention in the 2022 Small World in Motion Competition.
Technique: confocal microscopy
Magnification: 60X (objective lens magnification)

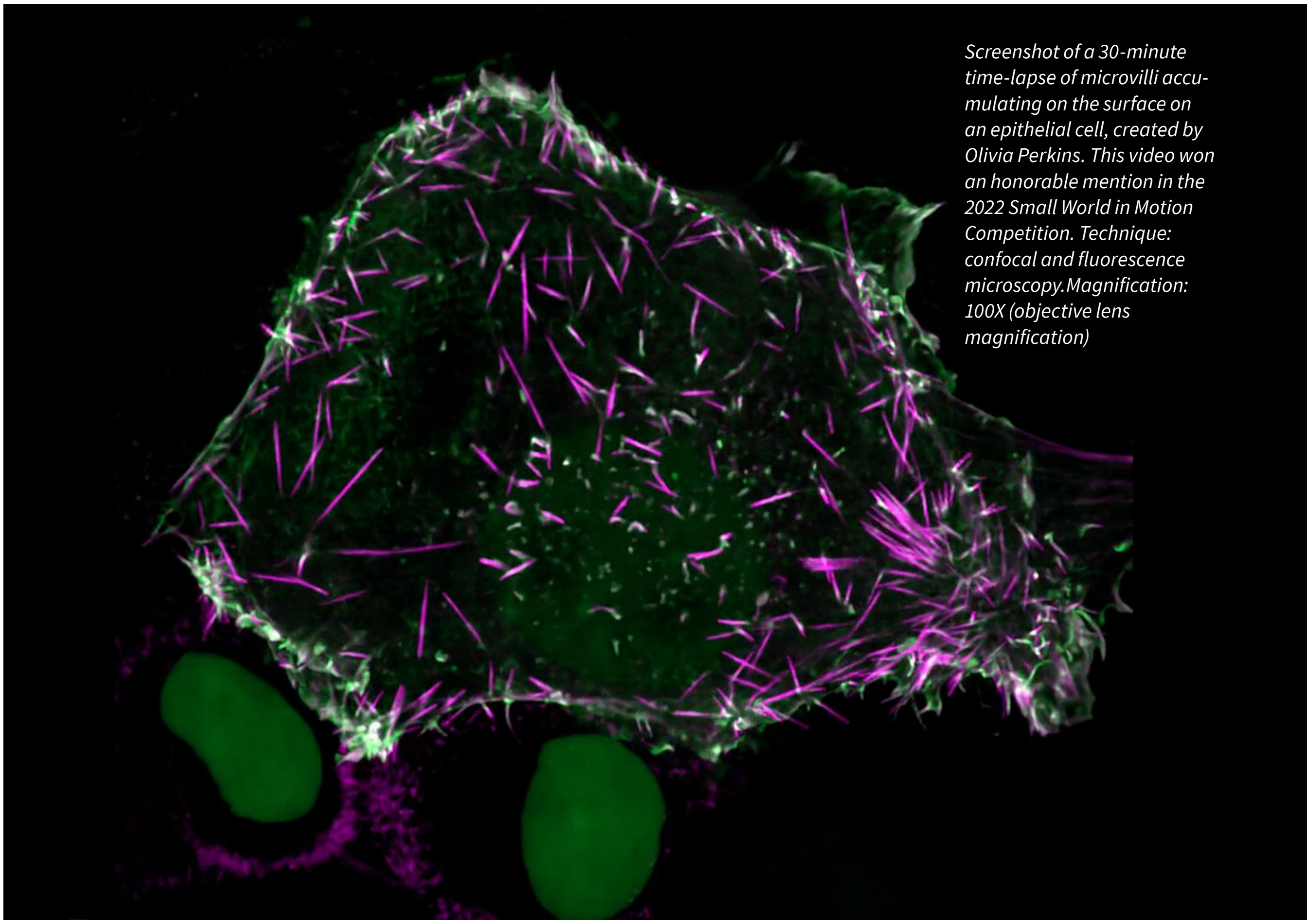


within five suite locations, CISR has established an easily accessible imaging resource for students and staff. CISR personnel are always on hand to train researchers on the proper use of the microscopes as well as assist in data processing and analysis.

CISR keeps up with the newest microscopes and techniques. Most recently, CISR acquired a lattice light-sheet microscope and a focused ion beam scanning electron microscope. The light-sheet microscope enables fast, three-dimensional imaging of live cells without phototoxicity—which happens when too much excitation light damages the cell—thanks to thin sheets of light passing through the sample one slice at a time. The addition of the FIB-SEM is especially exciting, as this new technology applies the high-resolution power of SEM to the three-dimensional space, allowing CISR users to create in-depth maps of entire cells or subcellular structures.

Burnette and Perkins made use of CISR microscopes—including the structured illumination microscope and the spinning disk confocal microscope—and training, which set them up for recognition by Small World.

Many of CISR's resources are funded by shared instrumentation grants or center grant supplements as noted in the numerous scientific publications that recognize the use of the CISR core each year. As CISR continues to acquire the latest and greatest microscopes, the future of Vanderbilt imaging is truly limitless.



Screenshot of a 30-minute time-lapse of microvilli accumulating on the surface on an epithelial cell, created by Olivia Perkins. This video won an honorable mention in the 2022 Small World in Motion Competition. Technique: confocal and fluorescence microscopy.Magnification: 100X (objective lens magnification)

ASPIRE data science internship provides mutual benefits to companies and students

By Dora Obodo

The Office of Biomedical Research Education and Training's Career Development ASPIRE program has been hosting an internship program for graduate students and postdoctoral fellows for eight years. The internship program, an invaluable resource for trainees interested in non-academic roles in the biomedical industry, has facilitated just over 200 internships to date through partnerships with a wide range of organizations.

In particular, the ASPIRE data science internship with Decode Health demonstrates how students can break into growing fields. Decode Health is a health care artificial intelligence company that empowers pharmaceutical companies and their tech partners by delivering proactive health care innovations to advance precision medicine.

Decode Health co-founder and CEO **Chase Spurlock**, PhD'14, takes a hands-on approach to training by integrating interns throughout the company's operations, ensuring that they develop in areas aligned with their interests.

"Interns have the opportunity to touch every aspect of the company," said Spurlock, whose degree is in microbe-host interactions. "We're very intentional about having people join us who are interested not only in being on the data team, but also seeing how Decode's products and services come together."

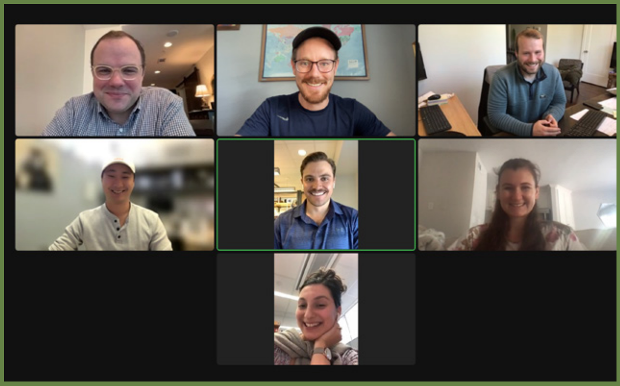
Since 2018, the Decode Health team has hosted nine successful interns, several of whom continued to pursue data science roles afterwards.

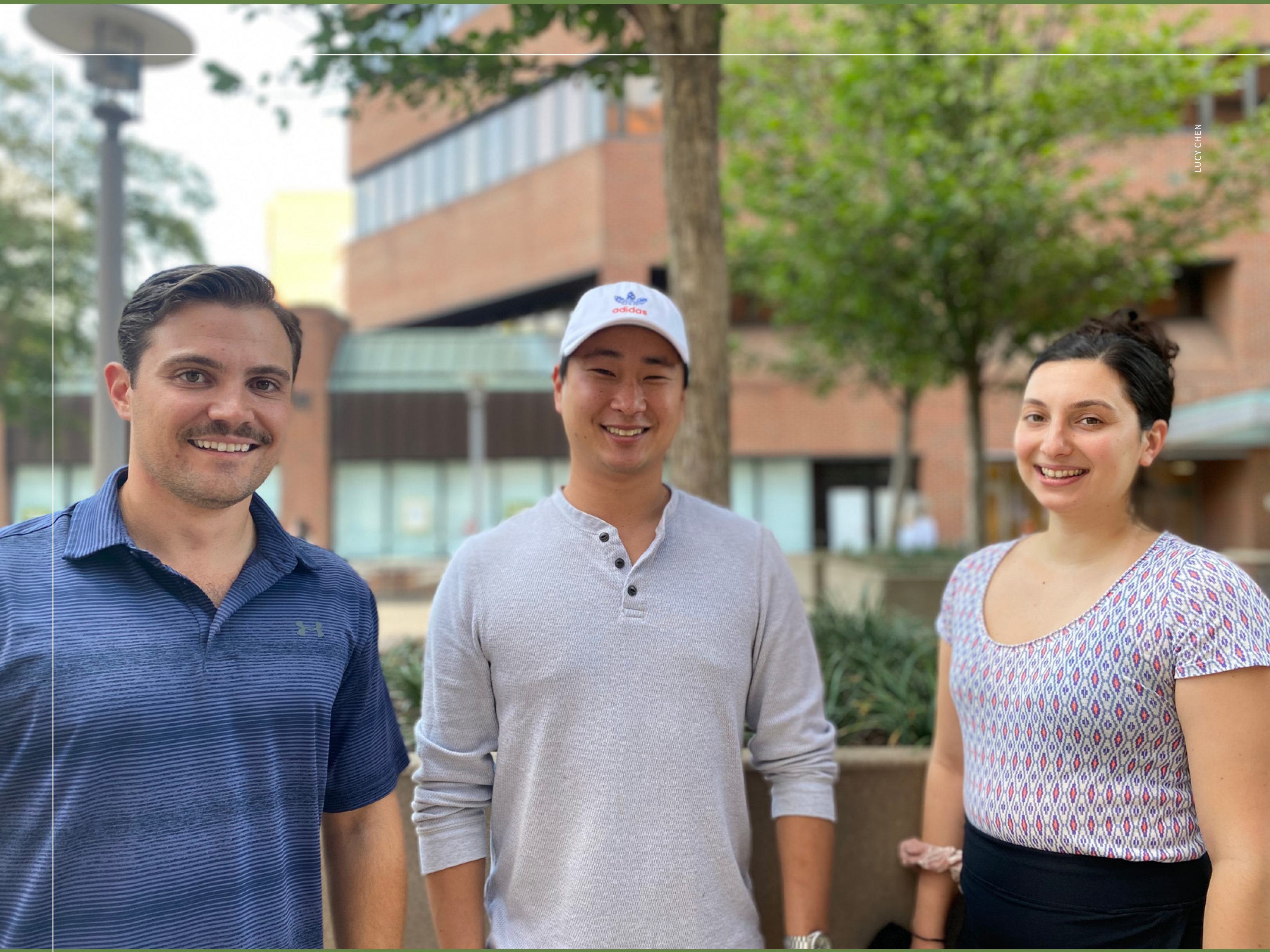
"Industry is a completely different work environment than academia because people think about and prioritize different things here," said **Darwin Fu**, PhD'17, currently a data scientist at Bluesight , a medication intelligence and software company. "Seeing that during an internship really softens the transition."

Like many of his biomedical scientist colleagues, **Aaron May-Zhang**, Fellow'20, senior bioinformatics scientist at Fluent BioSciences Inc., was interested in data science but had little experience during his postdoctoral training at Vanderbilt.

Right: Decode Health interns Cody Heiser, left, Tim Scott, middle, and Verda Agan

A Zoom meeting (below) featuring (from left to right) Chase Spurlock, Jamieson Gray, and Lukasz Wylezinski on the top row, Tim Scott, Cody Heiser, and Sarah Groves on the middle row, and Verda Agan on the bottom. Spurlock is co-founder and CEO, Jamieson is chief of staff, and Lukasz is director of data analytics in research and development of Decode Health. Scott, Heiser, Groves, and Agan were all interns.





"My internship experience allowed me to be an attractive candidate to Fluent Biosciences because their day-to-day roles were similar to what I was experiencing in my internship," he said. "I was able to point to specific outcomes and efforts that were highly relevant skills to the company."

During the internship, students work on self-driven projects that can develop into pipelines to help advance customer goals. Students with highly successful projects can take on advanced responsibilities as their skills improve. **Cody Heiser**, PhD'23, a recent graduate from the Chemical and Physical Biology program who interned at Decode Health for a year and a half, progressed from a data analyst role into data engineering. "I got to wear a lot of different hats along the R&D spectrum in a dynamic environment where everybody has to contribute on so many different levels. The internship gave me experiences to point to and say, 'Here are the challenges that I've seen in an industry space, and this is how I contributed to overcome those challenges,'" he said. Heiser is now a senior scientist at Regeneron.

For Spurlock and the Decode Health team, the ASPIRE partnership has also been incredibly rewarding. Not only do the internships provide bright, talented self-starters to the company, but they also afford trainees with necessary experiences to boost their competitiveness and foster industry-academia connections.

Are you interested in hosting Vanderbilt Ph.D. students or postdoctoral fellows at your organization? Get full details on page 3.

Accolade corner

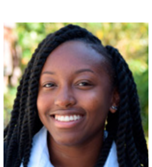
The hard work of the faculty, staff, postdocs, and graduate students who conduct basic biomedical research at Vanderbilt continues to be recognized on the local and national level. Here we list a few of the researchers whose work has been recently recognized.

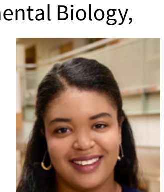
Erin Calipari (Pharmacology) received a 2023 American Psychological Association Distinguished Scientific Award for an Early Career Contribution to Psychology for her work in behavioral and cognitive neuroscience.

Larry Marnett (Biochemistry) and **Thao Le** (Molecular Physiology and Biophysics, Julio Ayala lab) were among those honored at the inaugural Graduate School Honors Banquet. Marnett received the Excellence in Graduate Student Mentoring Award and Le received the Excellence in Leadership Award.

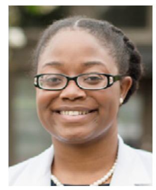
Veronika Kondev (Neuroscience, Sachin Patel and Brad Grueter labs) and **Ayesha Muhammed** (Human Genetics, Dan Roden lab) were named the 2023 Founder's Medalists for the Graduate School and the School of Medicine, respectively.

Neil Osheroff (Biochemistry) was the opening keynote speaker at the APMEC 2023 and received the Mentoring, Innovation, and Leadership in Educational Scholarship Award. He was also this year's recipient of the AAMC Alpha Omega Alpha Glaser Award.





Deronisha Arceneaux (Cell and Developmental Biology, Ken Lau lab) and **Kimberlyn Ellis** (Human Genetics, Lea Davis lab) were named HHMI Gilliam Fellows.



Yasminye Pettway (Molecular Physiology and Biophysics, Alvin Powers lab) was selected as the 2023 Vanderbilt Prize Student Scholar.

The 2023 recipients of the Dean's Award for Exceptional Achievement in Graduate Studies, their programs, and their mentors are:

- **Brooke Christensen**, Neuroscience. Advised by Erin Calipari.
- **Steven Wall**, Microbe-Host Interactions. Advised by Ivelin Georgiev.
- **Matthew O'Neill**, Human Genetics. Advised by Dr. Dan Roden.
- **Jenny Tran**, Biochemistry. Advised by Breann Brown.
- **Tara Mack**, Human Genetics. Advised by Dr. Alexander Bick and Lea Davis.
- **Marianne Casilio**, Hearing and Speech Sciences. Advised by Stephen Wilson (University of Queensland).
- **Marina Hanna**, Neuroscience. Advised by Vivian Gama.
- **Allison Lake**, Human Genetics. Advised by Lea Davis.
- **Margret Fye**, Cell and Developmental Biology. Advised by Irina Kaverina.
- **Kirsty Erickson**, Neuroscience. Advised by Cody Siciliano.

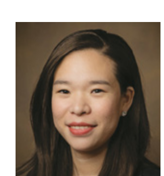
Rafael Arrojo e Drigo (Molecular Physiology and Biophysics) received the Robert L. Sorenson Young Investigator Award from the Midwest Islet Club.

The W. M. Keck Foundation Board of Directors awarded a three-year, $1.2 million grant to **Chuck Sanders** (Biochemistry) and **Roy Zent** (Medicine) for a project titled "Genetic Intolerance Patterns as a Treasure Map to Genes that Define Us as Human."

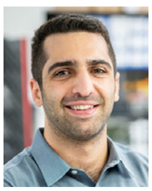
Snigdha Mukerjee (Cody Siciliano lab) was awarded a NARSAD Young Investigator Grant from the Brain & Behavior Research Foundation.

JooEun Kang, MD/PhD'23, received the Somerfeld-Ziskind Research Award from the Society of Biological Psychiatry for a first author paper that she wrote in the Ruderfer lab, "Dissecting the Shared Genetic Architecture of Suicide Attempt, Psychiatric Disorders, and Known Risk Factors."

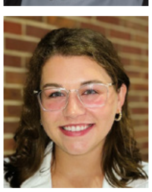
Neil Dani (Cell and Developmental Biology) was named a Rita Allen Foundation Scholar. This prestigious grant program supports early-career biomedical scientists conducting innovative research.



Ayaka Sugiura (Microbe-Host Interactions, Jeff Rathmell lab) and **Camille Wang** (Neuroscience, Lisa Monteggia and Ege Kavalali labs), aspiring physician-scientists, are among the 2023 recipients of highly competitive P.E.O. Scholar Awards.

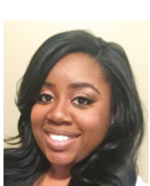



Emily Hodges (Biochemistry) and **Cody Siciliano** (Pharmacology) were selected as 2023 Dean's Faculty Fellows of the School of Medicine Basic Sciences. This award recognizes early-career faculty members with impressive records of scientific accomplishments.

Darian Carroll Thomas (Molecular Physiology and Biophysics, Maureen Gannon lab) and **Jordyn Barr** (Biological Sciences, Julián Hillyer lab) were among the five graduate students selected as the 2023–24 SEC Emerging Scholars.

James O'Connor, PhD'22, received the 2023 Larry Sandler Award from the Genetics Society of America. This international award is presented to a recent graduate with the best Ph.D. dissertation on *Drosophila*.

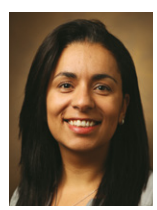


Jessica Thomas (Roger Colbran lab) received the 2023 Henry Grass Rising Stars in Neuroscience Award from the Grass Foundation.

Ronald Emeson (Pharmacology) received the 2022 Innovation Award from the International Rett Syndrome Foundation.

Loic Fort (Ian Macara lab) was named a fellow in *Development*'s inaugural Pathway to Independence program.

Juan Carvajal García (Houra Merrikh lab) received a Helen Hay Whitney Foundation Postdoctoral Research Fellowship.



Mariana Byndloss (Pathology, Microbiology and Immunology) was selected as a Burroughs Wellcome Fund 2023 Investigator in the Pathogenesis of Infectious Disease.

Zer Vue (Antentor Hinton Jr. lab) received the 2023 M&M Postdoctoral Scholar Award, sponsored by the Microscopy Society of America.

Hey, graduate and postdoc alumni!

Have something to share with us, such as a personal or professional accomplishment? Scan the QR code or visit https://redcap.link/BasicSciencesClassNotes and tell us about it. We'll give you a shoutout in our next issue.

Class Notes

2012

Christina Keeton, PhD'12 (Biochemistry), recently became the associate director of graduate and postdoctoral scholar coaching and engagement at the Vanderbilt University Career Center.

2018

Chuck Herring, PhD'18 (Cell and Developmental Biology), was recently named winner of the Emma Whitelaw ECR Publication Award, an award for early-career researchers.

2019

Aparna Shekar, PhD'19 (Pharmacology), recently became the director of therapeutic strategy (Neuroscience) at Novartis.

Elizabeth Gibson, PhD'19 (Pharmacology), was promoted from to associate director in the Clinical Pharmacology, Pharmacometrics, and Bioanalysis group at Bristol Myers Squibb.

2020

Tyler Perfitt, PhD'20 (Molecular Physiology and Biophysics), recently started a new position as scientist I in neuroscience biology at Atalanta Therapeutics in Boston, Massachusetts.

2021

Jordyn Wilcox, PhD'21 (Neuroscience), **Fellow'22**, recently became an assistant teaching professor at the University of Notre Dame. She teaches undergraduates in psychology and neuroscience, contributing to the neuroscience and behavior major.

2023

Heather Caslin, Fellow'23, became an assistant professor of health and human performance at the University of Houston this fall.

Erin Green, Fellow'23, became an assistant professor in the Department of Microbiology at the University of Chicago this summer.

Tyler Hansen, PhD'23 (Biochemistry), is a postdoctoral fellow with Luis Barreiro at the University of Chicago.

Kavi Mehta, Fellow'23, is an assistant professor at the University of Wisconsin-Madison as of this summer.

Bradley Reinfeld, MD/PhD'23 (Cancer Biology), is completing his internal residency training at the Ronald Reagan UCLA Medical Center. He seeks to become a physician-scientist studying the metabolic milieu of kidney cancer to ultimately find better treatment combinations.

School *of* Medicine Basic Sciences

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