Vestigo

ISSUE 6, DECEMBER 2024

VANDERBILT UNIVERSITY **SCHOOL OF MEDICINE BASIC SCIENCES**

Strong then, strong now: Vanderbilt investigators push boundaries in diabetes research

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Innovation Ignition Fund: Derisking early-stage drug discovery targeting cardiovascular disease

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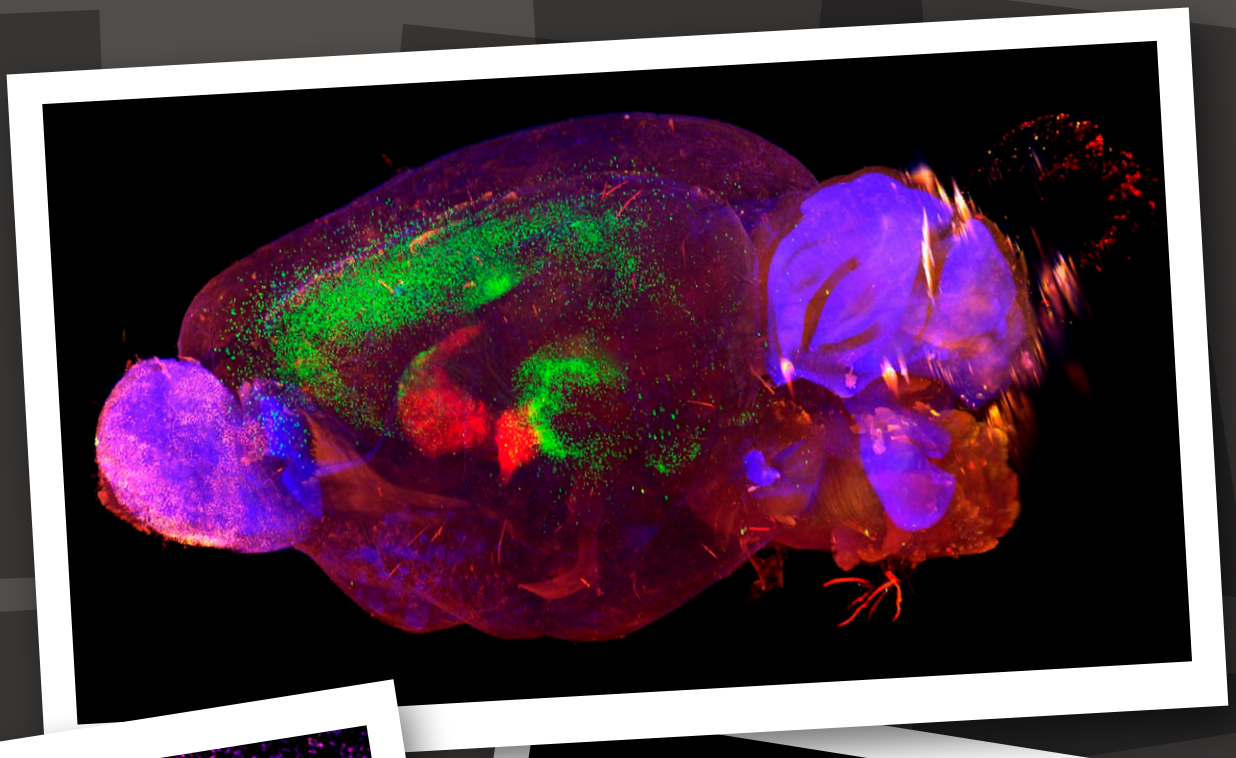
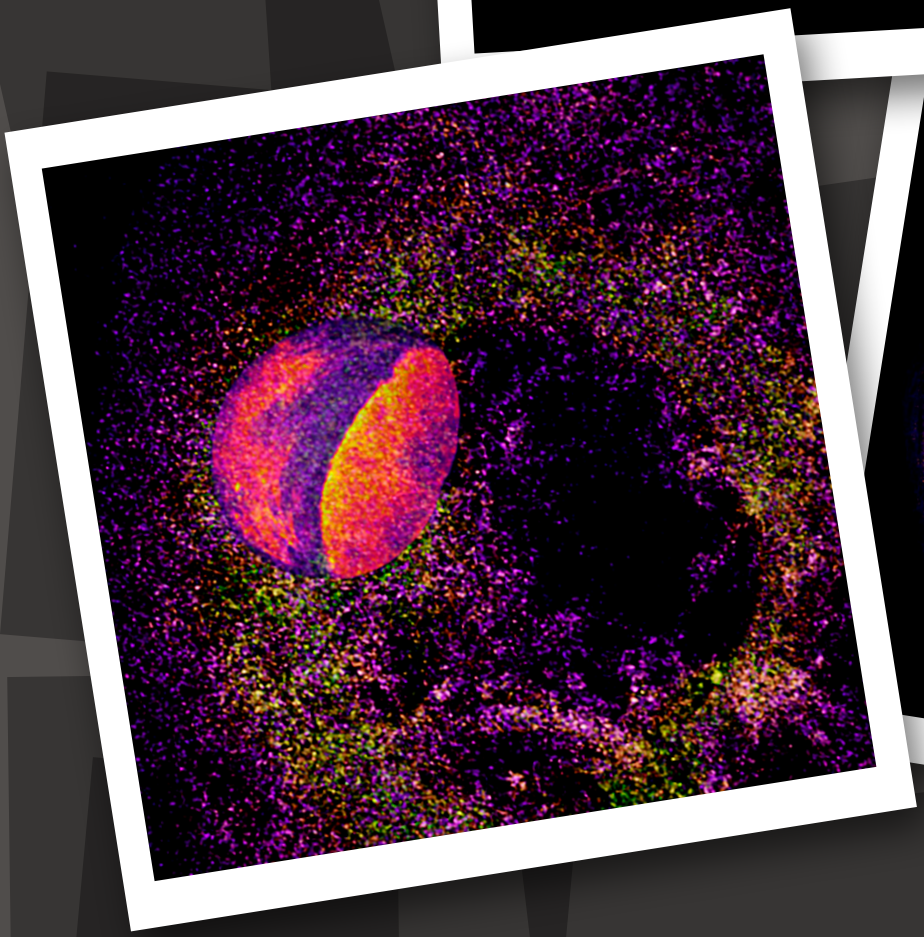
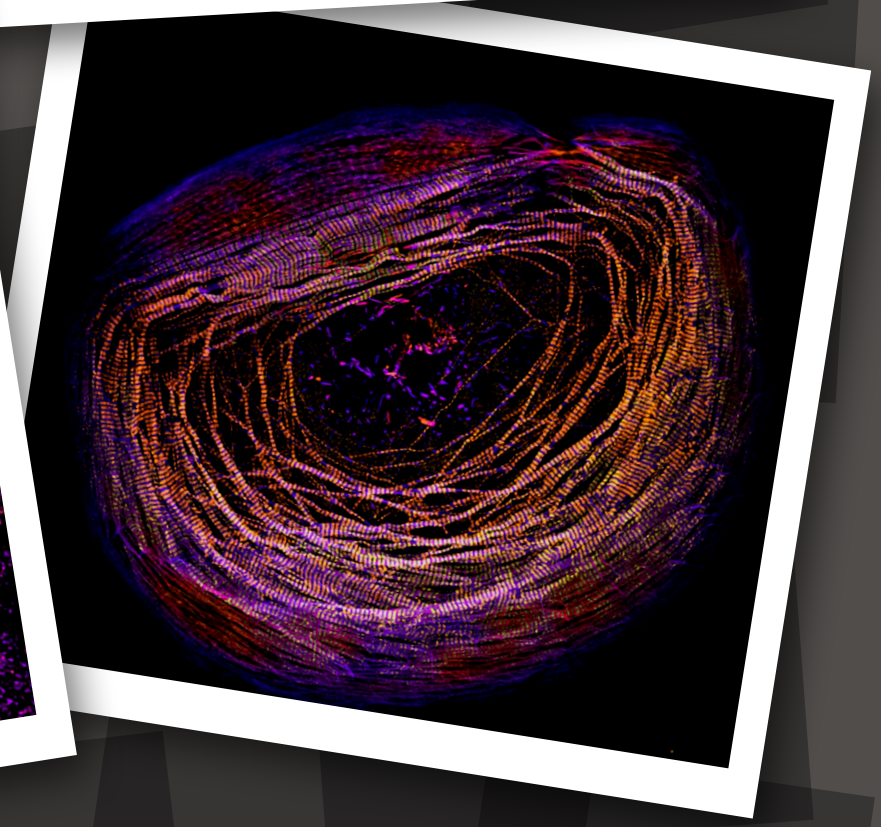
Vanderbilt launches plan to improve environmental sustainability of labs

This year we held the first-ever Cell Imaging Shared Resource Life Is Beautiful Image Contest, designed to showcase the beautiful images captured by CISR users as part of their biomedical research at Vanderbilt. Here are the 2024 winners.







Top: The first place image, by **Shane Watson**, *shows a whole mouse brain injected with two separate viruses: a Cre-dependent starter virus and a modified rabies virus. The starter virus infected Cre-expressing D2-type medium spiny neurons in the dorsal striatum (red).The modified rabies virus entered those same MSNs and traveled one synapse backward to denote retrograde, direct synaptic connections (green). This means that every green dot is an individual neuron that synapses directly onto the red, infected MSNs in the dorsal striatum.*

Left: The third place image, by **Emma Koory**, *shows a clefted nucleus amongst cellular mRNA, which was labeled with fluorescence in situ hybridization. This particular probe labels the polyA tail of all cellular mRNA. The nucleus was stained with DAPI. The mRNA channel was depth coded, resulting in multicolor dots. The nucleus was colored using the mpl-inferno LUT in Fiji.*

Right: The second place image, by **James Hayes**, *shows a cardiac myocyte cell, one of thousands that your heart uses to drive your heartbeat. The primary structures pictured in the cell are known as sarcomeres, which are the contractile units of muscle. The darker purple in the image shows sarcomere actin filaments stained with phalloidin. The lighter gold and yellow colors are myosin filaments stained with an antibody. Myosin filaments pull on the sarcomere actin filaments to produce force, driving the heartbeat.*

In this issue

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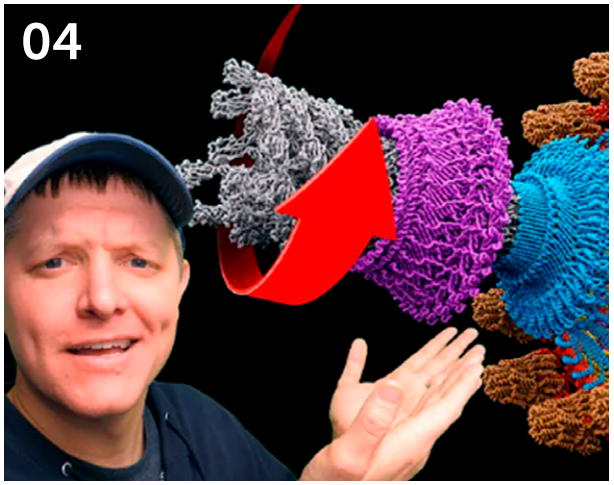
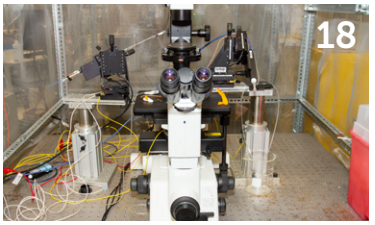
Cover: This image, taken by recent alum Darian Carroll, is a pancreatic islet from a 3-year-old nonhuman primate. Pancreatic islets are responsible for creating and secreting insulin, and Carroll studied them while a student in the lab of Maureen Gannon, professor of medicine. Insulin is shown in green, a mitochondrial marker in magenta, and DNA in blue.

Microscope and technique: Spinning disk confocal immunofluorescent microscopy using a Nikon CSU-W1 with super resolution by optical pixel reassignment taken with a 100X objective





IN EVERY 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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Vanderbilt School of Medicine Basic Sciences

Dear alums and friends:

JOHN RUSSELL

In the previous issue of *Vestigo*, we paused to look back at 150 years of innovative research. In this issue, we look ahead to new and amazing research breakthroughs coming out of our laboratories and their potential impact in treating and eliminating specific diseases.

Widespread antimicrobial resistance has created both a global crisis and a challenge for physicians and researchers. Two recent discoveries from Basic Sciences labs provide promising new avenues to combat persistent and treatment-resistant pathogens. One remarkable finding comes from our researchers who have uncovered fascinating details about the molecular machinery that powers bacterial flagella (page 4). Their work, which clarifies the intricate workings of these microscopic propellers, suggests that disrupting the flagellar motor could render certain bacteria immobile and unable to infect host cells. A second team of researchers has discovered the first evolution-inhibiting chemical compound that prevents drug resistance from developing in bacteria in the first place, a potential tool in the fight against superbugs (page 5).

Another recent advance with major implications for the clinic is a new method that could revolutionize disease diagnosis and monitoring and open the door to the use of "liquid biopsies," minimally invasive blood tests that could replace traditional tissue biopsies for certain conditions (page 3). The potential benefit to patients is huge, as liquid biopsies are generally safer and more accessible, and they can provide real-time insights into disease progression and treatment response.

And of course, our researchers are continuing to use and expand on their work with assistance from artificial intelligence and machine learning (pages 10, 23). You may have noticed how pervasive AI is becoming in our culture, and certainly it has a role to play in biomedical research.

These are just a few examples of the transformative research taking place in our Basic Sciences laboratories. I am truly excited to see the real-world impact these innovations will have in the years to come. I invite you to explore the following articles to learn more about these, and more, remarkable discoveries.

Sincerely,

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

WHAT'S NEW IN SCIENCE?

Vanderbilt scientists develop new tool that could lead to noninvasive "liquid biopsies"

Biopsies are clinical tools commonly used to diagnose a variety of diseases or to monitor tissue for abnormal growth or even rejection of a transplant. During biopsies, tissue samples are removed from the body so they can be examined more closely, but depending on the type of tissue that's needed, the procedure can be rather invasive.

Researchers from the School of Medicine Basic Sciences recently developed an analytical tool that could lead to the use of "liquid biopsies" as a substitute for traditional biopsies for certain patients or diseases. The tool, called EV Fingerprinting, was the culmination of the dissertation work of **Ariana von Lersner**, a former graduate student and current postdoctoral scholar in the laboratory of **Alissa Weaver**, Cornelius Vanderbilt Professor of Cell and Developmental Biology and was described in a paper published in *ACS Nano* in April 2024.

The "EV" in EV Fingerprinting stands for extracellular vesicles, which are membrane-bound particles that contain biologically active cargo and that contribute to cell-cell communication in health and disease. Although EVs have been observed since at least the 1980s, their origin and purpose have not been clearly defined. The last two decades have seen research into EVs skyrocket, and EVs have been found to have roles in endocrine processes, immune responses, and even cancer progression in a variety of species, including humans.

The term "EV" encompasses vesicles of various sizes and cargos, each likely tailored to different functions. Changes in the heterogeneity of EVs in an organism can reflect changes in biological state—for example, a cancer state vs. a normal, nondisease state—which can serve as a clinically informative biomarker.

"Fingerprinting allows you to characterize EVs with minimal sample preparation in a high-throughput manner, and allows you to better classify the types of vesicles in the sample," von Lersner said.

The technique involves isolating EVs from the rest of the cellular content in a sample, labeling them with a fluorescent lipophilic dye that intercalates into the EVs' lipid bilayer, and running them through a flow cytometer, an instrument that shoots a laser at a sample and collects information about how the light is refracted or emitted. The collected information is compiled into a "fingerprint" that can be used to perform quantitative analyses of distinct EV populations and determine how they are altered by experimental manipulation, molecular perturbation, or disease state.

EV Fingerprinting is an unprecedented advancement toward the characterization of EVs because it can analyze the composition of the lipid bilayers of the EVs in a sample and break the sample down into individual EV populations, which previous bulk analysis methods could not do. Using the composition of the lipid bilayers to separate EV populations is a novel approach that capitalizes on an EV characteristic that had been previously overlooked by the field.

HARRISON MCCLARY

Alissa Weaver, left, and Ariana von Lersner

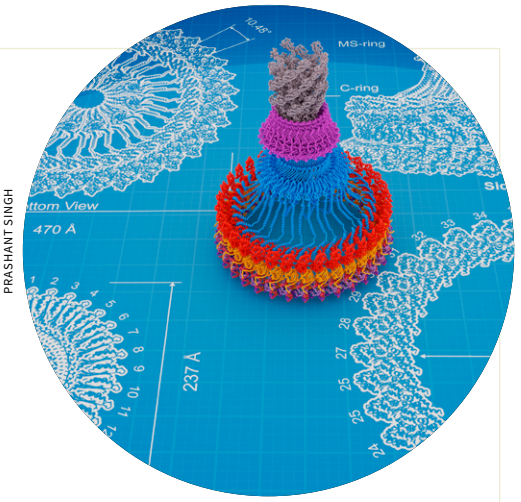
The work was completed thanks to the contributions of Vanderbilt collaborators from the departments of cell and developmental biology, chemical and biomolecular engineering, and pathology, microbiology and immunology and the Center for EV Research, and external collaborators from the Cedars-Sinai Medical Center and Genentech. The Center for EV Research, established in 2021, is managed under Weaver's direction and provides shared instrumentation and training for EV work, fosters interdepartmental discussion and collaboration through monthly seminars and annual retreats, and provides members with funds to conduct or share EV-related work at conferences.

"EV Fingerprinting is furthering the development of liquid biopsies in which the EVs can be used as biomarkers for diseases such as cancers or neurological disorders," von Lersner said.

If you find yourself needing a biopsy one day and can forgo the traditional kind in favor of a simple blood draw, you may have these researchers to thank. — **By Lorena Infante Lara**

WHAT'S NEW IN SCIENCE?

'Smarter Every Day' explores how bacteria move to survive—and make us sick



PRASHANT SINGH

3D construction of the bacterial motor, created by Prashant Singh.

In a recent episode of *Smarter Every Day*, YouTube sensation and host Destin Sandlin talks with Vanderbilt Professor **Tina Iverson** and Senior Research Associate **Prashant Singh** about bacterial "motors" and how they work in the microorganisms that make us sick. The video racked up more than 1.4 million views in its first day.

Humans have always battled infections caused by bacteria—everything from abscessed teeth and strep throat to botulism and pneumonia. The single-celled organisms cause about 8 million deaths each year worldwide, and they constantly adapt to resist the antibiotics we have developed to kill them.

Iverson, who holds the Louise B. McGavock Chair and is a professor of pharmacology, and Singh, with other researchers around the world, learned that bacteria change direction through chemotaxis: a process in which a molecular motor drives a bacterium's whiplike flagella to act like a boat propeller, pushing the bacteria around to look for food, avoid danger, and find comfortable places to multiply—thus causing infections. Understanding chemotaxis, researchers say, may help us learn how to prevent those infections from taking hold.

As antibiotic resistance grows, making infections increasingly difficult to treat, the team is investigating how other bacterial components interact with this motor. Using this knowledge, they seek to develop new treatments for persistent and drug-resistant infections.

"Innovative research like this exemplifies the groundbreaking work our faculty and collaborators are doing to address global health challenges," said **Provost C. Cybele Raver**. "By unraveling the mechanisms of bacterial movement, we are paving the way for novel treatments that can save millions of lives."

Chemotaxis is essential for virulence in animals and a potential target for new therapeutics, but the process itself needs to be better understood.

The Iverson lab, in collaboration with researchers at the University of California, San Francisco; Stanford University; and The Weizmann Institute of Science in Israel, provided new insights on chemotaxis in a paper published in *Nature Microbiology*.

Chemotaxis requires a small motor to turn a flagellum—a hairlike appendage on bacteria that spins to provide propulsion, like a boat motor. Rotating the flagellum clockwise or counterclockwise at different rates allows bacteria to move toward or away from stimuli. Current research hasn't come up with an agreed-upon architecture of the central components of the motor that powers the flagellum, which has hindered researchers' understanding of and ability to target chemotaxis with drugs. The current work, spearheaded by senior research associate in the Iverson lab Prashant Singh, puts forth new information about how a motor component called a switch reverses rotation and transmits torque to the flagellum.

To do this, the researchers looked at *Salmonella enterica*, a bacterium responsible for approximately 60,000 deaths globally per year, as a model. After isolating and purifying *S. enterica* motors stabilized in different swimming configurations, the collaborators leveraged the power of Vanderbilt's Titan Krios, a $10M cryo-electron microscope acquired by the School of Medicine Basic Sciences that was made available through the Center for Structural Biology's Cryo-EM Facility.

The structures provided the researchers with information about how the bacterial motor powers clockwise and counterclockwise rotation of the flagellum, which allows a bacterium to swim straight or switch directions while swimming. It also helped them understand how proteins bind to the motor to help regulate bacterial movement.

These results are applicable to a broad range of infections. For instance, the Salmonella chemotaxis machinery is nearly identical to that of *Escherichia coli*, which is responsible for over 250,000 infections per year in the U.S. alone. Because chemotaxis is required for infection, selectively disrupting the interactions that allow pathogens to form a reservoir within an organism can help to prevent recurrent infections without impacting the normal microbiome.

The Iverson lab is now working to identify how an expanded range of different protein partners bind to the flagellar motor during chemotaxis, and they hope that this will lead to ways to disrupt chemotaxis during infection.

— By Lorena Infante Lara

Vanderbilt biochemists discover breakthrough evolution-resistant compound to combat antibiotic resistance

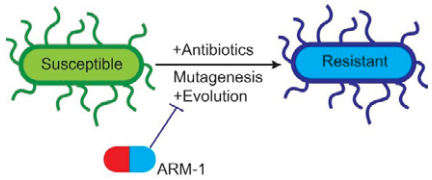
Vanderbilt scientist **Houra Merrikh** led a team of researchers who discovered the first evolution-resistant chemical compound that prevents drug resistance development in bacteria. The compound is also a drug development platform that targets antimicrobial resistance during treatment of infections with antibiotics and evolution in general, Merrikh said.


VANDERBILT UNIVERSITY
Houra Merrikh

The World Health Organization ranks AMR in human and animal populations as one of the top 10 global health risks, according to United Nations report. By the year 2050, as many as 10 million lives could be lost every year to this issue, potentially devastating economies and severely disrupting agricultural output.

AMR develops when bacteria, viruses, parasites, or fungi become unaffected by antimicrobial treatments that had previously worked. Earlier research by the Vanderbilt team showed that DNA translocase Mfd—a protein responsible for moving molecules across cell membranes—causes genetic mutations and speeds up the development of AMR.

In this study the biochemists, including Research Assistant Professor of Chemistry **Kwangho Kim** and Professor of Biochemistry **Martin Egli**, used a high-throughput screen of living cells to discover a small molecule that inhibits mutations caused by Mfd. In addition to diminishing genetic mutations, the molecule named ARM-1 slows the development of antibiotic resistance across a broad spectrum of bacterial pathogens. These findings suggest that combining a to-be-developed drug that inhibits Mfd with traditional antibiotics is a promising strategy to prevent the progression of antibiotic resistance during the clinical treatment of infectious diseases.



Graphical abstract from Carvajal-García et al., 2024, NAR Molecular Medicine shared in accordance with a with a CC BY license.

Following this study, the team will be optimizing ARM-1 for clinical translation. "Our goal is to move the identified compound into medicinal chemistry and develop a clinically effective drug," said Merrikh, who is also a member of the Vanderbilt Institute for Chemical Biology. "We will focus on difficult-to-treat infections like cystic fibrosis, urinary tract infections, and tuberculosis infections."

— **By Marissa Shapiro**

Lau lab publishes authoritative reference article on the hallmarks of precancer

Every oncologist and cancer researcher is familiar with the hallmarks of cancer, a series of functional capabilities that human cells acquire as they transition from a normal state to a neoplastic state (a state of excessive and abnormal growth). These hallmarks have been used (and updated) during the last quarter of a century as a "conceptual scaffold" to help "rationalize the complex phenotypes of diverse human tumor types and variants in terms of a common set of underlying cellular parameters" (Douglas Hanahan, 2022, *Cancer Discovery*).


VANDERBILT UNIVERSITY
Ken Lau

Now, **Ken Lau**, professor of cell and developmental biology, and **Neelendu Dey**, assistant professor of medicine at the University of Washington, and colleagues have laid out the principles governing the biology of early, precancerous lesions, which are different from the principles that govern cancers. Their authoritative perspective was published in *Cancer Discovery* in April 2024.

A large body of research details how lifestyle factors can predispose a person to cancer initiation and development, but how those macroenvironmental risk factors are manifested in cells and molecules is poorly understood. Lau, Dey, and colleagues shed light on these points.

"Precancers are defined as 'at-risk tissues and lesions' that develop into cancer," Lau said. "Given the effectiveness of early interventions against cancers, we hope to establish some principles that the research community can follow when looking at precancers."

These principles include age-related genetic alterations, epigenetic changes, metabolic alterations, the hijacking of regenerative cell state transitions, the disruption of immune surveillance and "inflammaging," and remodeling of the tissue microenvironment mediated by senescence or biological aging. Inflammaging refers to the state of chronic, sterile, and low-grade inflammation that naturally occurs with advanced age.

"By understanding the hallmarks of precancer, we hope that we can further develop early detection, stratification, and intervention strategies at the precancer stage," Lau said.

Just as the hallmarks of cancer are updated as we develop new knowledge, Lau and colleagues hope to update the hallmarks of precancer as we learn more about them.

Zhengyi Chen *and* **Sarah E. Glass**, *graduate students in the Chemical and Physical Biology program and the Department of Cell and Developmental Biology, respectively, were co-first authors with Mary M. Stangis from the University of Wisconsin-Madison, Jimin Min from the University of Texas MD Anderson Cancer Center, Jordan O. Jackson from the University of Washington, and Megan D. Radyk from University of Michigan Medical School.* **Robert Coffey**, *professor of medicine and cell and developmental biology, and* **Martha Shrubsole**, *research professor of medicine, were also co-authors on the paper.* — **By Lorena Infante Lara**

WHAT'S NEW IN SCIENCE?

Combining unique methods, Kuriyan lab discovers new protein functions; explores physical space of proteins

Researchers in the lab of **John Kuriyan**, University Distinguished Professor of biochemistry and chemistry and dean of the School of Medicine Basic Sciences, have revealed a key element of how a molecular machine responsible for high-speed DNA replication works. The results of their study build on growing theories of molecular evolution.

Clamp loaders—proteins that help load DNA replication machinery onto the DNA—have a variety of biological functions that change as their structure evolves. These proteins are found in all of life—from single-celled organisms to humans. Over the last decade, the structure and function of the clamp loader were thought to be well understood based on a handful of snapshots of its three-dimensional structure. This research, led by co-first authors postdoctoral fellow **Kendra Marcus** and research assistant professor **Yongjian Huang**, revealed the bigger picture.


VANDERBILT UNIVERSITY

John Kuriyan

"By combining deep mutagenesis and cryogenic electron microscopy, we found a key structural intermediate that was not seen in these [snapshots] and illustrated the conformational changes needed for the clamp loader to do its job," Marcus said. "Not only this, but we see regions of the protein that we thought were 'unimportant' participate in highly coordinated processes."

The unique pairing of deep mutagenesis and cryo-EM is what led to this discovery. Deep mutagenesis maps important regions of a protein by revealing its mutational sensitivity, or how a protein responds to a mutation, and cryo-EM produces three-dimensional visualizations that aren't usually seen in crystal structures. Studying the mutational sensitivity of proteins sheds light on how the protein architecture influences its function and how evolution can tune these variables to give proteins new tasks.

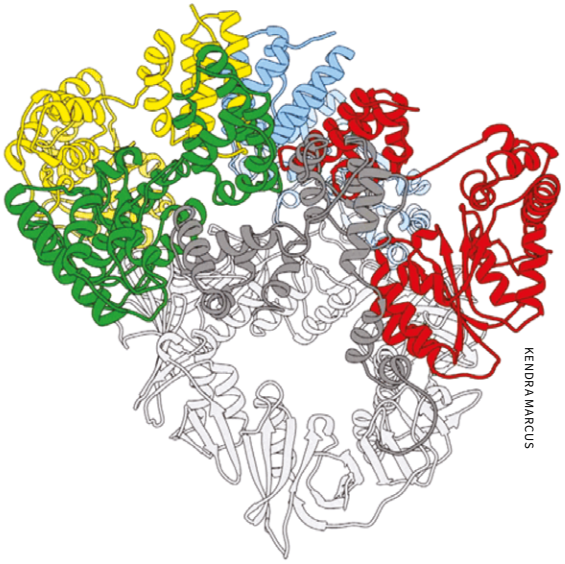
The researchers first inferred a new state of the clamp loader based on the deep mutagenesis data and then visualized it using cryo-EM, which revealed a previously unseen conformational state, or arrangement of atoms that give the clamp loader its shape.

"One of the unique strengths of cryo-EM lies in its power to capture the ensemble of conformational states adopted by these macromolecular machines, such as the clamp loader," Huang said. "In this study, cryo-EM allows us to visualize the molecular details of a newly discovered conformational state and the critical conformational changes required for the function of clamp loader."

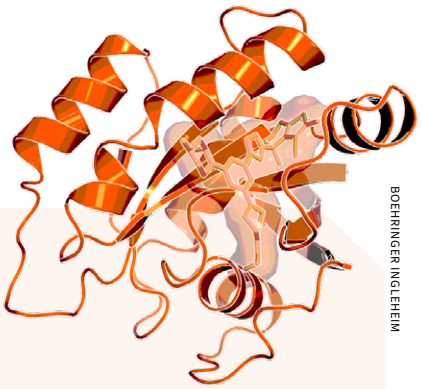
These findings have implications in evolutionary theory and how proteins use "insignificant" places in these molecular machines to become conditionally important in the adaptation of new functions, Marcus said. Following this discovery, the Kuriyan lab is now leveraging machine learning techniques to design and test new clamp loader proteins based on the lab's current findings. These types of experiments offer tremendous utility toward understanding how proteins change function because of disease-related mutations or in response to drugs.

"We hope that these results inspire biochemists and molecular biophysicists to apply creative methods to explore the physical space of proteins," Marcus said. "This work illustrates how evolutionary theory can elevate our structurally oriented understanding of protein functions." — **By Marissa Shapiro**

> "We hope that these results inspire biochemists and molecular biophysicists to apply creative methods to explore the physical space of proteins."
>
> **— Kendra Marcus, postdoctoral fellow**


KENDRA MARCUS

The T4 bacteriophage clamp loader morphs between inactive and active states. When bound to DNA, the clamp loader is "pulled" into a spiral conformation, creating an "active" conformation. When the DNA disengages from the clamp loader, the complex relaxes into a more planar, inactive state.



BOEHRINGER INGLEHEIM

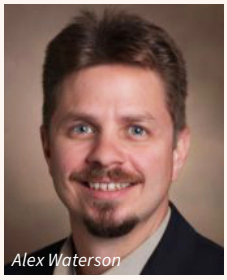
X-ray structure of the complex of BI-0474 with KRAS^{G12C}

Cancer-killing compound discovered at Vanderbilt is now available through Boehringer Ingelheim open science portal opnMe

Researchers in the lab of **Stephen Fesik**, Orrin H. Ingram II Chair in Cancer Research and professor of biochemistry, have added BI-0474 as the second molecule co-discovered by Vanderbilt to the open science portal opnMe.com, an initiative being driven by biopharmaceutical company Boehringer Ingelheim.

BI-0474 is an irreversible covalent inhibitor of KRAS^{G12C}, a mutant KRAS in which a glycine amino acid of the protein is replaced by a cysteine. BI-0474 holds the promise of blocking the cancer-causing functions of this mutation, which is one of the most common found in KRAS. KRAS is one of the most commonly mutated proteins in cancer, driving 32 percent of lung cancers, 40 percent of colorectal cancers, and 85 percent to 90 percent of pancreatic cancer cases. It has been thought to be an undruggable target since its discovery in 1983, but recent advancements have resulted in agents that can successfully target KRAS^{G12C}.

VANDERBILT UNIVERSITY



Alex Waterson

"The value of putting BI-0474 on opnMe is to allow global scientists to find creative uses for the compound, which may ultimately benefit cancer patients," said **Alex Waterson**, research professor of pharmacology and associate director of drug discovery in the Vanderbilt Institute for Chemical Biology. "It gives researchers who may not have had access to a well-characterized G12C inhibitor before the opportunity to learn. Who knows what science will develop!"

The researchers started their work by trying to build a comprehensive attack on RAS. Preliminary KRAS research in the Fesik lab identified compounds binding at one of the protein's two binding sites. However, the binding strength (affinity) of these molecules was very weak. This led the lab to invent a new technique to block that site, allowing them to find new chemical matter that interacts with a second site near the G12C mutation.

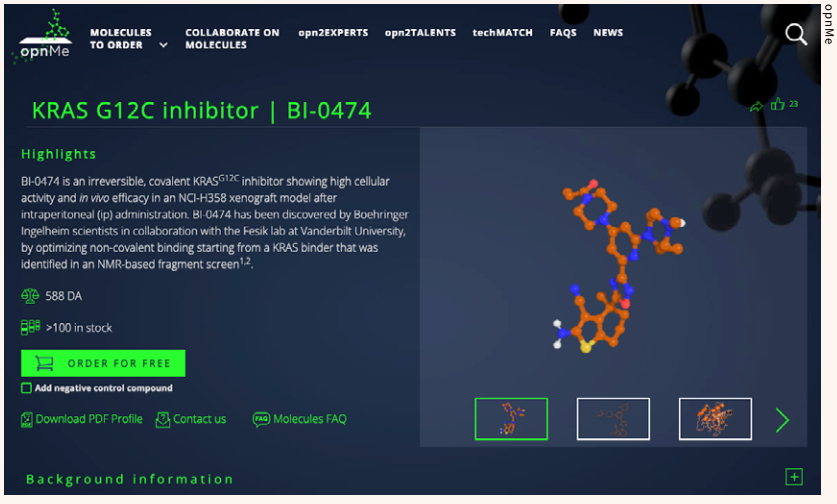
Uniquely, the approach that led to BI-0474 started with the optimization of a reversibly binding fragment that was attached to an electrophile designed to engage the cysteine. BI-0474, like other G12C-targeted compounds, works by taking advantage of the cysteine mutation. Some of the first successful attempts to target KRAS have targeted KRAS^{G12C} because of its sulfur, which allows researchers to make inhibitors that form a strong covalent bond with KRAS. "Working with the sulfur—the only strongly nucleophilic amino acid—as a handle allowed us to take advantage of a reaction with it in a way that can't easily be done with any other amino acid," Waterson said. "We were trying to approach it from the reversible binder first and then add a cysteine binding function, rather than start with something that reacts first and then make it better."

According to Boehringer Ingelheim, BI-0474 is a highly potent KRAS^{G12C} inhibitor showing a high second-order rate (k^{inact}/K_i) and low K_i in mass spectrometry experiments detecting covalent protein modification of KRAS^{G12C}. It also shows in vivo biomarker modulation and in vivo efficacy in KRAS^{G12C}-mutated xenograft models after intraperitoneal administration.

In addition to Fesik and Waterson, Vanderbilt researchers who contributed to this work include Research Assistant Professor **Jason Phan**, former postdoctoral research fellows **Andrew Little** and **Jason Abbott**, and former graduate student **Qi Sun**.

"The joint discovery of KRAS^{G12C} inhibitor BI-0474 together with our partners from Vanderbilt University represents a remarkable success in our endeavor to combat one of the most commonly mutated oncogenetic drivers of cancer," said Norbert Kraut, global head of cancer research of Boehringer Ingelheim. "I congratulate my colleagues as we have been able to release this well-characterized KRAS inhibitor now on our open innovation portal, opnMe.com, with the goal to share it with scientists worldwide to come up with new therapeutic strategies to transform patients' lives." — **By Marissa Shapiro**

The KRASG12C inhibitor is freely available on opnMe.



WHAT'S NEW IN SCIENCE?

Research Snapshot:

Protons can tune synaptic signaling by changing the shape of a protein receptor

THE IDEA

Synaptic plasticity, the ability of synapses to strengthen or weaken over time in response to changes in their activity, is a central foundation of learning and memory. At synapses, presynaptic cells transmit signals to postsynaptic cells through a dance that is orchestrated by neurotransmitters, protons, receptors, scaffolding proteins, signaling molecules, and more.

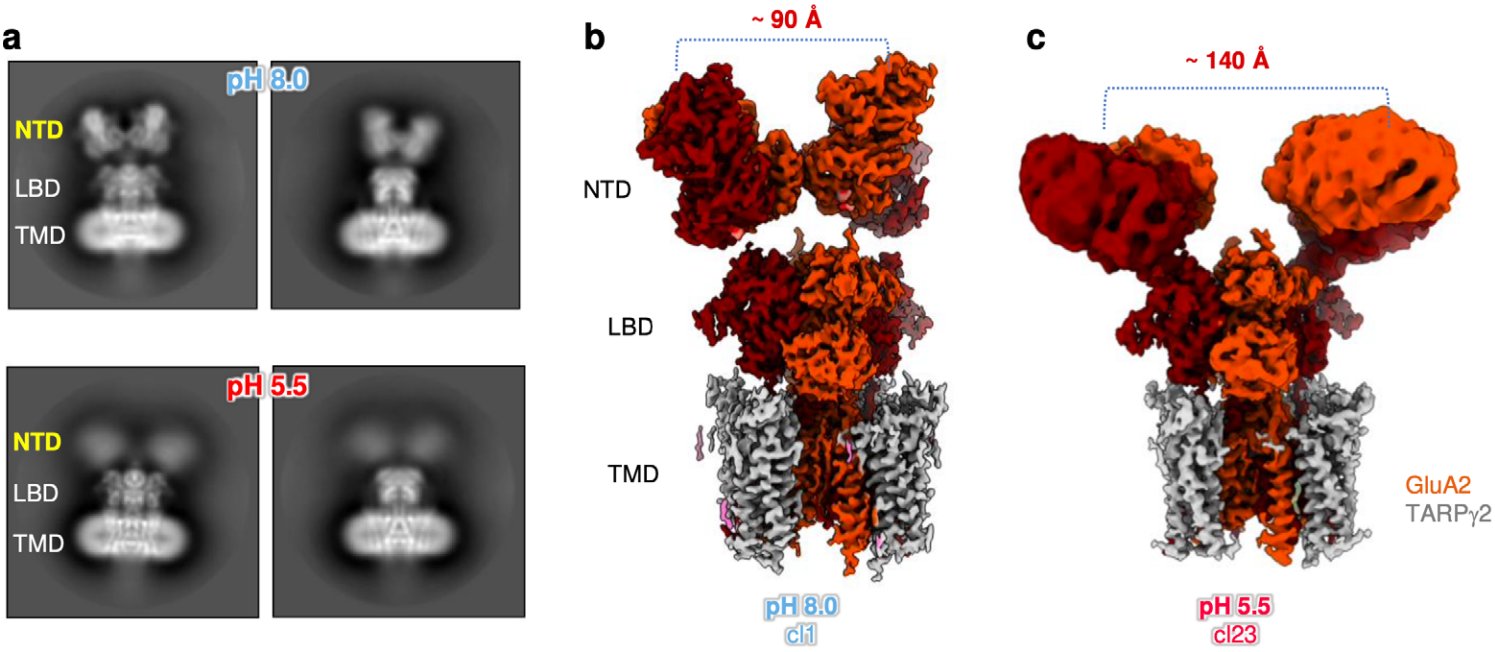
AMPA receptors, ligand-gated ion channels that mediate fast, excitatory synaptic transmissions, are activated by glutamate, the primary neurotransmitter of the mammalian brain. Surprisingly, however, AMPARs have a low affinity to glutamate, so they anchor themselves in close physical proximity to the site of glutamate release for optimal activation. The anchoring is mediated in part by their N-terminal domains.

During synaptic transmission, some protons are released together with glutamate, and the co-released protons participate in synaptic signaling mediated by the AMPARs. However, how protons modify AMPAR signaling was unknown.

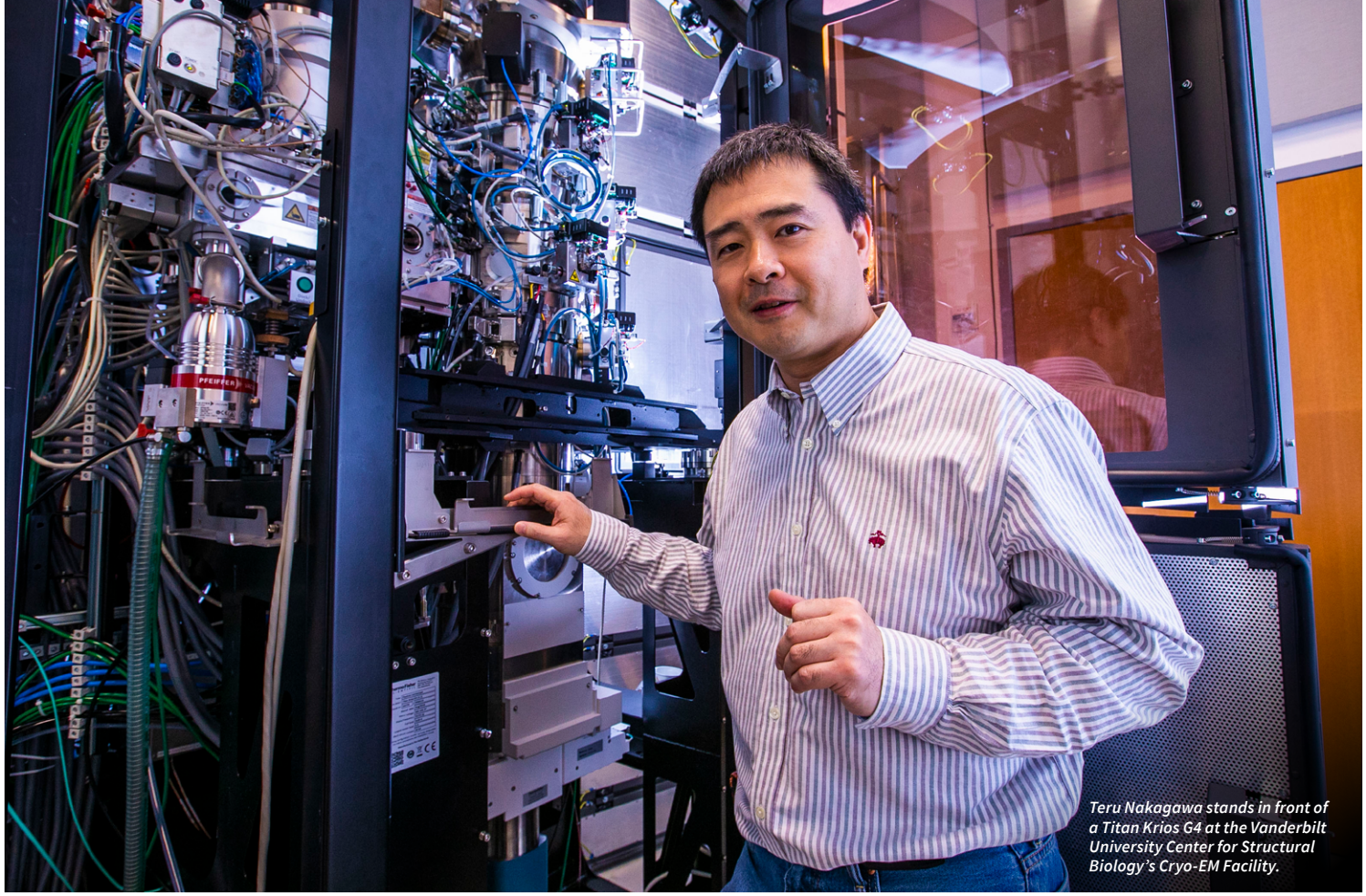
Now, research from the labs of **Dr. Teru Nakagawa**, professor of molecular physiology and biophysics, and Ingo Greger, group leader at the MRC Laboratory of Molecular Biology in Cambridge, England, reveals that a brief decrease in pH—a brief increase in the concentration of protons—can lead to changes in AMPAR's structure, thereby modulating its location and gating kinetics.

WHAT IT MEANS

Certain health conditions, such as ischemia (reduced blood flow and oxygenation) and stroke, are known for creating acidic environments in the brain, so understanding the role of protons on neuronal function can lead to a more nuanced understanding of brain injury and recovery.



This figure from the paper shows the splaying apart of the N-terminal domain of AMPAR. The left panels show cryo-EM images of the receptor at a higher pH (top) and at lower pH (bottom). The structures on the right, created from the cryo-EM images, show how the distance between the halves of the NTD increases from ~90 Å at pH 8.8 to ~140 Å at pH 5.5. (Image cropped and shared in accordance with a CC BY 4.0 license. Ivica et al., 2024, Nature Structural and Molecular Biology.*)*



Teru Nakagawa stands in front of a Titan Krios G4 at the Vanderbilt University Center for Structural Biology's Cryo-EM Facility.

ANNE RAYNER

Nakagawa's new research, published in *Nature Structural and Molecular Biology*, shows that when protons are released at the synapse and interact with a particular amino acid in an AMPAR, they cause the receptor's N-terminal domain to splay in half. The effects of the splaying are twofold: It slows the receptor's recovery before it can activate again, and it increases receptor diffusion by breaking the receptor's anchor from the optimal location for activation, ultimately reducing AMPAR activity and impacting synaptic strength and plasticity.

WHAT'S NEXT

The molecular processes behind cognition, learning, and memory formation are not well understood, yet scientists know that AMPARs are central to these processes. In addition to their role in normal physiology, deficiencies in AMPAR functioning have been linked to a variety of neurological and psychiatric disorders such as seizures, Alzheimer's disease, major depressive disorder, limbic encephalitis, intellectual disability, and autism spectrum disorder.

Nakagawa's work on resolving the role of protons during synaptic transmission will have particular implications for our understanding of short-term and long-term synaptic plasticity.

GO DEEPER

The paper "Proton-triggered rearrangement of the AMPA receptor N-terminal domains impacts receptor kinetics and synaptic localisation" was published in *Nature Structural and Molecular Biology* in August 2024. **— By Lorena Infante Lara**

> "Synaptic plasticity, the ability of synapses to strengthen or weaken over time in response to changes in their activity, is a central foundation of learning and memory."
>
> **— Teru Nakagawa, professor of molecular physiology and biophysics**

WHAT'S NEW IN SCIENCE?

Research Snapshot:
Exploring the range of AlphaFold2's utility within the realm of protein dynamics

THE IDEA

AlphaFold, the revolutionary artificial intelligence program developed by DeepMind (a subsidiary of Alphabet, Google's parent company), uses machine learning to predict the 3D structures of proteins. Traditionally, protein structures are determined experimentally using methods such as X-ray crystallography or cryo-electron microscopy; however, proteins often adopt multiple conformational states, which may require multiple experimental structures over time to identify them. The development of new computational tools such as AlphaFold can cut down on the time needed to fully understand the relationship between a protein's structure and function.

The AlphaFold software—now in its third iteration, AlphaFold3—has dramatically changed the field of structural biology. Yet not every tool is without its drawbacks, and new tools must be pushed and prodded to determine the full extent of their potential.

To this point, a group of School of Medicine Basic Sciences researchers led by **Dr. Benjamin P. Brown**, assistant professor of pharmacology and member of the Center for Applied Artificial Intelligence in Protein Dynamics, set out to investigate the extent to which AlphaFold2 has learned biologically meaningful energetics of protein conformations.

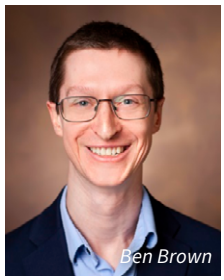
The collaboration brought Brown together with Research Associate Professor of Molecular Physiology and Biophysics **Richard A. Stein**, Research Professor of Chemistry and Associate Professor of Pharmacology **Jens Meiler**, and Professor of Molecular Physiology and Biophysics **Hassane Mchaourab** and resulted in a publication in the *Journal of Chemical Theory and Computation*. Mchaourab, one of the corresponding authors, is the founding director of Vanderbilt's Center for Applied AI in Protein Dynamics.

WHY IT MATTERS

The likelihood that a protein will find itself in a given conformational state is directly related to the relative energetics of all accessible conformations. According to Brown, predicting which conformation a given protein will find itself in is extremely computationally expensive and scales poorly with the size of the system. The researchers strive to develop approaches that make inferring dynamic properties of proteins more computationally tractable.

To that end, Brown and colleagues used AlphaFold2 to see whether it had learned thermodynamic information, specifically as it relates to conformational free energies, and whether it could approximate the conformational flexibility of proteins.

The experiments yielded two main conclusions. First, even though the final output of AlphaFold2 is a static, non-moving structure, AlphaFold2 learns information that can suggest important dynamical properties of proteins. Second, AlphaFold2 is not entirely "mutation sensitive," in other words, it does not necessarily correctly predict changes in the structure of a protein when a single amino acid is changed to a different amino acid. However, the researchers found that this does not mean that AlphaFold2 views each


VANDERBILT UNIVERSITY
Ben Brown

Research Snapshot:
Hodges lab sheds new light on mechanisms of gene regulatory divergence between species

The idea

Closely related animal species can look physically different, but you might be surprised to learn that those differences can result not only from DNA sequence changes that alter proteins' structure or function, but also because changes in the DNA affect how those proteins are expressed. To add to that, not all differences between species can be explained by DNA sequence changes alone.


VANDERBILT UNIVERSITY
Emily Hodges

Molecular biologist **Emily Hodges**, assistant professor of biochemistry, studies the regulatory elements of our genome and is interested in parsing how changes in DNA sequence affect gene regulation.

The expression of genes is controlled by DNA sequence regulatory elements such as gene enhancers, which help increase the expression of a target gene. Species-specific changes in enhancer function can result from DNA sequence changes that occur directly within a single enhancer *(cis)* or within the cellular environment in a way that can affect thousands of enhancers *(trans)*. For instance, a transcription factor—a mobile protein that drives expression of a target gene—is a *trans* regulatory element that can bind and control enhancers on different chromosomes. Historically, scientists have had trouble determining the individual contributions of these two mechanisms to gene expression divergence.

The labs of Hodges and former colleague **Tony Capra**, who is now an associate professor of epidemiology and biostatistics at the University of California, San Francisco, used ATAC-STARR-seq—a genome-scale reporter technique developed by the Hodges lab—to disentangle the relative contributions of *cis* and *trans* regulatory mechanisms to gene regulatory divergence between the closely related humans and rhesus macaques.

With ATAC-STARR-seq, the researchers—led by recent Hodges lab graduate **Tyler Hansen** and recent Capra lab graduate **Sarah Fong**—looked at the effects of different DNA sequences (*cis* changes)

of those sequences identically, and that, in fact, it appears be sensitive to where in the sequence the mutation occurs and can provide functional insight such as which parts of a protein control its motion.

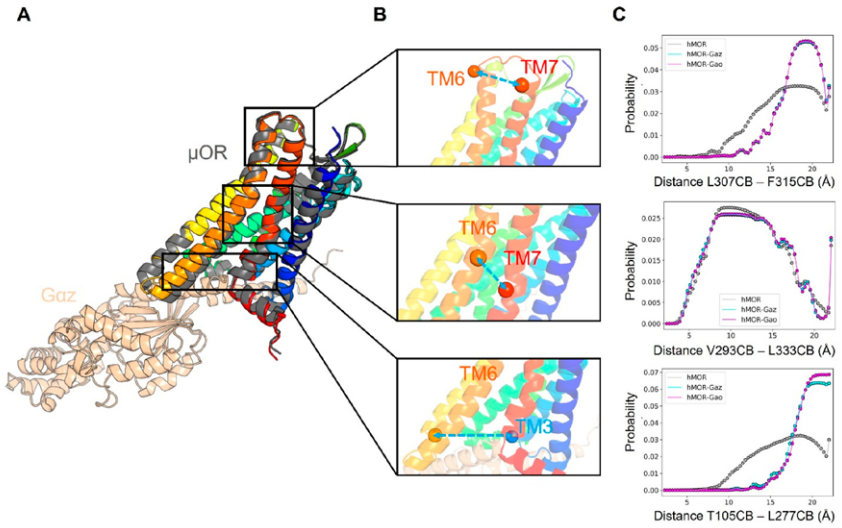
WHAT'S NEXT

A critical aspect of Brown et al.'s approach is that their results do not require the complete prediction of an entire protein structure using AlphaFold2, which can be deployed with less computational expense than mainstream methods such as molecular dynamics simulations.

"With this work, we hope that other researchers will use our approach to identify regions of proteins that are important for conformational dynamics, that impart allosteric function, and that may be susceptible to mutation-induced diseases," Brown said. "We also hope that our research can help computational researchers identify collective variables for simulation and analysis."

This manuscript is a substantial contribution toward the development of rapid methods to evaluate the functional properties of proteins. The refinement of artificial intelligence tools and the development of new applications of such tools that can be harnessed by increasing portions of the scientific community will open new research avenues that would otherwise have been prohibitively expensive or physically impossible for the average laboratory.

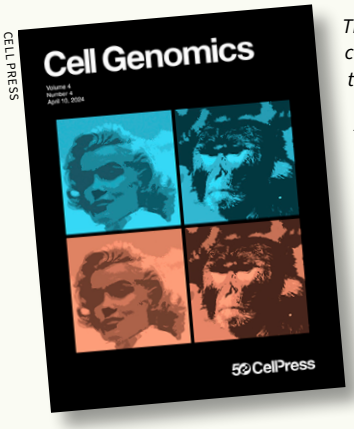
"AlphaFold3 was just released by Google DeepMind yesterday [May 9], and already people are sharing their insights into its potential," Brown said. "Congratulations to the Google DeepMind team! We look forward to seeing what impactful applications people derive from this next instantiation of AI in biomolecular modeling."



Structure of the human μ-opioid receptor predicted in the absence or presence of human Gaz. Brown et al., 2024, Journal of Chemical Theory and Computation. *Shared under a CC-BY-NC-ND 4.0 license.*

GO DEEPER

The paper "Approximating Projections of Conformational Boltzmann Distributions with AlphaFold2 Predictions: Opportunities and Limitations" was published in the *Journal of Chemical Theory and Computation* in January 2024. — **By Lorena Infante Lara**



The April 10, 2024, Cell Genomics *cover references the work done by the Hodges and Capra labs.*

within the context of different cellular environments (*trans* changes) and vice versa and found a substantially higher number of *trans* changes to gene regulatory activity than previously observed.

Why it matters

Differences between species are often attributed to sequence *(cis)* variation, but the Hodges and Capra labs uncovered a substantial role for cell environment *(trans)* differences in driving gene regulatory divergence between species. This work challenges current thinking that cis regulatory changes underlie most divergence in regulatory activity and argues a critical role for trans regulatory changes in driving gene regulatory evolution.

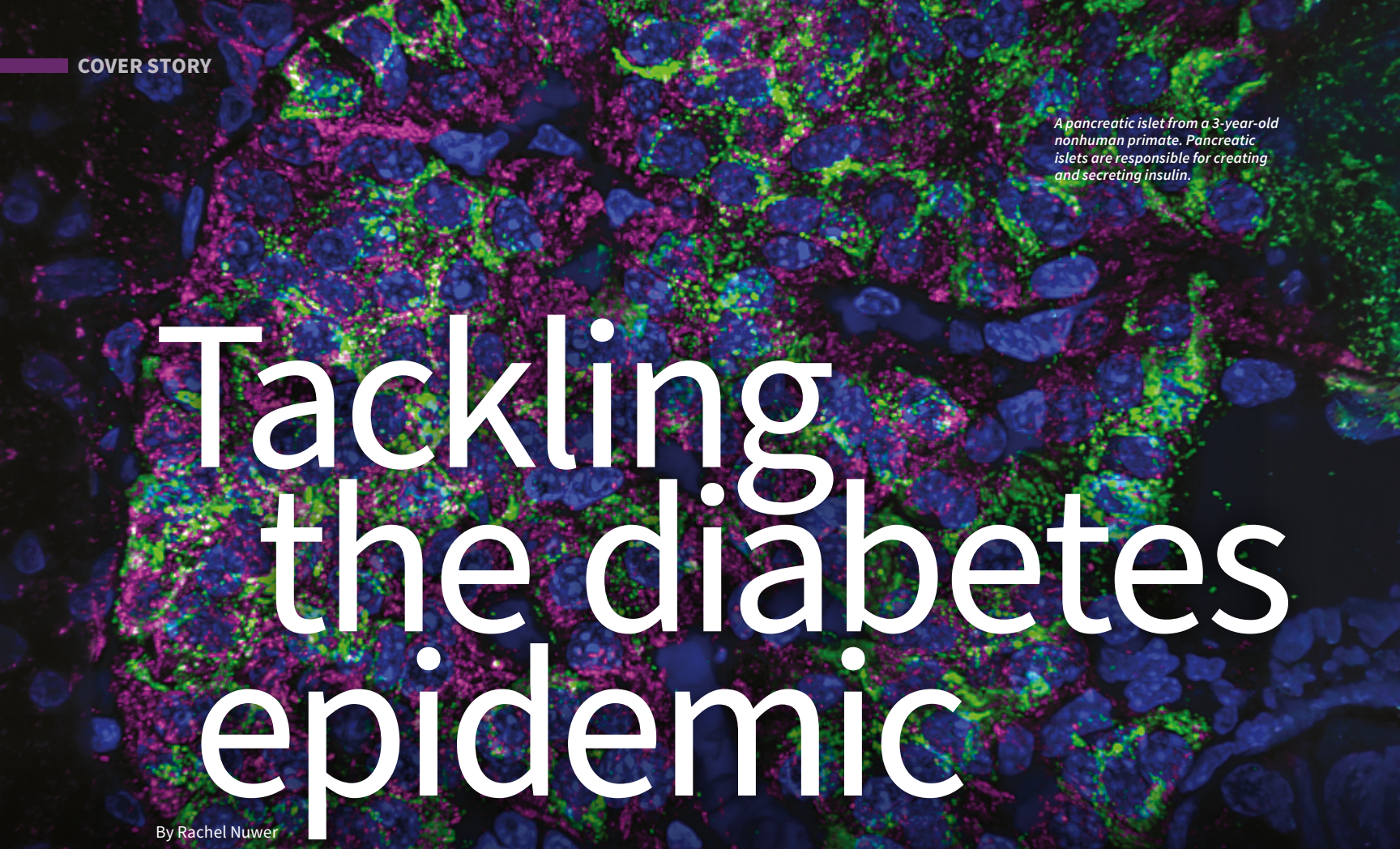
Parsing the relative contributions of *cis* and *trans* mechanisms of gene regulatory divergence has implications for the fields of gene regulation, human population genetics, and primate evolution.

What's next

Moving forward, Hodges is looking to extend the findings beyond human evolution to understand how *cis* and *trans* mechanisms of gene regulation contribute to differences in human disease risk. These questions are critical for understanding diseases like cancer where the interplay between sequence changes, epigenetics, and cellular environment strongly impacts disease outcomes.

— **By Lorena Infante Lara**

Rhesus macaques are anatomically and physiologically similar to humans. By Davidvraju – Own work, CC BY-SA 4.0.



A pancreatic islet from a 3-year-old nonhuman primate. Pancreatic islets are responsible for creating and secreting insulin.

Tackling the diabetes epidemic

By Rachel Nuwer

For more than 50 years, Vanderbilt has been a global leader in the quest to understand, prevent and treat diabetes

Alan Cherrington still clearly remembers the day that unexpectedly led him to what is today the Vanderbilt University School of Medicine Basic Sciences, where he is now a professor of molecular physiology and biophysics. It was 1972, and Cherrington was a doctoral candidate at the University of Toronto. He was finishing work developing a novel experimental animal model that would offer greater insight for understanding human metabolism and already had a postdoctoral position lined up in Switzerland.

Those plans changed when Cherrington met **Dr. Charles Rawlinson "Rollo" Park**, a pioneering diabetes researcher from Vanderbilt who was the first to prove that insulin could stimulate the transport of glucose into cells. Park was chair of what was then called the Department of Physiology—now the Department of Molecular Physiology and Biophysics—and had come to the University of Toronto to give a guest seminar. But he was also on the lookout for promising recruits to bring back with him to Nashville.

In a one-on-one meeting with Cherrington, Park made a convincing case that the research being done at Vanderbilt was "world class" and that Vanderbilt was "one of the best places to come and study diabetes." Park discussed his colleagues' plans to establish the country's first diabetes research center with support from the National Institutes of Health and talked about his lab's efforts to understand the molecular details of how diabetes causes glucose metabolism to go awry. He also highlighted the Nobel Prize in Medicine or Physiology that **Dr. Earl Sutherland**, a professor of physiology in the Vanderbilt School of Medicine, had just won the year before for decoding the mechanics of hormonal action.

Park ultimately delivered a proposition that would change Cherrington's life: "Come to Vanderbilt." Cherrington and his wife gave in, canceled their plans for Switzerland, and moved to Nashville instead. Their two-year stay turned into 52 years and counting—a decision that Cherrington views as one of the best he's ever made.

DARIAN CARROLL

Connecting the past to the present—and beyond

A direct line can be drawn from the pioneering diabetes research conducted at Vanderbilt in the early days and the world-class work that continues today—including through the recent recruitment of new investigators in diabetes-related basic and clinical science. "Decades of knowledge and know-how are concentrated here," said **Rafael Arrojo e Drigo**, an assistant professor in molecular physiology and biophysics who was recruited in 2020.

"Diabetes involves or affects many different organs—the brain, liver, kidney, and pancreas—and it involves genetics, signaling pathways, physiology, developmental biology, and the environment," said **Dr. Alvin Powers**, professor of molecular physiology and biophysics and medicine. It is a multifaceted disease with multiple causes that does not affect everyone in the same way.

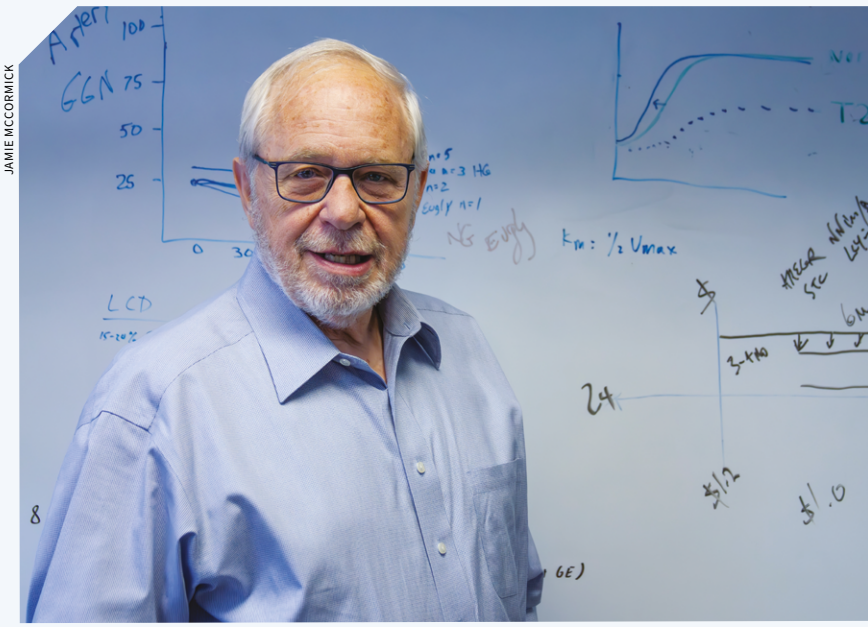
Researchers such as **Maureen Gannon**, professor of molecular physiology and biophysics and medicine and associate dean for faculty development at the Vanderbilt University Medical Center, focus their investigations on understanding what drives the differences in how diabetes manifests in different people with the aim of better tailoring interventions. "Can we identify those people who would benefit from a certain treatment, instead of going through the trial and error of trying five different things before seeing what hits?" Gannon said. "Vanderbilt is in a really good position to lead in this area."

Vanderbilt researchers study diabetes at every level, from the molecular underpinnings of insulin production and secretion across a cell's lifetime, to the overlap between diabetes and comorbidities and complications like obesity, cardiovascular disease, aging, and Alzheimer's disease. Researchers here are developing new paradigms for treating and preventing type 1 and type 2 diabetes, including through work on pancreatic islets, the clusters of cells in the pancreas that produce hormones that regulate blood sugar levels; techniques for preventing the immune system from destroying insulin-producing beta cells; investigations into the potential to revive "exhausted" beta cells in the pancreas; and studies on the mechanism of action for medical weight loss drugs like Ozempic.

They also conduct translational and population-based research in subjects like health care inequity, cost and delivery. "Talking about diabetes and its causes and clinical care must also include consideration of the social determinants of health and health equity," Powers said.

A legacy of excellence

Vanderbilt became a leading institution for diabetes research thanks in large part to the efforts of early leaders like Park, who actively recruited top-tier and up-and-coming scientists alike. Sutherland, for example, was recruited by Park and conducted some of his 1971 Nobel Prize-winning work on a molecular phenomenon called the second messenger theory while at Vanderbilt. **Tetsuro Kono**, who discovered the molecular transporters responsible for moving glucose into cells, and **Dr. John Exton**, who worked on gluconeogenesis—one of the ways the liver produces glucose—were two additional key recruits.



JAMIE MCCORMICK

Allen Cherrington, professor of molecular physiology and biophysics

"A lot of early work done here was centered around how hormones work on cells," said **Roger Colbran**, vice chair of the Department of Molecular Physiology and Biophysics. "To a large extent, efforts at Vanderbilt deciphered many key actions of hormones, including insulin and how it works to increase glucose flux into cells."

In 1965, **Dr. Oscar Crofford**, a clinician and investigator who conducted research on how fat cells contribute to diabetes, became Vanderbilt's first full-time diabetes specialist. He spearheaded and was the principal investigator for a pioneering clinical trial called the Diabetes Control and Complications Trial that proved that many diabetes complications could be mitigated by tightly controlling the patient's blood glucose levels.

In addition to his research excellence, Crofford's other claim to fame was the role he played in creating the Diabetes Research and Training Center, an NIH-supported hub that brings together basic and clinical scientists across different disciplines in the common pursuit of improving the understanding, prevention, and treatment of diabetes and its complications.

Crofford and others lobbied Congress to mandate

funds for diabetes research, and, in 1973, these efforts contributed to the NIH announcing the creation of a series of Diabetes Research Centers. Vanderbilt's DRTC was the first of what are now 17 such centers around the country. Working with **Dr. Rod Lorenz**, a pediatric endocrinologist who studied how to best deliver insulin to and care for diabetes patients, Crofford ensured that the DRTC had a strong clinical focus to complement and enhance the basic science research headed by Park, Sutherland, and others.

The DRTC quickly became a major draw for even more diabetes-related talent to come to Vanderbilt, especially because of the center's mission to facilitate career development of junior investigators. The DRTC is now home to five diabetes-related training grants for medical and graduate students and postdoctoral fellows, one of which was just renewed in August. "This T32 grant, which provides funding to support students and postdoctoral fellows who are working at the interface of engineering and diabetes, fits perfectly into our efforts to train the next generation of scientists in diabetes," Powers said.

The DRTC also awards seed money for early-stage diabetes-related projects with an emphasis on work proposed by new investigators in the field. The center sets aside funding for enrichment programming as well, including hosting guest seminars and mini meetings, like Vanderbilt's annual Diabetes Research Day.

When **Dr. Daryl Granner**, a leading pioneer in molecular biology, was recruited to replace Park as chair of the Department of Physiology in 1984, he added a new emphasis on developing cutting-edge molecular biological and biophysical tools to study gene expression and other signaling processes. After Crofford's retirement, Granner became the director of the DRTC and oversaw the creation of several research cores—facilities with expert-managed technologies in specialized techniques like genomics and microscopy.

In 2001, the DRTC got another upgrade when then-Associate Professor **Owen McGuinness** and Professor **David Wasserman** from the Department of Molecular Physiology and Biophysics were awarded an NIH grant to create a new center that would provide experimental services in mouse models of diabetes and related metabolic diseases. Since then, the Vanderbilt Mouse Metabolic Phenotyping Center has performed sophisticated experimental services in collaboration with investigators across the U.S. Wasserman served as the VMMPC director from its founding until his death last June. Under his leadership, around 250 visiting researchers came to learn phenotyping techniques from Vanderbilt facility.

Julio Ayala, associate professor of molecular physiology and biophysics, was selected to replace Wasserman earlier this fall. He said that Wasserman's efforts to share the VMMPC's expertise amplified Vanderbilt and the DRTC's role in driving diabetes and metabolism research around the world. "That excellence continues today," Ayala said.

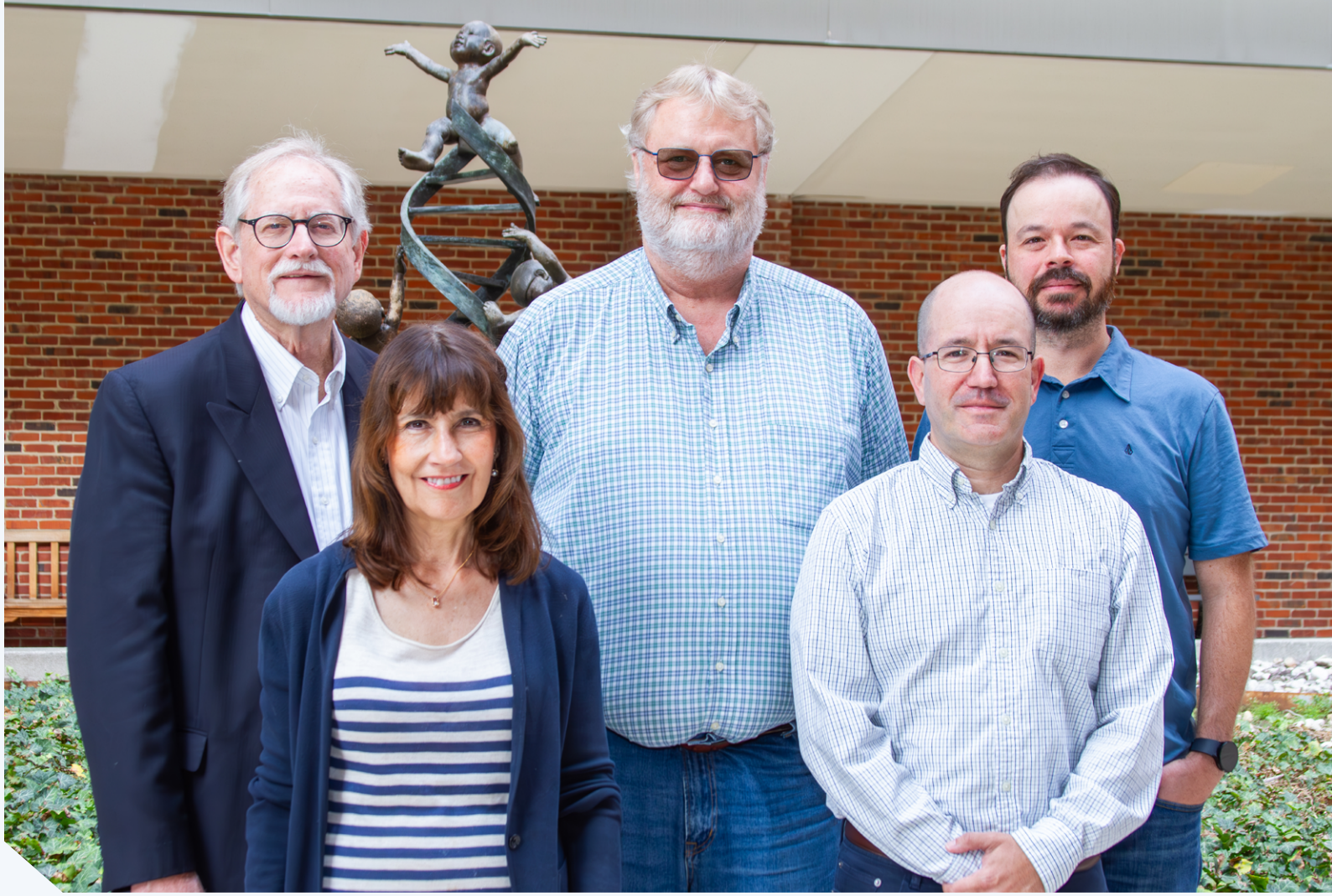
> "If you were to draw a map and link all the diabetes researchers in the U.S., a lot of them would link to Vanderbilt in one way or another."
>
> **— Rafael Arrojo e Drigo, assistant professor of molecular physiology and biophysics**

A culture of collaboration

Vanderbilt and VUMC split into separate entities in 2016, but researchers at both institutions have continued strong collaborations. In some ways, Ayala said, diabetes research has been "the glue to maintain those interactions." The DRTC has more than 140 members from 15 departments across both campuses.

The blend of basic and clinical science also highlights the DRTC's "commitment to bringing these two overarching approaches together," said **Dr. Nancy Carrasco**, the Joe C. Davis Chair of the Department of Molecular Physiology and Biophysics. Basic and clinical research "are essential to making fundamental scientific breakthroughs that can be translated into newer, better strategies for improving patient health," Carrasco said. This unified approach amplifies the impact that either research avenue could have on its own: Being proximate to clinicians helps basic researchers stay focused on problems that are relevant to patients and doctors, and interacting with basic researchers gives clinicians a deeper knowledge of the underpinnings of the diseases they're treating.

According to Gannon, these interactions are also boosted by a genuine spirit of collaboration that permeates the diabetes community at both Vanderbilt and VUMC. "I was a skeptical New Yorker when I came here, but it really is true that we have a culture of collaboration and collegiality," she said. "You can't move forward in



JAMIE MCCORMICK

From left to right: Alvin Powers, Nancy Carrasco, Roger Colbran, Julio Ayala, and Rafael Arrojo e Drigo

understanding diabetes and finding new pathways for prevention and cures if everyone is in their own lab not talking to anyone." Gannon said that Vanderbilt and VUMC researchers "share ideas, help each other, give advice, and critique each other," and, as a result, of the more than 500 diabetes- and obesity-related papers published by Vanderbilt groups in the last five years, half had more than one DRTC investigator as an author.

Vanderbilt has continued its role as a leader in diabetes research on the national and international level as well. DRTC members have been heavily involved with both the Juvenile Diabetes Research Foundation and the American Diabetes Association. According to Cherrington, the president of the American Diabetes Association is "*the* authority figure around the world in diabetes"—a position that he, Crofford, and Powers have all held.

Vanderbilt's campus continues to bring researchers from multiple institutions together. From 2001 to 2015, **Dr. Mark Magnuson**, professor of molecular physiology and biophysics, headed the NIH-funded Beta Cell Biology Consortium, a group of researchers who sought to understand how beta cells develop and eventually fail. That program's success led to a second, currently active consortium, the Human Islet Research Network, whose investigators now work to better understand immunology and other aspects of type 1 diabetes. HIRN comprises investigators from Vanderbilt and other institutions, which has helped spread Vanderbilt's influence to a broader group of scientists.

As Arrojo e Drigo said, "If you were to draw a map and link all the diabetes researchers in the U.S., a lot of them would link to Vanderbilt in one way or another." He predicts that, in the coming years, those links will only become richer.

"That's why I originally came here: to be in a place that's always been and continues to be at the forefront of diabetes research," Arrojo e Drigo said.

Diabetes is a terrible disease that causes suffering and death in a growing number of people throughout the world. And yet there is hope thanks to the tireless work of diabetes and metabolism researchers, work that has led to profound breakthroughs that have improved patients' lives throughout the last century. And if the growing impact of a new generation of drugs that treat diabetes is anything to go by, the next century promises even a bigger revolution. ■

VCAR Science Day brings leading addiction researchers together

By Alexandra Scammell

ALEXANDRA SCAMMELL

Within the industrial-style doors of Ruby Nashville, an event venue located off the southern end of Vanderbilt's campus, the Vanderbilt Center for Addiction Research hosted its annual Science Day on April 18.

"I am super excited about today," said **Erin S. Calipari**, director of VCAR, at the start of the day.

VCAR is advancing our understanding of the intricate mechanisms underlying the development of addiction and substance use disorder in the brain, providing community outreach to destigmatize addiction and developing new pharmaceutical strategies to treat addiction. Science Day, which started as an annual event in 2017, features the latest research in addiction, including investigations into alcohol, opioids, and stimulants. "Addiction is a really complex disorder," Calipari said. "It affects every system in the brain."

The research highlighted at the event this year focused on a few of those brain systems, delving into the basic mechanisms and systems that drugs are shown to impact.

The event attracted attendees and speakers of the highest caliber in the field of addiction research from top institutions from around the world. From Sydney, Australia, where Mel Sharpe, senior lecturer at the University of Sydney, hails from, to Vanderbilt's own Perception Plasticity & Learning Lab, where **Kari Hoffman**, associate professor of psychology, works, and everything in between. Sharpe and Hoffman were both presenters at Science Day.

According to Calipari, the event helped the VCAR team conceptualize how their work fits into "the bigger picture of the brain and how the brain works."

The day featured three sessions, "Learning and Memory," "Brain Mechanisms of Reward," and "Circuits of Social Behavior," that were chaired by some of VCAR's own graduate students and fellows. Graduate student **Kirsty Erickson**, who chaired the second session, calls herself the "resident bartender and cocaine dealer to the mice."

Research from the School of Medicine Basic Sciences was featured throughout the day. **Maxime Chevee**, a postdoctoral fellow who joined the Calipari lab in August 2020, where he studies the neural mechanisms underlying habit formation, gave a presentation on food restriction and its effects on region-specific dopamine release to promote learning.

Michelle Bedenbaugh, research assistant professor in the Department of Molecular Physiology and Biophysics who will soon be moving on to the University of Florida to start her own lab, discussed the sexually dimorphic effects of the melanocortin 3 receptor network on feeding and stress, but not anxiety behaviors.

The last Basic Sciences graduate student to present her work was **Zahra Farahbakhsh** from the lab of Cody Siciliano, assistant professor of pharmacology, who discussed phenotypic screening of a type of opioid receptor in a preclinical model of alcohol use disorder.

Calipari also made sure to emphasize VCAR's small-but-mighty team, which includes grad students and postdoctoral fellows. "This group is not that big … but [we are] accomplishing great things," she said. Recently, the National Institutes of Health awarded Calipari and colleagues a five-year, nearly $9 million grant that will help establish the Vanderbilt AUD Research and Education Center, which will advance Vanderbilt's leadership in neuroscience, addiction research, and new approaches to studying alcohol use disorder (learn more on page 23).

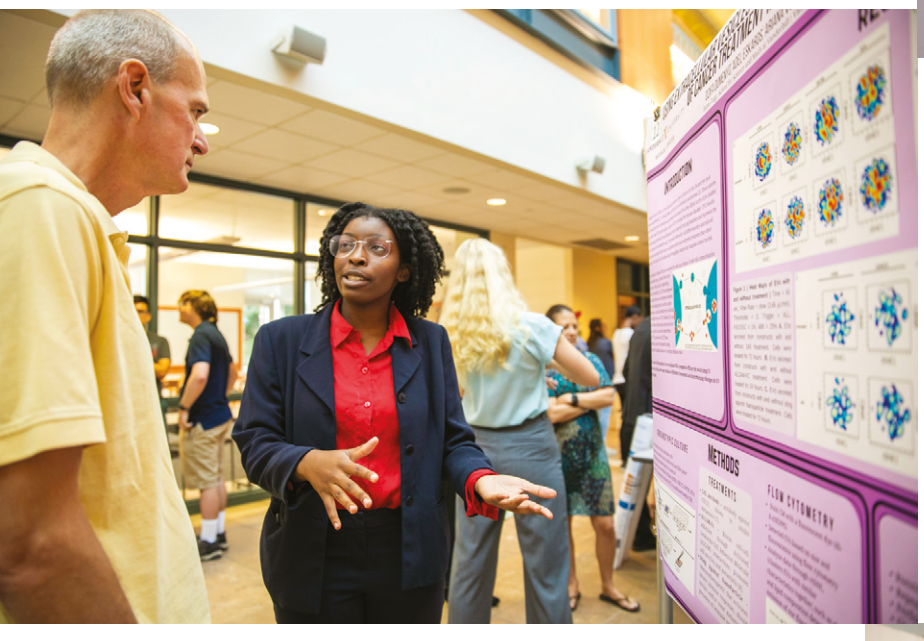
"This [grant] is going to be a really great opportunity for us to collaborate together and have other people come to the alcohol field," Calipari said. To the event's participants, she added, "We are so excited to partner with you to do that."

Promising initiatives are ahead for Vanderbilt's community of addiction researchers, but the last five years have also been impactful for VCAR's labs. "You guys have been killing it, so thank you," Calipari said to the attendees.

VCAR is supported by Discovery Vanderbilt, an initiative of the Office of the Provost and one of three pathways in the Vanderbilt's Dare to Grow campaign, established to support and extend the resources underpinning Vanderbilt's most innovative research and education.

VANDERBILT
School *of* Medicine Basic Sciences

MAKE A GIFT TO SUPPORT LIFESAVING DISCOVERIES AT THE VANDERBILT CENTER FOR ADDICTION RESEARCH



Substance use disorder is on the rise across the nation and has a devastating impact on our society. The Vanderbilt Center for Addiction Research at the School of Medicine Basic Sciences is **committed to alleviating the burden of this disease** through high-risk, high-reward research, translational drug applications, and community education.

Support for groundbreaking discoveries is a key priority of Vanderbilt's Dare to Grow fundraising campaign. **Dare to make a difference and make a gift of any size today.**

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MEET THE DEPARTMENTS:

Pharmacology

A research enterprise on a pillar of excellence

By Emily Hawes and Lorena Infante Lara

The Vanderbilt University School of Medicine Basic Sciences encompasses four departments: Biochemistry, Cell and Developmental Biology, Molecular Physiology and Biophysics, and Pharmacology. Through this article series, we are featuring each one, highlighting their proudest accomplishments, unique strengths, and visions for the future.

JAMIE MCCORMICK

Graduate student Morgan Ottley, left, and postdoc Baris Tosun working in the pharmacology lab of Richard Sando

GROUNDWORK FOR SUCCESS

Vanderbilt's pharmacology department is one of the oldest programs in the country, and it has maintained a superlative status by continually adapting to overcome new challenges and provide the best possible training. The department's first three chairs oversaw it for nearly seven decades, but each chair was critical in pushing the department's research and innovation momentum forward.

The enterprise began with **Dr. Canby Robinson**—the first dean of the medical school and a key driving force behind its establishment—hiring **Dr. Paul Lamson** in 1923 to be the first chair of the nascent department. Lamson fostered a culture of innovation in large part through his own actions: He built one of the first artificial hearts and was the first scientist to artificially induce cirrhosis of the liver.

Lamson's tenure lasted until 1953 when **Dr. Allan D. Bass** took over. Bass was a prolific scientist whose research career spanned four decades and subjects as varied as anthelmintics (a type of antiparasitic drug), skin-sterilizing agents, sulfonamides, adrenal corticosteroids, hormones, and chemical transmitters. He transformed the department from the relatively small entity it was then to a program that attained national recognition for its research excellence. In fact, in recognition of his legacy, the Department of Pharmacology established the Allan D. Bass Lectureship in the late 1970s and the Allan D. Bass Chair in 1995.

Joel G. Hardman, a research giant who first came to Vanderbilt to complete a postdoctoral fellowship with **Dr. Earl Sutherland** and was chair of the department from 1975 to 1990, discovered an enzyme called guanylate cyclase. It synthesizes cyclic GMP from GTP, a source for energy in the body similar to its better-known cousin, ATP. Hardman's finding led to the understanding that cGMP—like cAMP, which Sutherland discovered and which earned him the Nobel Prize in medicine or physiology in 1971—can serve as an intracellular second messenger.

ALL PHOTOS BY VANDERBILT UNIVERSITY

From left to right: Lee Limbird, Elaine Sanders-Bush, Heidi Hamm, and Lisa Monteggia

WOMEN LEADING THE WAY

Since Hardman, there have been five more department chairs—three of them female. According to **Ege Kavalali**, the current chair, a huge part of the department's research impact and a key factor distinguishing it from its peers is the strength of its female faculty.

The three chairs—**Lee Limbird**, **Elaine Sanders-Bush**, and **Heidi Hamm**—each left their mark on the department in ways that are still felt today.

Limbird became the department's first female chair in 1991, and under her leadership it became one of the top pharmacology departments in the nation in terms of federal funding levels, graduate training, and research publication impact. She is known for her pioneering research on alpha-2 adrenergic receptors and how they relate to the regulation of blood pressure, sedation, pain suppression, and opioid drug action.

Additionally, Limbird is known for her "legendary" devotion to mentoring graduate students, postdoctoral fellows, and young faculty, as attested by a 2013 award announcement by the American Society for Pharmacology and Experimental Therapeutics.

Although Sanders-Bush was only interim chair during the turn of the millennium, she was a Vanderbilt staple from the moment she joined as faculty in 1969 to her retirement in 2010. Her research was instrumental in helping scientists understand the structure, function, and regulation of serotonin—a major neurotransmitter—and two serotonin receptor subtypes. Sanders-Bush's work set the stage for the current growing field of potential psychedelic-based neurotherapeutics.

Like Limbird, Sanders-Bush placed a significant emphasis on mentoring trainees, particularly those from minority groups, which led to the department's 2006 establishment of the Elaine Sanders-Bush Award for Mentoring Graduate and/or Medical Students. Sanders-Bush also established and directed both Vanderbilt's neuroscience Ph.D. program and the Vanderbilt Brain Institute.

Hamm, pharmacology's most recent female chair, held the post for almost a decade and a half and remains on the faculty. Her research focus has centered on G protein-coupled receptor signaling and the structure and function of GTP binding proteins, and her efforts have resulted in the discovery of novel targets for G-protein signaling. Thanks to her leadership, the department quintupled the size of its National Institutes of Health budget, catapulting it to the top of NIH-funded pharmacology departments in the nation during her tenure as chair, which ended in 2014.

JAMIE MCCORMICK

Ege Kavalali

The department's record of influential female faculty in pharmacology continues with **Lisa Monteggia**. Monteggia is the Barlow Family Director of the VBI, and she studies the molecular and cellular mechanisms that underlie psychiatric disorders and their treatment, including antidepressant action. Her studies on rapid antidepressant action, particularly the fact-acting antidepressant effect of ketamine, have been groundbreaking and have recently earned her membership in the National Academy of Medicine.

HIGHLIGHTING STUDENTS

Vanderbilt's biomedical doctoral students enroll through its Interdisciplinary Graduate Program in the Biological and Biomedical Sciences or its Quantitative and Chemical Biology umbrella programs. After a year of classes and research rotations, students choose a permanent home in one of 11 programs

> A huge part of the department's research impact and a key factor distinguishing it from its peers is the strength of its female faculty.

or departments—including pharmacology—where they finish their training.

The Department of Pharmacology wasn't always the training powerhouse it is today. Prior to 1953, only two students had received a Ph.D. from the department. Thanks to a shift in focus, Bass increased that number to more than 60 graduates during his 20-year tenure. Today, the department typically enrolls about 25 students and grants five doctorates each year.

A huge part of the department's training success comes from its emphasis on listening to and implementing student feedback. For example, the department recently underwent an overhaul of the qualifying exam, an assessment designed to evaluate the knowledge a student gained during their coursework and apply it to their thesis work, based on feedback from students. course curriculum in 2021 by offering more elective courses, providing students with an opportunity to further tailor their education. Students are also welcome to give input into the department's choice of seminar or retreat speakers, even beyond the annual Joel G. Hardman Student-Invited Pharmacology Forum.

"My time at Vanderbilt set the foundation for everything," said **Andrew Tapper**, PhD'01, director of the Brudnick Neuropsychiatric Research Institute at the UMass Chan Medical School. "What I loved about the pharmacology department was that they ensure that you not only are an expert on your project in the lab, but also that you acquire comprehensive foundational knowledge in general pharmacology and physiology, which is something I use to this day."

STANDOUT FACULTY

Current research in the department focuses on five major areas: signal transduction, neuroscience, bioactive lipid metabolism, genetic basis of cardiovascular dysfunction, and drug metabolism. The department maintains close ties with the Warren Center for Neuroscience Drug Discovery, the Vanderbilt Brain Institute, and the Vanderbilt Center for Addiction Research, and its cross-disciplinary research allows for the recruitment of high-caliber faculty from a wide variety of backgrounds.

Currently, the department has 26 tenured or tenure-track faculty. Following are highlights of the current and incoming junior faculty, whose early-stage career accomplishments are but a glimmer of what their trajectories promise.

Cody Siciliano, assistant professor in the department and a member of VCAR, joined Vanderbilt in 2019. His lab investigates the neural mechanisms involved in individual decision-making and how two people may have different responses when confronted with the same situation. Siciliano received a $100,000 award from the Stanley Cohen Innovation Fund in 2020 and was added to the *Forbes* 30 under 30 – Science list in 2021.

Current research in the department focuses on five major areas: signal transduction, neuroscience, bioactive lipid metabolism, genetic basis of cardiovascular dysfunction, and drug metabolism.

Richard Sando is an assistant professor and a member of the VBI who joined the faculty in 2020 after a postdoctoral fellowship with Nobel laureate Dr. Thomas Südhof at Stanford University. His research focuses on how synapses in the central nervous system assemble and function. In 2022, Sando was awarded the Sloan Research Fellowship, one of the most competitive and prestigious awards available to early-career researchers.

Prashant Donthamsetti arrived in 2022 from the University of California, Berkeley, where he completed postdoctoral work in the lab of Ehud Isacoff. At Berkeley, he developed novel tools to interrogate the function of G-protein coupled receptors in intact living systems using light, marking his arrival to Vanderbilt with an extremely novel and groundbreaking research portfolio in the nascent field of opto-pharmacology. His recent work on photoswitchable allosteric agonists brings a new dimension to drug discovery as conventional drugs are not typically selective for specific receptors and cannot be controlled with spatiotemporal precision.

Dr. Benjamin Brown, PhD'22, MD'23, is a recent graduate from Vanderbilt's own Medical Scientist Training Program and started his faculty career as a research assistant professor of chemistry but joined pharmacology in 2024. He is a member of VCAR and the Center for Applied Artificial Intelligence in Protein Dynamics and has already made waves and earned funding from the National Institute on Drug Abuse for "highly innovative studies [that] represent the future of addiction science."

Quynh Anh Nguyen, another highly accomplished young investigator with a background in synaptic signaling and neurophysiology, developed novel tools while a postdoctoral fellow at Stanford to interrogate the function of neuronal circuits that gives rise to network imbalances and epilepsy while a postdoctoral fellow at Stanford. Her research seamlessly bridges fields of cell biology, neurological disorders, neurogenetics, neuropharmacology, and signal transduction.

Finally, **Shan Meltzer** and **Valentina Cigliola** joined the department's ranks as assistant professors this past summer and early fall. Meltzer holds the Leonard and Isabelle Goldenson Fellowship and the William Randolph Hearst Fellowship at Harvard Medical School and is a Howard Hughes Medical Institute Hanna H. Gray Fellow at Harvard and HHMI until 2027. Previously under the direction of Harvard's David Ginty, Meltzer currently studies the molecular mechanisms of somatosensory circuit assembly.

Cigliola already has a major discovery under her belt: she identified a novel transcriptional pathway in zebrafish that is driven by heparin-binding EGF-like growth factor, which robustly regulates spinal cord regeneration and circuit re-assembly after injury. At Vanderbilt, she will pursue this novel pathway to identify further upstream and downstream mechanisms and to investigate why similar mechanisms are not in play in mammals. The latter question has far-reaching implications not only for spinal cord regeneration in humans but also neuronal circuit rewiring and plasticity in the central nervous system.

Given the fantastic pool of talent that the department attracts, it is no wonder that Kavalali, the current chair, gets excited thinking about the department's future. "Creativity is the currency of science, and I have enjoyed working with our faculty to foster the creativity and outstanding training environment that have enabled new discoveries," Kavalali said. "We are responsible for carrying the research torch forward, into new depths and new fields, and I know the department is up to the task."

Amy Stark, a graduate student and a former member of the Pharmacology Graduate Student Association, said that the faculty are "excited to teach and mentor the students."

Stark said that the WCNDD is one of the big draws for students because "Vanderbilt is the place to do academic drug discovery and students can learn from and work with the some of the best faculty in the field."

The first exam is an oral assessment of the student's knowledge about the principles of pharmacology, tailored to their own research focus. This assessment forces students to take the general knowledge they gain during their first two years of graduate school and apply it to a unique system. In the second part of the qualifying exam, students orally discuss their specific thesis project, walking through the experiments they plan to do and the knowledge that their work will hopefully add to the field.

JAMIE MCCORMICK

Sando lab postdoc Baris Tosun

Laurent Audoly, PhD'97, a self-described "company builder" who earned his Ph.D. in pharmacology, has founded at least five science-related business enterprises and is part of the Basic Sciences Council of Visitors.

Erin Calipari, who joined the department in 2017, was until very recently part of this standout group of junior faculty but was recently promoted to associate professor. Her stardom, however, continues to shine. Calipari's work focuses on the processes the brain uses to encode information and how these processes are dysregulated in drug addiction. She was named a Dean's Faculty Fellow of the School of Medicine Basic Sciences in 2021 and was awarded the Faculty Mentor of the Year Award in 2022. She also recently became the director of the Vanderbilt Center for Addiction Research and established the Vanderbilt AUD Research and Education Center to combat alcohol use disorder with research, education, and community outreach (learn more on page 23). Through frequent interviews and other media engagements, Calipari helps to spread the outstanding image of the Vanderbilt Department of Pharmacology to the public.

"I am honored to serve as the chair of one of the most prominent departments of pharmacology in the country," Kavalali said. ■

Davies, Doran win inaugural Innovation Ignition Fund grant to pursue anti-inflammatory drug discovery

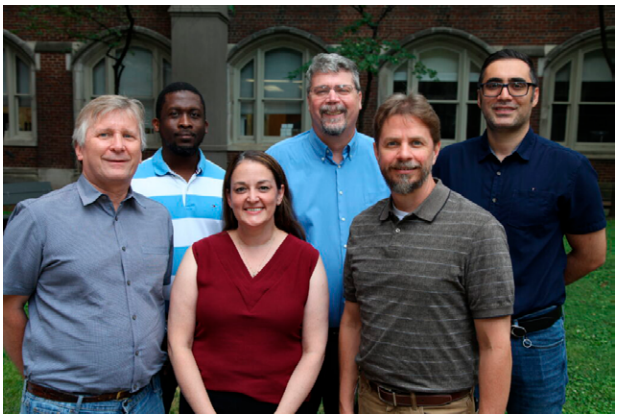
By Marissa Shapiro

Sean Davies, associate professor and associate director of graduate studies in the Department of Pharmacology, is the first to receive support from the Innovation Ignition Fund for his project "Activation of NAPE-PLD as a Strategy for Treatment of Atherosclerotic Cardiovascular Disease." His co-lead on the project is **Dr. Amanda Doran**, assistant professor of medicine and molecular physiology and biophysics. Davies lab postdoctoral fellow **Reza Fadaei** rounds out the team.

Despite advances in the treatment of atherosclerotic cardiovascular disease—a general term for any disease of the blood vessels or heart caused by plaque buildup in artery walls—400,000 people in the U.S. still die of this disorder, and nearly half of all patients experience recurring cardiovascular events each year.

Researchers have found evidence that improving the resolution of inflammation, particularly a step called efferocytosis, can limit the progression of ASCVD. The enzyme NAPE-PLD holds promise to treat ASCVD because of its effects on efferocytosis.

STEPHEN DOSTER



From left to right, Gary Sulikowski, Abdul-Musawwir Alli-Oluwafuyi (former Davies lab postdoc), Sean Davies, Alex Waterson, Reza Fadaei

After a screening of 40,000 compounds from the High Throughput Screening Facility compound library, Davies and his team identified more than 50 compounds that increase NAPE-PLD activity. The next steps in this drug discovery project, which the Innovation Ignition Fund will support, are to confirm that these compounds activate NAPE-PLD in macrophages, a type of white blood cell that plays a critical role in initiation, maintenance, and resolution of inflammation. They will then move their research along to proof-of-concept studies to further illustrate how these compounds can treat ASCVD and potentially other inflammatory diseases.

"The goal of the Innovation Ignition Fund is to support innovative ideas in drug development, and we look forward to seeing how Davies and Doran's work in this important area progresses," said **John Kuriyan**, dean of the School of Medicine Basic Sciences and University Distinguished Professor of Biochemistry and Chemistry.

Davies has studied how NAPE-PLD can be used to treat ASCVD throughout his research career. He is one of the project leaders on a PO1 program project grant to study the role of high-density lipoprotein in ASCVD and related diseases that is now in its eighth year of funding from the National Heart, Lung, and Blood Institute. That project also recently won a Scaling Success award from the Office of the Vice Provost for Research and Innovation to conduct and interpret various experiments and to develop a medicinal chemistry plan. Doran is a leading clinical researcher in role of efferocytosis and the resolution of inflammation in atherosclerosis and will provide critical insights as this work progresses toward the clinic.

"I am very grateful that funding by the Innovation Ignition program will allow us to really push forward this drug discovery project in a major way," Davies said. "The long-term goal of my lab has always been to translate what we learn from our basic research in lipid signaling into new treatments for cardiometabolic diseases. This funding provides us the chance to fully optimize and characterize our small molecule activators of NAPE-PLD so that we can rigorously test their potential impact on cardiovascular disease."

In addition to $500,000 in funding over two years, their efforts will be supported by scientific guidance from **Gary Sulikowski**, Stevenson Professor of Chemistry, and professor of pharmacology, and director of the Vanderbilt Institute of Chemical Biology, and other scientific leaders in Basic Sciences, including Research Professor of Pharmacology **Alex Waterson** and Research Associate Professor of Biochemistry **Josh Bauer**. The researchers will also take advantage of the VICB's HTS Facility and Molecular Design and Synthesis Center to conduct their work.

"The new approach proposed by Sean Davies and his team, which has the potential for broader applications of these therapeutics beyond ASCVD, suggests wider translational potential and impact," said **Selene Colon**, assistant dean for research. "This project exemplifies the innovative and transformative thinking within the School of Medicine Basic Sciences and wholly represents the spirit behind the Innovation Ignition Fund."

The Innovation Ignition Fund, piloted by Basic Sciences and OVPRI, was created to support small molecule therapeutic projects at the very early target-validation and lead-optimization stages.

Vanderbilt University receives prestigious NIH grants to establish new center to tackle alcohol use disorder and leverage AI to understand opioid addiction

By Herschel Pollard, edited by Marissa Shapiro and Lorena Infante Lara

Vanderbilt University has received an $8.9 million grant from the National Institutes of Health to establish the Vanderbilt AUD Research and Education Center, bolstering the university's leadership in neuroscience, addiction research, and innovative approaches to the study of alcohol use disorder.

VAREC will facilitate collaborative efforts among diverse researchers at Vanderbilt and across the country, enhancing the university's role in alcohol and addiction research both locally and nationally. "This milestone underscores our unwavering commitment to solving society's most pressing problems, like understanding the complexities of the brain and addiction," Provost **C. Cybele Raver** said.

The new center's "precision neuroscience" approach will leverage human and animal models to identify the causes of and potential treatments for AUD and will provide public education on the disorder. The center will work closely with the Vanderbilt Center for Addiction Research, which has similar goals.

The grant's principal investigators are **Erin Calipari**, director of VCAR; **Danny Winder**, adjoint professor of molecular physiology and biophysics at Vanderbilt and chair of the Department of Neurobiology at UMass Chan Medical School; **Jennifer Blackford**, adjoint professor of psychiatry and behavioral sciences at Vanderbilt and director of research at the Munroe-Meyer Institute at the University of Nebraska Medical Center; and **Cody Siciliano**, assistant professor of pharmacology. Calipari, Blackford, and Winder are VAREC's assistant director, associate director, and director, respectively.

In addition to AUD research, Vanderbilt is also making strides in tackling the opioid epidemic. Researcher **Dr. Ben Brown**, assistant professor of pharmacology and a faculty affiliate of VCAR and the Center for Applied Artificial Intelligence in Protein Dynamics, was recently awarded a $1.5 million grant from the National Institute on Drug Abuse to develop artificial intelligence that can analyze billions of potential opioid drugs to reveal detailed insights into how they interact with key proteins.

Brown focuses on understanding how opioid molecules interact with Mμ-opioid receptors in the central nervous system, which modulate pain, stress, mood, and other functions. Drugs that target these receptors are powerful analgesics but are also highly addictive. By computationally modeling the dynamic physical movements of these drug-protein interactions, Brown aims to identify or design new opioid-based painkillers that are less addictive.

"The energy and enthusiasm Ben brings to his science and scientific collaborations are outstanding, and it is fitting that he be recognized as a young pioneer in his field," said **Hassane Mchaourab**, director of the Center for Applied AI in Protein Dynamics.

Both VAREC and Brown's research exemplify Vanderbilt's multifaceted approach to addressing the pressing public health challenges of substance use disorders. VAREC's dual focus on research and dissemination will not only bolster the university's capabilities, but will enhance its standing as a hub for scientific discovery and public education on AUD.

JAMIE M. CORMICK

Erin Calipari, left, and Ben Brown

"Addiction is a disease. Promoting a deeper understanding of addiction fosters compassion and paves the way for solutions that can bring healing and hope to those affected by it," said **John Kuriyan**, dean of the School of Medicine Basic Sciences.

VAREC plans to establish a course and provide scholarships for researchers from across the country to learn innovative neuroscience technologies at Vanderbilt, as well as a summer student program with stipends for underrepresented students to work in addiction labs on campus. "The hope is that we can get the next generation excited about doing addiction work," Calipari said. Calipari is also an associate professor in the Department of Pharmacology.

Through these initiatives and cutting-edge research, Vanderbilt is poised to make significant strides in understanding and treating substance use disorders, while also sharing information with the public and making a tangible difference in the community.

"The great thing about this NIH grant is that it's renewable at the end of the funding period, which will ensure that this work will continue at Vanderbilt far into the future," Calipari said.

Vanderbilt School of Medicine Basic Sciences among nation's top NIH-funded departments

The four School of Medicine Basic Sciences departments—Biochemistry, Cell and Developmental Biology, Pharmacology, and Molecular Physiology and Biophysics—pulled in more than $65 million in National Institutes of Health funding in fiscal year 2023, as reported by the Blue Ridge Institute for Medical Research. The School of Medicine ranked 10th in the nation in total research grant support during the same period with $527.7 million.

Funding for basic science research supports the exploration of the intricate processes that cause health problems, identification of diseases in their early stages, development of treatments to cure disease, and ways to prevent the factors that cause medical conditions.

Chazin named senior associate dean of biomedical research education and training

By Marissa Shapiro

Walter Chazin, Chancellor's Chair in Medicine and professor of biochemistry and chemistry, has been named senior associate dean of Biomedical Research Education and Training. **Kathleen Gould**, Louise B. McGavock Chair, stepped down from the role after 14 years with the BRET office to return her focus to her research program in the Department of Cell and Developmental Biology.

"I am grateful to Professor Gould for her leadership and dedication to Vanderbilt's graduate students and postdoctoral fellows," said **John Kuriyan**, dean of the School of Medicine Basic Sciences. "I look forward to continuing to work with her in her faculty position."

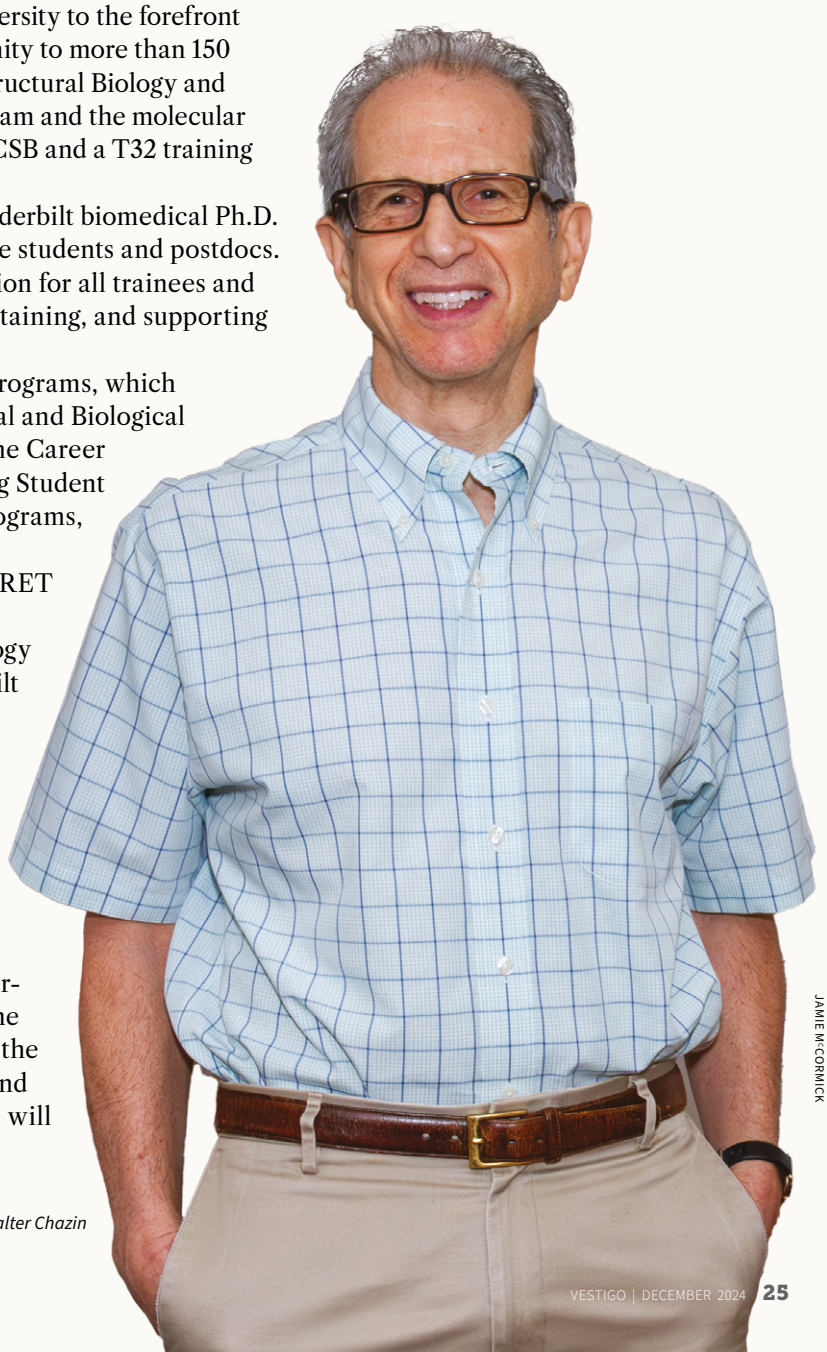
Chazin joined Vanderbilt in 1999 and has brought the university to the forefront of integrative structural biology, growing its research community to more than 150 scientists. Chazin is the founding director of the Center for Structural Biology and the director of the Chemical and Physical Biology Ph.D. program and the molecular biophysics training program. The MBTP is sponsored by the CSB and a T32 training grant from the National Institutes of Health.

The BRET office provides support and resources for Vanderbilt biomedical Ph.D. students, postdoctoral fellows, and faculty who train graduate students and postdocs. They are committed to fostering equity, diversity, and inclusion for all trainees and community members and are intentional about recruiting, retaining, and supporting diverse and underrepresented groups.

In his new role, Chazin leads the BRET office staff and programs, which include the Interdisciplinary Graduate Program in Biomedical and Biological Sciences, the Quantitative and Chemical Biology program, the Career Development ASPIRE Program, the Initiative for Maximizing Student Development, the Office of Outcomes Research, summer programs, health and wellness initiatives, and more.

Gould, his predecessor, was appointed associate dean of BRET in 2012 and senior associate dean in 2021, having served as director of Graduate Studies for Cell and Developmental Biology starting in 2006 and having created and directed the Vanderbilt International Scholar Program from 2010 to 2016. She was responsible for leading the development and implementation of the ASPIRE program, the revision of the first-year curriculum of the IGP, the partnership with the offices of faculty development within the School of Medicine to institute faculty mentor training, and multiple other initiatives aimed at improving the training environment for students and postdocs.

"Graduate students are the lifeblood of the scientific enterprise, and biomedical training continues to be the cornerstone of our work," Kuriyan said. "I am continuously impressed by the BRET team's recruitment and support of graduate students and postdoctoral fellows and am confident that Professor Chazin will not only maintain but also accelerate this trajectory."



Walter Chazin

JAMIE MCCORMICK

VANDERBILT UNIVERSITY

THE CAPRIOLI WAY

By Stephen Doster

It started with a hacksaw and a multimillion-dollar instrument. **Richard Caprioli**, then a postdoctoral fellow, was given the hacksaw to cut the instrument in half during his first day in the lab of John Beynon, professor of chemistry at Purdue University and author of one of the earliest books on mass spectrometry. Caprioli installed a new detector in the cut-open instrument and developed a yearning to "do innovative things with instruments," particularly with mass spectrometry. This yearning has accompanied Caprioli throughout his career and has resulted in him becoming a pioneer of new mass spec techniques, such as imaging mass spec.

Caprioli, the Stanford Moore Professor of Biochemistry at the School of Medicine Basic Sciences until his retirement earlier this year, didn't have a genuine science bent growing up, although he and his brothers had the notion of one day opening a pharmacy. After completing high school in his native Deer Park, New York, Caprioli got a fellowship from the National Science Foundation to do undergraduate research at the Columbia University College of Pharmacy.

Caprioli worked for a professor who was looking at different types of penicillin to figure out how to change its structure to make it just as effective but not have side effects. As an undergrad, Caprioli synthesized three or four new penicillins, including one that was extremely active—more so than the normal penicillin G, benzylpenicillin. "Sadly, it had really negative side effects, so it never got anywhere," Caprioli said. "But that was my exposure to real molecular science. I loved creating something and then seeing if it would have a positive health effect." At Columbia, Caprioli caught the bug for using his hands to create something.

Medical school briefly beckoned before Caprioli focused his attention on basic science. In 1965 he was accepted into Columbia's Ph.D. program under the guidance of biochemist David Rittenberg. Rittenberg pioneered the isotopic tagging of molecules and was a "fantastic mentor," whom Caprioli credits for instilling in him his own desire to teach and train students. "It came from him, there's no doubt," Caprioli said.

"He not only brought a capability for protein mass spectrometry that we didn't have, but he also introduced us to imaging mass spectrometry." —**Larry Marnett**

"He would have said, 'If you want to label me a researcher or this or that, okay, but the one word I want is teacher.' That resonated with me."

Breaking eggs to make omelets—and better instruments

Caprioli's first experience with a mass spectrometer occurred in the Rittenberg lab. 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, to quantify known molecular compounds and to determine the structure and chemical properties of molecules.

The instrument he used was an old-fashioned isotope ratio mass spectrometer made of glass that had a boiling mercury pump. "Every day I had to put dry ice and alcohol or acetone in this thing and hope that none of the boiling mercury got out," he said. But he was convinced that there was a larger role for mass spec in biology and biochemistry than was being explored solely through isotope ratio mass spec, so he applied for a postdoctoral position at Purdue with Beynon, a Welsh chemist and physicist known for his work in mass spec.

That's where the hacksaw story comes in. Caprioli produced a lot of papers thanks to the modified instrument, which allowed for "a whole new way of using a mass spectrometer" than was previously possible. Better yet, it taught Caprioli a valuable lesson: new equipment, even expensive equipment, could be modified.

Expertise pays off

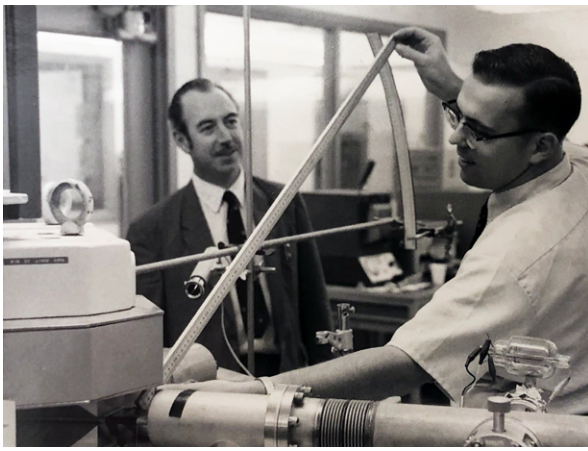
One day, Rittenberg and a redheaded stranger wearing boots, jeans, and a cowboy hat approached Caprioli. The cowboy, the renowned James "Red" Duke, best known for being the first surgeon to attend to President John F. Kennedy after he was shot in Dallas in 1963, was there to learn everything Caprioli could teach him about mass spec.

Several years later, Caprioli, by then an assistant professor of chemistry at Purdue, got a call from Duke inviting him to become part of a new medical school in Houston. "I don't want to go to Texas," Caprioli said to Duke, who offered to host him for a lecture and scientific discussions instead. Despite his initial reservations, Caprioli accepted an offer once he was on site and remained at the University of Texas Medical Center for 20 years teaching biochemistry to medical students, running a research program, and serving as director of the mass spec-based analytical center.

Vanderbilt beckons

In 1998, **Larry Marnett**, University Distinguished Professor and dean emeritus of Basic Sciences, led the search for a new director of the School of Medicine mass spec facility. One of the sources Marnett relied on was Bob Murphy, a distinguished mass spectrometrist, who recommended Caprioli as someone he should contact. By that time Caprioli had already made his mark on the field with micro-electrospray mass spec.

"Richard was doing cutting-edge research and had experience running a medical center–wide core facility," Marnett said. "He not only brought a capability for protein mass spectrometry that we didn't have, but he also introduced us to imaging mass spectrometry." Imaging mass spec retains information about where the molecules are located within thinly sliced tissue samples. At the time, imaging mass spec was just in its infancy and was poised to transform biological mass spec.

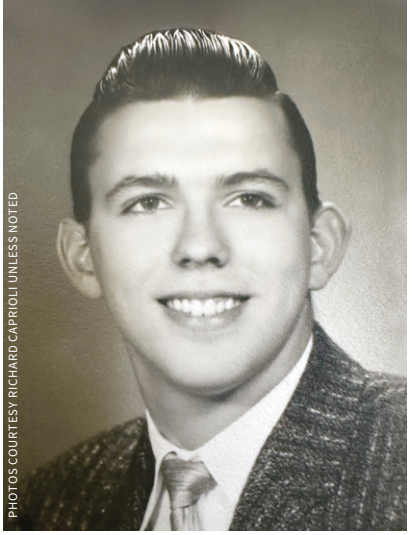


John Benyon, left, and Richard Caprioli

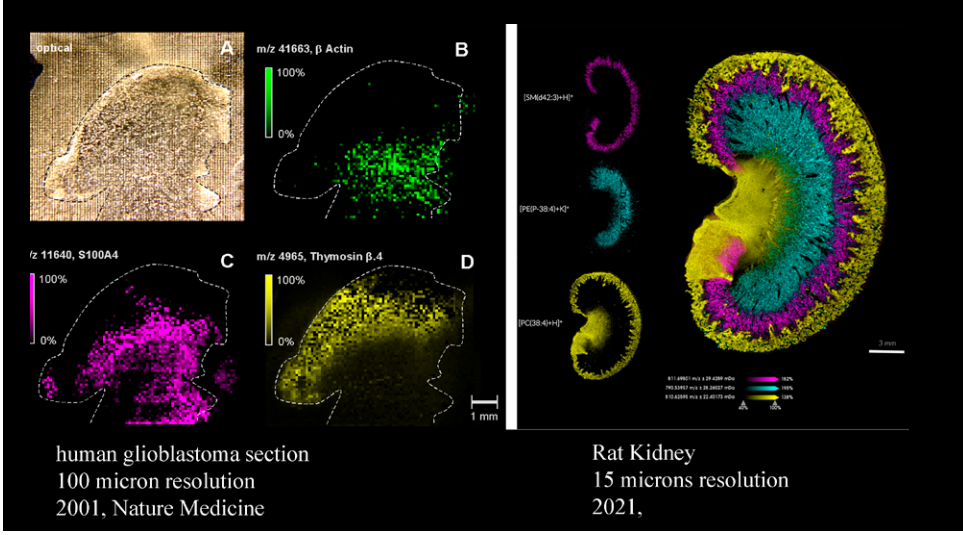
"I liked Texas, but when I interviewed at Vanderbilt, I could see a much more dynamic place, and I could see a better interaction with clinicians," Caprioli said. "I liked the collegiality that I saw here."

Crafting a place of excellence

Over the years, mass spec has been used to help diagnose genetic diseases in newborns, detect the

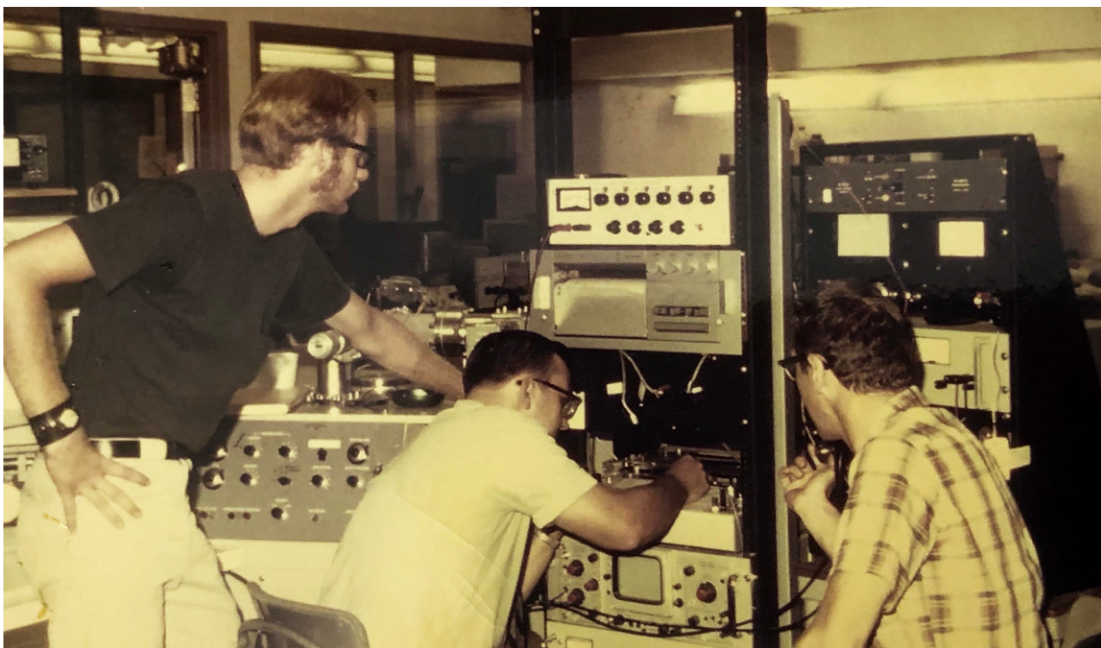


PHOTOS COURTESY RICHARD CAPRIOLI UNLESS NOTED



Clockwise from the top left: Caprioli as a toddler in his native New York; Caprioli in high school; technological advances over the span of 20 years have dramatically increased the resolution of images generated with imaging mass spec; Caprioli at his desk in 1998; Caprioli (third from the left in the front row) teaching Nobel Prize winner John Fenn; Caprioli and two colleagues at Purdue University in 1970; Caprioli at the Mass Spectrometry Research Center at Vanderbilt; Caprioli using his innovative thinking outside of the lab and inside the kitchen.

VANDERBILT UNIVERSITY



use of steroids in athletes, monitor patients' breathing during surgery, locate oil deposits by measuring petroleum content in rocks, and more.

"Richard has innovated multiple technologies, and his impact on the field of mass spectrometry has been enormous," **Kevin Schey**, Stevenson Professor of Biochemistry, said. Schey is also the deputy director of the Mass Spectrometry Research Center, which Caprioli led until his retirement.

Caprioli's work has created new possibilities for understanding the relationships between molecular and cellular organization in tissue microenvironments, ultimately providing a precision medicine toolbox for uncovering the molecular underpinnings of normal aging and disease.

Caprioli is best known for developing matrix-assisted laser desorption/ionization imaging mass spec, for which he received the John B. Fenn Distinguished Contribution in Mass Spectrometry Award from the American Society for Mass Spectrometry in 2014. MALDI imaging mass spec allows proteins, lipids, metabolites, and drugs to be localized in tissues with near single-cell resolution. This technology has had a major impact on biomedical research by providing scientists with the ability to determine spatially resolved molecular compositions in tissues in a variety of disease settings or within the context of different drug treatments. The pharmaceutical industry has adopted this technology to track drugs and their metabolites within tissues and to clarify mechanisms of toxicity.

In 2015 Caprioli's group achieved the first fusion of mass spec and microscopy, allowing scientists to see the molecular make-up of tissues in high resolution, an advance that could drastically improve the diagnosis and treatment of cancer.

Caprioli and his staff have transformed Vanderbilt's MSRC into a world-class facility that houses dozens of state-of-the-art instruments and consistently recruits the brightest minds in the field. The MSRC provides mass spec services in proteomics, small molecule (drugs, metabolites, lipids) mass spec, and imaging mass spec to the Vanderbilt community. It also attracts scientists from around the globe who attend annual lectures and workshops to learn the workings of MALDI imaging mass spec.

The center has supported many individual federal grants as well as large center grants, including from the Vanderbilt Ingram Cancer Center, the Vanderbilt Digestive Disease Center, and the Vanderbilt Vision Research Center. In 2023 Bruker Daltonics—a manufacturer of scientific instruments for molecular and materials research, including mass spectrometers—established a strategic partnership with Vanderbilt by creating a Mass Spectrometry Center of Excellence, the first of its kind, housed within the MSRC.

"Through vision and leadership of the MSRC, Richard has led the way in developing imaging mass spectrometry, continually pushing the boundaries of what is possible to enable molecular imaging at cellular resolution," said **Jeffrey Spraggins**, associate professor of cell and developmental biology and Caprioli's successor as director of the MSRC.

Inspiring innovation

Passing on his knowledge to the next generation of scientists is a passion of Caprioli's. "I've always told my students that I don't give Ph.D.'s—they earn them," he said. Caprioli's mentoring philosophy involves letting his students decide on their own experiments, even when he doesn't think they will work. "When something works, a student might think, 'I understand it.' No, you don't—you were lucky. But things that don't work, you go back and do an autopsy on them. You learn all kinds of things."

His mentoring style appears to be working, as his students usually have jobs waiting for them as soon as they graduate. The fact that every medium to large pharmaceutical company has an imaging mass spec laboratory—based on Caprioli innovations—also helps.

From hacksaw to band saw

Besides mass spectrometry and fast cars—Caprioli has driven a Ferrari since before coming to Vanderbilt—woodworking holds a special place in his heart. Five years ago, Caprioli built a 4,000-square-foot cabin atop a mountain surrounded by 30 acres of land in the Smoky Mountains. There, after retiring from Vanderbilt in August, he will apply the same inventive mindset he brings to science in his woodworking shop.

"Innovation is the commonality with science and woodworking," he said. "You can make things that don't exist; they come out of your mind. It's innovation."

It's the Caprioli way. ■

Basic Sciences trainees visit Boston's biotech with ASPIRE on the Road

By Christopher Williams and Kateryna Nabukhotna

COURTESY OF SANOFI AT CAMBRIDGE CROSSING

Above: The ASPIRE on the Road group after a tour at Sanofi's Cambridge Crossing location

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

Deciding on one's future beyond graduate school or a postdoc fellowship is a daunting task. But for us and 10 other School of Medicine Basic Sciences students, the BRET office helped facilitate the next steps in our careers.

Our group of trainees had the unique opportunity to travel to Boston in May to visit biomedical companies new and old, large and small, through the ASPIRE on the Road program. Throughout the tours, we found comfort among the familiar, including our favorite lab equipment, caffeine-fueled science, and the smiles of fellow Commodores.

Before hitting the road, all 12 participants submitted a cover letter and resume to the BRET office in which we demonstrated our interest in the program and the pursuit of a career in industry. Many of us were unsure of precisely what to expect on this trip, but thankfully **Ashley Brady**, assistant dean of biomedical career engagement and strategic partnerships and the trip's organizer, went to great lengths to ensure we were exceptionally well prepared for any and all professional situations. We gathered for two meetings before the trip in which we discussed trip logistics, how to dress, backgrounds of the companies we were visiting, the individuals from each company who would host us during these visits, and more. By the time we landed in Boston, we were ready to go!

Our first stop on the trip was MOMA Therapeutics, a biotech company with fewer than 100 employees that specializes in developing small-molecule inhibitors of MOlecular MAchines (enzymes that create force, work, and motion and that give the company its name). A panel of employees from different departments within the company showed us just how vital collaborative work is at a smaller organization, where enthusiasm to learn and help others is indispensable when driving innovation.

On day two of our trip we visited several larger pharmaceutical companies, including Sanofi,

Johnson & Johnson, and Merck. Our conversations with employees at these companies covered just about everything, including company structure and organization, hiring processes and tips for application success, the enormous breadth of positions and functional roles within these organizations, and more.

"It was so inspiring to meet the next generation of scientific talent! The ASPIRE program is such a valuable resource for the biomedical graduate program by providing a way to introduce some of Vanderbilt's graduate students to careers outside of academia and, importantly, to network with former alums," said **Roshi Afshar**, PhD'05, principal scientist at Johnson & Johnson Innovative Medicine. "I appreciated the questions and interest the students had as they gained exposure to what life is like for different roles in industry, and, as someone who knows firsthand how difficult that leap from academics to industry can be, I hope they were able to take home some nuggets of inspiration and learnings as they navigate the next phase of their careers."

The next day included visits to incubator spaces that house (very) small biotech startups that often have just a few employees. Many of these companies occupy less bench space than our own labs at Vanderbilt but maintain access to what is otherwise prohibitively expensive equipment and resources.

Before returning to Nashville, we made one last stop at Dewpoint Therapeutics, a smaller biotech company that targets biomolecular condensates. Researchers at Dewpoint showed us how their novel compound-screening pipeline integrates artificial intelligence to discover compounds that modulate the behavior of cells.

Each company—regardless of size—provided not only sleek and modern lab spaces with powerful equipment and ample resources for cutting-edge research, but also made sure employees were well hydrated and caffeinated. Espresso machines, sparkling water dispensers, and cold brew on tap were fixtures of each laboratory visit that we were always sure to take advantage of!

An exciting networking opportunity took place during the Vanderbilt Alumni Networking Happy Hour. Before this event, we were provided a list of attendees and their current occupations so that we could identify specific people we hoped to connect with. The happy hour kicked off with a greeting from the dean of the School of Medicine Basic Sciences, **John Kuriyan**, and provided an immediate sense of Vanderbilt community. As the evening went on, we had friendly, helpful, and meaningful conversations with Vanderbilt alums and ended up meeting and interacting with more people than we originally anticipated.

A significant and unique aspect of the trip was the ability to gain firsthand information about industry career paths directly from scientists who had a range of roles within different companies. As many of us have a long-term objective to transition to a career in industry, we were specifically curious about what we could currently do as graduate students and postdocs to increase our chances of being successful applicants for industry roles.

ASHLEY BRADY

A captive audience at Dewpoint Therapeutics

We learned specifics about each company's positions and interview processes. These behind-the-scenes details were tremendously helpful as we look to start navigating the application process and search for the appropriate job match. We also garnered general insights into the qualities and skills that are crucial for getting a job in industry; employees at each company repeatedly mentioned networking as one of the essential factors that can help us stand out from other applicants. Having internal reference contacts can also make a notable difference during the hiring team's decision-making process.

The ASPIRE on the Road trip was an outstanding opportunity for each of us to grow our networks. At every company, we met scientists at different career stages who specialize in various research areas, which enabled us to establish the most relevant networking contacts based on our individual scientific and career interests.

It was a pleasure to be a part of this year's ASPIRE on the Road group. Although most of us did not know each other before the trip, all trip participants became quick friends who connected thanks to our common interests. It quickly became apparent that the group consisted of ambitious, curious, open-minded, and driven people ready to ask questions and maximize opportunities. We networked with each other and bonded throughout the trip, particularly during an inspirational walking tour of Kendall Square, one of the most innovative spots on the planet due to its high concentration of biotech and pharma companies.

We returned to Nashville feeling inspired and ready to make well-informed career decisions that will hopefully bring us one step closer to our future dream jobs! ■

FRED GUENGERICH:

50 years of sowing seeds and harvesting rewards

By Stephen Doster

ADOBE STOCK

PHOTOS COURTESY OF FRED GUENGERICH.

Numbers can tell a story. For **Fred Guengerich**, PhD'73, professor of biochemistry, the story of his 50-plus years in science can be told through his 99 semesters on Vanderbilt University's faculty; the 22 graduate students and 141 postdoctoral fellows and visiting scientists he has mentored; the 772 primary research papers, 324 invited reviews and chapters, and 138 book chapters and published proceedings he has authored; and the more than 128,200 times he has been cited.

But even those numbers don't tell the whole story.

The early days

Guengerich's tale began on an Illinois farm on New Year's Day in 1949. He was the first member of his family to be born in the U.S., as they had migrated from Germany in 1913. Life was grueling for his father, who often worked 100 hours a week, but he inspired in his son a "warm spot in my heart for hard-working immigrants."

By age 10 Guengerich could operate a tractor. At 12 he was driving stick-shift trucks. Six-day work weeks, exposure to the elements, and no time for vacations ingrained in him a work ethic that has served him well throughout his professional life. "It may not seem very relevant to a career in science, but I learned much about hard work, self-reliance, and mental toughness from my father," Guengerich said. "Compared to baling hay, working in the laboratory is much easier and much more interesting."

Guengerich, approximately 5 years old, sitting on a corn picker

Guengerich excelled in agriculture and chemistry in high school, but soon realized that following in his father's footsteps was not in his future. Instead, he enrolled in the University of Illinois to study food science and technology. His sophomore adviser, Carl Davis, saw the potential in him and suggested he apply for summer work in the biochemistry lab of Harry Broquist.

The summer research project involved working on pathways of alkaloid biosynthesis in the mold *Rhizoctonia leguminicola*, a fungus that affects plants and causes black patch disease in horses and cattle. "Once I started I never wanted to do anything else for a career but be a biochemist," Guengerich said.

As Guengerich later related in a recollection published in 2005 in *IUBMB Life*, "I was not aware of this as a student, but people take notice of your good qualities as well as the bad." His stint with Broquist turned into a lifelong friendship.

Finding his own path

Broquist accepted a faculty position at Vanderbilt in 1969 and Guengerich followed him in 1970, enrolling in graduate school to study biochemistry. He started with a small annual stipend and an individual National Institutes of Health fellowship.

At that time graduate students were required to pass a foreign language exam in either German, French, or Russian. Although his father spoke a Bavarian German dialect with a "thick" accent, Guengerich didn't learn the language at home. He took an introductory German class, read German chemical and medical journals, and passed the exam on his first attempt.

His last year of graduate school proved to be a memorable one: Guengerich met a "beautiful, red-headed nurse." He and the nurse, Cheryl Powell, were married in December 1973 shortly after Guengerich started a new job as a postdoctoral fellow. "We have been happy together since then," he said.

The new job—a position in the lab of Minor J. "Jud" Coon, best known for his research on cytochrome P450—took him from Nashville to the University of Michigan in Ann Arbor, Michigan. It was a fortuitous match that gave Guengerich a lifelong research focus. "It was Jud Coon who really taught me how to be a professor, although I did not always realize it at the time," Guengerich said.

Cytochrome P450 enzymes are the main catalysts that break down drugs in the body. Variability in these enzymes is a major factor in how long they are active in the body and in drug-drug interactions. Cytochrome

P450 enzymes are also the main ones involved in steroid metabolism, and changes in their expression level can cause serious endocrinological problems. "When some are too active, they are targets for cancer-treating drugs such as the aromatase inhibitors for breast cancer," Guengerich said. "I was attracted by the enzymes because I thought there might be practical applications for P450 research someday, especially if I decided to go into industry, but I did not expect to keep working on the same enzymes for the rest of my life."

Guengerich completed his Ph.D. in a remarkable three years, and, in 1975—barely five years after obtaining his undergraduate degree—returned to Vanderbilt as an assistant professor. He was promoted to associate professor with tenure five years later and became a full professor—at a young 34—in 1983.

Don't take it from us–take it from his trainees

The impact of Guengerich's mentoring can be felt through the work and words of former trainees, many of whom have embarked on their own stellar careers.

"Fred has always maintained an unparalleled love for science," **Asit Parikh**, PhD'98, MD'00, president and CEO of MOMA Therapeutics and former Guengerich lab member, said. "He led by example, as exemplified by his ritual Saturday mornings in the lab where he conducted his own experiments—most unusual for a scientist at his level!" Parikh has been able to lean on his former mentor over the years and appreciates his equanimity not just in science but in regards to people and decision-making. When it comes to the work he expects from his lab members, Parikh said that what Guengerich "wanted to see was effort and excellence in the pursuit of science, whether the science was pure or applied, and he would lend his full support as soon as that bar was achieved" regardless of gender, race, religion, or socioeconomic status. "I am deeply grateful to have him as a friend and mentor," Parikh said.

Former postdoc **Hiroshi Yamazaki**, now a professor at Showa Pharmaceutical University, recalls how Guengerich has worked with many international collaborators, students, and postdocs. "He learned much of other cultures through the individuals and gave us great, kind, and continuous support and impact on our training and career," Yamazaki said.

Laura Furge, PhD'98, a former Guengerich lab graduate student and current provost and professor of chemistry at Muhlenberg College, values Guengerich's mentorship so much that she has sent six research students to work under him. "Fred has been a constant mentor, colleague, and now friend," she said. "In 1994, he got me started in research and gave me the confidence to be successful and to push myself. Every morning on my desk there would be new papers to read, manuscript markups, and notes to remind me that I was part of a team." Even though she has left his lab, Guengerich has been available to celebrate successes and to encourage Furge through challenges. "While my current role as a provost has taken me away from the lab, I've tried to model the same level of relentless support for my colleagues that I have felt these past 25 years from Fred."

Former postdoc **Robert Eoff**, currently a professor of biochemistry and molecular biology at the University of Arkansas for Medical Sciences, has similar feelings about the impact that Guengerich has had on his life. "Very few people have influenced my life as much as Fred," he said. "The constancy of his work ethic, intellectual prowess, and drive to have a long-lasting and meaningful body of scientific work are all inspirational." Eoff also prizes Guengerich's mentorship, and credits it with helping to hone many of his most valuable professional skills, such as "being consistent in your work, staying organized and ahead of schedule, keeping lines of communication open, and having belief in one's own abilities—traits I saw him apply every day."

A lasting legacy

John Exton, professor emeritus of molecular physiology and biophysics, now deceased, once told Guengerich: "You often come back to your lab from committee meetings and wonder if your presence there mattered—usually not." But in contrast, as an editor, Guengerich said, "You make the real decisions—decisions that (usually) stick and that can shape an entire research field." He learned that firsthand when he joined the editorial board of the *Journal of Biological Chemistry* in 1984 and eventually became an associate editor. He remains involved with the journal and most recently has served as interim editor-in-chief and deputy editor.

Guengerich flirted with fame in 2004 when he and a former postdoc, **Elizabeth Gillam**, made international headlines by discovering a liver enzyme that turned a bacterium blue. The media speculated on its significance toward the creation of blue roses and blue cotton, which do not occur naturally, but sadly, the potential game changer did not pan out. Regardless, the discovery garnered him a spot in a mid-2000s edition of Trivial Pursuit, the popular trivia board game.

When Guengerich began his academic career, most of his peers handwrote articles on legal pads. But unlike he and most of his peers today, he still literally puts pen to the paper when starting new work. "I still write up initial drafts of long things—papers, grants, manuscript reviews—in longhand. As **Lubomir Hnilica**, a former faculty colleague at Vanderbilt, used to say, 'I think with my pencil.'" Guengerich's long-time administrative assistant, **Kathy Trisler**, then transcribes his work. "When I first started working for Fred in 1999, I was so happy that he preferred to handwrite his letters, manuscripts, etc.," she said. "I was not very good at transcribing from recordings, but I was fast at typing what I read. So, we were a good fit."

His handwriting-and-thinking approach is clearly working, seeing as he is one of the most-cited authors in his field. "Dr. Guengerich's accomplishments in scientific research are extraordinary," said **David Cortez**, Richard N. Armstrong, Ph.D. Professor of Innovation in Biochemistry and chair of the Department of Biochemistry. "He is a world leader in the field of cytochrome P450 biochemistry. He has made major contributions to our understanding of cytochromes P450 as central enzymes in metabolic and biosynthetic pathways, xenobiotic processing, drug catabolism, biotechnology, health, and disease."

When he's not in the lab or at conferences, Guengerich pursues fishing and photography. He has traveled the world with his camera, from Africa and Antarctica to South America and Oceania. "Photography is interesting for a scientist: It allows you to combine technical skill with art and composition," he said.

Former postdoc Eoff encapsulates Guengerich's versatility: "Fred is an exemplary scientist and leader, a devoted husband and father, and a gifted photographer. He even runs a farm!" he said. "I wouldn't be where I am today without Fred, and I will always be grateful for the opportunity to be one of his [mentees]."

Without a doubt, Guengerich can look back contentedly on his career. "I consider myself a very fortunate person—I am paid to do things I like," he said. "I owe a lot to biochemistry and have absolutely no regrets."

Turns out that, in a way, Guengerich did follow in the footsteps of his father: sowing seeds and harvesting the fruits of hard labor. ■

From left to right: Former postdocs and graduate students at a meeting in Fukuoka, Japan, in December 2012 celebrating the 50th anniversary of the discovery of cytochrome P450; Guengerich and Harry Broquist in 2007; Guengerich in college in the early 1970s with the then-popular Beckman Model DU spectrophotometer; Jud Coon, left, presenting Guengerich the William C. Rose Award at the ASBMB annual meeting in 2005; Guengerich with his camera.

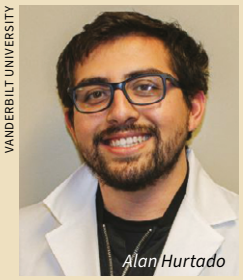
Alan Hurtado, Ph.D. candidate in the Chemical and Physical Biology Program, was named inaugural Linda Sealy Emerging Scholar Travel Award recipient

By Marissa Shapiro

Alan Hurtado, a chemical and physical biology Ph.D. candidate in the lab of **Edward Levine**, has been awarded the first Linda Sealy Emerging Scholar Travel Award.

The award was established to enhance the STEM talent pipeline by promoting a more inclusive environment that supports trainees from diverse backgrounds. Hurtado and Levine will receive $4,000 to attend a national conference in Hurtado's research field. The award was named for **Linda Sealy**, associate professor emerita of molecular physiology and biophysics and associate dean for diversity, equity, and inclusion from 2017 to 2020.

Hurtado's graduate research seeks to uncover the transcriptional and epigenetic mechanisms that maintain retinal progenitor cell lineage during development. His main goal is to identify the interconnectedness of activating and repressing eye lineage pathways that regulate retina and retina pigment epithelium differentiation. Hurtado is specifically interested in understanding how these mechanisms prevent retinal progenitor cells from changing tissue lineages during development. Hurtado and Levine, who is the William A. Black Professor of Ophthalmology and a professor of cell and developmental biology, will use the award to attend the Association for Research in Vision and Ophthalmology annual meeting, the leading conference in their field of work, in 2025.



VANDERBILT UNIVERSITY

Alan Hurtado

"I am honored to have been selected as a recipient for the Linda Sealy Emerging Scholar Travel Award," Hurtado said. "Networking is an indispensable aspect of research, and it is crucial for finding collaborators and job opportunities. My career goal is to get a tenure-track faculty position at an R1 institution, so being connected with experts and being familiar with the research that is being conducted is imperative for further developing my career options." While at the conference, Hurtado plans to share his work with researchers and professionals with different areas of expertise to help him continue building his graduate project. "Knowing that my mentor will play a proactive role in my interactions during the meeting gives me the confidence that I will maximize my time at the conference," he said.

Hurtado joined Vanderbilt in 2021 and received an Institutional Training Grant from the National Institutes of Health and a Provost's Graduate Fellowship from Vanderbilt University the same year. The following year, he received a National Science Foundation Graduate Research Fellowship.

On campus, Hurtado leads the Vanderbilt chapter of the Society for the Advancement of Chicanos/Hispanics and Native Americans in Science, an all-inclusive, student-run chapter welcoming anyone who has the desire to support and contribute to fostering scientists from underrepresented communities. Hurtado is also the vice president of student support for the Chemical and Physical Biology Graduate Student Association. Hurtado has also served as a peer mentor for multiple first-year students from the Initiative for Maximizing Student Development and Quantitative and Chemical Biology programs.

Hurtado was selected by a committee chaired by **Vivian Gama**, associate dean for equity and inclusive mentoring and associate professor of cell and developmental biology, **Felysha Jenkins**, assistant dean for diversity, equity, and inclusion, and **Ken Lau**, professor of cell and developmental biology and associate professor of surgery. The award was established with funds provided by the Howard Hughes Medical Institute Gilliam Fellows Program, the School of Medicine Basic Sciences, and the Department of Cell and Developmental Biology.

"I am so proud that we were able to recruit Alan to Vanderbilt in the spring of 2021 right before I retired, as he is clearly an amazing scholar and richly deserving of this award," Sealy said. "It's wonderful to know that the Basic Sciences, through the efforts of Vivian, Ken, and Felysha, are providing this travel opportunity for Alan and his mentor, Ed Levine, which will no doubt advance Alan's career." Sealy extended the congratulations to Levine and added that, "by making the mentor's engagement part of the selection criteria, this award importantly conveys to the entire biomedical research community that quality mentorship is valued at Vanderbilt."

VANDERBILT UNIVERSITY

Linda Sealy

Biomedical Ph.D. alum career goals and outcomes revealed in new research

A team from the Office of Biomedical Research Education and Training published a longitudinal study of the career goals and outcomes of up to 1,452 biomedical sciences Ph.D. graduates. The study provides clarity on how students' career goals change during graduate school and how career goals at graduation connect to career outcomes.

The article, "From goal to outcome: Analyzing the progression of biomedical sciences PhD careers in a longitudinal study using an expanded taxonomy," has broad implications for academic and biomedical research communities, funding organizations, employers and Ph.D. trainees in the face of a changing workforce and economy. The article was published in the Federation of American Societies for Experimental Biology journal *FASEB BioAdvances* in October 2024.

This research connects career goals during graduate school with career outcomes and shows the career evolution of Ph.D. alums longitudinally during the crucial, career-defining 10 years after graduation with a Ph.D.

The job landscape for Ph.D. graduates has changed over the past decade, in part due to the country's shift toward a knowledge-based economy. There are greater chances for people with advanced thinking, analysis and communication skills developed during their Ph.D. studies to work for private companies in 2023 than in 2013. This shift is intensified by the stagnation or lessening of the number of permanent faculty positions in universities during this time. The result is that fewer Ph.D. graduates are taking the traditional route of becoming professors in universities.

"This trend is especially true for biomedical science Ph.D. graduates," said **Abby Brown**, first author of the article, director of outcomes research for BRET and assistant professor of molecular physiology and biophysics. "The number of Ph.D. degrees granted by U.S. institutions has quadrupled in the last 40 years, while available tenure-track faculty jobs have remained steady."

While there are numerous compelling career prospects for Ph.D. scientists, little is known about the factors that influence their career choices. Equally lacking is data about career path progression and how it aligns with the aspirations of Ph.D. students during their studies.

To address these gaps, the BRET team's study followed the careers of 1,452 Vanderbilt biomedical Ph.D. alums who graduated between 1997 and 2021, for up to 10 years after their thesis defense. Their work was guided by their goal of more closely aligning the structure of biomedical Ph.D. training programs with career development initiatives for Vanderbilt trainees and with national workforce trends.

"We found that most students changed their career goals during graduate school, which speaks to the importance of universities and graduate programs providing opportunities for Ph.D. students to explore career options and their interests," said **Kim Petrie**, principal investigator on the study, assistant dean for biomedical career development for BRET and associate professor of medical education and administration. "Our findings emphasize that Ph.D. students need a wide range of career development opportunities and career mentoring during graduate school to help them transition efficiently to their future careers inside and beyond academia."

Other findings include:

Overall, about 30 percent of students were interested in research-intensive faculty jobs at the time of doctoral defense.

Students who became more interested in pursuing a faculty job during graduate school cited a high-quality mentoring experience or increased confidence in their ability to succeed.

Many alums ultimately pursued different careers than their stated career goal at the end of graduate school, suggesting that alums also switch goals during postdoctoral training.

By 10 years after graduation, about one-third of alums were in academic research positions. The remaining alums were employed in other types of roles in academia, industry, government and nonprofits.

In line with national trends in postdoctoral employment over time, there is a declining number of Ph.D. students pursuing postdoctoral training.

The article co-authors include **Lindsay Meyers**, assistant dean for operations and administration, **Janani Varadarajan**, assistant director of postdoc support and Office of Outcomes Research project manager, **Nicholas Ward**, Office of Outcomes Research program manager, **Jean-Philippe Cartailler**, director of Creative Data Solutions in the Vanderbilt Center for Stem Cell Biology, **Roger Chalkley**, former senior associate dean of BRET and professor emeritus of molecular physiology and biophysics, and **Kathleen L. Gould**, Louise B. McGavock Professor of Cell and Developmental Biology.

JAMIE M°CORMICK

From left to right, Jan Varadarajan, Abby Brown, Kim Petrie, Kathleen Gould, and Lindsay Meyers

Vanderbilt University launches sustainable lab program

VANDERBILT Sustainable Labs

The new Vanderbilt Sustainable Labs program, an initiative from Environmental Health, Safety and Sustainability in the Division of Administration, provides guidance and a voluntary certification designation for laboratory members to reduce the environmental impact of their lab activities.

Laboratory spaces traditionally consume about five times more energy per square foot than standard office spaces, making them a crucial focal point for university sustainability efforts. The VSL program not only meets this challenge but also supports the entire university in meeting its ambitious carbon and waste reduction goals.

"The launch of the Vanderbilt Sustainable Labs program represents a significant milestone in our ongoing commitment to environmental stewardship and sustainability," said **Andrea George**, assistant vice chancellor for EHSS. "By engaging our laboratory community in sustainable practices, we are not only reducing the university's environmental impact but also supporting Vanderbilt's culture of innovative, safe and responsible research."

The VSL program offers two resources:

- **Sustainable Lab Guide:** This comprehensive guide for laboratory members offers practical strategies to minimize the environmental impact of lab activities.
- **Sustainable Lab Certification Program:** Labs can voluntarily participate in this program by completing a self-certification form. After meeting impactful sustainability criteria, lab teams receive a sustainable lab certification badge, which can be showcased to highlight their commitment to sustainability.

The program is the result of collaborative efforts between EHSS and the Green Team, a group of researchers passionate about sustainability within the Center for Structural Biology and the Molecular Biophysics Training Program.

"Laboratory spaces are essential for research and discovery, but they also have a substantial environmental impact," said **Borden Lacy**, Green Team member and a professor of pathology, microbiology and immunology. "The VSL program underscores our commitment to sustainability by empowering Vanderbilt labs to adopt eco-friendly practices without compromising scientific excellence."

Peer advisers are available to support labs in implementing sustainable strategies and completing the certification checklist. Email futurevusustainability@vanderbilt.edu to learn more.

For more information about the Vanderbilt Sustainable Labs program, including resources and how to get involved, visit the VSL website at vu.edu/vsl.

PHOTOS BY JAMIE MCCORMICK

Top: A Green Team member demonstrates how closing the sash on a fume hood when it is not in use is one of the best ways to save energy in a lab.

Bottom: A Green Team member demonstrates how maintaining equipment regularly, organizing cold samples, and setting ultra low temperature freezers to -70˚C instead of -80˚C are techniques to reduce the environmental impact of your lab's refrigerators and freezers.

School of Medicine Basic Sciences Staff Spotlight Roundup

By Alexandra Scammell

The School of Medicine Basic Sciences consists of a remarkable community that is dedicated to advancing the study of human biology, health, and disease. In addition to the award-winning faculty and students who are at the forefront of our cutting-edge research, a large part of our school's success can be attributed to our staff. They work hard to ensure the exceptional exploration into basic biomedical science that takes place at our school.

We sat down with a few of our staff members who told us a little about themselves: **Karen Davis** is the program coordinator for the Center for Structural Biology, **Stephen Doster** is the associate program director of academic and educational support in Basic Sciences, and **Mary Gray Lindstrom** is the program manager for the career development ASPIRE program and the ASPIRE Path in Molecular Medicine in the Office of Biomedical Research and Training Education.

How long have you been working for Vanderbilt?

Davis: Since 2012! I like the people I work with and the feeling of being a part of something bigger than myself.

Doster: I started working for the Vanderbilt Institute of Chemical Biology in 2004 and I transitioned to Basic Sciences when it was created in 2016. Belief in the mission to improve human health keeps me coming in. My co-workers make the good days great and the worst days not so bad.

Lindstrom: I started in the College of Arts and Science in 2018 and transitioned to BRET in 2022. I've been truly so thankful for my team members, especially in the Career Development ASPIRE program. I hope to continue to try to learn from them all!

What is your favorite project you have completed in Basic Sciences?

Davis: I'll always remember the first symposium I worked in 2014, the "Biomolecular Structure, Dynamics and Function: Protein Membranes Symposium." We had a dance party one night during the event. I might have done the MC Hammer dance. And no, you can't touch this!

Doster: I have been interviewing long-time employees for their memories of how things have evolved at Vanderbilt since they started working here. Some of them have been at Vanderbilt more than 40 years. One of them, Fred Guengerich, drove a farm tractor at age 7. He's now one of the most cited researchers in his field of study.

Lindstrom: The 2024 ASPIRE Career Symposium! We invited 11 alums to share their career paths and network with the students.

What is a fun fact about you?

Davis: I'm a huge soccer fan! I started coaching at Nashville Youth Soccer Association in 2006 and I currently coach two coed NYSA recreational soccer teams. What can I say? I love being called coach!

Doster: I have a British passport. Fortunately, I'm familiar with the language, too. And I like to write. Believe it or not, Vanderbilt's main library has three of my nonfiction books on its shelves.

Lindstrom: My double name comes from my grandmothers. Mary Neil Lindstrom and Wilma Gray Biggs.

COURTESY OF KAREN DAVIS

MARISSA SHAPIRO

COURTESY OF MARY GRAY LINDSTROM

Top to bottom: Karen Davis, Stephen Doster, and Mary Gray Lindstrom

Vanderbilt students explore STEM policy in Washington, D.C.

Edited by Alexandra Scammell

Three Vanderbilt graduate students traveled to Washington, D.C., for the Catalyzing Advocacy in Science and Engineering Workshop hosted by the American Association for the Advancement of Science. The workshop provides an opportunity for students from around the country to learn from experts about the role of science in policymaking and the federal policymaking process. The Vanderbilt Office of Federal Relations has been sponsoring graduate students to participate in the AAAS CASE Workshop for a decade.

The program aims to empower students to leverage their scientific expertise to shape public policy. Sessions covered a spectrum of topics, ranging from science policy, career pathways, and the federal budget process to science communication skills and advocacy. Participants also learned how congressional offices and federal agencies operate and what it's like to work there.

On the final day of the workshop, the Vanderbilt graduate students met with staff in four congressional offices, specifically those working at the intersection of science and policy. The staffers shared their perspectives on how scientists can advocate to shape public policy. The meetings were arranged by Vanderbilt's Federal Relations team, offering a uniquely comprehensive experience for the Vanderbilt students.

"As a Ph.D. student knowing I don't want to continue into academia, science policy is the answer to so many questions I had about how to use my expertise in the government sector," said **Lauren Bellocchio**, Ph.D. candidate in chemistry. "This workshop taught me about how the federal budget is used for promoting science and technology policy, and I gained the invaluable firsthand experience of speaking directly with policymakers on Capitol Hill."

Logan Northcutt, Ph.D. candidate in cancer biology, said, "I really learned a lot about policymaking and how funding for science is influenced by government priorities. I would highly recommend the AAAS CASE Workshop to anyone who is interested in science policy."

Vanderbilt's Office of Federal Relations works in close partnership with the Graduate Leadership Institute and the Office of Biomedical Research Education and Training ASPIRE program, who select the students who participate each year.

"I'm thrilled to continue bringing students to Capitol Hill as part of the AAAS CASE program," said **Heather Bloemhard**, associate director of federal relations. "The workshop is an excellent opportunity for both professional development and civic education; it is gratifying to see them gain valuable insights into science policy and advocacy and learn how they can have a meaningful impact on policy as both citizens and scientists."

For students and postdocs interested in exploring careers in science policy or advocacy, Vanderbilt's Office of Federal Relations hosts a biennial Federal STEM Policy and Advocacy Seminar. This program, inspired by the AAAS CASE Workshop, offers content tailored to the interests of the Vanderbilt community. The most recent seminar was held in October in Washington, D.C.

HEATHER BLOEMHARD

Vanderbilt students Lauren Bellocchio, Audrey Arner, and Logan Northcutt outside the U.S. Capitol

Faculty transitions

By Lorena Infante Lara

The academic landscape can seem like an unmoving entity, but it's the people within it that make it tick and grow to new frontiers. No outlook on our School of Medicine Basic Sciences is complete without recognizing significant faculty transitions, including well-deserved promotions, exciting new appointments, and bittersweet departures as esteemed colleagues embark on new journeys at other institutions.

DEPARTURES

Alyssa Hasty

Hasty

Hasty, formerly the senior associate dean for faculty in Basic Sciences, became vice provost and senior associate dean for faculty affairs and career development at the University of Texas Southwestern Medical Center in August 2024.

Dr. Vito Quaranta

Quantana

Quaranta, former co-director of the Quantitative and Chemical Biology program and director of the Quantitative Systems Biology Center, has been appointed professor emeritus of biochemistry and pharmacology. He has also started a new position as a strategic advisor to the provost at the Institute for Experiential AI at Northeastern University.

David Wasserman

Wasserman

Wasserman, Annie Mary Lyle Professor and professor of molecular physiology and biophysics, died June 20 in Nashville due to health issues. He was 66.

Danny Winder

Winder

Winder, former director of the Center for Addiction Research and professor of molecular physiology and biophysics, joined the ranks of the UMass Chan Medical School as their new chair of the Department of Neurobiology.

PROMOTIONS

The following people have been promoted so far during 2024. Congratulations!

BIOCHEMISTRY:

Wade Calcutt, **W. Hayes McDonald**, **Michelle Reyzer**, **Kristie Rose**, and **Ansari Aleem** were promoted to research associate professors.

CELL AND DEVELOPMENTAL BIOLOGY:

Angela Kruse was promoted to research associate professor.
Marija Žanić was promoted to professor.

MOLECULAR PHYSIOLOGY AND BIOPHYSICS:

Erkan Karakas was promoted to associate professor.
Wenbiao Chen was promoted to professor.
Dale Edgerton was promoted to research professor.

PHARMACOLOGY:

Pankaj Sharma was promoted to research assistant professor.

NEW LEADERSHIP:

Erin Calipari was appointed as director of the Vanderbilt Center for Addiction Research.
Walter Chazin was appointed as senior associate dean of Biomedical Research, Education and Training.

NEW FACULTY

So far during 2024 we have brought on five new faculty into our departments. Here are the new recruits!

BIOCHEMISTRY:

Anna Edmondson and **Katrin Karbstein** were appointed as professors.
Rahul Bhowmick and **Sezen Meydan** were appointed as assistant professors.
Jinhui Dong and **James Marks** were appointed as research assistant professors.

CELL AND DEVELOPMENTAL BIOLOGY:

Madeline Colley was appointed as a research instructor.
Dr. Erin Plosa received a secondary appointment as an associate professor.

MOLECULAR PHYSIOLOGY AND BIOPHYSICS:

Karin Bosma, Katie Coate, and **Stephenie Wankowicz** were appointed as assistant professors.
Alejandra Paola Torres Manzo and **Zer Vue** were appointed as research instructors.

PHARMACOLOGY:

Ben Brown, Valentina Cigliola, Shan Meltzer, and **Quynh Anh Nguyen** were appointed as assistant professors.
Aaron Bender and **Kristen Gilliland** were appointed as research assistant professors.
Salvatore Incontro, Snigdha Mukerjee, and **Suzanne Nolan-Strle** were appointed as research instructors.

Vanderbilt basic science alum Q&A: Sonja Fulmer

By Alexandra Scammell

The School of Medicine Basic Sciences has seen remarkable and diverse students come through its doors, collaborate and learn from distinguished faculty, then graduate from one of our nationally ranked departments. But where are they now?

They go on to become leaders at notable institutions, universities, governmental entities, and research and development companies, among other organizations. Some of the places where our alums work are the U.S. Department of Health and Human Services, St. Jude Children's Research Hospital, Pfizer Inc., the Food and Drug Administration, and Oak Ridge National Laboratory, to name but a few. And some even decide to stay at Vanderbilt!

We sat down with Fulmer to discuss her experience studying basic science and how it played a role in her successful career.

COURTESY OF SONJA FULMER

Fulmer

What activities at Vanderbilt had the most significant impact on your career path?

I appreciated Vanderbilt's focus on highlighting and explaining different career paths. While I was completing my Ph.D., the BRET office held a series of "alternative" career seminars. The seminar speakers explained how Ph.D.'s in biomedical sciences contribute to many different industries, beyond following a more traditional path in academia. I had originally planned to pursue an academic career path, hoping to be my own PI and direct my own research group, but I found that learning about alternative career paths showed how I could impact the world in other ways.

Although I will always dream of experiments that I could have done and scientific problems that I could have solved, I feel that I've found the right path for me at the FDA. I remain driven by the same desire to improve public health but now I apply my training not by designing experiments and writing grants, but by shaping the regulatory policy for digital health. Who would have thought?

Were there any specific mentors or professors who played a crucial role in shaping your career aspirations?

My principal investigator for my graduate work, **Brandt Eichman**, was consistently supportive of my professional growth while I completed my Ph.D. Whenever I checked in with him about pursuing a project to advance my experience in science policy, he encouraged me to take advantage of opportunities, including participating in internships during the time I would otherwise be in the lab.

In addition to Brandt's support, **Bruce Damon**, program director for my degree program, played a crucial role in my career progression. Bruce informed me of the postdoc fellowship program that led me to the FDA. As a fellow of the American Institute for Medical and Biological Engineering, Bruce connected the dots between my interest in science policy and a new scholars program developed by AIMBE. This fellowship allowed me to make connections at FDA that led to a permanent position and was the start to my (to-date) 10-year career in FDA policy development.

In what ways did your involvement in additional projects or internships during your time at Vanderbilt contribute to your current success?

Thanks to Brandt's support, I was able to participate in several projects and internships beyond the traditional scope of Ph.D. lab work and dissertation writing. I was a legislative policy intern for Life Science Tennessee, which is a statewide, nonprofit organization that strives to advance and promote the life science industry in Tennessee. During my internship, I organized the group's advocacy days in Nashville and Washington, D.C., to connect industry and academic representatives to state and federal policymakers.

I can't underestimate the value of the scientific education I received at Vanderbilt.

I also co-created Vanderbilt's first Students for Science Policy program to help Vandy graduate students and postdocs learn how scientists influence policy decision-making throughout the government. This program, like the BRET careers program, provided seminars on science policy topics that are not traditionally included in academic training.

I also participated in the Nashville Adventure Science Center's Communication Fellowship program, which enabled me to hone my science communication skills. Effective communication is a vital part of all scientists' work. Developing this skill has been crucial for me throughout my career. In my current role, I need to be able to explain complex topics to other scientists and engineers, lawyers, public health experts, patients, and health care providers.

How did the networking opportunities provided at Vanderbilt contribute to your professional connections and career advancement?

Let me first admit that networking was not top of mind while I was in graduate school, in part because I thought I didn't enjoy it much. I've since come to find that there are ways to enjoy and benefit from networking opportunities, even if it doesn't come easily to you. First, find a networking buddy that will go to events with you. Then, have a few topics in mind that you like asking people about.

What skills or knowledge gained during your time at Vanderbilt have been most valuable in your current role or industry?

I can't underestimate the value of the scientific education I received at Vanderbilt. The courses, research, and people all contributed to my multidisciplinary understanding of basic sciences and their application to human health. This education has formed an important foundation for the work I do now, which also spans many disciplines and clinical problems.

Beyond the science, my graduate program at Vanderbilt contributed to the development of important "soft" skills, such as my ability to clearly and concisely present on complex topics, and ask the right questions about those topics. When presenting to leadership who have limited time to hear all the nuances of an issue, the clear articulation of options and impacts is crucial. When you are the leader making a decision, thinking critically and asking the important questions can make all the difference in successful leadership.

How has the interdisciplinary nature of biomedical research training played a role in your ability to collaborate with professionals from different fields in your career?

The FDA includes experts across all scientific disciplines and beyond, including legal, public health, education, and management experts. I need to be able to negotiate with, influence, and collaborate with them all to achieve our public health goals. I studied at the intersection of three fundamental sciences to complete my degree in chemical and physical biology, leading to my development as an interdisciplinary scientist. Now, as the deputy director for the Digital Health Center of Excellence, which also sits at the intersection of technology and health care, I manage a team of experts across many engineering, technology, and clinical disciplines. Our work extends across the FDA and the whole of government to advance the development of safe and effective digital health technology. Because I have an interdisciplinary background, I can advance solutions to problems that require collaboration from diverse groups of experts.

Looking back, is there any advice you would give to current biomedical students based on the lessons you've learned in your career?

Two important things: first, demonstrate your interest in a career path, and second, tell someone what you're interested in doing. Tell lots of people. You never know who may be able to help you find an internship or connection that can help you along the way. If you've demonstrated that interest (by learning more, participating in an internship, and taking on those challenges), the people you tell will see how you can be successful in those roles and make connections that can advance you on your career journey.

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 who have been recently celebrated.

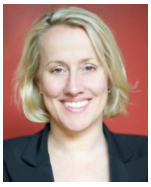
Tina Iverson (Pharmacology) received an Innovation Catalyst Fund award for the February 2024 cycle and was named associate dean for faculty of Basic Sciences.

Dr. Alissa Weaver (Cell and Developmental Biology) won the 2024 Chancellor's Award for Research based on research in *Developmental Cell* that is crucial for advancing extracellular vesicle–based therapies.

Antentor Hinton Jr. (Molecular Physiology and Biophysics) was named faculty mentor of the year by the Vanderbilt Postdoctoral Association and the Office of Postdoctoral Affairs.

Cody Siciliano (Pharmacology) received the third of Vanderbilt's Keck Foundation grants since 2020 for his research on oral chemesthesis.

Jennifer Pietenpol (Biochemistry) has been named the 2024 Science of Oncology Award recipient by the American Society of Clinical Oncology for her many contributions to the cancer field.



Carrie Jones (Pharmacology) received this year's Excellence in Undergraduate Research Mentoring Award for her work understanding schizophrenia, Alzheimer's disease, and addiction and her dedication to supporting students in her lab.

Lisa Monteggia (Pharmacology) received the 2024 Distinguished Alumni Award from the University of Illinois Urbana-Champaign College of Liberal Arts & Sciences for her contributions to neuroscience.

Erin Calipari (Pharmacology) and **Jeff Spraggins** (Cell and Developmental Biology) were selected for the 2024 cohort of Chancellor Faculty Fellows. Calipari also launched the AUD Research and Education Center with a five-year, $8.9 million P60 grant from the National Institutes of Health to study alcohol use disorder.

Andreanna Burman (Cell and Developmental Biology, Jim Goldenring and Izumi Kaji labs) was the grand-prize winner in this year's StemCellfie contest hosted by STEMCELL Technologies.

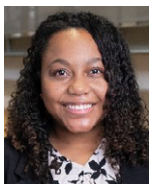
David Cortez (Biochemistry) won the Hans Neurath Award, a 2024 Protein Society award for recent contributions of exceptional merit to basic protein research.

Neil Osheroff (Biochemistry) was awarded the Lillian B. Nanney Award for Outstanding Service to the Vanderbilt University School of Medicine and VUMC Community of Educators by the Academy for Excellence.

Teresa Torres (Microbe-Host Interactions program) has become the first Vanderbilt graduate student to receive the K. Patricia Cross Future Leaders Award given by the American Association of Colleges and Universities.

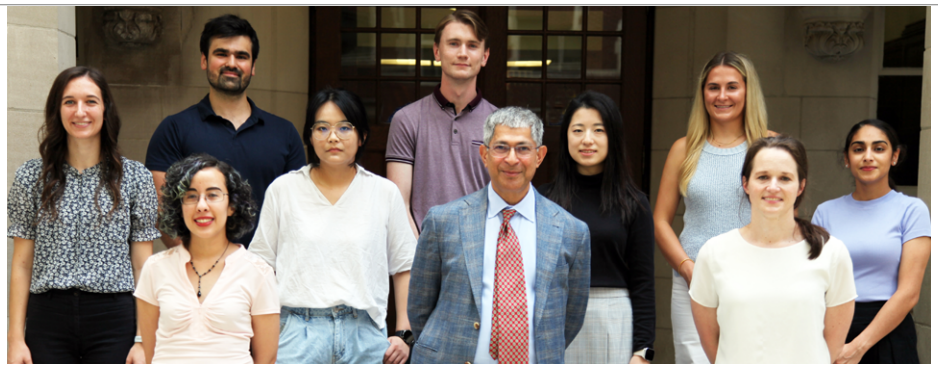
Kit Neikirk (Molecular Physiology and Biophysics, Antentor Hinton Jr. lab) has been named a 2024 Marshall Scholar by the British government.

Dr. Benjamin Brown (Pharmacology) was awarded an Avenir Award in Chemistry and Pharmacology of Substance Use Disorders by the National Institute on Drug Abuse.



Darian Carroll (Molecular Physiology and Biophysics) and **Jose Zepeda** (Pharmacology) were two of the Graduate School Sesquicentennial Scholarship Exhibition & Celebration winners.

Sean Davies (Pharmacology) and co-lead **Dr. Amanda Doran** (Molecular Physiology and Biophysics) were the first to receive support from the Innovation Ignition Fund. **Gary Sulikowski** (Pharmacology) and **Alex Waterson** (Pharmacology) will provide scientific guidance for this project.



The 2024 recipients of the Dean's Award for Exceptional Achievement in Graduate Studies and Dean of the School of Medicine Basic Sciences **John Kuriyan**. From left to right, they are:

- **Alyssa Parker**, Human Genetics
- **Alejandra Flores**, Microbe-Host Interactions
- **Soren Emerson**, Neuroscience
- **Junmin Hua**, Cell and Developmental Biology
- **Kevin McCarty**, Biochemistry
- **John Kurian**
- **Zhengyi Chen**, Chemical and Physical Biology
- **Avery Bogart**, Molecular Pathology and Immunology
- **Amber Crabtree**, Molecular Physiology and Biophysics
- **Harsimran Kaur**, Chemical and Physical Biology
- (Not pictured) **Caroline Bodnya**, Cell and Developmental Biology

Through Research Development and Support, the Office of the Vice Provost for Research and Innovation offers Seeding Success Grants to support new work or directions with strong potential for impact or funding from federal, foundation, or industry sponsors. Basic Sciences recipients from the 2023–24 academic year were:

Fall 2023: **Yongjian Huang** (Biochemistry), **Neil Dani** (Cell and Developmental Biology)

Spring 2024: **Vivian Gama** (Cell and Developmental Biology), **Wenbiao Chen** (Molecular Physiology and Biophysics)

The following 14 biomedical sciences students from across the School of Medicine Basic Sciences and the School of Medicine were awarded the 2024 Provost Pathbreaking Discovery Award from the Graduate School:

- **Darian Carroll**, Molecular Physiology and Biophysics
- **Marianne Casilio**, Hearing and Speech Sciences
- **Ryan Fansler**, Microbe-Host Interactions
- **Zahra Farahbakhsh**, Neuroscience
- **Azuah Gonzalez**, Molecular Pathology and Immunology
- **Monika Grabowska**, Bioinformatics
- **Mirazul Islam**, Cell and Developmental Biology
- **Tara Mack**, Human Genetics
- **Kara McNamara**, Cancer Biology
- **Amy Stark**, Pharmacology
- **Shengxin Tu**, Biostatistics
- **Paige Vega**, Cell and Developmental Biology
- **Cong Wang**, Epidemiology
- **Xiaoyu "Lily" Yu**, Biochemistry

Class Notes

2000s

Renee Iacona, PhD'08, has been named AstraZeneca's chief operating officer for oncology R&D in addition to her role as vice president of oncology biometrics.

2010s

Nicole Perry-Hauser, PhD'19, has accepted a position as a lecturer, on a research and teaching track, at the School of Molecular Biosciences at the University of Glasgow. Her lab will open in March 2025 and will focus on exploring the role of adhesion GPCRs in neuropsychiatric disorders.

Aimee Potter, PhD'19, became an assistant professor of microbiology and immunology at the University of Iowa.

2020s

Keyada Frye, PhD'20, Fellow'21, was recently promoted to senior clinical research associate at PPD, part of ThermoFisher Scientific.

Austin Featherstone, PhD'20, started a new job as a senior scientist at the Naval Medical Research Command Center at Fort Detrick in Frederick, Maryland.

Manuel Castro, PhD'22, was promoted to Scientist II at Altos Labs.

Tyler Hansen, PhD'23, started a new position as a senior scientist in R&D at Tempus.

Kacie Dunham-Carr, PhD'24, started a postdoctoral fellowship with Boston Children's Hospital and Harvard Medical School.

Jennifer Shuman, PhD'24, was recently hired as a consultant with EverGlade Consulting.

COURTESY OF AUSTIN FEATHERSTONE

Featherstone and his wife, Carrie, as they move into their new home in Frederick.

Hey, graduate and postdoc alums!

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 on our socials and in our next issue.

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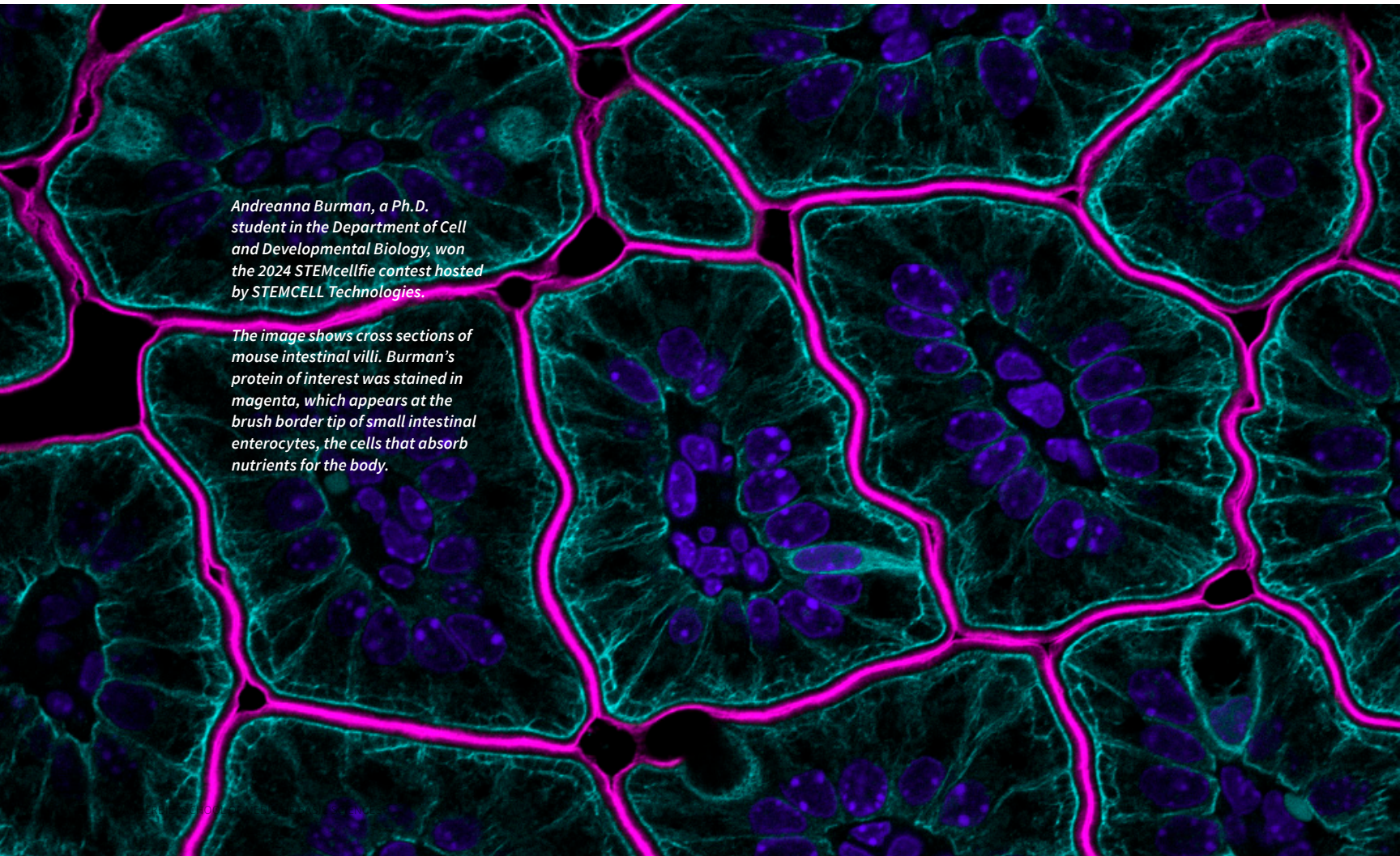

Andreanna Burman, a Ph.D. student in the Department of Cell and Developmental Biology, won the 2024 STEMcellfie contest hosted by STEMCELL Technologies.

The image shows cross sections of mouse intestinal villi. Burman's protein of interest was stained in magenta, which appears at the brush border tip of small intestinal enterocytes, the cells that absorb nutrients for the body.