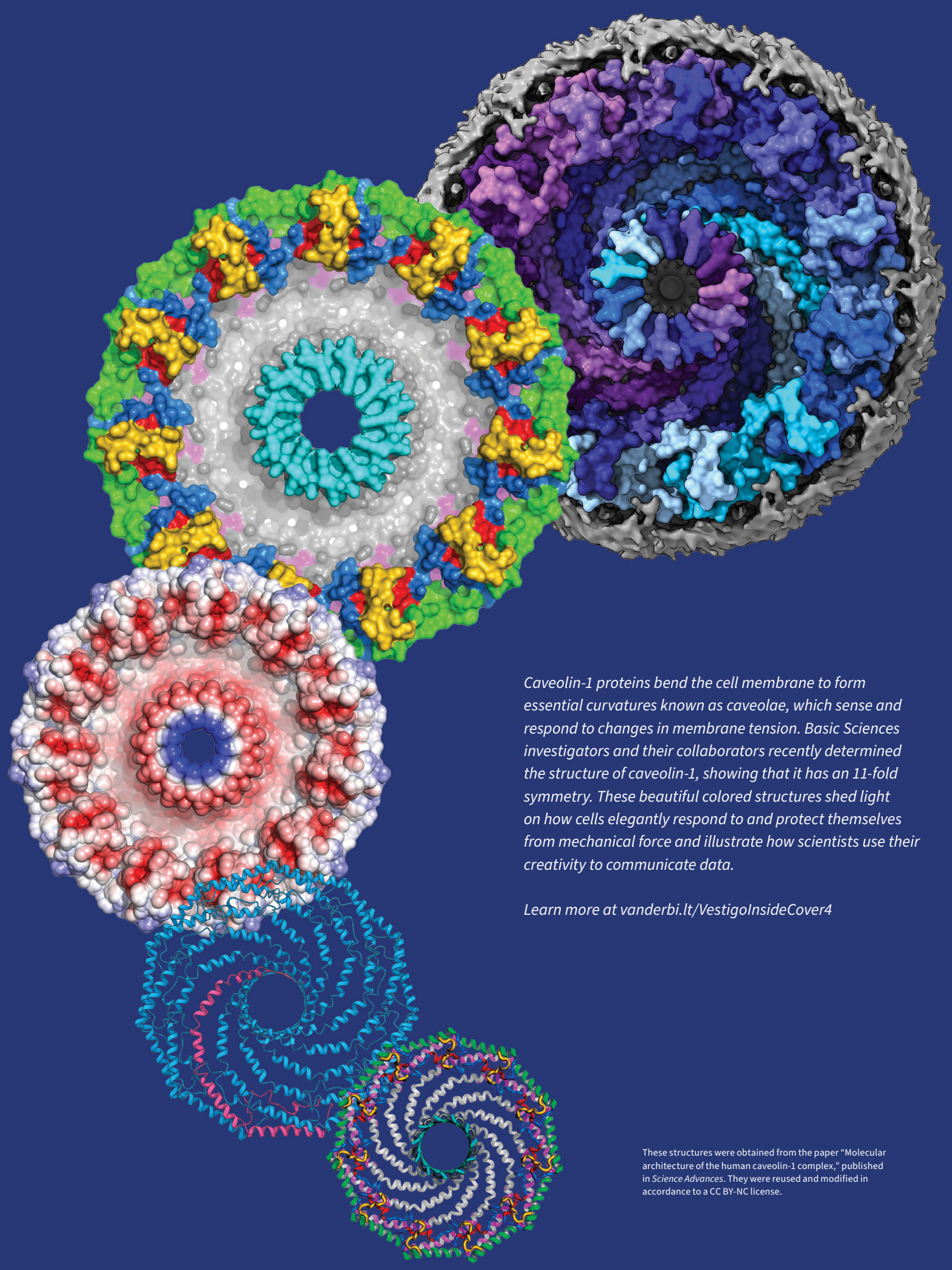
Vestigo

ISSUE 4, 2022

VANDERBILT UNIVERSITY **SCHOOL OF MEDICINE** | **BASIC SCIENCES**



Caveolin-1 proteins bend the cell membrane to form essential curvatures known as caveolae, which sense and respond to changes in membrane tension. Basic Sciences investigators and their collaborators recently determined the structure of caveolin-1, showing that it has an 11-fold symmetry. These beautiful colored structures shed light on how cells elegantly respond to and protect themselves from mechanical force and illustrate how scientists use their creativity to communicate data.

Learn more at vanderbi.lt/VestigoInsideCover4

In this issue

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Cover: In celebration of Larry Marnett's tenure as dean, this cover is dedicated to his work with COX-2, a human enzyme that is targeted by non-steroidal anti-inflammatory drugs. This image, drawn by Kendra H. Oliver, is based on the structure of the NSAID isoxicam when bound to COX-2, a structure that Marnett's lab determined nearly eight years ago (2014). Water molecules mediate a crucial aspect of this interaction at amino acid residues R120 and Y385. Oxicams (including isoxicam) are the only class of NSAIDs for which water-mediated binding to COX-2 is observed. The structure, including the water molecules, is essential for explaining the structure-activity of this series of drugs.

JOHN RUSSELL

KENDRA H. OLIVER

MICHAEL FANT

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 nest 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 http://vanderbi.lt/BasicSciencesNewsSignUp

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COVER STORY

DISCOVERY

INNOVATION

IMPACT

SPECIAL ISSUE

JOHN RUSSELL

Dear alumni and friends:

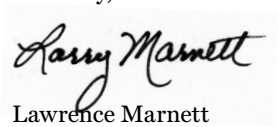
Welcome to *Vestigo*! This is the last time I will have the pleasure of extending this greeting as I will soon be stepping down as dean. I've enjoyed my six or so years as the founding dean of the School of Medicine Basic Sciences and will miss the challenges and opportunities they have brought. But I am looking forward to returning to my laboratory to continue our exploration of endocannabinoid signaling in inflammation, early detection of cancer, and endogenous sources of DNA damage. You can read more about my tenure as dean and my lab's research on page 22.

The school is very well positioned for the future. We have exceptional faculty, students, staff, and postdocs in our labs and a dedicated administrative staff to support our research and educational mission (pages 18 and 26). We have put new programs in place to improve our training and administration, and we have invested heavily in infrastructure. We will be developing many exciting initiatives over the next few years, and I anticipate watching them unfold and participating in them as a faculty member.

I am extremely grateful to the many people whose investments in Vanderbilt have enabled me to lead and build Basic Sciences. Through these investments and the collegiality of our campus, we have connected individuals from multiple schools, departments, and centers to create new research initiatives while tackling problems that arose along the way. That gestalt makes Vanderbilt a great place to work and train, and I hope you enjoy learning more about our unique community through the many great articles and features in this issue of *Vestigo*.

My sincerest thanks to every member of our community for making the past six years so exciting, challenging, and rewarding. It has been an honor to be your dean.

Sincerely,



Lawrence Marnett
Dean of Basic Sciences

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WHAT'S NEW IN SCIENCE?

New list identifies genes and proteins that cause 72 of the most common genetic diseases

Chuck Sanders, associate dean for research in the School of Medicine Basic Sciences and professor of biochemistry, and **Tucker Apgar**, an undergraduate student in the Sanders lab, have compiled the first comprehensive list of genes and proteins that cause the 72 most common genetic diseases.

While many of these diseases are classified as "rare" diseases, successful drug development efforts to treat any of these conditions would be beneficial to society and would likely be profitable. In fact, despite the "rare" classification these diseases afflict at least one in 20,000 individuals, and improving treatment options would provide better quality of life for patients and caretakers alike.

One disease on the list, cystic fibrosis, is a poster child for rare diseases. Cystic fibrosis is a genetic disease that results in frequent lung infections, causing severe damage to the lungs, and limiting an individual's ability to breathe. A recently developed drug cocktail will extend the lifetimes of many CF patients and, despite the small number of worldwide patients, will likely be a billion-dollar therapeutic.

STEPHEN DOSTER

First author: Tucker Apgar, undergraduate student

The investigators hope that this list will help motivate new projects that unravel how mutations in these genes and proteins lead to disease. While nearly half of the diseases listed are associated with mutations in a single gene, some of the diseases are associated with mutations in any one of a number of different proteins.

"We hope this list will spur rational therapeutic development for as many of these diseases as possible," Sanders said. Spearheading the effort will be the Sanders lab, which has already started a new project based on one of the gene-disease relationships described in the compendium.
— By Aaron Conley and Emily Overway

***Apgar, T.L.**, Sanders, C.R. (2021). Compendium of causative genes and their encoded proteins for common monogenic disorders.* Protein Science *31(1), 75–91. doi.org/10.1002/pro.4183.*

Researchers complete first-ever gene expression map of an entire nervous system

Research Assistant Professor **Seth Taylor** and Professor Emeritus **David Miller**, both in the Department of Cell and Developmental Biology, have established a gene expression atlas for the nervous system of the nematode worm *Caenorhabditis elegans*, along with scientists from Columbia University and Yale University.

First author: Seth Taylor, research assistant professor and former postdoctoral fellow

Their data complement the known wiring diagram of the *C. elegans* nervous system—a network of identifiable, labeled neurons connected by chemical and electrical synapses—and for the first time create a complete picture of gene expression for every neuron in an entire nervous system.

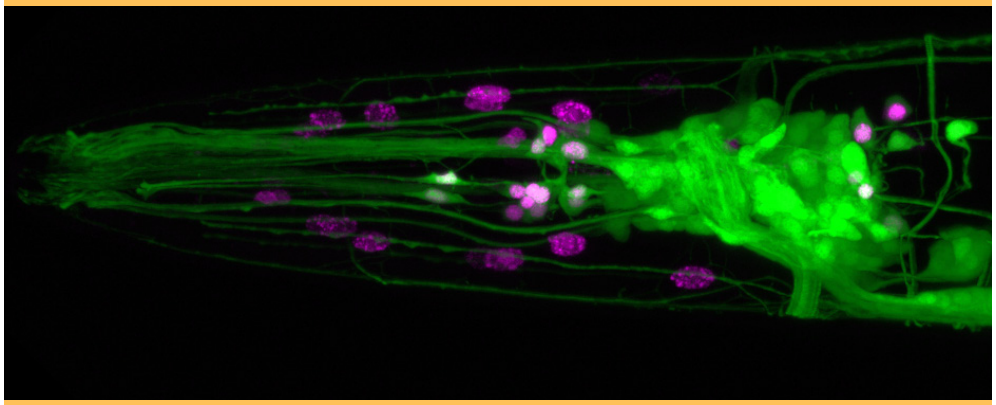
The researchers used flow cytometry to capture every type of neuron for gene expression profiling, and have shared these data for anyone to investigate how individual genes in neurons contribute to the function of a nervous system. To illustrate this approach, they used computational methods to identify DNA regions that control gene expression in specific neurons, as well as adhesion proteins that may sustain the formation of synapses—the connections between neurons that drive brain activity.

With only 302 neurons the *C. elegans* nervous system is much smaller and simpler than the human brain with its 100 billion neurons. However, "because the genetic rules that direct the development and function of the worm nervous system are also likely to operate in mammals, we expect that this unique gene expression data set will serve as a valuable foundation for deciphering the genetic underpinnings of the human brain," Miller said.

By sharing their data, the researchers aim to create opportunities for other scientists studying the nervous system and how genetic defects shape the brain's function and design. "These data will facilitate hypothesis-driven research into how genes specify different neuron types, how they make and maintain connections, and how they influence behavior," Miller said. **— By Marissa Shapiro**

***Taylor, S.R.**, Santpere, G., Weinreb, A., Barrett, A., ... Miller, D.M. (2021). Molecular topography of an entire nervous system.* Cell *184(16), 4329–4347.e23. doi.org/10.1016/j.cell.2021.06.023.*

SETH TAYLOR



The C. elegans *brain with all neurons expressing green fluorescent protein and a subset of neurons involved in feeding expressing a magenta nuclear marker.*

Targeting the reward system to lessen alcohol consumption

When individuals see or do things they enjoy, a reward system is activated in the brain, encouraging them to repeat the action. Many activities turn on this system, such as eating good food, being in love—and consuming alcohol.

For some individuals, the desire to consume alcohol is uncontrollable and compulsive—leading to a condition called alcohol use disorder. AUD impacts approximately 30 percent of Americans at some point during their lives and costs the United States nearly $250 billion annually. Current treatment options for AUD are limited and relapse rates are high.

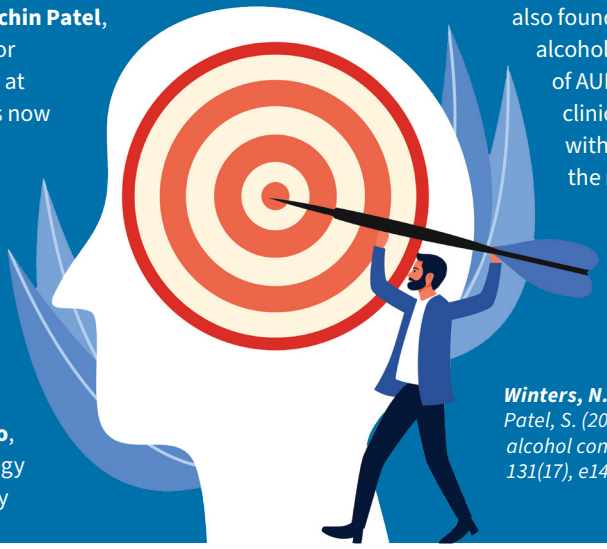
Co-first author: Gaurav Bedse, postdoctoral fellow

Nathan Winters, a graduate student in the Department of Pharmacology, **Gaurav Bedse**, a postdoctoral fellow in the Department of Psychiatry and Behavioral Sciences, and **Sachin Patel**, a former professor of pharmacology at Vanderbilt who is now at Northwestern University, set out to investigate how a brain chemical called 2-AG—an endocannabinoid that interacts heavily with the brain's reward system—may impact alcohol intake, with the goal of determining additional targets for the treatment of AUD. Their work, done in collaboration with the labs of Assistant Professor of Pharmacology **Cody Siciliano**, Associate Professor of Molecular Physiology and Biophysics **David Samuels**, University Professor of Biochemistry and Chemistry **Larry Marnett**, and Professor of Molecular Physiology and Biophysics **Danny Winder**, was published in *The Journal of Clinical Investigation*.

STEPHEN DOSTER

Co-first author: Nathan Winters, Ph.D. student

The researchers explored the 2-AG system's effects on alcohol intake in two ways: first by using a genetically modified mouse model that lacked the enzyme that makes 2-AG, and then by testing the impacts of a drug that inhibits that same enzyme. They found that both the genetically modified mice and the mice treated with the drug had a lower preference for alcohol than unmodified and untreated mice. Winters and collaborators also found that treatment with the drug lowered alcohol consumption in several different models of AUD, with results comparable to current clinically available treatments for AUD, albeit without an increase in anxiety or depression in the mice.



This collaborative work provides evidence that targeting the brain's 2-AG reward system with a drug may be a viable treatment option for some individuals with AUD. — **By Emily Overway**

Winters, N.D., Bedse, G., *Astafyev, A.A., Patrick T.A., ... Patel, S. (2021). Targeting diacylglycerol lipase reduces alcohol consumption in preclinical models.* J Clin Invest *131(17), e146861. doi.org/10.1172/JCI146861.*

Single-cell data curation with machine learning

Diabetes is caused by a combination of dysfunctional insulin-producing pancreatic β cells and an inability of the body to respond to the insulin produced. The two most common types of diabetes are type 1 and type 2, but there are other less common types, including maturity-onset diabetes of the young. MODY is caused by mutations in genes that affect insulin production, and treatments for patients differ depending on what mutation is causing the disease.

First author: Emily Walker, postdoctoral fellow

Former postdoctoral fellow **Emily Walker**, along with researchers from the labs of **Roland Stein**, **David Jacobson**, and **John Stafford**, professors of molecular physiology and biophysics, recently investigated the mechanisms leading to MODY in individuals with a mutation in the MafA Wprotein. MafA is highly expressed in β cells and is essential for proper insulin secretion. This particular MafA mutation significantly increases protein stability and is more likely to cause diabetes in men than in women. The work, published in Cell Reports, provides key insights into sex-specific molecular and genetic mechanisms controlling pancreatic β cell function.

The researchers genetically modified mice to express the mutant MafA protein. In four-week-old male mice, but not female mice, researchers found an increase in the amount of the MafA protein in β cells. Male mice with increased MafA levels developed symptoms of diabetes by five weeks of age.

In searching for molecular mechanisms responsible for diabetes development, Walker and colleagues discovered that β cells of male mice with this mutation showed accelerated aging and increased senescence, likely contributing to the development of β cell dysfunction. This critical research could pave the way to improved treatment options for individuals with this MODY mutation.
— **By Emily Overway**

Walker, E.M., *Cha, J., Tong, X., Guo, M., ... Stein, R. (2021). Sex-biased islet β cell dysfunction is caused by the MODY MAFA S64F variant by inducing premature aging and senescence in males.* Cell Reports *37(2), 109813. doi.org/10.1016/j.celrep.2021.109813.*

WHAT'S NEW IN SCIENCE?

Microtubule-associated protein discovery

Microtubules are essential for the proper functioning of our cells, fulfilling critical roles in cell structure, division, and development. Microtubule-associated proteins regulate microtubule growth in cells, but the direct effects of many of these proteins are understudied. Researchers from the lab of Associate Professor of Cell and Developmental Biology **Marija Žanić,** including first author and Research Instructor **Beth Lawrence**, postdoc **Göker Arpağ**, and former graduate student **Cayetana Arnaiz**, sought to understand the direct effects of SSNA1, a microtubule-associated protein, on microtubules through a variety of biochemical and microscopy techniques.

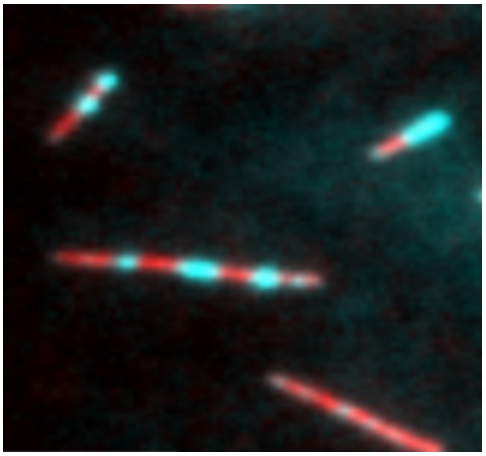
First author: Beth Lawrence, research instructor and former postdoctoral fellow

SSNA1 is implicated in Sjögren's syndrome, a highly prevalent autoimmune disease. SSNA1 plays important roles in cilia, the organelles that animal cells use to move and sense their environment, and during cell division and neuronal development. Prior to this study, the mechanism for how SSNA1 directly regulates microtubules was unknown.

Lawrence, who was formerly a postdoc in the Žanić lab, and colleagues found that SSNA1 is involved in regulating all aspects of dynamic instability, the alternating cycles of growth and shrinkage that newly formed and growing microtubules undergo. Specifically, the researchers found that SSNA1 acts to both slow the rate of microtubule growth and protect microtubules from shrinkage, is recruited at high concentrations to sites of damage on microtubules, and can protect microtubules against spastin, a microtubule-severing enzyme.

Given its apparent role in slowing the rate of growth and shrinkage—stabilizing microtubules at whatever their current length is—SSNA1 can be classified as a microtubule-stabilizing protein. SSNA1 also serves as a sensor, detecting microtubule damage irrespective of the cause. Lawrence and colleagues' discoveries of multiple direct functions of SSNA1 on microtubules reveal that SSNA1 may employ various mechanisms for regulating microtubules, which not only furthers biological knowledge, but could also lead to new treatments for Sjögren's syndrome. **— By Aran Sullivan**

The Žanić lab used total internal reflection fluorescence microscopy to monitor the interplay between microtubules (red), spastin (unlabeled), and SSNA1 (cyan).



ELIZABETH LAWRENCE

***Lawrence, E.J.**, Arpağ, G., Arnaiz, C., Žanić, M. (2021). SSNA1 stabilizes dynamic microtubules and detects microtubule damage.* eLife *10, e67282. doi.org/10.7554/eLife.67282.*

Discovery of small-molecule inhibitors of an immune regulator

Immunotherapy—treatments based on activating or educating immune cells to attack tumor cells—has demonstrated remarkable efficacy against some cancers. Nonetheless, not all patients respond, and there are many potential negative side effects. Researchers continue to investigate mechanisms that control the immune response to identify new ways to target it and improve existing therapies. One such novel target, a protein involved in the negative regulation of the immune response, is called TIM-3. TIM-3 is one of several proteins frequently found on so-called "deeply exhausted" T cells, which are no longer able to mount an effective immune defense against tumor cells.

First author: Tyson Rietz, recent Ph.D. graduate

Ongoing preclinical and early clinical research using antibody-based inhibitors of TIM-3 has yielded encouraging results. However, there is substantial interest in moving from antibody-based inhibitors to small molecule-based inhibitors which are much cheaper, easier to manufacture, and more easily manipulated to minimize side effects.

Researchers in the laboratory of **Stephen Fesik**, a professor of pharmacology and biochemistry who also holds the Orrin H. Ingram II Chair in Cancer Research, led by recent Ph.D. graduate **Tyson Rietz**, used a fragment-based discovery method to develop small molecule inhibitors of TIM-3. In "fragment-based discovery," researchers identify small molecules (fragments) that bind weakly to a target and combine several of these molecules to make a compound capable of binding more strongly, or with higher "affinity."

Fesik's group began by using a technique called protein-observed NMR spectroscopy, which identified several candidate fragments. They then used medicinal chemistry to combine several of them into optimized compounds they can study and further modify to enhance the compounds' binding affinity for TIM-3. They found that several of the high-affinity compounds interacted with the protein at a different binding site than the one that other proteins are known to interact with. Future work will determine if, aside from binding strongly, the compounds also inhibit the function of TIM-3.

Identification of these high-affinity compounds is an important step in the development of clinically useful TIM-3 small molecule inhibitors, which will hopefully serve as immunotherapeutic agents against cancers. In the meantime, the compounds generated here will be useful tools for researchers studying TIM-3 biology. **— By Wendy Bindeman**

***Rietz, T.A.**, Teuscher, K.B., Mills, J.J., Gogliotti, R.D., ... Fesik, S.W. (2021). Fragment-Based Discovery of Small Molecules Bound to T-Cell Immunoglobulin and Mucin Domain-Containing Molecule 3 (TIM-3).* J Med Chem *64(19), 14757–14772. doi.org/10.1021/acs.jmedchem.1c01336.*

Identifying mediators of the wound response

All organisms have a method of responding to wounds. Wounds can take many different forms, but the early wound response is remarkably consistent. During this time, cells near the site of injury experience an increase in internal calcium concentrations, which triggers a variety of effects to help the cells respond to the damage. These effects begin with the cells directly involved in the wound and extend out to neighboring cells over the course of a few seconds or minutes.

Fluctuation of calcium concentrations inside cells is a critical signaling mechanism active in a plethora of contexts. In the case of wound response, however, questions remain about how cells "sense" the initial wound event and how that initial calcium response is controlled.

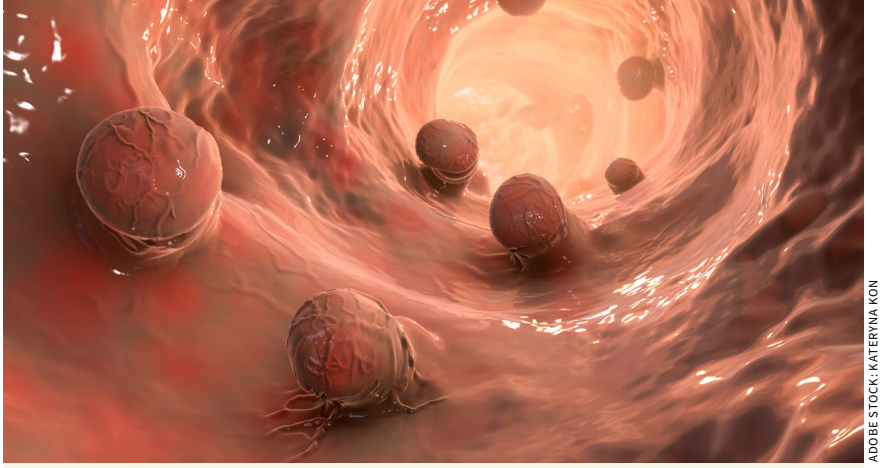
First author: James O'Connor, recent Ph.D. graduate

James O'Connor, a recent Ph.D. graduate from the Chemical and Physical Biology program, and colleagues in the lab of **Andrea Page-McCaw**, professor of cell and developmental biology, used a fruit fly model as well as a computational model generated based on their experimental data, and identified a pathway that cells use to detect wounds.

They found that, in fruit fly larvae, a wounding event activates several nonspecific proteases, enzymes capable of cleaving, or cutting, other proteins. These proteases act on growth-blocking peptides, inactive proteins present in the tissue that become active when cleaved, which in turn activate a protein called Methuselah-like 10. Mlth10 then activates a signaling cascade that terminates in a calcium response and feeds into known wound-response pathways.

Although there are no direct equivalents to Mlth10 or the growth-blocking peptides in mammals, this research represents an important step forward in understanding the mechanisms involved in wound detection. Similar wound response mechanisms—specifically, those based on protein cleavage by proteases released by injured cells—have been identified in many other organisms, which suggests that wound detection depends on ancient and highly conserved strategies. — **By Wendy Bindeman**

***O'Connor, J.T.**, Stevens, A.C., Shannon, E.K., Akbar, F.B., ... Page-McCaw, A. (2021). Proteolytic activation of Growth-blocking peptides triggers calcium responses through the GPCR Mthl10 during epithelial wound detection.* Developmental Cell *56(15), 2160–2175.e5. doi.org/10.1016/j.devcel.2021.06.020.*



ADOBE STOCK: KATERYNA KON

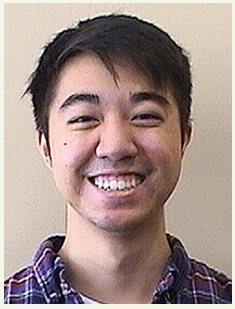
Developing a framework for precision surveillance of colorectal cancer

A team of Vanderbilt researchers has revealed some of the mechanisms by which polyps develop into colorectal cancer, setting the framework for improved surveillance for the cancer utilizing precision medicine.

Their study, published late last year in *Cell*, describes the creation of a single-cell transcriptomic and imaging atlas—a molecular "map" describing the complete set of mRNA transcripts coupled with microscopic images of specific tissues—of the two most common colorectal polyps found in humans: conventional adenomas and serrated polyps. They determined that adenomas arise from expansion of stem cells that are driven by activation of WNT signaling, which contributes to the development of cancer, while serrated polyps derive into cancer through a different process called gastric metaplasia.

Co-first author: Cherie' Scurrah, recent Ph.D. graduate

The cells from serrated polyps did not exhibit WNT pathway activation nor a stem cell signature. Moreover, the researchers observed that these cells had highly expressed genes not normally found in the colon, leading them to hypothesize that metaplasia, an abnormal change of cells into cells that are non-native to the tissue, plays a role in how serrated polyps become cancerous.



Co-first author: Bob Chen, recent Ph.D. graduate

The finding about metaplasia was surprising, the researchers said.

"Cellular plasticity through metaplasia is now recognized as a key pathway in cancer initiation, and there were pioneering contributions to this area by investigators here at Vanderbilt," said **Ken Lau**, associate professor of cell and developmental biology, one of the study's corresponding authors. "We now have provided evidence of this process and its downstream consequences in one of the largest single-cell transcriptomic studies of human participants from a single center to date."

Bob Chen and **Cherie' Scurrah**, recent Ph.D. graduates from the Chemical and Physical Biology program and the Department of Cell and Developmental Biology, respectively, are the paper's first authors. The corresponding authors are Lau, **Martha Shrubsole**, research professor of medicine, and **Dr. Robert Coffey Jr.**, professor of medicine and cell and developmental biology. — **By Tom Wilemon**

***Chen, B., Scurrah, C.R.**, McKinley, E.T., Simmons, A.J., ... Lau, K.S. (2021). Differential pre-malignant programs and microenvironment chart distinct paths to malignancy in human colorectal polyps.* Cell *184(26), 6262–6280.e26. doi.org/10.1016/j.cell.2021.11.031.*

The push and pull

By Aaron Conley

KENDRA H. OLIVER

Biomedical research unfolds new knowledge, building a deeper and more complicated understanding of the nature of life and disease than we've ever had before; mechanobiology, a relatively new field, is but a building block in this network of discovery. It is the study of how mechanical forces both within and external to cells play a role in cell function, homeostasis, division, cell fate, and other processes.

The first observations of mechanical force impacting the body were made around the turn of the 20th century. First, in the late 1800s, **Dr. Julius Wolff** observed how force affects bones and postulated Wolff's law, which states that bone in a healthy animal will adapt to the loads under which it is placed. Then, in 1895, **Dr. Wilhelm Roux** proposed that mechanical forces shape tissues and organs during embryonic development.

# of cells

Despite these initial advancements and theories, technologies to observe mechanical forces in the body were lacking until the mid-1990s. Since then, these technologies have continued to advance at a rapid pace to allow research at the intersection of biology, engineering, and physics.

"Understanding how mechanical force controls cell behavior is a new frontier," said **Matthew Tyska**, the Cornelius Vanderbilt Professor of Cell and Developmental Biology. "We know that force is important and that cells can sense and respond to it, but studying mechanics at that scale has been difficult because one cannot easily 'see' force like we can see other components of the cell. For that reason, mechanobiology is still an exciting nascent field, and with constant improvements in imaging technology, many fundamental insights are just waiting to be uncovered."

Marija Žanić, an associate professor also in cell and developmental biology, agrees. "Now we can think about the mechanics within cells," she said. "What kind of forces are necessary for cellular processes, and how are they exerted? In cell division, for example, all transformations that cells undergo require repositioning by pulling and pushing things apart, which requires mechanical force."

Vanderbilt's power in the realm of mechanobiology lies in the campus culture of collaboration that's palpable across all disciplines—basic, translational, and clinical sciences—and across scales—from the subcellular environment to human tissue. "At Vanderbilt you can find a collaborator in any area of research you want," said **Irina Kaverina**, professor of cell and developmental biology. Kaverina asserted that the university is "well known" for the collaborative relationships between labs and departments.

This cooperative environment is being further cultivated with the establishment of a new Center for Mechanobiology at Vanderbilt, co-led by Žanić and **Cynthia Reinhart-King**, a professor of biomedical engineering. The center will include co-located lab space for School of Medicine Basic Sciences, College of Arts and Science, and School of Engineering faculty in a newly built-out floor of the Engineering and Science Building.

"It is an exciting time to be working in mechanobiology as we continue to identify factors beyond solely genetics that play a role in disease," Reinhart-King said. "Vanderbilt has strong roots in mechanobiology due in part to our deep expertise in engineering and physical science, biology, and medicine, which coexist all on one campus." Reinhart-King also credits our "excellent facilities" that span multiple departments.

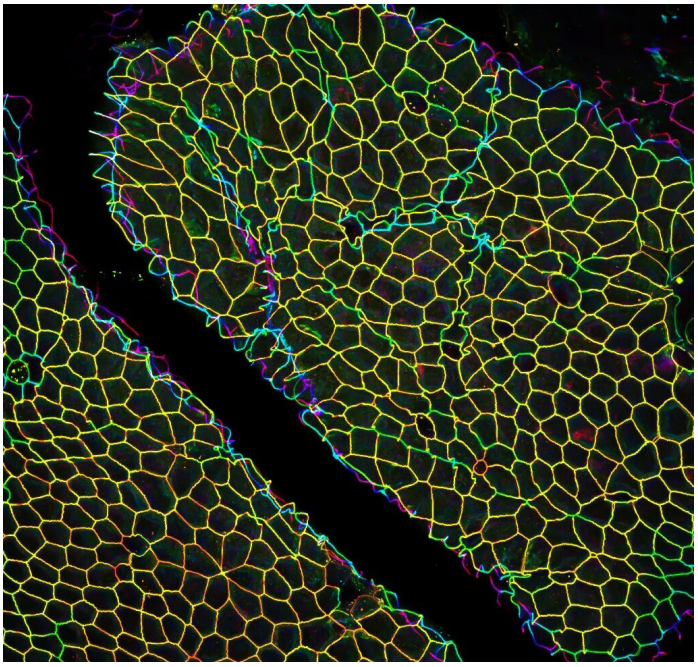
The pull of mechanobiology

The mechanobiology research within Basic Sciences is located primarily within the Department of Cell and Developmental Biology. Four key players are Associate Professor **Dylan Burnette**, Tyska, Žanić, and Kaverina.

The Burnette lab works to understand the growth of the human heart on the cellular level. This process, said Burnette, "is driven by specialized muscle cells known as cardiac myocytes that go through cell division and a subsequent enlargement." Myosin II, a motor protein, drives the physical forces behind the growth and development of these heart cells. However, the mechanisms of MII regulation in the heart—especially its interactions with the cell membrane, which control cell shape—are not fully understood.

Burnette's research group has made recent discoveries showing that MII turnover is an essential, dynamic process influencing the mechanical output of the actin cortex, a specialized, inner layer of the cell membrane. Burnette is employing key basic research techniques, including the use of nonmuscle cell lines and stem cell-derived cardiac myocytes and the development of zebrafish embryos, to study cellular mechanisms of cardiovascular disease on a single-cell level. His lab's findings could lay the foundation that influences future cardiovascular disease treatments.

Tyska's lab studies how cells use force-generating cytoskeletal proteins to control their shape, with a particular interest on the epithelial cells that line the surfaces of the body and organs. In the intestinal



The lumen of the intestine is lined with thin tendrils called villi that absorb nutrients for the body. An extensive network of epithelial cells, linked together by tight junctions, forms each intestinal villus. Tight junctions between cells allow them to pull on each other to create tension in the epithelial sheet, ultimately allowing for tissues to take on three-dimensional shapes. Here, tight junctions were stained and then pseudocolored to indicate relative depth.

tract, epithelial cells build a specialized surface known as the brush border, which allows nutrients to enter the body and serves as a barrier to the external environment. The Tyska lab uses cutting-edge imaging to study how epithelial cells create the brush border, how the brush border maintains stability and function in the intestine, and how changes in the brush border can lead to human diseases such as celiac disease or infections by pathogens such as *Escherichia coli*.

The imaging techniques that Tyska's group uses allow them to directly visualize the formation of the brush border and have begun to reveal how mechanical forces drive this process. Over the past 15 years, the Tyska lab has leveraged these approaches to make several fundamental and field-leading discoveries in epithelial cell biology.

The focus of the Žanić lab is on the behavior of the microtubule cytoskeleton, a cell component that is essential for life, as it provides mechanical support and structure to cells. Žanić describes microtubules, which are highly conserved biological polymers, as "incredibly dynamic, allowing them to build remarkable subcellular structures and exert mechanical forces to drive cell division and cell motility." However, she added, "Individual microtubules can experience structural damage due to the actions of molecular motor proteins, microtubule-severing enzymes, and mechanical forces within the cell."

In Žanić's most recent work (page 6), her team discovered that a specific protein, Sjögren's Syndrome Nuclear Autoantigen 1 or SSNA1, is a novel detector of microtubule damage. SSNA1 not only detects but can also stabilize and protect microtubules from damage. Given that SSNA1 is implicated in Sjögren's Syndrome—a highly prevalent autoimmune disease—further research of SSNA1's mechanisms of action may reveal potential avenues for the development of new treatment approaches for Sjögren's Syndrome and for other diseases affected by microtubule dysfunction.

Kaverina's lab also focuses on microtubules and has made significant discoveries that have replaced a previous dogma in the field about how and where microtubules are created. Her lab uses live-cell imaging to understand what happens in a cell, as well as where and when it happens. This has allowed for major discoveries, helping to establish principles of microtubule network architecture.

"It's like making a movie on the microscope, like having a small Hollywood studio in your lab," Kaverina said when describing what it feels like to use the newest tools in microscopy. Her research group uses these methods to not only understand the underlying principles of microtubule structure, function, and dynamics, but also how they impact diseases such as diabetes, cancer, and cardiovascular disease.

Recent work led by the Kaverina lab, published in *eLife* in collaboration with Žanić and others at Vanderbilt, showed that microtubules play a major role in the pancreas. The editors of *eLife* noted that the study "provides a yet uncharacterized dimension to the regulation of insulin secretion from the pancreas." With their work, the Kaverina lab is laying the foundation for future research that could provide new routes to treat diabetes.

"What we do is basic science," Kaverina said. "To repair any mechanism we need to understand why that mechanism works. To cure any disease, we need to understand the underlying physiology—on an organismal, cellular, and molecular level."

> "In cell division, for example, all transformations that cells undergo require repositioning by pulling and pushing things apart, which requires mechanical force."
>
> — **Marija Žanić**

An institutional commitment to diversity, equity, and inclusion

By Wendy Bindeman

Felysha Jenkins recently joined the Vanderbilt University School of Medicine Basic Sciences as its first diversity, equity, and inclusion program manager. She joined the program after the retirement of two Basic Sciences leaders—**Linda Sealy**, formerly the senior associate dean for DEI, and **Roger Chalkley**, formerly the senior associate dean for biomedical education, research, and training—who worked to increase Vanderbilt's diversity and build a more inclusive community.

Jenkins' new role focuses on further enhancing Vanderbilt's commitment to maintaining a diverse, equitable, and inclusive environment. "I am very thankful for Dr. Sealy's diversity efforts over the course of her career and the pathway forward she provided," Jenkins said. "My primary goal is to continue using evidence-based approaches to guide my work and our community."

Jenkins earned a master of arts in experimental psychology from Wake Forest University and a doctorate in psychology from North Carolina State University. At NC State she also graduated from the Equal Opportunity Institute, a certificate program that offers enhanced training focused on improving equity and diversity in workplaces and schools. She is also a trained facilitator with the National Coalition Building Institute, an international leadership organization that provides comprehensive, DEI-focused leadership training. She officially joined Vanderbilt in September 2021.

Larry Marnett, dean of basic sciences, said he was "delighted we were able to recruit Dr. Jenkins in our national search." He added, "She has a wealth of experience and the scholarly background to advance our efforts in inclusive excellence and be an incredible resource for the community."

Many of the department's DEI efforts focus on racial equity. Jenkins said, "I feel like if we can start with conversations about race, remove fear from the conversation, and then give people knowledge about what race is, what racism is, what structural racism is, and how it influences our daily lives, that'll do a lot to help move us forward."

In time for Black History Month (February), Jenkins organized the 21-Day Racial Equity Habit-Building Challenge©, a department-wide opportunity for Basic Sciences students, postdocs, faculty, and staff to engage in self-paced learning and reflection to improve their understanding and practices around racial equity. In June, she co-organized, along with Assistant Professor of Molecular Physiology and Biophysics **Antentor Hinton Jr.**, a half-day symposium celebrating Juneteenth, which commemorates the official end to slavery in the United States. The event featured a talk discussing the meaning of the holiday, scientific talks by invited speakers and trainees, and a celebration of the first-ever Vanderbilt Basic Sciences Juneteenth Awards.

Jenkins works closely with the Basic Sciences DEI Committee, a volunteer-based group formed in the summer of 2020. It consists of student, postdoc, faculty, and staff representatives from the DEI committees of each of the four basic sciences departments (Biochemistry, Cell and Developmental Biology, Molecular Physiology and Biophysics, and Pharmacology), as well as the Program in Cancer Biology and the Vanderbilt Institute for Infection, Immunology, and Inflammation.

"My goal for working with the committee is to make sure we have a strong foundation of what DEI means so we can implement change within our areas of influence. I want everyone to understand how and why DEI benefits everyone and not just marginalized communities," Jenkins said. "We already have a group of people who want to do the work; I want to bring us together so that we can grow what we're doing and have them be ambassadors for DEI."

STEPHEN DOSTER

Some of Jenkins' other current projects include creating a Basic Sciences DEI calendar that includes the DEI events hosted by all the departmental subcommittees to streamline and build connections among the groups, as well as building a DEI library of relevant hard-copy books to make learning about different aspects of DEI more accessible to community members.

An additional upcoming focus will be on hidden disabilities—disabilities or conditions that impact people's daily lives that may not be visible to others, such as depression, diabetes, or chronic fatigue syndrome. Jenkins said, "We have to be cognizant of hidden disabilities and think about what that means for people when we're working on building an inclusive environment."

Jenkins looks forward to furthering Basic Sciences's commitment to being an inclusive and equitable environment for everyone who works and trains within the department. "I want people to feel free to reach out to me through email or phone or to just stop by my office: U1205B MRBIII," she said. "I'm here, and I'm ready to assist our community in any way that I can."

Meet the departments:

An inward look into biochemistry

By Wendy Bindeman

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

The Department of Biochemistry is nestled within the School of Medicine Basic Sciences, but even though the school was only established in 2015, the department has been an integral part of Vanderbilt since its foundation in 1925. Historically, the department was known for its prowess in nutrition and toxicology, although its areas of topical expertise have evolved over time.

Stanley Cohen, who received the Nobel Prize in Physiology or Medicine in 1986 for his discoveries related to growth factor signaling, conducted his prize-winning work as a faculty member in biochemistry and sparked the development of the department as a force to be reckoned with in the field of cellular signaling.

The department is currently led by **David Cortez**, professor of biochemistry and holder of the Richard N. Armstrong, Ph.D. Chair for Innovation in Biochemistry. It is a national powerhouse, occupying the No. 1 spot in funding from the National Institutes of Health for biochemistry departments nationwide for the past three years running, with more than $30 million in funding in 2021.

Cortez, who transitioned from interim chair to chair last summer, defines biochemistry as "the pursuit of the mechanistic understanding of biological processes at the molecular level." Biochemists, he said, "Delve deep down into the molecules of biology and study how their interactions and the processes happening within our cells yield biological outcomes."

The Department of Biochemistry currently has 23 primary tenure-track, 23 secondary, three educator-track, and 26 research-track faculty. An exceptional group of graduate, medical, and undergraduate students—and a large cohort of postdoctoral fellows—train in department laboratories.

Benefits of a unique structure

The biochemistry department, as part of Basic Sciences, is uniquely positioned compared to similar departments at other institutions. As it is separate from the Vanderbilt University Medical Center, the school's financial model is independent of clinical margin and is supported by the university's endowment. This allows for sustainable funding with strong and proactive investments into faculty, cutting-edge instrumentation, facilities, education and training, staff, and projects.

According to Cortez, this organizational structure provides "all of the advantages of being a department in a medical school and none of the disadvantages." Researchers can collaborate closely with clinicians at the medical center, yet retain access to resources and an administrative team focused on the needs of basic researchers, rather than having to split funding and attention with clinical endeavors.

Diverse research strengths and an emphasis on collaboration

Faculty within the department work on an incredibly diverse array of research topics, ranging from precise mechanistic studies of chemical reactions and proteins, all the way to the development of novel cancer therapeutics. Assisted by an excellent network of research cores and institutional centers, investigators are leaders in applying advanced approaches in biochemistry, cell biology, genetics, structural biology, mass spectrometry, and chemical biology to thematic areas that include DNA and RNA metabolism, enzymology, molecular cancer biology, molecular virology, and protein misfolding diseases.

ADOBE STOCK: PINKEYES

Collaborative projects are facilitated by shared instrumentation, open lab spaces, and research centers, including those led by biochemistry faculty, such as the Vanderbilt-Ingram Cancer Center, led by **Jennifer Pietenpol**; the Quantitative Systems Biology Center, led by **Vito Quaranta**; and the Mass Spectrometry Research Center, led by **Richard Caprioli**.

Structured activities open to anyone in the department—such as a cryo-electron microscopy discussion group—enable interactions between department members, whether they be students or senior faculty. Cryo-EM technology is currently undergoing rapid growth, so the discussion group ensures that faculty and trainees stay current on the latest developments in the field and provides an avenue to share expertise and communally solve problems. The highly active Biochemistry Student Association also sponsors activities such as social events and a bimonthly research colloquium.

Renowned faculty and mentors

Cortez, the current chair of the department, joined Vanderbilt in 2002 and has built a strong research program focusing on the mechanisms that maintain genome integrity. For "research bridging diverse disciplines, such as chemistry or physics, to solve biology's most important fundamental questions," he was awarded the Stanley Cohen Award by the School of Medicine in 2020.

In addition to his research accomplishments, Cortez is committed to fostering a positive training and mentoring environment for graduate students, postdocs, and early-career faculty. "The department really cares about mentoring," Cortez said. "And we make it intentional, so it's a great place to be a trainee because, in addition to great science and resources, we have great mentors."

The biochemistry department is replete with talented faculty at all career stages, including many with internal and external leadership positions, such as **Chuck Sanders**, associate dean for research for Basic Sciences.

Like Cortez, Sanders is an exemplary amalgam of research and mentoring excellence. An expert in membrane protein biology—reflected by his ongoing tenure as president of the Protein Society—Sanders also exhibits outstanding training practices that were recently recognized by the department with an Armstrong Mentoring Award, named in honor of the late Professor of Biochemistry **Richard Armstrong**.

Sanders was recruited to Vanderbilt by fellow biochemistry professor **Walter Chazin** and then-chair **Mike Waterman** in 2002—the same year as Cortez. He was initially attracted by the depth of expertise in the department and the opportunity to work with the Vanderbilt Center for Structural Biology. Broadly, his research focuses on "problems that are chemical or biochemical in nature but have direct medical relevance." In particular, the Sanders lab studies various membrane proteins and how their misfolding can result in disease, with an emphasis on understudied pathologies.

One current project in the Sanders lab centers on the role of peripheral myelin protein 22 in Charcot-Marie-Tooth disease, a genetic disorder of the peripheral nervous system. After 15 "painstaking years" of work, the Sanders lab identified the defects responsible for many cases of the disease in the mid-2010s. This work subsequently attracted the attention of Ancora Innovation, a company established by Vanderbilt in partnership with the investment company Deerfield Management. Ancora was designed to fund projects aimed toward the discovery of novel therapeutics to cure life-altering diseases, and is now supporting an early-phase drug discovery project guided by the Sanders lab's discoveries.

Rising stars

In addition to the cadre of experienced faculty, biochemistry is home to many early-career researchers. **Yi Ren**, one such rising star, is an assistant professor of biochemistry whose lab has made exciting discoveries about the machinery that exports messenger RNA out of the nucleus.

Ren joined Vanderbilt in 2016. She is a structural biologist by training with expertise in X-ray crystallography and cryo-EM, advanced techniques used to probe and determine the physical shape of proteins and other biological molecules. Her work demonstrates the power of coupling the services provided by core facilities to basic science questions that have the potential to yield translational applications.

Over time, her lab has found that many viruses—including the influenza virus, vesicular stomatitis virus, and SARS-CoV-2, the virus responsible for COVID-19—all interfere with the mRNA export process, thereby blocking host gene expression and interfering with the antiviral response.

> "I want to really push it to where Vanderbilt Biochemistry is recognized throughout the country and the world as a destination for biochemistry research and training."
>
> — **David Cortez**

"It's important to understand the basic science," Ren said, "Because if we understand how the machinery works, how certain viruses target host factors such as proteins involved in mRNA export, we can speed up our studies on the virus-host interaction." Understanding aspects of that interaction, in turn, may result in new opportunities for the development of antiviral treatments.

Ren has benefited from the department's mentoring and support structures for early-career faculty. Overall, she said, the department provides a "nurturing" environment for trainees and early-career faculty and "understands the importance of basic research." This last point is especially critical, according to Ren: "Because of the department's support, I feel comfortable taking risks and really working on what I would like to work on."

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The future of biochemistry

Cortez has high expectations for the biochemistry department moving forward. "I want to really push it to where Vanderbilt Biochemistry is recognized throughout the country and the world as a destination for biochemistry research and training," he said.

To meet this ambitious goal, Cortez has identified several areas of focus, such as the continual improvement of the training environment. "We want the culture here to allow all department members to be the best scientists, the best staff members, and the best students that they can be," Cortez said. "And that really starts with making sure it's an inclusive and equitable environment."

Another area of focus is the recruitment of new talent. **John York**, the previous chair, hired seven assistant professors and one professor to expand the department, and Cortez is eager to maintain that momentum. This year, and with help from the university's Destination Vanderbilt initiative, the department is focusing on recruitment at both the assistant and associate professor level. In addition, the department is establishing Destination Biochemistry Postdoctoral Scholar Awards to support the research of outstanding young scientists.

JOHN RUSSELL

David Cortez

Research infrastructure is an additional key area of investment for upcoming years. This includes everything from modernizing laboratory spaces and purchasing state-of-the-art equipment for departmental use to continuing to improve financial support structures through the creation of endowed chairs and the diversification of funding streams. Such resources, as Ren and Cortez both pointed out, provide researchers with the financial freedom to pursue exciting questions that can lead to unprecedented breakthroughs.

"We've had a really great history as a department and the trajectory we're on builds on that history," Cortez said. "The Department of Biochemistry is a destination for doing great science and learning how to be a great scientist. It is really a department that Vanderbilt can be proud of." ■

In excellent company!

Here are some of the faculty who call the Department of Biochemistry home. You can find the full list of faculty on the department website.

Manny Ascano, assistant professor of biochemistry
- Research focus: molecular virology
- Notable accomplishments: receipt of the Richard M. Caprioli Award for the creation of novel methods for studying RNA viruses

Breann Brown, assistant professor of biochemistry
- Research focus: structural biology of protein complexes regulating mitochondrial physiology
- Notable accomplishments: receipt of a 2021 NIH Director's New Innovator Award

Richard Caprioli, Stanford Moore Chair in Biochemistry and professor of biochemistry
- Research focus: development of advanced imaging methods using mass spectrometry
- Notable accomplishments: appointment as director of the Mass Spectrometry Research Center in 1998

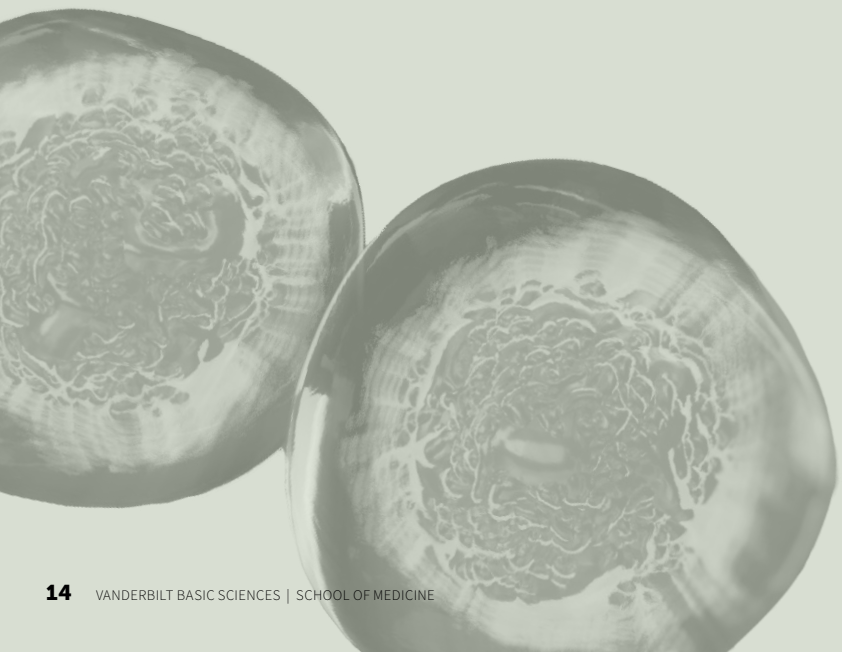
Stephen Fesik, Orrin H. Ingram II Chair in Cancer Research and professor of biochemistry and pharmacology
- Research focus: small-molecule drug discovery
- Notable accomplishments: invention of structure-activity relationships by nuclear magnetic resonance (SAR by NMR); development of drugs targeting BCL2 protein family for cancer therapy

Fred Guengerich, Tadashi Inagami, Ph.D. Chair in Biochemistry and professor of biochemistry
- Research focus: genetic toxicology
- Notable accomplishments: cited more than 100,000 times; selection as an inaugural fellow of the American Society for Biochemistry and Molecular Biology in 2021

Scott Hiebert, Hortense B. Ingram Chair in Cancer Research and professor of biochemistry
- Research focus: gene expression regulation related to acute leukemias
- Notable accomplishments: appointment to the National Cancer Advisory Board by President Barack Obama in 2016; appointment as acting chair of the NCAB for 2020–21.

Houra Merrikh, professor of biochemistry
- Research focus: replication-transcription conflicts; blocking the evolution of drug resistance
- Notable accomplishments: receipt of a 2021 Cohen Innovation Fund Award; two-time selection as finalist of the Blavatnik Awards

Jennifer Pietenpol, Benjamin F. Byrd Jr. Chair in Oncology and professor of biochemistry
- Research focus: triple-negative breast cancer; p53 family of tumor suppressors
- Notable accomplishments: appointment as director of the Vanderbilt-Ingram Cancer Center in 2008; appointment as executive vice president for research at VUMC in 2016



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Owen McGuinness (left) and David Wasserman (right).

The gold standard:

How a Vanderbilt group of innovators set the bar in metabolism research

By Kendra H. Oliver

Scientific discoveries are accelerated by portals that bridge gaps between scientists with different areas of expertise. One such portal is the Vanderbilt Mouse Metabolic Phenotyping Center, which has over its 20-year history become a national leader driving the field of metabolism research.

A National Institutes of Health-funded center associated with the School of Medicine Basic Sciences, the VMMPC provides scientists from a variety of backgrounds the tools necessary to rigorously study metabolic processes in mice carrying targeted gene mutations. VMMPC staff also provide the breadth of experience required to optimize experimental design and assist with interpretation of the resulting data. Since its inception, the VMMPC has been instrumental in the publication of 936 papers from Vanderbilt and other institutes around the world.

Innovations that sparked transformation

This story starts with now-retired Associate Professor **Masakazu "Masa" Shiota**, whose research interests were centered on the liver's role in glucose homeostasis and how conditions such as obesity and diabetes could lead to homeostatic dysregulation. Shiota directed the Small Animal Core in 1996, one of many cores operating as part of the Vanderbilt Diabetes Research and Training Center at that time, and provided services such as surgical procedures, glucose clamping (a method for quantifying insulin secretion and resistance), and blood pressure monitoring.

Originally serving only a small group of researchers, the Small Animal Core's impact was limited by the technical skill and time needed to complete experiments. "There was a year or two when the mouse procedures were done by Masa alone, as he preferred to do all the specialized procedures himself," recalled David Wasserman, current director of the VMMPC.

Indeed, Shiota was renowned for his research prowess. "His technical skills were otherworldly—he could easily see these minuscule vessels of the mouse, and he developed key surgical techniques and instruments that have been passed down through the VMMPC and have served as a platform for innovative science," Wasserman said. Wasserman is also the Annie Mary Lyle Professor and a professor of molecular physiology and biophysics in Basic Sciences.

Masakazu Shiota

Shiota's innovations were the springboard for the development of new diagnostic tests for mice. Variations in his techniques have been used to study how well the body responds to insulin and blood glucose, as well as other hormones and promising drug therapies. An important feature of these techniques is that they allow for the study of conscious,

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PHOTOS BY STEPHEN DOSTER

Merrygay James (left) and Martha Troutman (right), staff members at the VMMPC.

unrestrained mice that are free of stress, which is optimal not only for measuring insulin sensitivity and glucose levels but for the welfare of the animals.

A key apparatus Shiota developed, the Mouse Antenna for Sampling Access, is still important today for preparing mice for study. "We still call the apparatus 'the Masa,'" Wasserman said. "We freely publish our protocols, and because it was his innovation, I wanted to have his contributions immortalized. Now, people worldwide call it 'The M.A.S.A.'"

Here at Vanderbilt, Shiota's advances sparked a wildfire of innovation and ingenuity, centered around excellence and resource sharing, that laid the foundation for the construction of the highly successful VMMPC.

The right opportunity

Critically important to the establishment of the VMMPC was a request for applications issued by the National Institute of Diabetes and Digestive and Kidney Diseases, part of the NIH, in 2000. The RFA, which was issued in response to the burgeoning availability of mice bearing interesting genetic mutations, solicited funding proposals focused on improving methodologies for mouse research. The NIDDK had recognized the growing number of investigators who wished to use these genetically modified mice but lacked the necessary experience or technical skills in mouse metabolism research, and strove to provide them access to that expertise. **Mark Magnuson**, the Louise B. McGavock Professor and professor of molecular physiology and biophysics, recruited Wasserman to work together with **Owen McGuinness**, a fellow professor in the department, to develop and submit a proposal in response to the RFA.

Trained as a classical physiologist, Wasserman currently studies the role of physical exercise, insulin stimulation, and diet in metabolism. McGuinness is interested in the regulation of glucose metabolism during infection and inflammation and how it is influenced by obesity and variations in nutrition. Both Wasserman and McGuinness had limited experience working with mice back in 2000, but their expertise in physiology provided key insights into the application of metabolism studies to the mouse.

"Mark came to me and said, 'There's an RFA that's going to be coming out,' but I knew nothing about it," Wasserman said. At the time, Wasserman had only been working in mice for a short time, publishing one paper, and McGuinness had never done research in mice.

"So, there we were with little track record, just one paper between the two of us, and we put together a grant," McGuinness said. "After submitting the grant, Dave contacted the grants manager, who told us that all the grants' scores were between 1.48 and 5, and that our score was 1.48—the top-rated grant application." The NIH grant application scoring system used a five-point rating scale in which 1 is exceptional and 5 is poor. "We were elated, and maybe a little intimidated," McGuinness said.

This initial grant, which led to the transformation of the Small Animal Core into the first of five national Mouse Metabolic Phenotypic Centers in 2001, was the core's first award in what would become a long line of grants.

The right opportunity, with the right people

Much of the VMMPC's success can be attributed to the way that Wasserman and McGuinness combined their expertise in the physiology of larger animals to exploit the compilation of small-animal techniques that Shiota developed.

"My training is in classical physiology, just like Dave's," McGuinness said. "His background was in exercise metabolism while mine was in inflammatory stress, infection, and metabolism." For both Wasserman and McGuinness, it's all about scale. "I think what has made us and continues to make us so successful is that we started with larger models and scaled down to the mouse," said Wasserman. "The principles behind the measurement of dynamic changes in metabolism are the same regardless of whether one studies a human or a mouse."

For people who study small animals, it is a challenge to measure something in the same animal over time, but McGuinness and

Wasserman figured out how to do it by "micro-ing" their approach to be mouse sized. "We also recognized that the quality of data was only as good as the quality of the health of the mouse and the quality of the experimental tools we used," McGuinness said. "We understood that if we studied stressed or unhealthy animals, we were going to mask the role of our gene mutations."

Wasserman and McGuinness share an understanding that their experiments are relevant to human physiology, and this provides them a high-level perspective that had previously been siloed away from mouse biology. "The problems and theory of studying people and mice are the same," Wasserman said. "Many of the people who were studying mice when we began had experience with isolated cells but had not been confronted with the integrated nature of studies of the whole organism."

The right opportunity, with the right people, in the right place

An additional major factor that contributes to the VMMPC's ongoing success is Vanderbilt's outstanding ecosystem for discovery, with its strong institutional emphasis on collaboration and shared resources across campus communities. For example, as the associate director of the VMMPC and the associate director of the Vanderbilt Diabetes Research and Training Center, McGuinness is deeply engaged in both groups. "Owen's integral involvement in both the DRTC and the VMMPC has been key to the interactions of these two NIDDK-funded entities," Wasserman said. The interplay of the two groups improves the research environment of the diabetes community at Vanderbilt.

Another advantage driving the VMMPC's success originated with Shiota and centers on sharing technical innovations. Vanderbilt "optimizes" investigator interactions and access to core facilities, and the proximity of DRTC investigators and VMMPC infrastructure assists in the development of new technology and, according to McGuinness, makes it very easy to share resources and collaborate.

"We share our methods both within and outside of the Vanderbilt community," McGuinness said. "And because the VMMPC is focused on education and outreach within the national research community, our impact extends well beyond Vanderbilt's boundaries."

Learning for oneself, sharing for others

Once they addressed the technical difficulties of working with such a small species, the VMMPC was faced with the challenge of communicating its approaches to the broader scientific community.

"From the outset of the VMMPC it became clear that many investigators wanted to learn how we did difficult procedures in a species as small as mice," Wasserman said. "It also became clear that much of the work being done in mice was technically crude and was difficult to interpret."

The VMMPC's drive for effective practices changed the way that metabolic measurements in the mouse were performed, which, coupled with a national need for guidance and assistance in using these techniques, led to an educational initiative that has gained national recognition and unequivocally made the VMMPC the premier center for the study of mouse metabolism.

Taking the VMMPC courses—a series of technical didactic and lab-based courses that started in 2004—is a rite of passage for many researchers who study metabolism in the mouse. "Through our courses, we have lowered the energy barrier for performing experiments in the mouse and analyzing the data these experiments yield," McGuinness said. The VMMPC has taught a technique called glucose clamping, for example, to more than 200 people from more than 20 countries. And although most researchers have learned this and other techniques through the courses, many seek the VMMPC's expertise through their own initiative and separately from the structured courses.

"Many of the people who were studying mice when we began had experience with isolated cells but had not been confronted with the integrated nature of studies of the whole organism."

– David Wasserman

For many researchers in the metabolism field, the VMMPC is the epicenter for state-of-the-art practices and the home of entire communities surrounding its programs. "It's been told to me that the road to study metabolism goes through Vanderbilt," Wasserman said.

Beyond academia

Because of their expertise, the VMMPC has caught the attention of the pharmaceutical and biotechnology industries. The VMMPC offers technical services and provides intellectual contributions that are beyond those readily available to many companies, leading to partnerships that have taken many forms. Some companies do the animal research for prospective drugs using the resources of the VMMPC. Others leverage its technical expertise and knowledge on a more periodic basis.

One biotech company in particular had a new therapeutic candidate but did not have a clear idea of how to test it in the whole organism. By that time, the VMMPC had developed a novel approach employing stable isotopes that could be used to study how lipids accumulate in the liver. Joining efforts, the VMMPC used this new method on the candidate drug, resulting in more insight into its effects than the company could have acquired on its own. Using the VMMPC as a partner will expedite the company's development of a promising new therapy for obesity and diabetes.

Honoring Shiota's core values

The VMMPC has undergone a transformation over more than 20 years, during which time it has shaped the expectations and requirements for the other four NIH-funded MMPCs nationwide. Through its technical innovations and scientific communications, it has set standards for metabolic research, methodology, rigor, and reproducibility. But for McGuinness and Wasserman, it comes back to Shiota.

"We've evolved and greatly broadened our skills since we began," Wasserman said. "But it originated with Masa. Masa's willingness to teach the core technologies he developed to our staff propagated the techniques and was a lesson in the importance of sharing technology." Following in Shiota's footsteps came with unintended but welcome consequences: the creation of an undeniably strong metabolism research community at Vanderbilt, and the certainty that the VMMPC will continue to grow and develop for many years to come. ■

Essential to their core

By Jan Read

The foundational research of Vanderbilt University School of Medicine Basic Sciences fuels discovery and innovation that brings vital therapies to people in need, ultimately improving health and working toward curing diseases. These efforts require investments in cutting-edge technologies and in the experts to run them.

Basic Sciences researchers enjoy the valuable resources available through our more than 20 core facilities. This portfolio of laboratories and shared resources amplifies investigative efforts by providing access to specialized equipment, services, and expertise beyond what is typically available in a single lab. While most of the core facilities are associated with one of the school's seven research centers, they are available to all investigators.

In appreciation of our cores, we're highlighting the roles they play in our community.

Under the spotlight

Vanderbilt's Cancer & Immunology Core, which hosts the **Mass Cytometry Center of Excellence**, provides bench-to-data services in techniques that include mass cytometry, a fusion of mass spectrometry and traditional flow cytometry. Mass cytometry allows for the investigation of cell identity and behavior by measuring protein levels and activation states.

Proteins are key executors of biological processes, and cytometry can simultaneously track sets of more than 45 proteins in millions of human tissue cells. Using metal-conjugated antibodies, mass cytometry helps researchers pinpoint rare cells and associate them with key proteins in biological samples, including cells from patients at Vanderbilt and mouse models.

The CIC is targeted toward beginning users and others interested in fee-for-service experimental or data analysis services. It provides mass cytometry and other services, such as tailored data analysis, using well-established standardized protocols, panels of antibodies, and machine-learning tools. The CIC helps users get their first mass cytometry figure and/or carry out studies in areas where the technology development has been robust, such as monitoring human T-cell subsets.

In turn, the MCCE is geared toward advanced users, providing them with the ability to generate their own metal-conjugated antibodies, collect their own samples, or analyze their own data. Investigators have access to cutting-edge equipment and advanced training and can learn any part of high-dimensional cytometry.

Creative Data Solutions offers bioinformatics and informatics research services. Its vision is to have a measurable impact on the ability of research investigators to both publish their work and obtain funding. By merging scientific experience with technical know-how, CDS tackles projects that require skills and experience in data management, processing, and analysis. CDS uses bioinformatics and computational approaches to convert data to knowledge, maintains a strong informatics skill set necessary for unraveling and integrating data sets originating from various sources and technologies, and delivers visually pleasing solutions for communicating science. CDS is part of the Vanderbilt Center for Stem Cell Biology.

The **Vanderbilt Genome Editing Resource** assists investigators in generating, maintaining, and storing genetically modified mice and cells.

Over the past three decades, VGER has served 320 investigators and has produced thousands of genetically altered mice and embryonic stem cells, resulting in at least 630 peer-reviewed publications. In addition to the production of genome-edited mice and human induced pluripotent stem cells, VGER offers sperm and embryo cryopreservation (freezing), in vitro fertilization and embryo transfers, and genome-editing design services.

VGER maintains the local Vanderbilt Cryopreserved Mouse Repository, a collection of cryopreserved mouse models, which facilitates compliance with National Institutes of Health sharing policies and enables the distribution of mice to interested investigators, even at other institutions.

How can our cores help you?

ACCRE, the Advanced Computing Center for Research and Education, is Vanderbilt's premier resource for high-performance computing needs in a wide variety of fields, including genetics research, particle/nuclear physics, astronomy, computational chemistry, and structural biology.

The **Biomolecular NMR Facility** uses nuclear magnetic resonance spectroscopy to provide information on the structure and dynamics of biological macromolecules. The facility also offers assistance in designing experiments, training, and software.

The **Cell and Developmental Biology Equipment Resource** maintains a large, diverse set of instruments, including autoclaves, centrifuges, cold storage, incubator shakers, and advanced microscopes. The equipment is available to the campus community.

The **Mass Spectrometry Research Center** houses three cores. The **Mass Spectrometry Core Lab** provides instrumentation to support the identification and structural analysis of small biological molecules, as well as assays of drugs and metabolites in physiologic fluids. Services include assay development, discovery metabolomics, and untargeted lipidomics. Consultation, collaboration, and data interpretation are available. The **Tissue Imaging Mass Spectrometry Core** uses MALDI-MS—matrix-assisted laser desorption/ionization mass spectrometry—to analyze complex proteomes of tissue and biofluid samples to help detect disease states, responses to therapy, and drug toxicity. Imaging mass spectrometry provides molecular images of proteins, lipids, and/or metabolites from tissue samples. Finally, the **Proteomics Core Laboratory** provides instrumentation and strategies to analyze proteins and proteomes. Services include quantitative analysis of protein expression, post-translational modification analysis, analysis of protein-protein interactions, and hydrogen-deuterium exchange mass spectrometry. Tools and expertise are integrated with bioinformatics workflows to interpret, assemble, and generate biologically meaningful insights from the data.

Poster Printing offers low-cost, fast-turnaround printing for Vanderbilt's biomedical sciences graduate programs. The service often prints dozens of posters leading up to large scientific meetings.

The **Mouse Neurobehavior Lab** develops and performs experiments on mice for investigators in areas that include gross neurological, sensory, motor, and learning/cognition functions, as well as behaviors related to anxiety, motivation, aggression, and more.

The **Cell Imaging Shared Resource** is a core that includes **CISR-Electron Microscopy** and the **CISR-Nikon Center of Excellence**, and it provides state-of-the-art equipment and expert technical support for the imaging and analysis of fixed and live specimens using light and electron microscopy.

The **Vanderbilt Antibody and Protein Resource** core partners with scientists to express and purify proteins of biomedical importance and to develop specific antibodies and nanobodies that recognize a wide variety of target proteins.

The **Vanderbilt Mouse Metabolic Phenotyping Center** is supported by the National Institute of Diabetes and Digestive and Kidney Diseases-funded Vanderbilt Diabetes Research and Training Center and by Mouse Metabolic Phenotyping Center NIH grants. This resource contains two cores to study primarily mice but also rats: the **Metabolic Regulation Core** and the **Body Weight Regulation Core**. These cores provide a centralized home for the development, optimization, and standardization of highly specialized tests and emphasize studies of the whole organism. Both cores provide a variety of surgical procedures and use flexible platforms to study nutrient metabolism and energy balance that can be readily adapted for specific experimental requirements.

The **High-Throughput Screening Facility** provides instrumentation, distribution of compound libraries and drug sets, high-throughput screening services, and informatics solutions to support investigators in the identification and investigation of new compounds for basic research and pharmacological discovery.

The **Molecular Design and Synthesis Center**, formerly the Chemical Synthesis Core, supports investigators in preclinical drug discovery lead development and helps basic science researchers develop chemical tools to further understand biological processes.

The **Small Molecule NMR Facility Core** comprises four Bruker nuclear magnetic resonance spectrometers ranging from 400 MHz to 600 MHz. It is geared toward researchers who require analysis of small molecules, such as synthetic organic compounds, natural products, polymers, or metabolites, that require small blocks of acquisition time (minutes), compared to the Biomolecular NMR Facility (above), which is geared toward larger samples that require longer blocks of acquisition time (hours or days). The small-molecule NMR core offers training classes in basic 1D NMR spectroscopy and advanced 2D NMR techniques.

The **Neurochemistry Core** provides high-sensitivity and fast-throughput analytical services to measure biogenic amine neurotransmitters and metabolites, plus amino acids and their neurotransmitters, in tissue samples.

Ushering in a new age of biomedical innovation at Vanderbilt

By Charleson S. Bell

My brow furrowed as I gripped the leather armrests of the low rider chair. I slowly reclined with an expression of feigned ambivalence as I glanced at my preceptor, Professor of Biomedical Engineering **Todd Giorgio**. The urgent news from the technology transfer officers sitting before us seemed to impact him equally.

It was spring of 2012. The prior day, I'd received a call from venture capitalists informing me that they were interested in investing in my biomedical innovation. They told me that the investment procedure would require me—a graduate student at the time—to launch a biomedical corporation. I was invited to accept the investment and relocate to Memphis to participate in the first medical device business accelerator of its kind.

As the call ended, the investors mentioned that they would be reaching out to Vanderbilt to inform them of the exciting but atypical development. This is why this meeting was so urgent, I said to myself in Todd's office.

"To our knowledge, this has never happened at Vanderbilt before," the tech transfer officers told us.

Those words would shape the entirety of my entrepreneurial journey.

A dedication to entrepreneurship

After that meeting, I took a leave of absence from my Ph.D. program and moved to Memphis to launch my company, BioNanovations. I returned to Vanderbilt for advice but was surprised to learn that the only resource for innovation on campus was a single professor from the business school, **David Owens**. I earned an opportunity to relocate to Silicon Valley in an effort to raise funds from higher-risk investors; yet, despite my nearly successful efforts to assemble a syndicated investment, I failed to acquire the development capital necessary to propel the product through the FDA regulatory process.

This failure, however, only deepened my resolve to make a positive impact. I completed my Ph.D. in biomedical engineering and joined the faculty at Vanderbilt as a research assistant professor. I also consulted at the Wond'ry—Vanderbilt's Innovation Center, led today by Professor Owens—where I helped the assistant director, **Deanna Meador**, as she led the design of prosperous entrepreneurship courses.

STEPHEN DOSTER

"To our knowledge, this has never happened at Vanderbilt before."

Almost exactly ten years later, those words ring truer than before. Today, we seek to help establish that which was missing when I was a student—a biomedical innovation continuum and an inclusive innovation ecosystem in which stakeholders are no longer forced to leave the magnolias of Vanderbilt to produce ventures that bestow positive impact on our region, country, and the world. I welcome you to join us in this new mission and usher in this new age of biomedical innovation at Vanderbilt, together.

Since then, multiple stakeholder-led endeavors have been transformed into government-funded companies, their solutions merely ideas on napkins less than 18 months before. Together, we sought to make it so that no Vanderbilt-affiliated stakeholder would struggle to learn commercialization processes to translate their innovations into impactful solutions. In 2022, under the guidance of Vanderbilt's leadership, innovation is becoming a crucial aspect of our culture.

The Biomedical Innovation Continuum

In my new role as director of biomedical innovation at the Wond'ry, I was tasked with identifying the impediments to and the opportunities and programmatic solutions for enabling biomedical innovation at Vanderbilt and in Nashville.

At Vanderbilt, a world leader in biomedical research, biomedical innovation is but the tip of the spear of our foray into innovation achievement. The development of an end-to-end continuum that merges human-centered, customer-focused, evidence-based commercialization processes with biomedical research is the key to cultivating a pipeline of Vanderbilt-affiliated startups. The vision is to enable a diverse group of innovators to seed the region, become prominent, and create a unique, influential startup culture—an emergent eclecticism—that creates an enhanced capacity for the empathetic discovery of needs and implementation of solutions across all geographic, demographic, and socioeconomic lines.

The Biomedical Innovation Continuum builds on the Wond'ry's entrepreneurship courses by connecting them to the innovation specialties—like basic science research—across schools and departments on campus. For example, a Basic Sciences stakeholder developing a unique computational tool or a novel cancer-targeting molecule may leverage the offerings of the continuum by participating in Wond'ry programming and working with the Center for Technology Transfer and Commercialization. This team of campus resources can then help the innovator formulate a robust business model to commercialize the technology toward an impactful, profitable product or partnership with biotech or pharma enterprises.

This continuum-based ecosystem will instill Vanderbilt-affiliated innovators with the capability to contribute their transformational visions to humanity. Nashville, in the midst of explosive growth, is primed for the establishment of biomedical firms to launch a sustainable innovation ecosystem. Emergent eclecticism will be achieved in this region with Vanderbilt as its anchor. ■

The academic startup guy:

Larry Marnett, founding dean of Basic Sciences

By Leigh MacMillan

JOHN RUSSELL

In the early 1960s, young **Larry Marnett** received his amateur radio license from the Federal Communications Commission. He put up an antenna outside his Kansas City, Kansas, home and began tapping away in Morse code.

"It was just so cool to be 'talking' to someone in California or Canada," Marnett recalled. After a conversation, radio operators often exchanged notes on postcards with their call signs. Marnett had postcards pinned up all over his walls.

"I remember one time I thought I was talking to somebody in Colombia. He was kind of going in and out, and I wasn't really sure that we had actually talked," Marnett said. "A week or so later, I got a postcard from him, so I knew that I had talked to somebody in another country that wasn't even contiguous with the United States.

"It gave me an appreciation that there are people in other places who think the way I do. I would dream about what they were like and what their lives were like."

Dreaming. Connecting. These themes run through Marnett's life. They have powered his five-plus decades of research and his progressively more complex roles in academic leadership.

Later this year, Marnett will step down as dean of the Vanderbilt University School of Medicine Basic Sciences, a "school within a school" that he and a dedicated team have built over the past six years. He will return to his research lab full time, knowing that Basic Sciences is thriving as one of the nation's top biomedical research and doctoral programs.

Becoming a scientist

Marnett didn't set out to be an academic leader. He didn't even set out to be a scientist when he started his freshman year at Rockhurst College in Kansas City, Missouri. He had not taken a chemistry course in high school and was struggling with it in college. By the end of the first semester though, he managed to score the highest grade on the final, prompting the professor to invite him to try out research.

"I started kind of putzing around in his lab, and then he arranged a summer position for me in an inorganic chemistry lab," Marnett said. "It was a small school, and it wasn't much, but I found a home, and it was fun."

By the time he was a senior, it was clear that he would pursue graduate studies. He chose the chemistry program at Duke University, where he became the first graduate student to work with **Ned Porter**, a new faculty member in the department, studying free radical chemistry.

Marnett recalls two particular events that occurred during graduate school: a career-changing conversation and a life-shaping connection.

The conversation: over beers one evening after a seminar, Porter asked Marnett what he was thinking about doing when he completed his Ph.D. Marnett listed some options that did not include academic research.

"What about academia?" Porter asked him. "I'm not good enough to go into academia," Marnett responded. "Yes, you are," Porter said.

"At that moment, this switch went off," Marnett remembered. "I thought, maybe I can do that. It was a really key moment in my career. Ned doesn't remember saying that," he said with a laugh.

And the connection: Marnett met and married **Nancy Brown**. They celebrated their 50th anniversary last year.

"I depend on my wife a lot. She's got a very good radar—she understands people, and she understands me," Marnett said of Nancy, whom he described as vivacious, energetic, and focused. "We complement each other well. I'm a dreamer, and she's a get-it-done kind of person."

Marnett completed his Ph.D. in 1973, and he and Nancy headed to Stockholm, Sweden, where Marnett worked with **Bengt Samuelsson** (who won the Nobel Prize in 1982 for his discoveries regarding prostaglandins and related compounds).

"I didn't know any biochemistry, but I had to learn it because I was teaching it. I was frequently just 10 minutes ahead of the students and always on the edge of terror that they would ask a question I didn't know how to answer."

"It was a super exciting time to be there. They had just isolated the prostaglandin endoperoxides that are the key intermediates in prostaglandin biosynthesis," Marnett said. "I remember the first week I was there, the guy working next to me was dumping platelet extracts on a rabbit aorta strip trying to identify the contractile substance, which turned out to be thromboxane A2.

"I got so turned on by this mix of chemistry and biochemistry and enzymology and pharmacology. I was hooked."

The experience laid the foundation for his career-long study of the prostaglandin-producing cyclooxygenase enzymes and, like his amateur radio experience, made him aware of the international connectedness of scientific research.

Research legacy

After a year (short postdoctoral fellowships were the norm at the time), Marnett wanted to get back to the U.S. to begin his search for a faculty position. He took a postdoctoral position at Wayne State University, where his intellect and work ethic were noticed, and within a year—despite a near-prohibition on hiring from within—he was appointed to the faculty.

"It was a great place for me to start my independent career because it was a chemistry department with a biochemistry division," Marnett said. "I didn't know any biochemistry, but I had to learn it because I was teaching it. I was frequently just 10 minutes ahead of the students and always on the edge of terror that they would ask a question I didn't know how to answer."

At Wayne State, Marnett advanced to full professor before moving to Vanderbilt in 1989. Multiple members of the Marnett research group moved with him to Vanderbilt, earning his laboratory the nickname "Lemmings."

"Larry has been a talented, creative, kind, and consistent academic mentor to all of his graduate students, postdocs, and research staff," said **Brenda Crews**, a senior research specialist who worked with Marnett from 1994 until her death in January. Consistent with the lab's nickname, she added, "I must confess that Larry's present lab would follow him off a cliff."

Among his group's many research discoveries over the years (published in more than 500 research articles), Marnett is most proud of:

- Being one of the first labs to study endogenous sources of DNA damage, and fully characterizing the chemistry and biology of the molecules generated by lipid oxidation and the DNA adducts that they form.
- Completely characterizing the structure and function of the interaction of nonsteroidal anti-inflammatory drugs (the oldest and most prescribed drugs) with the cyclooxygenase enzymes COX-1 and COX-2.
- Generating COX-2 specific imaging agents, which could be useful for detecting early cellular changes in cancer, by tethering fluorophores (molecules that fluoresce) and positron emission tomography ligands onto modified NSAIDs.
- Discovering that the endocannabinoid 2-arachidonylglycerol is a selective substrate for COX-2 and that the resulting glyceryl prostaglandins are biologically active.

This last area is where Marnett plans to put his energy going forward. After he steps down as dean, he will spend time on sabbatical recharging and traveling, but then he'll dive back into his research.

"This connection of COX-2 to endocannabinoids is very exciting, because from the standpoint of inflammation and behavior, those molecules have a biology of their own, and we've found novel ways for them to be mobilized. This is what's next; this is what I want to make sure we get done," he said.

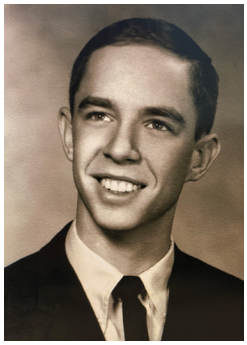
Academic startups

Marnett credits **Fred Guengerich** with recruiting him to Vanderbilt. After a symposium where they both spoke, Guengerich approached him, told him about being on a search committee for an endowed chair, and asked if Marnett knew "anybody great" who would be interested. Marnett said he would think about it.

"I called him a few days later and said, well Fred, I actually might be interested, but I don't know if you think I'm great," Marnett remembered. "He said, 'Oh, that's just what I wanted to hear.'"

The Mary Geddes Stahlman Chair in Cancer Research, which Marnett has held since he joined the faculty, was one of few endowed chairs at the School of Medicine at that time and was independent of a department. "I felt like I'd been recruited by the institution rather than a department; it gave me more of an institutional view from the start," Marnett said.

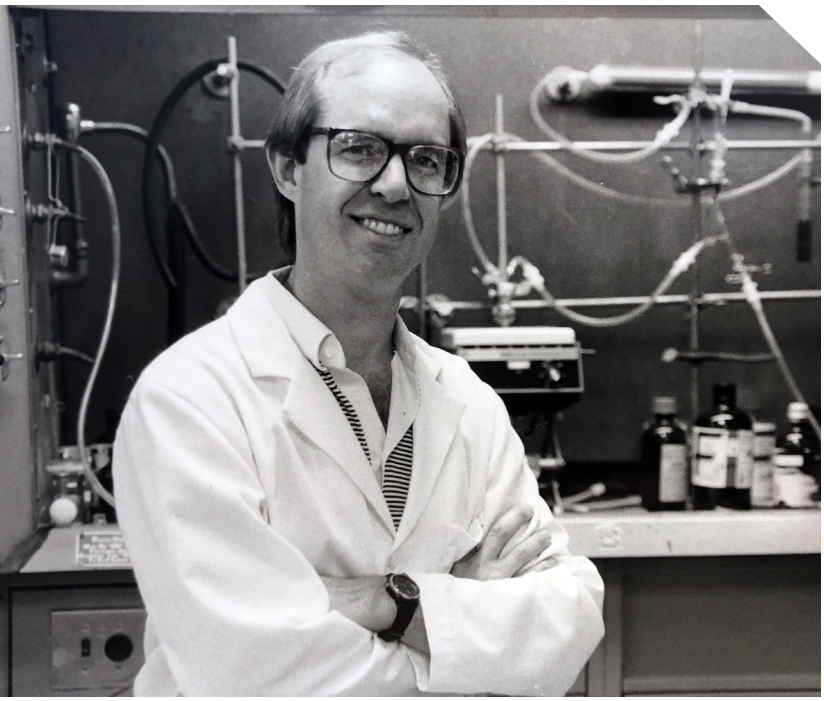
Marnett also was appointed director of the A.B. Hancock Jr. Memorial Laboratory for Cancer Research. He



PHOTOS COURTESY OF NANCY MARNETT

Top: Larry Marnett speaks at a conference. Bottom: Marnett's high school graduation photo from Rockhurst High in Kansas City.

used Hancock Lab funds to support institutional recruiting efforts and to provide "seed grants" for projects that moved investigators into new areas or made new connections. He found he had a knack for seeing opportunities for people to team up and do something unique.



Larry Marnett stands in front of a fume hood in his lab at Wayne State University.

"I loved catalyzing people to work together," Marnett said.

Things were humming along with these efforts, his group's research, and his editor-in-chief role for the journal he founded, *Chemical Research in Toxicology*, when **Harold "Hal" Moses** asked him in 1993 to be the first associate director for research of the the newly established Vanderbilt Cancer Center, now the Vanderbilt-Ingram Cancer Center.

"I thought, I don't know; it sounds fun; it's probably going to be a lot of work," Marnett said. "But here I was in a department with **Stanley Cohen** and Fred Guengerich and **Graham Carpenter**, really great scientists, and none of them had endowed chairs. I felt like I could repay this endowed chair that the institution had given me.

"I did not come to Vanderbilt to be a leader, and I quickly figured out what I'd gotten myself into," Marnett said, laughing.

He valued the opportunity to expand his research-catalyzing activities to a larger scale, invest in core facilities at a time when those resources did not exist, and learn leadership skills by absorbing lessons from Moses, a "fantastic mentor" to Marnett.

"I figured out that I'm an academic startup guy. When you're starting something, you can't really plan it out; you just have to do whatever needs to be done. There's a lot of energy, a lot of elbows in the air. It's exciting."

His next "startup" came in 2002, when he worked with Porter (whom he had helped recruit to the chemistry department at Vanderbilt) to establish the Vanderbilt Institute of Chemical Biology.

"I realized that there was a great opportunity for drug discovery around here, and chemical biology was just taking off as a discipline nationally," he said. "Ned and I started that, and it went really well. We recruited some real stars to Vanderbilt."

Building a unicorn

The creation of basic sciences presented an unexpected opportunity for Marnett. He had been named associate vice chancellor for research and senior associate dean for biomedical science in 2014, and he learned shortly after that the university and medical center would legally separate in 2016.

It had already been decided that the basic science departments would remain with the university, but no one knew exactly what that would look like. "Give us your ideas," **Jeff Balser**, dean of the School of Medicine, said to Marnett.

"That year and a half leading up to the split was a very unsettling time as we went back and forth on how Basic Sciences might be structured," said Marnett, who became dean of the new, undefined entity. "The first eight months after the split were complete chaos. We had no processes in place, and we didn't even know what the funds flow looked like."

Marnett assembled a team to help build this ultimate academic startup, including three associate deans: **Linda Sealy**, for diversity, equity, and inclusion; **Alyssa Hasty**, for faculty; and **Chuck Sanders**, for research. **Roger Chalkley** and **Kathy Gould** in the Office of Biomedical Research Education and Training supported Basic Sciences in areas related to graduate student and postdoctoral fellow training.

"Larry's passion is research, and he has the gift of being able to take pleasure in the research accomplishments of his colleagues," Sanders said. "I think this has been a major motivator for him in leading the creation of Basic Sciences and working 24/7 over the past six-plus years to ensure its success."

Marnett has prioritized programs to give faculty, staff, postdoctoral fellows, and students "as many resources as possible to function at their highest level," Hasty said. "Larry has a vision of what Basic Sciences can be in the future and seeks to establish and fund programs that will last long after he stops being our dean."

He also focused from the start on making diversity, equity, and inclusion an essential part of Basic Sciences, and this commitment "will be one of his lasting legacies," Sealy said. During Marnett's tenure, 60 percent of faculty recruits have been women or from underrepresented backgrounds.

"I feel privileged to have had this opportunity to start something really unique," Marnett said.

"Basic Sciences is a unicorn. We're sitting between a great university and a great medical center, and we're doing our own thing with access to all of the resources on both sides. We focus on research, and we train graduate students. It's almost like a research institute.

"It's been a lot of fun, and it's been hard … putting processes into place, and then, you know, a pandemic. I believe that the structure we've put together is set up for success and should be a model for how basic science is done at universities across the country, a model enabled by the close juxtaposition of the university and its medical school. I can't wait to see how it goes for the next 10 years."

Marnett will be watching from his lab, where he'll no doubt be dreaming and making new connections. ■

From Albert Camus to biology: A road less traveled

By Rachana Nitin

Dr. Asit Parikh, chief executive officer of MOMA Therapeutics, is an out-of-the-box thinker who encourages people to be creative in their approach to life. His numerous passions are reflected in his career trajectory, which has spanned French literature, molecular biology, medicine, and pharmaceutical research. He wears many hats across several aspects of his life: CEO, practicing physician, mentor, and a chair of the Vanderbilt University School of Medicine Basic Sciences Board of Visitors. I recently caught up with Parikh and had the privilege of talking to him about his scientific career.

What was your path to choosing science as a career?

I started off studying French literature at Northwestern University, and Camus was my favorite author. I spent a year abroad at the Sorbonne studying the Middle Age/Renaissance and 19th century periods. Although I really enjoyed it, I could not envision a long-term academic career in that field. In my senior year, I decided to give biology and medicine a chance and took a molecular biology class. There, I was assigned was a book by **Mark Ptashne**, *A Genetic Switch*. The combination of the book, the instructor, and the material really sparked my interest in medicine and biology. I took several more classes and decided to work in a laboratory and focus on a senior biology project.

What was your motivation for enrolling in Vanderbilt's Medical Scientist Training Program?

For my senior project I joined the lab of **Dr. Janardan "Jan" Reddy**. He was a talented scientist and researcher. Though I originally wanted to work in a lab to bolster my medical school application, Dr. Reddy's mentorship made me realize I also enjoyed basic science research. So, I decided to opt for the NIH-sponsored MSTP, leading to both M.D. and Ph.D. degrees, so I could study medicine as well as the research behind the medicine.

What has your career path been like?

I joined **Professor Fred Guengerich**'s lab for the Ph.D. portion of my MSTP training at Vanderbilt. There, I studied cytochrome P450 structure and function and earned a doctorate in biochemistry. After I graduated with my M.D., I did rotations at both Vanderbilt and Johns Hopkins University and an internal medicine residency at the University of Pennsylvania. I also completed a gastroenterology fellowship at Mass General Hospital and did postdoctoral work at MIT.

I moved to a research career in industry immediately after my fellowship with a job at Millennium Pharmaceuticals, which was subsequently acquired by Takeda Pharmaceuticals. There I led the clinical development of a monoclonal antibody that treats ulcerative colitis and Crohn's disease and built a pipeline focused on gastroenterology and liver disease. In 2021, I joined MOMA Therapeutics as the CEO.

Throughout, the belief that my work and research have the power to change the way that medicine is practiced has driven me forward. I also enjoy mentoring anyone who seeks help with their career or needs advice. People have always given me a lot of their time, and in return I try to pay it forward by being as generous with my time as possible.

Do you have any advice for budding scientists?

Stop worrying about what everyone else thinks and do what makes you happy. I learned this from Fred, my Ph.D. adviser: You have one life, and you should be in charge of it. Focus on finding a career that gives you satisfaction and fulfilment. If you focus on how everyone else is judging you, you lose time. It's great to see that students at Vanderbilt today are exposed to all kinds of career choices, which was not always the case when I was a student 25 years ago; it was Fred who helped me expand my horizons by helping me think through the pros and cons of pursuing an industry career. Also, don't fixate on what the path is "supposed" to look like: Be open to change and you could end up learning and enjoying something you didn't think you would.

PHOTOS COURTESY OF ASIT PARIKH

Core Competency

By Stephen Doster

Advancement against the most intractable health challenges requires the best minds, the latest tools, and exceptional training. The School of Medicine Basic Sciences offers those ingredients in its core facilities. But our cores are more than state-of-the-art equipment. Here, as part of *Vestigo's* regular support staff shoutout, we profile some of the people behind the curtain.

Caroline Roe, Cancer & Immunology Core

CIC Managing Director **Caroline Roe** grew up in a suburb of Milwaukee, Wisconsin, but earned a bachelor of science from the University of Minnesota Twin Cities. Roe relocated to Nashville in 2012 after enduring one too many cold Midwestern winters.

At Vanderbilt, Roe enjoys giving researchers who wouldn't normally employ cytometry, a tool to measure the number and characteristics of groups of cells, in their studies access to cutting-edge techniques.

One of Roe's favorite (non-research) memories at the CIC was of the time she had to move a piece of equipment across campus to their core space on the seventh floor of the Robinson Research Building. Her entire core, plus a "terrified" vendor engineer, had to roll a "bright, mango-colored machine bigger than a clothes dryer" through the tunnels of Medical Center North. "We moved perhaps a bit too quickly," Roe said, laughing.

To help her relax, Roe has practiced yoga for over a decade. She is especially proud of her extended side crow, a pose in which a person holds their body weight on their hands and hovers their head above the ground, legs held up high and to the side.

FDSS is in the house
Finding a compound to put in a mouse
Requires some throughput for a discovery
That might help Docs shorten your recovery
I'm sitting here praying for a hit
So my boss isn't like "'Yo, just quit"
But that's just the way grad school is, bro
You end up dreading science's "no"
High throughput screening is the way to go
Every other way is way too slow
I don't have one publication
So right now this project is mental exploration

Written by Krystian Kozek, MD/PhD'21, and Kristopher Abney in December 2014. Abney, a Meharry Medical College Ph.D. student, did his dissertation work alongside Kozek in the lab of Dave Weaver, associate professor of pharmacology.

Dehui "Debbie" Mi, High-Throughput Screening Facility

Debbie Mi hails from Wuhan, Hubei Province, China, but completed a doctoral degree in chemistry and biochemistry at Arizona State University.

"In Phoenix, roads were wide and straight like a checkerboard," she said of the place she learned to chase dust devils with her car. "People gave directions using the cardinal directions: north, south, east, and west. In Nashville, they only tell you to turn left or right!" Despite that, it was not until Mi came here that she really felt she was in the United States. "I feel a more pronounced and richer atmosphere of American traditions here to slowly and thoroughly appreciate," she said. "Where my heart settles is where my home is."

Through her role at the HTS, Mi enjoys helping investigators identify new compounds for pharmacological exploration. In her spare time, she reads and writes poetry in Chinese and English. One of her favorites, included here, was written by a core user on a white board at the HTS.

STEPHEN DOSTER

Markus Voehler, Biomolecular NMR Facility

Markus Voehler, an expert in nuclear magnetic resonance, hails from Switzerland. Voehler completed a bachelor of science in physical chemistry at the School of Engineering in Winterthur and cut his NMR teeth at his first job at the University of Zurich. There, he combined his interest in NMR with further education in electronics, instrumentation, analytics, and chemistry. He left Zurich in 1992 to pursue his dream of working in the United States, choosing to work at Vanderbilt for several years.

"My commitment was for three years," Voehler said. "That was 30 years ago, and I still like it here very much." Voehler earned a Ph.D. from Vanderbilt in 2007.

Voehler almost single-handedly runs the Biomolecular NMR Facility, which houses five NMR spectrometers. NMR spectroscopy uses magnets to observe the local magnetic fields around atomic nuclei of different molecules. Running the facility is hard work but occasionally provides comedic relief. "Not too long ago, the signal on one of our instruments suddenly and dramatically degraded," he recounted. "Upon removing the instrument's probe from the magnet, we found the culprit—a cockroach that died inside!"

Voehler likes biking, running, and traveling off the beaten path. His biggest aspirational goal for the year was to finish the St. Jude Rock 'n' Roll Nashville Marathon, which he accomplished in April. His next big goal is to submit and hopefully receive a large National Institutes of Health grant for shared-use instrumentation!

Eric Appelt, Advanced Computing Center for Research and Education

Eric Appelt is a rare species—a native Nashvillian! But although he was born and raised here, he moved to Ohio to attend Miami University for his undergraduate studies. Later on, while pursuing a physics Ph.D. at Vanderbilt, he spent several months near Geneva, Switzerland, working as a collaborator at the Large Hadron Collider.

"The CERN campus straddled the French-Swiss border, so during a given day I would move from one country to the next depending on what building I was in," he recalled.

Appelt is currently the senior software development and IT operations engineer at the Advanced Computing Center for Research and Education, a core he first learned about as a grad student. "I was a heavy user of ACCRE resources, so when I learned of a job opportunity there after graduating and moving on to software development, I was delighted to join the team," Appelt said.

Away from work, Appelt indulges his passion for bird photography. "We've got a lot of great parks in Nashville, like Edwin Warner and Radnor Lake, to go and find [birds], especially during the migration season."

This male indigo bunting was photographed by Eric Appelt in the summer of 2020. "They like to hunt bugs out in the milkweed patch just south of the Percy Warner Park Nature Center off Highway 100. There are lots of them there in the summer, but you'll likely only see them if you are looking carefully. They have a very distinctive song, too, which makes them easier to locate."

STEPHEN DOSTER

Erin Gribben, Vanderbilt Antibody and Protein Resource

Erin Gribben, originally from Chattanooga, Tennessee, attended the University of Georgia, earning a bachelor of science in forestry with an emphasis in fisheries and aquaculture. She got a master of science in wildlife and fisheries science at the University of Tennessee Knoxville before moving to the Washington University to do cancer research for eight years.

Gribben joined the Vanderbilt Antibody and Protein Resource 12 years ago and currently serves as the lab manager, focusing on producing monoclonal antibodies from hybridomas (a fusion of normal lymphocytes and lymphoma cells). In her time at VAPR, Gribben has survived a crisis or two.

"Once," she recalled, "Hundreds of cell lines thawed in a bone-dry liquid nitrogen tank. We worked for two years to recover those lines with about a 75 percent success rate." Thankfully, she learned a lot about nursing cells back to viable, healthy lines, which has come in handy when customers need to recover old cell lines they find deep in their freezers or tanks.

A former soccer player, Gribben coaches recreational soccer when not at work and is a board member of her daughter's middle school band program and her son's high school soccer program, which support and fundraise for the clubs.

STEPHEN DOSTER

Jenny Schafer, Cell Imaging Shared Resource

Jenny Schafer is the pride of Montevallo, a town about 30 miles south of Birmingham and the "geographic center" of Alabama. "It's amazing to me that there are more people on the Vanderbilt campus than in my hometown," Schafer said.

She first came to Vanderbilt as a postdoc in the lab of **James Goldenring**, professor of surgery, in 2006 after earning a Ph.D. at the University of Alabama at Birmingham. Schafer joined the Cell Imaging Shared Resource in 2014 and enjoys helping researchers with microscopy projects while broadening her own knowledge each day.

In her free time, Schafer turns to the musical arts. "I enjoy tap dancing, but I am also a Broadway aficionado!" she said. "I am still obsessed with *Hamilton*, even years after its release, and just saw it on stage for the second time. If anyone wants to talk *Hamilton* trivia, I'm available."

Pushing the boundaries of the academic ladder

By Lorena Infante Lara

In 1951, Martha Fant, a schoolteacher in Clarksdale, Mississippi, was pregnant with her second child. Living in the Jim Crow South, she and her husband, Wendell Fant, had access to few health care resources that were readily available to white Americans. Thankfully, the city of Mound Bayou, Mississippi, and its Taborian Hospital were only 30 miles away.

Mound Bayou, founded in 1887 by formerly enslaved persons, was a safe haven and relative oasis for Black residents of the Mississippi Delta. A variety of Black-owned businesses thrived there, and Black people were able to safely vote at a time when trying to exercise this basic right of citizenship could lead to death.

Taborian Hospital, which opened in 1942, was entirely staffed by Black health care workers. Its first chief surgeon, **Dr. Theodore Roosevelt Mason Howard**, became an important civil rights leader, working with and mentoring other young activists such as **Medgar Evers** and the **Rev. Jesse Jackson**. It was in this hub of civil rights activism that **Dr. Michael Fant**, Vanderbilt University's first Black M.D./Ph.D. student and the first Black student in one of its biomedical sciences Ph.D. programs, was born.

A model to follow

Fant is now a professor emeritus of pediatrics at the University of South Florida Morsani College of Medicine in Tampa, Florida, but his path was not a straight line connecting Mound Bayou to Tampa. It was, as it is for many Black Americans, a path that was winding and replete with hurdles and naysayers.

Fant's parents, both graduates of Lane College, a historically Black college and university in Jackson, Tennessee, were strong advocates for education, their family, and the Black community. They constantly modeled a life based on a strong intrinsic sense of dignity, self-worth, and excellence that was not swayed by others' opinions. A constant theme of his father's counsel was to "stay true to yourself, do things the right way, and pay no attention to the noise."

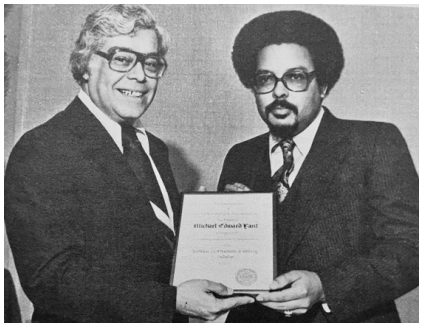
Wendell worked as a district executive for the Boy Scouts of America, recruiting, organizing, and training the volunteers who served as scout leaders. Because scouting was segregated at the time, he worked closely with many of the business, church, and educational leaders in the Black community to create the organizational structure that provided important developmental resources for Black boys and young Black men. Although so-called "Negro Boy Scouts" had fewer resources than white scouts, Wendell consistently set a high bar in terms of the recruitment and leadership metrics by which he and his coworkers, Black or white, were judged.

With Fant, the apple didn't fall far from the tree.

When he was five years old, Fant's family moved from Clarksdale to Memphis, Tennessee, where he grew up experiencing firsthand "colored-only" waiting rooms and water fountains and attending segregated schools where the textbooks were always hand-me-downs from neighboring white schools. However, "we were fortunate to have teachers who extended themselves to provide learning opportunities far beyond the restricted curricula and resources provided by the school district," Fant said.

When he was a junior in high school, Fant became involved with the National Association for the Advancement of Colored People's youth movement in Memphis. He regularly participated in protests at the Memphis City Hall on behalf of sanitation workers who were striking for higher wages and better working conditions, a strike that led to **Martin Luther King Jr.**'s fateful visit to Memphis. Fant was there for the march King led and for King's "I've Been to the Mountaintop" speech, given the day before his assassination in April of 1968.

ALL PHOTOS COURTESY OF MICHAEL FANT



At Vanderbilt, Dr. Fant undertook an M.D./Ph.D. combined degree program in Biochemistry and Nutrition. Winning the Goldberger Summer Nutrition Fellowship, SNMA's "Student of the Year" Award, and the Vivian Allen Fellowship, he organized and chaired a symposium on "Hypertension and Cardiovascular Disease: A Black Perspective." He worked with the medical school administration to bring about a significant increase in Vanderbilt's minority student enrollment, while continuing to interview regional applicants for admission to MIT. Co-author of twelve articles and nine abstracts, as well as the chapter of a book, Dr. Fant also

Above: Dr. Samuel Dagogo-Jack presents Michael Fant with a plaque following a lecture at the University of Tennessee. Right (clockwise from top left): Fant during the 1980 Commencement ceremony at Vanderbilt. Newspaper cutout describing Fant's burgeoning career. Fant receiving the 1979 William and Charlotte Cadbury Award from Dr. Gilbert Ortiz, then the chairman of the Awards Committee of the National Medical Fellowships Board of Directors.

Right: Andrew Young (second from left to right), American politician, diplomat, and activist, congratulates Fant (far right) and other medical students for winning National Merit Foundation merit awards for academic excellence, leadership, and service. Bottom right: Fant (middle) and his wife, Ana María, (right of him) at his retirement party in 2019 with some current and former fellows. Bottom left: Fant and his wife, Ana María, vacationing in Rome in 2015.

Ultimately, Fant overcame the institutionalized roadblocks, departing Memphis in 1969 for Cambridge, Massachusetts, to attend the Massachusetts Institute of Technology.

A twist of fate

Determined to become a physician, Fant enrolled in MIT's life sciences program, following a track in nutritional biochemistry and metabolism. There, he began to understand that nutritional intervention at the national and global levels was "more than just providing food and grain and throwing it at a community," Fant said. "It's infrastructure, economy, education, culture—it's a whole host of things. The major determinants of nutritional status in a community depend on multiple variables specific to that community."

As his studies progressed, Fant focused on the impact of malnutrition on human development. "I found myself growing angry at the fact that something as simple as a lack of nutrition during critical periods of postnatal development could permanently reduce a person's genetic potential at birth," Fant said, referring to the ways in which nutritional and environmental insults during critical developmental periods can permanently lead to the failure of a child to reach their full intellectual ability.

During his studies at MIT, Fant couldn't help but see the impact of malnutrition in the context of the profound inequity between white communities and communities of color locally and between the developed world and nations of color globally.

> "Because of my own independence, self-confidence, and support network, I had a very productive tenure at Vanderbilt."

"That the vast majority of cases where malnutrition was wiping out or stunting upward of 50 percent of a generation's genetic potential were occurring were places where there were people of color pissed me off," Fant said.

After MIT, Fant chose to continue his studies on malnutrition at the basic science level through the pursuit of a dual M.D./Ph.D. program. "When I looked around the country at programs, there were really only two or three options for me," he said. Among the choices was Vanderbilt and its Department of Biochemistry, which was chaired by **Dr. William Darby**, a leader in the field of nutrition. "He had a cohort of faculty with him that promised to provide me with the perfect environment to pursue the interests I developed at MIT," Fant said. The fact that Vanderbilt was closer to home helped seal his decision.

In 1972, Fant was admitted into Vanderbilt's dual M.D./Ph.D. program and geared up to dive into nutritional biochemistry under Darby's leadership. Yet fate—well, Darby—had other plans.

Before Fant started the program, Darby resigned as chair of biochemistry to serve as president of the Nutrition Foundation in New York. With his departure, the faculty Darby had assembled also began to leave, leaving Fant feeling like his primary reason for moving back to Tennessee had evaporated.

In the face of this uncertainty, Fant had to consider the options. "Do I stay? How do I make lemonade out of this?" Ultimately, he decided to stick it out.

Same goal, different focus

As Fant continued to assess the best way to pursue his long-term career plan, fate intervened again. **Raymond Harbison**, a young new faculty member with a primary appointment in pharmacology and a secondary in biochemistry, wanted to audit the anatomy class and was assigned to Fant's dissection table. Harbison introduced himself and asked each of the four students about their interests and their plans. Fant described his interest in the developmental consequences of malnutrition and how his intended program had been "short-circuited" by Darby's exit.

"Have you ever thought about the period of development before birth?" Harbison asked. He argued that far more consequential developmental events occurred before birth than after birth, that we knew essentially nothing about the period between conception and birth, and that we didn't understand how the placenta—a unique organ that helps to direct traffic at the maternal-fetal interface—functioned.

"At that point," Fant said, "My interest was piqued, and our conversations slowly pulled me into the world of placental biology. The opportunities to discover important new knowledge relevant to human development became very apparent and appealing." Shortly thereafter, Fant joined Harbison's lab as a graduate student in the Department of Biochemistry.

Breaking through the brick wall of homogeneity

Fant's arrival at Vanderbilt occurred prior to its extensive efforts to foster diversity, equity, and inclusion in the M.D./Ph.D. program and across the institution that have since propelled it to the forefront of biomedical graduate training for minority students. Thus, he found very little diversity in the undergraduate school and even less within the medical and biomedical spaces.

In 1966, **Dr. Levi Watkins Jr.** became the first Black student to be admitted to the School of Medicine, and he remained the only one until his graduation in 1970—also a first. By the time Fant enrolled as a medical student in 1973, there were still only three other Black students at the School of Medicine; Fant and two other students in his class collectively became the fifth through the seventh to enroll.

"The optimism I had when I entered Vanderbilt was quickly tempered by the realities of day-to-day life as a student," Fant said. "It was a bit disappointing, to say the least. I'd spent the last four years at MIT—surrounded by Harvard, Boston University,

Northeastern University—being conditioned by a relatively more progressive academic environment compared to other parts of the country." MIT had its own diversity challenges, but they continually engaged with students to address them.

Vanderbilt, it seemed to Fant, "was sociologically stuck in a 1950s time warp." When the Black students as a group or Fant individually attempted to raise concerns or address issues related to student recruitment, support, or even the scholarly examinations of racial disparities in health outcomes, there was a palpable resistance by administrators and leadership to acknowledge the existence or significance of these issues.

"Vanderbilt's mindset was, 'we don't have any diversity problems, there are no racial problems here, everything is fine as it is,'" Fant said. "Coming to Vanderbilt from MIT was, in many ways, a greater culture shock than going from Memphis to MIT."

While the country had largely gotten used to the idea of the "Black kid" wanting to be a "doctor," the expectation among many white people was that Black physicians would or should return to their communities and work in neighborhood clinics. Fant, who sought to become an academic physician and join the ranks of the faculty at a medical school, came to realize that many were not yet comfortable with a Black student having such aspirations.

"Why do you want to get a Ph.D.?" some members of the biochemistry faculty would ask. "You know how hard that's going to be, right? Why don't you just get the M.D. and then maybe, if you still want to do it later, you can come back to the Ph.D.?"

"Resistance, indifference, and efforts to dissuade and discourage were familiar forces I had to deal with. But I had seen it all before and understood it for what it was," Fant said. "Moreover, my success at MIT armed me with the sense of calm and confidence I needed to move forward."

Along the way, Fant was able to identify faculty members who provided a strong support network and served as a counterweight to the more negative forces at play. In addition to Harbison, his primary mentor, Fant became close friends with and was mentored by **Dr. Robert Harrison**, a Black basic scientist and a clinical endocrinologist who worked in the Department of Medicine, and the future **Dr. Robert Taylor**, one of the Black M.D. students in the year above him. Additionally, Fant received valuable mentoring and support from some faculty members, most notably from **Dr. Ian Burr, Dr. Robert Cotton**, and **Dr. Mildred Stahlman** in pediatrics, as well as **Frank Chytil, David Ong, David Puett** and **Robert Neal** in biochemistry. Several of these relationships endured and grew into lifelong friendships.

"Because of my own independence, self-confidence, and support network, I had a very productive tenure at Vanderbilt," Fant said. By the time he graduated, Fant had presented his research at several national and international scientific conferences, published nine publications in peer-reviewed journals, and received two national honors from the Kaiser Family Foundation.

"It was an experience that I really wouldn't trade because it created an unconventional yet critical pathway for me to do what I needed to do to become a successful physician-scientist."

Of mice, genes, and future generations

Fant completed the M.D./Ph.D. program in 1980 and left Vanderbilt to climb the academic ladder. He went on to specialize in pediatrics at Boston Children's Hospital and combined a neonatology fellowship at Harvard Medical School with a postdoc at MIT, training under **Dr. Mary Ellen Avery** and **Dr. Hamish Munro**, respectively.

After that, Fant embarked on his own independent academic career, which took him to the University of Texas Southwestern Medical Center in Dallas, the Washington University School of Medicine in St. Louis, the John P. and Kathrine G. McGovern Medical School at the University of Texas Health Science Center at Houston, and the University of South Florida Morsani College of Medicine in Tampa. During his tenure at USF, he also served as the program director for its Neonatal-Perinatal Fellowship Program.

As a graduate student, Fant had switched his focus from postnatal development to prenatal development, with particular interest in the role of the placenta. After arriving at UT Southwestern, a large portion of his research explored the role of insulin-like growth factors, such as IGF1, in placental development and function.

Fant's research interests later shifted to a gene called PLAC1 that was found to be strongly and primarily expressed in the placenta; he later demonstrated that it was also expressed throughout the embryo. To probe PLAC1's role, Fant's laboratory worked diligently to develop a knockout mouse model that did not express PLAC1 and demonstrated unequivocally that PLAC1 is essential for placental development as well as for brain development and function.

"Reaching a point in my career where I could say that we were able to contribute significant new knowledge to mammalian biology was immensely satisfying," Fant said. "Isn't that the point of it all?"

Throughout his academic career Fant has mentored a significant number of trainees at all levels of the educational pipeline in clinical medicine and basic research. "Sharing with young folks the excitement of taking care of sick newborns and of scientific inquiry relevant to that care while modeling the commitment and integrity required to pursue both properly was an immense privilege, and it was especially satisfying," Fant said.

Fant was granted the emeritus title in 2019 and is in the process of completing several remaining manuscripts and reviews. As for what comes next, he expects to find other roles where he can leverage his life experiences and expertise to contribute to the development of the next generation of physicians and scientists.

"I've retired from the job, but not the mission," Fant said. ■

Accolade corner

By Skylar Cuevas

The hard work of our faculty, staff, postdocs, and graduate students in the Vanderbilt University School of Medicine Basic Sciences continues to be recognized on the local and national level. Here we list a few of the researchers whose work has been recognized so far in 2022.

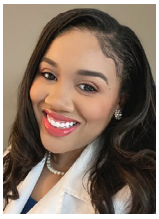
Graduate student **Noah Bradley** (Biological Sciences, Brandt Eichman lab) was named the 2022 recipient of the Karpay Award in Structural Biology.

The editorial board presents the Paper of the Year Award to the first author of the paper judged to be the best of the year from June of the previous year to May. The 2021 winner was **Colbie Chinowsky** (recent Cell and Developmental Biology graduate, Matt Tyska lab).

Postdoc **Ji-Woon Kim** (Lisa Monteggia lab) received a NARSAD Young Investigator Grant from the Brain & Behavior Research Foundation.

Postdoc **Seth Zost** (James Crowe lab) has been awarded the Claude Hannoun Prize for his research on COVID-19 and other life-threatening viral diseases.

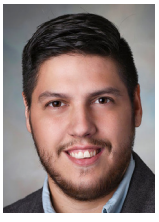
The multi-institutional Intersections Science Fellows Symposium recently named its 2021 fellows. Among the 30 selected was postdoc **Lillian Brady** (Erin Calipari lab). In addition, **Magdalene Ameka** (Alyssa Hasty lab) was selected as a 2021 associate.



Postdoc **Heather Beasley** (Antentor Hinton Jr. lab) and recent graduate **Shawna Brookens** (Mark Boothby lab, now at the University of Pennsylvania) are the 2021 recipients of the E. E. Just Postgraduate Fellowship in the Life Sciences, granted by the United Negro College Fund and Bristol-Myers Squibb.

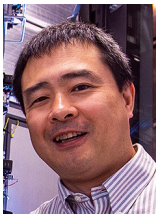
Madison Adolph, a postdoc in the lab of David Cortez, was named the Vanderbilt-Ingram Cancer Center Postdoc of the Year for her studies on replication stress responses.

Postdoc **Woongjae Yoo** (Mariana Byndloss lab) received the 2020–21 Sidney P. Colowick Outstanding Postdoc Award from the Molecular Pathogenesis Division.



M. Gunes Kutlu (Pharmacology), research instructor in the lab of Erin Calipari, has earned an NIH NCATS KL2 award.

Caroline Roe, managing director of the Mass Cytometry Center of Excellence, has been chosen as an emerging leader by the International Society for Advancement of Cytometry as part of its Shared Resource Lab Emerging Leader program.



ANNE RAYNER

The Stanley Cohen Innovation Fund annually supports innovative early-phase research projects that are high risk yet potentially high reward. This year, faculty members **Houra Merrikh**, professor of biochemistry, and **Teru Nakagawa**, associate professor of molecular physiology and biophysics, were granted one-year awards.

Warren Center for Neuroscience Drug Discovery Director and Professor of Pharmacology, Emeritus, **Jeff Conn** is one of 16 scientists to be welcomed as a 2021 fellow of the American Society for Pharmacology and Experimental Therapeutics.

JOHN RUSSELL

STEPHEN DOSTER

Assistant Professors of Biochemistry **Breann Brown** and **Will Wan** have received 2021 National Institutes of Health Director's Awards for their unconventional, bold approaches to research that advances knowledge and enhances health. Peabody College postdoc **Katherine Aboud** earned a similar award.

The V Foundation for Cancer Research has awarded a $600,000 grant to **Scott Hiebert**, the Hortense B. Ingram Professor of Cancer Research and professor of biochemistry, to pursue a possible precision therapy for a type of sarcoma that predominantly affects children.

STEPHEN DOSTER

The American Federation for Aging Research and the Glenn Foundation for Medical Research have awarded assistant professor of cell and developmental biology **Kris Burkewitz** a $100,000 grant to research the biological aging process.

Kathleen DelGiorno, assistant professor of cell and developmental biology, received a grant from the Sky Foundation for Pancreatic Cancer Research.

STEVE GREEN

Renã Robinson, associate professor of chemistry, has been named president of the National Organization for the Professional Advancement of Black Chemists and Chemical Engineers.

JOE HOWELL

The National Academy of Inventors has elected **John McLean**, the Stevenson Professor of Chemistry, a 2021 fellow. Election as an NAI fellow is the highest professional distinction granted solely to academic inventors.

ANNE RAYNER

Colleen Niswender, associate professor of pharmacology, has received the 2022 Scientific Achievement Award in Drug Discovery and Development from the American Society for Pharmacology and Experimental Therapeutics. Niswender has also earned a $300,000 grant from the International Rett Syndrome Foundation.

STEVE GREEN

Seven Vanderbilt faculty members have been elected fellows of the American Association for the Advancement of Science. This includes three with secondary appointments in Basic Sciences: **Brandt Eichman**, the William R. Kenan, Jr. Professor and chair of the Department of Biological Sciences, **Bjorn Knollmann**, the William Stokes Professor in Experimental Therapeutics and professor of medicine, and **Jens Meiler**, research professor of chemistry.

JOHN RUSSELL

Lisa Monteggia, professor of pharmacology and Barlow Family Director of the Vanderbilt Brain Institute, was appointed co-editor for the journal *Neuropsychopharmacology*. Monteggia is the first woman to be named to a leading role at the journal.

Jennifer Pietenpol, the Benjamin F. Byrd Jr. Professor of Oncology and professor of biochemistry, is stepping down as director of the Vanderbilt-Ingram Cancer Center and will assume a combined leadership role for VUMC as chief scientific and strategy officer.

The Office of the Dean of Basic Sciences has named the recipients of the 2022 Vanderbilt School of Medicine Basic Sciences Core Development Grants. The grants provide each awarded core with up to $50,000 toward the purchase of capital equipment, the development of a new core technology or service, or scientifically-driven lab renovations.

- *Cell Imaging Shared Resource*
  Jenny Schafer, research associate professor of cell and developmental biology
  Matt Tyska, Cornelius Vanderbilt Professor of cell and developmental biology
- *Center for Structural Biology Biomolecular NMR Facility*
  Markus Voehler, research assistant professor of chemistry
  Michael Stone, professor of chemistry
- *Mass Spectrometry Resouce Center Proteomics Core Laboratory*
  Kevin Schey, professor of biochemistry
  Kristie Rose, research assistant professor of biochemistry
  Hayes McDonald, research assistant professor of biochemistry
- *Center for Structural Biology Cryo-Electron Microscopy Facility*
  Scott Collier, Cryo-EM Facility co-director
  Melissa Chambers, Cryo-EM Facility co-director
  Terunaga Nakagawa, associate professor of molecular physiology and biophysics
- *Mouse Neurobehavioral Core*
  Fiona Harrison, associate professor of medicine
  John Allison, research assistant professor of pharmacology
- *Small Molecule NMR Facility Core*
  Donald Stec, Small Molecule NMR Facility Core director
  Gary Sulikowski, Stevenson Professor of Chemistry

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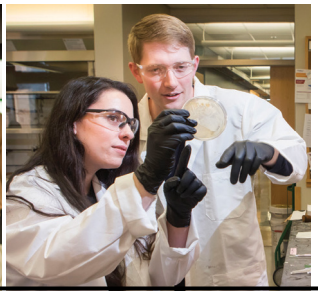

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