

BIOCHEMISTRY In Vivo

Department of Biochemistry - College of Agricultural and Life Sciences - UW-Madison

2023 Education | Research | Innovation



Table of Contents

From the Chair	1
New Faculty	
Snehal Chaudhari	
Monica Neugebauer	4
Research News	
When Antibiotics Deplete Microbiome, a Pathogen Takes Advant	<u>age</u> 5
Power of Reactive Molecule Harnessed to Explore Protein Inner V	
MCCET to Expand	7
Images Uncover How Enzyme Kicks Off DNA Replication	8
Beyond the Bench	
James Ntambi	9
Erica Shu	12
Aaron Hoskins	13
Judith Simcox	14
Vatsan Raman	15
Awards	
Scott Coyle	16
Elizabeth Wright	17
<u>James Ntambi</u>	17
Ophelia Venturelli	18
Philip Romero	18
Amy Weeks	19
Vatsan Raman	19
Collin Borcik	20
Daniel Parrell	20
Claire Palmer	21
Saeed Roschdi	21
Graduate Degrees.	22
More Honors & Awards	23
We Heard About You	26
In Memoriam	28
<u>Donors</u>	29
<u>Innovations</u>	Back Cover

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Cover: Photo by Beth Young

Students traveling to Uganda with Professor <u>James Ntambi</u> explore a banana grove on one of their field trips. Ntambi, who has been bringing students to his native Uganda since 2002, reflects the experiential study abroad programs in our Beyond the Bench feature, starting on p. 9.

This page: Artwork by Chloris Lowe

Hogiwe Hirokirere Hii, Connecting Paths preserves some of the wood from an elm tree fondly known as 'Elmer', which stood in the Biochemical Sciences Complex Plaza until it succumbed to Dutch elm disease in 2018. For Lowe, the artwork is about spacemaking and energy exchange. The hanging piece was installed in the Biochemical Sciences Building atrium in October 2023. Visit the News section of our website to watch a video and learn more.

From the Chair



Brian G. Fox

Here we are, nearing the end of 2023, and I'm happy to present you with the 2023 issue of *Biochemistry In Vivo*. The goal is to keep our worldwide network of members, alumni, supporters, and friends up to date on the department. This edition is full of new faces, new happenings, and continued impact. It is our sincere hope that you will find this newsletter enlightening and an inspiring call to engagement.

The cover image shows a group of undergraduates exploring Uganda as part of an immersive and interactive curriculum. The Uganda Program is led by Professor James Ntambi (also named this year as a Fellow of the American Society for Biochemistry and Molecular Biology). There are two tracks available to students in this program, each of which includes a three-week field experience in Uganda: Agriculture, Health & Nutrition, and UW Mobile Clinics & Health Care. Through these programs, students walk through agricultural fields, observe medical professionals at mobile health clinics in rural communities, discuss the fundamental importance of clean water and nutritious food, and learn about Ugandan culture and traditions. We are proud to share the history of the Uganda Program. The stories of generations of students who have participated in the Uganda Program shine a bright light on the transformational impact that your

support of this unique program could have.

The Uganda Program's interweaving of agriculture, health, and nutrition serves as a prime example of the interdisciplinary broad-based and nature of biochemistry. This edition of Biochemistry In Vivo introduces a new section, "Beyond the Bench," that highlights some of the ways in which our work extends beyond the Biochemical Sciences Complex to broaden educational opportunities within and beyond the department, build collaborative partnerships, and break down barriers to inquiry and discovery.

Innovation and creativity remain foundational to our department's educational opportunities and research programs. We introduced two assistant professors who arrived just before the start of the Fall 2023 semester. Snehal Chaudhari, who joined us from her postdoctoral work at Harvard University, studies the impact of the human gut microbiome on metabolic diseases. Her initial results indicate that small molecules synthesized by gut microbes have important, underappreciated influences on diabetes, obesity, and liver cirrhosis. Monica Neugebauer, who joined us from her postdoctoral work at the Broad Institute, is an engineer by initial training. She is starting a research program to use systems biology, principles of chemistry and mechanism, directed evolution, and other approaches to create enzyme catalysts that give new insight, minimize the use of toxic solvents, and create an expanded portfolio of renewable molecules for the bioeconomy and human well-being.

We also highlight the work of two recently promoted associate professors, both of whom bring systems-level approaches to their research programs. Ophelia Venturelli (who also received the ACS Synthetic Biology Young

Innovator Award and the UW–Madison Office of the Vice Chancellor for Research and Graduate Education's Early Career Innovator Award) seeks to understand the complex interactions that stabilize a microbiome. Vatsan Raman (who received an NSF Early Career Award and Wisconsin Alumni Research Foundation Accelerator Grant for technology de-risking) is developing engineered, highly-specific bacteriophages that can be used to eliminate bad actors in a microbiome.

Both Ophelia and Vatsan are also engineers by initial training, along with Assistant Professors Philip Romero (a co-PI on a UW-Madison Research Forward grant) and Scott Coyle (an NIH Director's New Innovator Award recipient). Scott will build on his creation of engineered protein circuits that can control cell metabolism which leads to oscillations at different rates. By linking these circuits to fluorescent reporters, a stunning visual readout of the behaviors of different cell types can be obtained. You can watch the movies here: https://go.wisc.edu/coyle research.

We also recognize Philip's receipt of a campus Research Forward grant with SMPH faculty to study angiotensin converting enzyme 2 (ACE2) as an engineered biotherapeutic agent to treat high blood pressure. This research, which probes relationships between protein sequence, structure, and function, is relevant to those who take Lisinopril, which is one of the top five most prescribed drugs in the US. Philip brings expertise in state-of the-art methods, including advances in DNA sequencing and synthesis, microfluidic screening, molecular modeling, machine learning, and optimization to address this important problem.

The newsletter highlights the translational innovation of Dr. Erica Shu. In addition to her role as teaching

Continued on next page

faculty in the department, Erica is an entrepreneur whose start-up company EzraBio, Inc. arose directly from challenges she faced and discoveries she made during her Ph.D. studies. The department is fortunate to have Erica's contributions to teaching and her entrepreneurial vision enriching our collective experiences. Her path from discovery to company is another compelling embodiment of our department's work extending beyond the bench.

We continue to see the incredible impact of the department decision to bring the cryo-EM revolution to UW-Madison. Professor Elizabeth Wright (also UW Vilas Associate Award recipient this year) leads our enterprise, with a departmental center (Cryo-Electron Microscopy Research Center, CEMRC) and an NIH-funded Cryo-ET Network Hub Center (Midwest Center for Cryo-Electron Tomography, MCCET) now established. These two centers are becoming a premier site for research and training, and over 150 faculty, staff, and students have passed various levels of certification for microscope operation.

Late in 2022, NIH approached Elizabeth with an offer to double the size of MCCET by adding new staff and a new Titan Krios microscope. After a few rounds of negotiations, we are now in the process of designing a new lab space, purchasing of three new microscopes, and hiring new staff. The Daniel F. Klessig Cryo-EM Research Support Fund is now established through the generosity of Daniel Klessig, BS'74, and Judith Hope Klessig. We greatly appreciate how Dan and Judy's innovative approach and thinking have helped us move forward.

Among the biochemists using cryo-EM in their research is Assistant Professor Ci Ji Lim, whose recent work is highlighted in this publication. Using cryo-EM to capture images of DNA replication in action, Ci Ji's research

gives new insights into the function and structure of enzymes essential to the process.

To briefly note to friends of the 1.1 GHz NMRFAM, solid state NMR spectrometer received by Professors Chad Rienstra and Katherine Henzler-Wildman as part of the NSF-funded Network for Advanced NMR (NAN) is now at field after an initial failed installation in July, return of the instrument, and offsetting benefit of recovery of a large fraction of the valuable liquid helium used for cooldown into the campus recycling utility. I am appreciative of all the individuals who have contributed to this success. Check the News section of our website in the new year for more information.

Please applaud the awards received by members of our community beyond those mentioned above, including the selection of Assistant Professor Judith Simcox as a Howard Hughes Medical Institute Freeman Hrabowski Scholar and Assistant Professor Amy Weeks as an International Protein Society Young Investigator, and the election of Professor Aaron Hoskins to the Board of Directors of the RNA Society. Aaron and Professor Christina Hull from the Department of Biomolecular Chemistry, along with their graduate students Megan McKeon and Sierra Love, won a Badger Challenge Award to carry out collaborative cancer research.

We also recognize prestigious awards received by several postdoctoral fellows. Collin Borcik received a National Institutes of Health Ruth L. Kirschstein Postdoctoral Fellowship (F32), Claire Palmer received a US Department of Agriculture National Institute of Food and Agriculture Fellowship, and Daniel Parrell received the Great Lakes Bioenergy Research Center Outreach and Service Award.

In our news about graduate students, twenty students in the Integrated Program in Biochemistry received M.S. and Ph.D. degrees this year. Graduate student Saeed Roschdi was selected as a Louis and Elsa Thomsen Wisconsin Distinguished Graduate Fellow by the College of Agricultural and Life Sciences (CALS), and our graduate students received many other competitive awards including five NSF Graduate Research Fellowships and other fellowships from UW Foundation endowments established by our generous friends to support the mission of the department.

The department thrives on the diversity, skills, and commitment of its members, alumni, supporters, and friends. As outlined above, we are dedicated to excellence in all facets of our lives. If you can, please join us by becoming a donor to the Department of Biochemistry. Our need for your support in these challenging times is greater than ever, and so we request your consideration of generosity in three areas: named fellowships for support of students across all genders, ethnicities, and need levels; named professorships to support the innovative work of the faculty; and, named opportunities to support our nationally-recognized facilities.

If you are so inclined, please contact us, or the University of Wisconsin Foundation, about your interests in supporting a brighter future for the department. Details on how to contact the department can be found at the front of this newsletter, and details for contacting the Foundation are on page 29. We encourage you to interact with us, and we look forward to receiving your comments, advice, and referrals as we continue to affirm our commitment to excellence. Also, let us know if you would like to see a topic featured in a future edition of the newsletter.

Our doors are open now, and if you are in Madison, please come by for a visit. We look forward to staying connected in the year ahead, and we send warm wishes for 2024.

Profile: Snehal Chaudhari

This August, we welcomed <u>Snehal</u> <u>Chaudhari</u> to the faculty as an assistant professor.

The Chaudhari Lab will investigate relationships between the gut microbiome and metabolic diseases. Another focus of the lab will be how gut bacteria research can be used to identify and inform therapeutic treatments.

Chaudhari, a cell biologist by training, sees the Department of Biochemistry as the perfect venue for her research to grow. "Biochemistry is a fundamental part of cell biology," says Chaudhari, "it is an interplay of small molecules, of proteins, and how they affect the health of a cell."

What excites Chaudhari the most about joining the department and the UW–Madison community are the opportunities for interdisciplinary collaboration — within the department, in her lab, and across campus.

"I did my graduate work at state schools," says Chaudhari. "I see the power of being in a state school like UW-Madison, where we have the freedom and resources to follow the science, wherever it may take us. Having access to experts from so many different fields, that's its own form of scientific freedom."

The value Chaudhari places on multidisciplinary research stems in large part from her own multifaceted education. Chaudhari grew up in Mumbai, India and completed her undergraduate studies in biotechnology close to home. She then moved to the United States, where she earned a M.S. from Pennsylvania State University and a Ph.D. from the University of Georgia. Along the way, her interests shifted from plant physiology to immunology to cell biology as she was exposed to more modes of research and inquiry.

In Chaudhari's graduate program at the University of Georgia, students

arrived with a general idea of their areas of interest but had the opportunity to explore new interests during lab rotations. It was during her lab rotations that Chaudhari first encountered research with *C. elegans* — a roundworm model organism upon which she would eventually build her doctoral research.

"I focused on host-microbiome interactions at a basic level using *C. elegans*," recalls Chaudhari. "I studied how the bacteria *E. coli*, when consumed by *C. elegans*, affects metabolic pathways in germ stem cells. I found that *E. coli* strains produce unique small molecules that can influence stem cell signaling and aging in *C. elegans*. This was my first research publication as a Ph.D. student, and years later, still one of my favorite discoveries."

Working with *C. elegans* opened the door for Chaudhari into research that could explore fundamental elements of host-bacteria relationships using *in vitro* cell culture and *in vivo* models. After graduate school, Chaudhari continued to investigate bacterial interactions as a postdoctoral trainee at Harvard Medical School, where she studied the role of the gut microbiome in metabolic diseases such as diabetes, obesity, and liver cirrhosis.

Now, her research integrates small molecule chemistry and cell biology to further explore host-microbiome interactions. The Chaudhari Lab will take a multidisciplinary approach toward exploring the microbiome, incorporating analytical chemistry, genetic engineering, cell culture assays, and *in vivo* model systems.

"I want to investigate how our gut microbiota biochemically impacts us," explains Chaudhari. "What small molecules are bacteria producing, and how are these impacting the host? What signaling pathways are involved in eliciting host responses? How are these



Snehal Chaudhari

interactions contributing to health and disease?"

Along with her expertise, Chaudhari brings to her lab — and the students she will advise — a passion for discovery. She says, "I love the thrill of discovery, and this is a very exciting time to be in the microbiome field. Groundbreaking discoveries have been made in microbiome research in the past decade, and I believe there is room for making many more. I want to have an interdisciplinary lab where we integrate different types of skills and research platforms to explore the microbiome in new ways."

Profile: Monica Neugebauer



Monica Neugebauer

This September, we welcomed Monica Neugebauer to the faculty as an assistant professor.

The Neugebauer Lab will focus on the discovery and evolution of enzymes to unlock their catalytic capabilities for use in biochemical reactions.

"This university is an ideal place for interdisciplinary research, which allows us to tackle problems in new and innovative ways," says Neugebauer of her decision to join UW–Madison. "There are strengths across many departments — including biochemistry, chemistry, and chemical engineering — and there is a collaborative and collegial environment." Neugebauer will also be an affiliate in the Department of Chemistry.

Neugebauer majored in engineering at MIT before joining the doctoral program in engineering at University of California Berkeley. However, she was always drawn to chemistry. While at UC Berkeley, Neugebauer explored opportunities that would merge her background in engineering with her interest in chemistry, eventually leading her to join a lab group focusing on engineering bacteria and enzymes to

facilitate biochemical experiments and reactions.

"Bacteria have evolved to produce enzymes that give them a survival advantage and do really useful things in nature," explains Neugebauer. "And those enzymes can also be quite useful for humans who are doing chemical reactions that are difficult to achieve with traditional tools and methods. For example, there are enzymes that can make a very selective modification to a molecule, such as removing a single hydrogen and replacing it with a halogen."

Neugebauer was fascinated by the notion that enzymes which exist because they provide an evolutionary advantage to bacteria can also be harnessed for use by humans. As a postdoctoral researcher at the Broad Institute, she began to investigate ways that enzyme evolution could be manipulated beyond what is commonly found in nature to produce new enzymes with desirable characteristics.

"Bacteria haven't evolved for the purpose of producing enzymes that are useful for humans," says Neugebauer, "but there are ways that we can, in a laboratory, encourage enzyme evolution to result in something that's useful for people."

Her work explored how enzyme evolution can be manipulated for the purpose of gene editing, with the goal of therapeutic treatments for genetic diseases.

Now, Neugebauer's work will combine the discovery, evolution, and engineering of new enzymes — especially enzymes with metal cofactors — to establish tools that pave the way for research and discovery. Neugebauer says, "In my lab, I'm interested in using enzymes as tools that can help us study basic biology — how human cells are working — which, in turn, can help us

understand mechanisms of diseases and how we might be able to prevent them."

Neugebauer is also interested in exploring the ways that enzyme engineering can reduce waste, resulting in more sustainable tools for biochemists. "Enzymes can help us improve on the reactions that we can already do synthetically," says Neugebauer. "Using enzymes can sometimes reduce the number of steps in a reaction, which can save money and result in a smaller environmental impact. We can also use enzymes to reduce toxic byproducts or the use of harsh solvents used in reactions."

In addition to her expertise in enzymology and engineering, Neugebauer brings to her work an enthusiastic love for mentorship and research. "I think enthusiasm goes a long way in science," reflects Neugebauer. "Enthusiasm and resilience. Most of the time, research doesn't go right the first time. It's important to be excited about the process and to find joy in trying again."

When Antibiotics Deplete Gut Microbiome, a Gut Pathogen Takes Advantage

The human intestine is home to a diverse ecosystem of bacteria — often referred to as the gut microbiome — that, among many other things, helps to ward off infection. Disruptions to this delicate ecosystem can make way for pathogenic bacteria to proliferate.

In research published in <u>PLOS</u> <u>Biology</u>, associate professor <u>Ophelia Venturelli</u> reveals new insights into how interactions within bacterial communities in the human gut impact our ability to treat a deleterious bacterial infection using antibiotics.

"A lot of antibiotic studies look at how the antibiotic effects the pathogen. But pathogens aren't living in our bodies in isolation," explains Venturelli.

Venturelli and Susan Hromada, who completed her doctoral research in the Venturelli Lab, explored interactions among antibiotics, bacteria found in the gut microbiome, and the bacterial pathogen *Clostridioides difficile*. The pathogen infects the human gastrointestinal system and is difficult to treat with antibiotics. In fact, *C. diff* can proliferate with greater intensity *after* some antibiotic treatments.

"There are studies demonstrating how interspecies interactions among bacteria alter *C. diff's* growth," says Hromada. "But almost nothing was known about how these interactions alter *C. diff's* susceptibility to antibiotics," information that could be useful in designing effective treatments.

"Bacteria aren't always inhibited by each other," says Venturelli, "but it seems as though *C. diff* doesn't compete well with other bacteria. That really impacts *C. diff's* ability to cause severe infection."

While antibiotics can help to control bacterial infections, they may also inhibit the growth of beneficial bacteria in the gut, making the environment more suitable for *C. diff*.

This is what Venturelli and

Hromada found in their study by examining how *C. diff* responds to two different clinically relevant antibiotics, metronidazole and vancomycin, in the presence of other gut bacteria. They also used a combination of computational modeling and high-throughput laboratory experiments to identify *C. diff's* response to combinations of gut microbiome bacteria and the presence or absence of antibiotics.

"In the presence of bacteria that are both sensitive to the antibiotic and compete with *C. diff*, we generally see an increase in *C. diff* growth when the competing bacteria are inhibited by the antibiotic," Venturelli says. "The general pattern we see is that most bacterial interspecies interactions seem to promote *C. diff* growth in response to antibiotics instead of sensitizing it."

Venturelli and Hromada also looked closely at how one bacterium, *Desulfovibrio piger* (*D. piger*), impacts *C. diff's* susceptibility to antibiotics.

"When *D. piger* was present, Hromada explains, "*C. diff* could withstand substantially higher concentrations of the antibiotic than when *C. diff* was on its own." This response is due to unique properties of both the antibiotic and *D. piger*.

"Metronidazole is a unique antibiotic. It enters the bacterial cell as a pro-drug, or a drug that is inactive," says Venturelli. "The bacterial cell has to import the antibiotic, and enzymes inside the cell activate the antibiotic."

But antibiotic activation is inhibited by the presence of *D. piger*, which depletes key bioavailable metals in the gut environment, resulting in a metal starvation response in *C. diff*. Without access to these necessary metals, *C. diff* is not able to produce the enzymes needed to activate metronidazole.

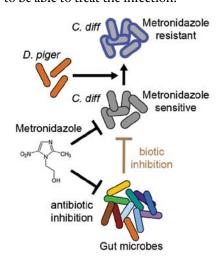
The research points to how crucial it is to study *C. diff* in the context of



Ophelia Venturelli

the gut ecosystem. Venturelli hopes that this work will contribute to a deeper understanding of the microbial interactions that inhibit *C. diff* treatment and, eventually, will lead to new discoveries about interactions that can suppress *C. diff* infection.

"Some day, we may be able to tailor antimicrobial treatments to be specific to the pathogen," says Venturelli. "We'd be able to look at someone's gut microbiome and know what they need to be able to treat the infection."



The presence of diverse gut microbes inhibit growth of *C. diff*. Addition of the antibiotic metronidazole inhibits growth among many gut microbes as well as *C. diff*. In the presence of the microbe *D. piger, C. diff* is no longer susceptible to metronidazole. Image courtesy of Venturelli Lab.

Power of Reactive Molecule Harnessed to Explore Protein Inner Workings



Michael Sussman

Picture a television. There's a screen on the front, some buttons along one side, vents in the back so it doesn't overheat, and inputs for specific cords on the other side. The connections — what makes the television work — are nestled within a black box (literally and figuratively). If you open the black box and line up the television's mechanical components, it may not be obvious how they work together. To truly understand how the television works, you need more information about the purpose of each component and how it functions in concert with other components.

Scientists have faced a similar challenge when studying proteins: the external, structural components are evident, but it's difficult to see 'inside' without pulling the protein apart, which results in biomolecular chains and fragments that no longer fit together.

The order of amino acids — a protein's primary structure — is only part of what determines the shape, and the function, of the protein. Interactions among amino acids result in the twists, folds, and coils that give each protein a distinct tertiary structure which, in turn, determines how it interacts with other molecules.

For example, when a protein is twisted into its three-dimensional structure, the chain of amino acids may

fold in such a way that hydrophobic amino acids cluster together to form hydrophobic pockets. These pockets, protected within the protein's structure and insulated from the environment around the protein, create regions with unique properties.

"In a protein with hydrophobic transmembrane domains, it's not so hard to identify those domains from the primary sequence," explains Benjamin Minkoff, a scientist in the Sussman Lab. "But if you're trying to identify other patches in a protein that have hydrophobic characteristics, they aren't always as obvious. The interplay of the amino acids means that, without empirical evidence, it's incredibly hard to predict where hydrophobic pockets or regions actually are."

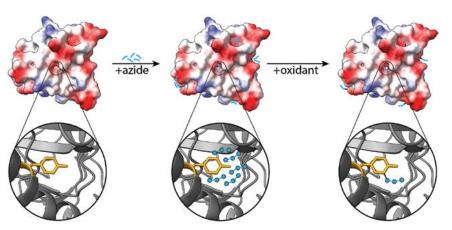
The Sussman Lab is developing tools that will provide researchers with the evidence needed to pinpoint the exact location of hydrophobic microenvironments within a protein's folds without damaging the protein.

Simply adding one more nitrogen atom to N_2 gas results in the solid, charged compound called azide. Thanks in part to its reactivity, azide is

widely used in chemical and biological research. In research published in the *American Chemical Society Chemical Biology*, the Sussman Lab identified a new use for this compound: the small, negatively charged azide molecule is attracted to proteins' hydrophobic microenvironments and can be used to locate and identify these hydrophobic regions without disrupting the structure of the protein. A form of azide called an azido radical can establish stabilizing covalent bonds with amino acids around hydrophobic regions.

The scientists explored azide's affinity for binding to hydrophobic microdomains in model proteins as well as dozens of proteins in the model plant organism, *Arabidopsis thaliana*. Their new research indicates that the radicalized molecule's ability to bind to proteins is more universal than was previously understood.

Findings will be investigated further to determine whether there are residues or other byproducts of the binding process that might impact how therapeutic drugs interact with proteins, with an eye toward using azide to assist in drug delivery pathways.



This image depicts, from left to right: a region in a protein, azide added to the protein's environment, azide attaching to a binding site within a protein. Image courtesy of the Sussman Lab.

Midwest Center for Cryo-Electron Tomography to Expand

The UW-Madison is home to the Midwest Center for Cryo-Electron Tomography (MCCET). Since this NIH-funded center opened in 2021, UW has become a national epicenter of cryo-electron tomography (cryo-ET) and innovative biomedical and life sciences research using cryo-ET techniques.

MCCET will now be expanding, thanks to \$15 million in supplemental funding from the National Institutes of Health <u>Transformative High-Resolution Cryo-Electron Microscopy Program</u>. The program supports broadening access to cryo-ET for biomedical researchers.

"The goal with this funding is to provide center users with access to instruments that are at the technological cutting edge and to extend the range of workflows available," says professor Elizabeth Wright, who directs MCCET. "The new instrumentation will allow us to increase throughput in the center by providing solutions for faster sample milling with less sample damage, and improved imaging for large cell, organism, and tissue samples."

MCCET is the central Hub for the National Network of Cryo-ET Centers, which consists of four cryo-ET research centers across the United States. The Network currently supports 148 research projects from about 350 principal investigators and their trainees, and receives requests from 15-30 new projects each quarter. "This expansion is essential for MCCET and for the entire network," says Wright. "With the existing microscopes running at full capacity, it would take approximately 2.8 years to collect the necessary cryo-ET data for all current projects."

The supplemental funding from the NIH will support recruiting new staff at MCCET, as well as installing advanced microscopes, other equipment, and

software updates. These additions — which will allow the center to process samples with greater efficiency and improve image quality and quantities — have the potential to reduce wait time for researchers and will help expand currently available workflows with newer research strategies. Construction on the new spaces is expected to begin in early 2024.

Cryo-electron microscopy (cryo-EM) allows researchers to study biological molecules and cells at ultracold temperatures, stopping biological processes in action and capturing images of cellular structures frozen in time with details revealed at the size of single molecules of water. Through cryo-electron tomography (cryo-ET), researchers can examine the three-dimensional structures of organisms, cells and organelles, and viruses in their native states by using a computer to reassemble images from 2D slices taken from the frozen sample at many different angles.

MCCET's staff and equipment provide researchers at UW and across the world with support for sample preparation, imaging, and computation, as well as training on these processes. Using these technologies, researchers have studied the structure, function, and processes of biomolecules and biomolecular phenomena on the smallest scales, from protein structure, bacterial motility, and mechanisms

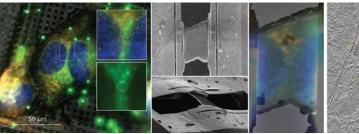


Elizabeth Wright

essential to DNA replication, to virus structure and brain cell morphology.

A core aspect of MCCET's work and that of the National Network of Cryo-ET Centers, which is fully funded through the NIH, is to open the door to discovery by making cryo-ET accessible to all researchers who may not otherwise have access to resources available to scientists at UW–Madison or their home institutions.

"We are extremely grateful to the NIH for their continued support of MCCET, the National Network of Cryo-ET Centers, and members of the cryo-EM, structural biology, and cell biology communities," says Wright. "This additional funding will ensure that we are able to improve the capabilities of our facility, which will mean that MCCET and its staff can reach and help more investigators in need of cryo-ET resources, access, and training."





Precise 3D targeted on-the-fly correlative cryo-iFLM-FIB-milling-ET. Image panel credited to Jae Yang from Wright Lab & MCCET and Veronika Vrbovská from Thermo Fisher Scientific.

New Images Uncover How Enzyme Kicks Off DNA Replication



Ci Ji Lim

Biochemistry researchers have used high-resolution imaging to gain a more nuanced understanding of the structure and multiple functions of an enzyme integral to DNA replication.

As the cells in our bodies replicate, our genetic code is passed from one cellular generation to the next, all while remaining largely unchanged. The process requires a precise and intricate dance among multiple enzymes and between enzyme sub-units.

Assistant professor <u>Ci Ji Lim</u> is interested in learning more about the choreography within one such enzyme: DNA polymerase alpha-primase (Polaprimase for short).

Polα-primase helps to create new strands of DNA by building short strands of genetic material called primers. First, the enzyme attaches to a strand of DNA template and lays down a short length of genetic material called RNA primer. The enzyme then lays down a second length of genetic material, contiguous to the first, called DNA primer. Only when the hybrid RNA-DNA primer is built can DNA replication proceed.

Unlike many other polymerases, $Pol\alpha$ -primase lacks the ability to proofread its own work. As a result, although the RNA-DNA primer may contain mistakes, it establishes a point

from which more accurate polymerases can finish the job of DNA replication.

Last year, the Lim Lab explored Pola-primase's role in DNA replication at the ends of chromosomes. This year, they investigated the steps by which Pola-primase builds RNA-DNA primers. The new research is a collaboration with the lab of Tahir Tahirov, a professor in the University of Nebraska Medical Center.

Scientists now have greater insight into the moment Polα-primase switches from making RNA primer to extending RNA primer with DNA. Their study in *Nature Structural & Molecular Biology* confirms mechanisms that allow Polα-primase to toggle between its sub-units to build RNA-DNA primer and also provides insights into how the enzyme stops building primer and detaches from the DNA template.

New images of Pol α -primase, collected using cryo-electron microscopy (cryo-EM) single-particle analysis, confirm a prevailing hypothesis: the region of Pol α -primase responsible for building the RNA primer remains attached to the primer even as the DNA portion of the primer is established.

Lim says these results suggest that the enzyme holds on to the RNA primer while building the DNA primer as a failsafe. "Think of a safety harness for a rock climber," says Lim.

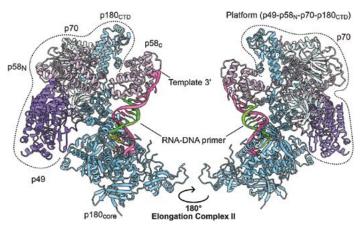
If the DNA polymerase subunit of $Pol\alpha$ -primase becomes dislodged before sufficient DNA is added to the primer, the incomplete primer, which remains bound to the enzyme, can rapidly be reengaged by the polymerase.

"We found that Polα-primase continues to hold on to the RNA primer while the enzyme is extending the primer with DNA," explains Lim. "There have been predictions about this, but we didn't have direct evidence. Now, we've caught it in action."

The researchers also hint at how Pol α -primase stops building RNA-DNA primer before handing its work off to other components of the DNA replication process.

These new findings prompt Lim and his collaborators to ask even more questions about how the Polaprimase machinery works during DNA replication. For Lim, this is exciting territory.

"We want to know how this multifaceted enzyme acts and interacts through every stage of action," says Lim, "to understand how genetic information is copied during DNA replication in cells."



Cryo-EM structural snapshot of human DNA polymerase alphaprimase machinery self-terminating its primer DNA elongation. Image courtesy of the Lim Lab.

James Ntambi Reflects on Decades of Study Abroad

Professor James Ntambi has brought groups of undergraduate students to his native country of Uganda since 2002. The Uganda Program (Nutritional Sciences course 421) has gained notoriety among biochemistry majors, and students in scientific disciplines across the UW–Madison campus. Students receive global health experience credits for their participation.

Ntambi's research, which focuses on the genetic regulation of metabolism in health and disease, was strongly influenced by his firsthand observations of malnutrition and other food-related illnesses. He has paved the way for students to gain their own observational understanding of metabolic disorders while connecting with communities through study abroad programs he established at UW with John Ferrick, former CALS associate director of international programs, and Solomy Ntambi, a pediatric social worker at American Family Children's Hospital. More than 600 students have participated in these programs, which give them opportunities to explore public health, agriculture, medical care, and public policy — fields in which biochemistry majors often seek careers after graduating — in between semesters.



James Ntambi

Ntambi, who conducted research in Kenya and Tanzania after completing his undergraduate work in Uganda, first came to the United States as a Fulbright Scholar at Johns Hopkins University in 1980, where he completed his graduate and post-doctoral work in biochemistry and molecular biology. He joined UW–Madison 1992. Renata Solan, science writer for the Department of Biochemistry, talked with Ntambi about his more than thirty years at the university and his more than twenty years of experience building experiential programs.



: What inspired you to bring students from Wisconsin to Uganda?

When I first came to this department, I taught a class on metabolism. We covered metabolic pathways that lead to noncommunicable diseases, such as diseases due to protein deficiencies or high-fat and high-carbohydrate diets. There are diseases still prevalent in many parts of the world that are not common here in Madison. The impact is so different when [students] see it for themselves, rather than reading about it in a book. So, I set up a study abroad program which could offer students experiences outside the classroom and the lab. The students who come on our trips have gained a more global perspective about how researchers think about metabolic diseases and how doctors treat the diseases. They also see how communities and doctors are trying to prevent these diseases through agricultural practices, nutritional interventions, and scientific education.



: How does your research intersect with, and inform, the Uganda study abroad programs?

The research I do on metabolism addresses some noncommunicable diseases like diabetes, hypertension, obesity, fatty liver disease, and so on. In some communities in Uganda, people are developing these metabolic diseases. The knowledge we have been building in my lab helps to develop strategies to manage and prevent metabolic diseases. I bring this knowledge with me when I visit [Uganda], and I work with doctors and health care professionals. Together, the students and people in the communities we visit learn about disease prevention strategies.

Continued on next page







From top to bottom: students learning alongside community members; hands holding fruit from a coffee plant; visiting students with local community members. Photos courtesy of James Ntambi, taken by students during the winter and summer programs.

Q: You have been taking students to Uganda for decades. How has the program changed over time?

Originally, the program focused on building partnerships with other universities, professors, and researchers. But it is communities in rural areas, not the universities, that are most impacted by the health and agricultural systems we are visiting. Now, most of our activities are community-based. We visit agricultural fields and stations, we visit nutritional clinics, we go to schools, we look at places where people suffer from common metabolic diseases, like diabetes and hypertension. We get an opportunity to build relationships. We learn from them; they learn from us. And every time we go back, we check on what we did last time, see if the activities were impactful, and make changes based on what the communities need.

• What can students expect to do during the program in Uganda?

The summer students work and observe doctors and other health care providers at community-based mobile clinics — which the program has helped to set up — and talk to patients. They see how the doctors there diagnose medical conditions and what treatments they turn to. The winter students see how agricultural practices and availability of food impacts health and wellness. We also help to set up small home gardens. Even if someone doesn't have much room, they can use sacks as containers to grow vegetables and students see how, in the smallest of spaces, families can grow enough vegetables to feed their children for weeks.

A goal of the trip is for students to see how different systems — health, nutrition, agriculture — are all connected. For example, we visit markets and farms and every year we think about why, if there is plenty of food, do kids become nutrient deficient? Why do they suffer from nutrition-related diseases? Then we visit the nutritional clinic in the country's major referral hospital, as well as a community nutrition clinic where we sit down with the children and their mothers and talk about diet, about what food is available. Through these conversations, our students end up really learning about culture, how people interact with each other, and the kind of problems present in the communities.

Every evening, we debrief and talk about what we have learned. We compare what happens here in the U.S. and Uganda, the ways our health care and agricultural systems are different. There are ways that our systems are better and ways that they're worse. The students learn to think about diversity in health care and agriculture, about community and collaboration.

: How does the program enhance the students' coursework and labwork at UW?

The program is really about relationships and how we communicate with each other, and the impact that can have. Students make connections between what we're seeing and the biochemical mechanisms behind the metabolic diseases we study. They start to think about our own health care system and the balance of disease prevention and treatment. The students and the communities both learn about the role nutrition plays in preventative care. People used to think that nutrition was just eating food. We're learning and teaching about how the food you eat is handled by your body and how that impacts your health. The knowledge our students gain in the classroom, the work we do on the bench, all of that is translated into a common language to educate people about food, nutrition, and health.

How have you seen the program impact your students beyond their time in Uganda?

Many of the students go into careers in public health fields. They start thinking about their futures in medical and nutritional sciences in terms of global health and global agricultural issues.

Some students are so inspired that their work in Uganda continues after graduation. They go back and visit the villages where we worked. They see opportunities to do more. They want a continuing relationship. A group of students started the Village Health Project to install clean water systems in Uganda. Access to clean water can be a major barrier to health. The students began it as a student organization, and now it's also a nonprofit.

O: What do you see for the future of this program?

I'd like to stay involved and help to keep it going after I retire. I would like to keep building opportunities for all students to go to Uganda if they want to. In Biochemistry, we can award some students with travel funds to come on the program, but not every student has the resources or support to pay for the program.

The experience is valuable to students, and since we've worked in these communities for many years, the trust is there. We work with leadership, with health care providers, with farmers, and with community members. They see that we are coming from UW–Madison, and they are excited to work with us. We've taken the time to build those relationships. People know who we are and know they can trust us. I want future students to have the opportunity to build off that.

Student Voices

"The trip prompted me to kind of take more of an interest in holistic perspectives on health, which is something that Professor Ntambi really emphasized. After the trip, I added a certificate in global health and expanded my coursework to include more classes on health and nutrition policy, as well as agriculture and environmental policy."

Brooke Hartwig: August 2022 Major in neurobiology Certificate in public health

"I was unsure if medicine was the right career for me, and then I went to Uganda. We met with one of the doctors who was also doing public health work, and I could see myself doing something similar here in America. I want to practice medicine like that — balancing public health work with treating patients."

Jaskiran Kaur Sandhu: August 2022 Major in biology Certificates in health policy and global health

"The Uganda Program is really tailored to biochemistry majors because of Professor Ntambi's expertise. I wasn't as familiar with thinking about agriculture in the context of biochemistry, so that was a really cool aspect of the trip. And, I got to hear how people from other disciplines experienced each day. We would have an opportunity to ask and answer questions about what we'd seen, what we'd experienced."

Beth Young: January 2023 Major in biochemistry

"I do research in the Ntambi Lab on genes related to diabetes. The disease can be so deadly and it affects so many people, not only here but in Uganda and all over the world. In Uganda, I had the opportunity to see how doctors are treating some of the diseases that we study in our lab and how the diseases impact people's lives. I am returning to Uganda this winter to learn more about how nutrition and agriculture are linked to human health."

Jacqueline Miller: August 2022 and January 2024 Majors in biochemistry, chemistry, and Italian

Read more

Madison Startup Offers New Tools for Analyzing Protein Synthesis



Erica Shu, Ph.D.

When Erica Shu was beginning her doctoral research at Cornell University with advisor Shu-Bing Qian in 2016, the process to acquire the data she needed was slow and laborious, and results often weren't reproducible.

Shu, now teaching faculty in the Department of Biochemistry, was studying how and why protein synthesis can go awry. Dysregulation in protein production can have profound effects on human health, leading to diseases such as diabetes, heart disease, and cancer.

Shu was examining ribosomes, organelles that translate messenger RNA (mRNA) into the nucleotide chains that make up proteins. Through a technique called ribosomal profiling, Shu sought insight into how protein synthesis is initiated and regulated — with an eye toward developing therapeutic tools to re-stabilize protein synthesis that has gone off-kilter.

"It took a lot of work," Shu says. "It was time-consuming and the data was not that reliable. We decided to figure out our own ways to improve the system." In addition, the available technology required such large samples that analyzing tissue from patient biopsies wasn't always possible.

Driven by a demand in academia and industry for more robust ribosomal profiling tools, Shu and Qian worked together to develop Qez-seq, a technology that completes analysis of a ribosomal profile in just six hours (shortening the processing time by about 75%), at greater accuracy and with smaller samples than ever before.

The pair founded <u>EzraBio</u>, Inc., a biotechnology startup, to make Qez-seq available to researchers. The company has two offices, one in Ithaca, NY, and the other in Madison, WI at Forward BIOLABS.

Shu and Qian see in EzraBio, Inc. the potential to progress the field of protein synthesis analysis and support the development of future therapeutic treatments. Now, EzraBio, Inc. is expanding.

Shu received funding from the UW–Madison Discovery to Product (D2P) State Economic Engagement and Development (SEED) program. The SEED program supports growth of technology-based startup companies, evaluating projects on their innovation and potential benefits to Wisconsin's economy. Funding through the D2P SEED program is matched by support from the Wisconsin Economic Development Corporation (WEDC).

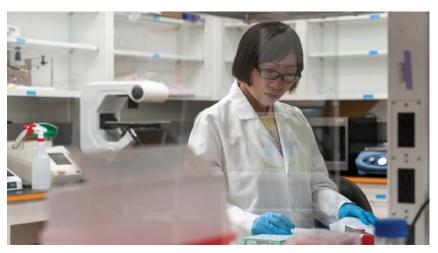
"This grant is special because of its focus on the Wisconsin economy," says

Shu. "Applying for this grant meant thinking about forming partnerships and collaborations. I'm thinking about how to support local clients and how to get our supplies from local suppliers."

As the company expands, Shu also plans to establish career-building employment opportunities for recent college graduates. Shu, who teaches an introductory course for first-year biochemistry students and a capstone course for senior undergraduates, firsthand UW-Madison witnesses students' progress during their time at the university. She says that EzraBio, Inc. can supplement local employment opportunities for biochemistry majors and keep knowledge and skills in the state of Wisconsin.

"I work with students at the university, and I hope I will be able to hire people who just graduated. I'd like to hopefully assist students with opportunities that will help them later in their career," Shu says.

Shu hopes that, as Madison's role as a growing hub for biotechnology continues to grow, so will EzraBio, Inc., making their ribosomal profiling technology readily available to researchers around the country.



Erica Shu works in EzraBio, Inc.'s lab space at Forward BIOLABS in Madison, WI.

Aaron Hoskins and Christina Hull among the 2022 Badger Challenge awardees



Christina Hull, Megan McKeon, Sierra Love, Aaron Hoskins, from left

The Badger Challenge, an annual fundraising race held each fall, was established in 2016 to support ground-breaking investigations in cancer research at UW–Madison. All proceeds raised through the race fund cancer research initiatives. A Badger Challenge Award started supporting two doctoral students, Sierra Love (Hoskins Lab) and Megan McKeon (Hull Lab) this year.

Their collaborative research will explore potential new treatments for fungal infection by uniting two labs with seemingly unrelated approaches. The Hoskins Lab typically focuses on pre-mRNA splicing — an essential step in eukaryotic gene expression — and its relationship with human diseases. The Hull Lab, in the Department of Biomolecular Chemistry, works on identifying mechanisms for human fungal pathogen germination and growth.

But the collaboration was a natural fit. "My lab was initially looking for things that could treat human cancers and the Hull Lab was looking for things that can be directly used as antifungal drugs," says Hoskins. "Research in both of our labs was approaching the same question — is RNA splicing a good target for antifungal therapy?"

Like bacteria and viruses, fungal spores are all around us. While it is

rare for a healthy person to become sick from breathing fungal spores, in people who are immunocompromised, some fungal spores can cause serious, and potentially fatal, infection. Cancer patients undergoing chemotherapy are often given prophylactic antifungal treatments to prevent such infections, but antifungal treatments pose their own toxicity to humans, and long-term treatment can result in fungi developing drug-resistant mutations.

The Hoskins and Hull collaboration is exploring possibilities for more effective and less toxic antifungal treatments using RNA splicing inhibitors.

When RNA splicing is inhibited or otherwise goes awry, it can result in cell death or illness in the impacted organism. This can be exploited for medical treatment, as splicing inhibitors can be used to target specific pathogens. Preliminary research out of the Hoskins and Hull Labs suggests that splicing inhibitors can inhibit germination and growth in *Cryptococcus* — a fungus that causes fatal meningitis in humans — and that splicing inhibitors may also work in concert with current antifungal drugs to further protect from infection.

The new research builds off these findings to examine how multiple pathogenic fungi respond to splicing inhibitors alone and with the aid of antifungal drugs. "This project promises to provide critically needed treatment options for cancer patients and identify antifungal agents for broader use as fungal infection rates continue to rise worldwide," says Hull.

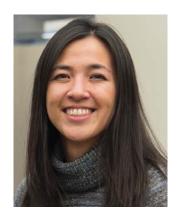
The complementary skillsets that Love and McKeon have developed at UW–Madison are essential to this research. McKeon's research looks at how fungal spores are formed, how they mature, and how they germinate. Love, meanwhile, has been studying RNA splicing inhibition. She explains, "My role in this project will be doing a bunch of drug screenings" to learn more about how *Cryptococcus* growth and proliferation respond to a combination of splicing inhibitors and known therapeutic antifungal drugs.

Their partnership arose from exploring interdisciplinary approaches to scientific inquiry. "The [graduate] programs provide a lot of opportunities for collaboration and professional development," adds Love. "That's really what science is about. Nothing happens in a vacuum."

The Badger Challenge Award also provides Love, McKeon, and their research advisors with an opportunity to build on their skills and try something new. "It's definitely a new direction for us," says Hoskins. "We've been thinking of inhibitors of RNA splicing for a while now, but the antifungal approach is something that I never thought about before we started getting the data in, and it's something my lab wasn't funded to do, either."

"The Badger Challenge Award has been fundamental in starting up a collaboration that we never expected in the first place," says Love. "Getting projects like this off the ground can have a big impact if you're given the opportunity to see where it can go."

Judith Simcox Named HHMI Freeman Hrabowski Scholar



Judith Simcox

If you walk into the office of assistant professor Judith Simcox you're likely to find that she's not alone. This is because Simcox values mentorship and inclusive science as much as she does the ground-breaking research coming out of her lab.

"I want to radically shift the way we do research," says Simcox. "And that's not just in the discoveries that I'm hoping to lead; it's how we do community-based research and how we include communities in that research."

Simcox's research seeks to fill in gaps in knowledge — holdovers from an era when biomedical research focused almost exclusively on men of Western-European descent — about relationships between lipids and cardiovascular disease. Current medical approaches for controlling cardiovascular disease are not equally effective across populations, due in part to the many and varied causes for disease. Without global knowledge about which lipids are associated with cardiovascular disease in a diversity of populations, preventative care, diagnosis, treatment are less effective.

Through mass spectrometry, which can measure hundreds of thousands of lipids in the plasma of blood samples, researchers in the Simcox Lab studies previously under-explored lipids, some of which may serve as biomarkers for cardiovascular disease, based on biochemical characteristics. From there, Simcox's group can identify similarities and differences — including the lipids' origins, their roles in health and disease, how they're transported, and how they're regulated — in the lipids associated with cardiovascular disease among populations.

"It's truly lipidomics on everyone!" says Simcox, whose lab has already found distinct makeups of lipids among Native American communities in Wisconsin, including collaborations with the Menominee and Oneida Nations.

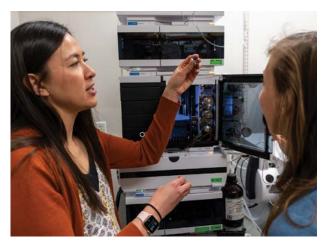
The science behind the research, however, is just one part of what is needed for this research to be successful. The Simcox Lab is working with community members to build relationships, establish trust, and set protocols to ensure that people within these communities benefit from the research. When data for Simcox's work is derived from blood samples collected from citizens of Native American Tribes, for example, the data are ultimately owned by the Tribes themselves, not the researchers.

Simcox is also hiring and mentoring researchers from within communities have been historically overlooked excluded biomedical research. "When people who members the community working on these projects," says Simcox, "it leads to better questions."

Simcox's emphasis on mentorship and inclusive science has been recognized by the Howard Hughes Medical Institute (HHMI), who named Simcox in the first cohort of their Freeman Hrabowski Scholars Program. The new program supports early career faculty committed to advancing diversity, equity, and inclusion in science.

"This award is not just about excellence in science, but also in mentorship," explains Simcox of funding, which is for \$2 million over five years. "We must define excellence by both innovative research and investing in the scientific community. HHMI does a good job at that, and I feel really honored."

With this funding, Simcox is looking to support the next generation of investigators by adding three postdoctoral researchers to her team. Simcox says of junior scientists, "If I could tell them one thing, it's that their perspective is valuable to science and the way we approach things. It has to be matched with the discipline and rigor of the scientific method, but their unique perspective is important to overcome the challenges we are facing in the world."



Simcox and Jessica Davidson, an Integrated Program in Biochemistry graduate student in the Simcox Lab, looking at a vial containing a lipid extract from human plasma before running it on a mass spectrometer.

Vatsan Raman Earns NSF CAREER Award

A ssociate professor <u>Vatsan Raman</u> has partnered with two undergraduate microbiology laboratory classes, integrating support for and from the classes into his research.

"It is like symbiosis; both we and the students benefit from it," says Raman.

Raman and his team of researchers are interested in investigating and replicating strategies that bacteriophages — viruses that infect bacteria — have developed to successfully invade host bacteria and survive.

"Bacteriophages are perhaps one of the longest evolutionary experiments on Earth," says Raman. "The bacteriophages are constantly trying to find new ways into the bacteria and the bacteria are constantly trying to evade infection. They're in an arms race, evolving genetic strategies to outdo each other."

This arms race may offer key insights into combating bacterial infections that are difficult to treat with current therapeutic methods. By identifying and replicating strategies that bacteriophages have developed to successfully invade host bacteria and survive, Raman hopes to produce phages that target specific bacteria, such as pathogenic bacteria associated with human diseases. Such phage therapies could treat bacterial infections without using antibiotics that often affect the human body's entire ecosystem of bacteria.

"The first step is to figure out how the bacteriophage gets into the bacteria and completes its lifecycle without being shut down by the host," explains Raman. "Then, we have to identify obstacles that bacteria have developed to protect themselves from bacteriophage infection, and use synthetic biology strategies to engineer bacteriophages that can counteract the obstacles."

This means examining millions of mutations to determine which ones have the potential to be therapeutically significant — essentially, looking for needles in a haystack.

With such large-scale datasets, however, it is unfeasible for the Raman Lab alone to produce detailed measurements on each potentially beneficial mutation, which can number in the hundreds.

Examining mountains of data became doable thanks to their collaboration with undergraduate lab classes. "We pick out the mutants of interest. The students categorize detailed measurements, and we'll learn a lot from their results," says Raman. The students, in turn, use the Raman Lab's protocol to learn lab techniques and participate in biochemical research.

Raman's innovative means of building integration between education and research earned him a 2023 NSF CAREER Award. The award will support Raman's lab-based and educational outreach work related to bacteriophages.

"The NSF CAREER Award is an endorsement by the scientific community," says Raman, who is also a professor in the Department of

Bacteriology, as well as an affiliated professor in the department of Chemical and Biological Engineering. "It's an opportunity to develop cool, cutting-edge science that is integrated with education and outreach. This integration makes the NSF CAREER award quite unique."

In addition to their collaboration with undergraduate classes, the Raman Lab is developing hands-on tools for gradeschool educators to give lessons on bacteriophages. The educational tools,

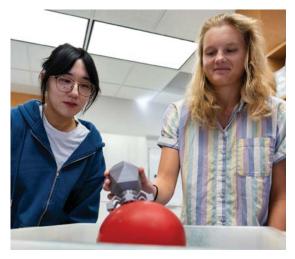


Vatsan Raman

including 3-D printed models of bacteriophages and water-filled balloons to represent bacteria, were piloted with hands-on demonstrations at this year's Wisconsin Science Expeditions.

"The kids loved it," Raman says. And he's looking forward to seeing how these educational collaborations develop and grow.

"Outreach and education are such important parts of the CAREER Award," says Raman, "and now we can build on these ideas and opportunities."



Rebecca Back (left) and Sarah Schmidt-Dannert, graduate students in the Raman Lab, illustrate how a bacteriophage acts on a bacterium, using a demonstration developed by the lab for outreach and public engagement.

Scott Coyle Breaks Through the Noise of Cellular Signaling



Scott Coyle

You're in a room, and everyone is talking at the same time. It's loud and chaotic. You hear many voices, and while you occasionally pick out a word, for the most part it's all noise. You can't identify where each voice is coming from or who it belongs to, let alone understand a conversation.

This is how assistant professor Scott Coyle describes what it's like for scientists to try and pinpoint the location, direction and intensity of signals being sent by individual cells in a multicellular system.

But isolating the signals of individual cells is exactly what Coyle is working to do.

"When we're trying to see what's happening in a cell in real time, we typically use reporter molecules that glow in response to activities of interest happening inside the cell. This includes tracking where a protein is moving, looking to see where a signal is brightest to identify differences in protein synthesis, things like that," explains Coyle, who received a Packard Fellowship in 2020.

This method has significant limitations, though. Coyle explains, when molecules in many cells are glowing in close proximity to one another, it can be difficult to determine the individual cells responsible for the

activity.

His progress towards developing tools that allow scientists to pinpoint individual cell activity has earned him a 2023 National Institutes of Health (NIH) Director's New Innovator Award. The \$1.5 million award supports exceptionally creative early career investigators embarking on innovative, high-impact projects.

Researchers in the Coyle Lab use synthetic biology to design protein circuits — networks of proteins that interact to induce a new function in a cell. These circuits can be designed to help scientists understand cellular processes by emitting structured data about cellular form and function that is comparatively easy to measure and analyze.

Coyle's work aims to broaden the ways researchers are able to ask questions about the dynamic patterns of biochemical activity that cells coordinate. Those patterns impact the development, growth, and health of cells.

The tool Coyle has developed allows researchers to tag individual cells with a protein that emits unique, oscillating signals. These signals can be computationally analyzed to learn about an individual cell's shape, location, and signaling activity. Coyle says the tool is analogous to an FM radio dial, with each cell transmitting data on its own radio signal.

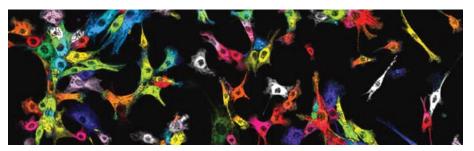
"When you turn on a radio, you don't hear anything until you lock into a specific frequency," says Coyle. "This works similarly — we can lock into a cell's specific frequency. The signals can be isolated from each other so you only hear what you want to hear. This gives us an innovative way to unambiguously assign activity data to individual cells in a multicellular system."

The result is dazzling, brightly colored images (reminiscent of a dorm room poster to the untrained eye) representing a spatial and temporal snapshot of cellular activity and communication, produced by color codes that are assigned to different cell types.

With the NIH funding, Coyle will apply these tools to explore dynamics of cellular signaling pathways in tumors. Many cancers are the result of corrupted signaling pathways and a more nuanced understanding of those pathway disruptions may be a key step in developing targeted treatments.

The prestigious NIH award will also allow Coyle to expand his lab by hiring scientists and acquiring the equipment necessary to continue testing and fine tuning his new technology.

"This technology could define a new paradigm for how we visualize and manipulate living cells," says Coyle. "Biological systems are dynamic, and we need tools that will allow us to explore how cells behave in a biological context."



Individual cancer cells are color-coded based on their signaling activity using a novel circuit technology developed in the Coyle Lab. Image taken by Rohith Rajasekaran.

Elizabeth Wright Named Vilas Associate

Professor and Morgridge Institute for Research investigator Elizabeth Wright was selected as a 2023-2024 Vilas Associate, awarded by the Office of the Vice Chancellor for Research and Graduate Education. The Vilas Associates award recognizes new and ongoing research of the highest quality and significance.

Wright's research lab develops cryoelectron microscopy (cryo-EM), cryoelectron tomography, and correlative imaging technologies. Group members explore a range of topics in bacteriology, cell biology, and virology, including bacterial motility and adherence, human cell regulatory function and dysfunction, and virus entry and assembly.

In addition to her research lab, Wright directs the UW–Madison <u>Cryo-</u>

Electron Microscopy Research Center and the NIH-funded Midwest Center for Cryo-Electron Tomography.

As a Vilas Associate, Wright's research will focus on developing cryo-EM imaging and data analysis technologies that will be used to explore enveloped virus infection, replication, and assembly *in situ*.

"Our cryo-EM and correlative imaging technology developments will transform how we investigate complex viral, cellular, and tissue-level systems, and our work on respiratory syncytial virus [RSV] and human metapneumovirus [HMPV] will provide structural foundations for understanding processes associated with virus assembly and infection to support drug discovery avenues," says Wright.

Recipients of the Vilas Associates



Elizabeth Wright

award receive summer research salary support and flexible research funds over the two years of the award. Winners are chosen competitively by the Divisional Research Committees of the Office of the Vice Chancellor for Research and Graduate Education.

James Ntambi Named ASBMB Fellow

Professor James Ntambi was named a fellow of the American Society for Biochemistry and Molecular Biology (ASBMB). The 20 fellows named in 2023 are recognized for their outstanding commitment to the ASBMB through participation in the society in addition to their accomplishments in research, education, mentorship, diversity and inclusion, advocacy, and service to the scientific community.

Ntambi was elected to the ASBMB Council in 2018 and re-elected in 2021. He has organized ASBMB conferences and symposia for the society's annual meeting, served as a judge for the annual undergraduate poster competition, and brought many

students into the ASBMB community. He won the 2013 ASBMB Award for Exemplary Contributions to Education and serves as an editorial board member of the *Journal of Biological Chemistry*.

"ASBMB encourages people at all career stages to excel through opportunities for networking and interactive meetings, professional development, access to scientific journals, and more. I'm proud to be a member — and now a fellow — of this supportive international scientific and educational organization," Ntambi says.

At UW-Madison, his research group studies the genetic regulation of metabolism in health and disease. In 2002, Ntambi started a study abroad program in Uganda that has impacted



James Ntambi

hundreds of students.

On page 9 you can learn more about the program through our Q&A with Ntambi.

Ophelia Venturelli Receives Early Career & Young Innovator Awards



Ophelia Venturelli

This year, Ophelia Venturelli was promoted to associate professor and received two early career and young innovator awards.

The American Chemical Society (ACS) Synthetic Biology Young Innovator Award recognizes Venturelli for her accomplishments as an early career investigator. She was recognized for her pioneering and interdisciplinary research toward programming the spatiotemporal behaviors of microbiomes, for her commitment to open science, and for her commitment to fostering a more diverse and supportive scientific community.

The Office of the Vice Chancellor for Research and Graduate Education's <u>Early Career Innovator Award</u> recognizes Venturelli for her activities in technology transfer and commercialization. The technologies

created by the Venturelli Lab have broad applicability in human health, animal health, sustainability, agriculture, and other industries.

The Venturelli Lab seeks to elucidate the molecular and ecological design principles of microbial communities using tools from systems and synthetic biology. The tools created by the group enable companies and academic researchers to better understand the complicated ecosystem that microbial communities create.

Research Forward with Philip Romero



Phil Romero

Por many post-myocardial infarction patients, progressive adverse cardiac remodeling occurs, leading to heart failure. Despite multiple drugs to treat heart failure, approximately half of individuals with heart failure die within five years of their diagnosis.

Assistant professor Philip Romero is working on opening new avenues for treating heart failure. He's collaborating with co-principal investigators and other researchers working in Medicine (Timothy Kamp, Department of Medicine), Surgery (Matthew Brown, Department of Surgery), and Radiology (Aaron LeBeau, Department of Radiology) to explore uses of a biotherapeutic hormone, Angiotensin-Converting Enzyme 2 (ACE2).

ACE2 may uniquely blunt the proinflammatory and pro-fibrotic signaling after myocardial infection and reduce the replacement of heart muscle by scar tissue.

Funding for the <u>research project</u> is provided by <u>Research Forward</u>, a competition sponsored by the Office of the Vice Chancellor for Research and

Graduate Education and supported by the Wisconsin Alumni Research Foundation (WARF). Research Forward is intended to stimulate and support highly innovative, collaborative, inclusive, and transformative research at the university.

The Romero Lab studies the design principles of proteins and how they can be applied to engineer new molecular functions. A large part of their work focuses on developing new methods to probe relationships between protein sequence, structure, and function by leveraging advances in DNA sequencing and synthesis, microfluidic screening, molecular modeling, machine learning, and optimization.

Amy Weeks Earns International Proteolysis Society Young Investigator Award

Assistant professor Amy Weeks has been awarded a Young Investigator Award by the International Proteolysis Society. The International Proteolysis Society was founded in September 1999 to serve as a focus for scientists working on all aspects of proteolytic enzymes, their substrates, and inhibitors.

Weeks, who received a Packard Fellowship in 2021 and an NIH Director's New Innovator Award in 2022, focuses on developing tools to map the proteome. As opposed to the full genome, which refers to the entire the collection of genes encoded in DNA, the proteome is the set of proteins encoded in the genes present in a cell at any given time. While the genome is static, the proteome is dynamic.

Through her exploration of the proteome, Weeks develops and applies tools to examine the thousands of modifications made within human cells in the proteins that the cell produces. These tools allow researchers to identify such modifications — and their impacts — in both time and space within the cell. The Young Investigator Award recognizes this work, which bridges the gap between spatial analysis of the proteome and research approaches to identifying protein function.

Weeks's research not only provides insight into biological function within cells, but also explores potential new biomarkers and therapeutic targets for human disease. Her lab draws from diverse disciplines, including protein



Amy Weeks

engineering, chemical biology, cell biology, and proteomics, using a host of different tools and technologies.

Vatsan Raman Funded by WARF Accelerator

A ssociate professor <u>Vatsan Raman</u> and postdoctoral researcher Phil Huss have been awarded funding from the <u>WARF Accelerator</u> for their proposal, "Using ORACLE-engineered Bacteriophages to Edit Microbial Communities."

WARF Accelerator provides resources for inventors, including industry expertise and targeted funding, to help de-risk commercially promising and urgent technologies and advance them closer to the marketplace. The award will help to commercialize the technology developed in the Raman Lab to create synthetic, therapeutic bacteriophages — viruses that infect

bacteria — for treating drug-resistant bacterial infections and microbiomelinked diseases.

The ORACLE (Optimized Recombination, Accumulation and Library Expression) technology can be used to help engineer phages with desired functions by systematically mapping how changes to phage genomes affect how the phage interacts with its host. The result is a library of variants which researchers can use to determine each mutations impact on phage structure and function.

This work builds on the Raman Lab's research, which takes systems and synthetic biology approaches



Vatsan Raman

to understanding and engineering biological systems at protein-wide and genome-wide scales.

Collin Borcik Receives NIH Postdoctoral Fellowship



Collin Borcik

Collin Borcik, a postdoctoral researcher in the Rienstra Lab, was awarded a year-long National Institutes of Health Ruth L. Kirschstein Postdoctoral Fellowship (F32) for his project, "Structural Biology and Biophysics of Alpha-Synuclein Fibrils by Solid State NMR."

Fibrils arising from the aggregation of alpha-synuclein — a protein found in the human central nervous system — are a diagnostic hallmark in several

neurodegenerative diseases, including Parkinson's Disease and Lewy body dementia.

Earlier this year, Borcik was part of a team that identified the structure of alpha-synuclein fibrils in brain tissue samples from people with Lewy body dementia. His F32 project aims to do the same for brain tissue samples affected by Parkinson's Disease with dementia.

Borcik's research uses solid state nuclear magnetic resonance (ssNMR) to learn more about precise structural characteristics of the fibrils.

"I'm looking at correlations among atoms and working outward to determine the structure," explains Borcik. "This allows us to...incorporate precise interactions and close contact among atoms into our structural models."

Borcik is uniquely positioned to carry out this research. UW–Madison is home to the NIH-funded National Magnetic Resonance Facility at Madison (NMRFAM), where Borcik

will be using ssNMR to assess fibril structure of brain samples. NMRFAM is co-directed by Borcik's postdoctoral advisor, Chad Rienstra, and Katherine Henzler-Wildman, both professors in the Department of Biochemistry.

"We have the institutional knowledge and equipment to investigate emerging questions that may translate to clinical impact. The research environment here is perfect for me to investigate my own curiosities," Borcik says.

This work will build on knowledge and techniques Borcik has been developing in the Rienstra Lab.

"Collin has developed new sample preparation methods and innovative strategies for obtaining higher quality experimental data using solid state nuclear magnetic resonance," says Rienstra. "I can't wait to see the outcomes of this research to help us understand how small molecules can be used to diagnose and treat neurodegenerative disease."

Daniel Parrell Wins GLBRC Outreach and Service Award



Daniel Parrell

Daniel Parrell, a postdoctoral researcher in the Wright Lab, won a 2023 Outreach and Service

Award from the Great Lakes Bioenergy Research Center (GLBRC). The award recognizes GLBRC members who have demonstrated a spirit of generosity in sharing science with the public. Parrell serves as co-director of the UW-Biocore's Wisconsin Heights Summer Science Camp, where he was once a camper. He enjoys helping students find their interest in science. "We all interact with science every single day. We all see the world around us and make conclusions based on the things that we see," he says. "It's really impactful to show kids that you don't have to be in a lab coat in order to be a scientist. Scientists are people of all races, people of all genders."

Parrell has also talked with policymakers about the importance of bioenergy research. He helped lead a tour of the Cryo-Electron Microscopy Research Center at UW–Madison for Congressional representatives, showcasing how federal grants are furthering scientific innovation.

"Outreach helps educate the public on the important work that we do at our public universities," Parrell says. "It's important that as scientists, we're able to communicate with the public about what we're doing and how it is affecting them."

Claire Palmer Earns USDA Grant to Explore Sustainable Alternative to Fertilizer

dded nitrogen is essential for A maintaining yield in agricultural systems; however, current nitrogen fertilizer strategies are inefficient and pose negative environmental impacts. Most processes to generate nitrogen fertilizer require natural gas, which is both non-renewable and polluting. What's more, once applied to the field, weather conditions can cause fertilizer to run off the field, making its way into water systems. The result is that the fertilizer does not always support crop growth and can cause environmental damage such as algae blooms in lakes and contaminated drinking water.

Claire Palmer, a postdoctoral researcher in the <u>Venturelli Lab</u>, earned a <u>National Institute of Food and Agriculture (NIFA) award</u> from the U.S. Department of Agriculture to support

her exploration into more sustainable alternatives to current nitrogen fertilizer strategies. The grant will support her research for two years.

Palmer is interested in harnessing the nitrogen-providing power of microbes living in the soil and on corn roots to supply crops with nitrogen, a process described in the 2021 edition of *In Vivo*. She will be studying interactions within the community of microbes living around the roots of corn plants and investigating how these interactions impact the nitrogen available to the plant. Her goal is to identify and design "microbial mixtures" which could be applied to soil as a sustainable alternative to current nitrogen fertilizer options.

"I'm really excited to be working on greener alternatives to current fertilizers strategies," says Palmer. "I've always been



Claire Palmer

interested in how we can use microbes to solve problems and build more sustainable practices, so setting up this project in the Venturelli Lab has been a joy. This was a new project in the lab when I started two years ago and it's very affirming to hear from the reviewers at NIFA that they're excited by my ideas."

Saeed Roschdi Awarded Wisconsin Distinguished Graduate Fellowship

aeed Roschdi, a graduate student in the Butcher Lab, was awarded a 2023-24 Louis and Elsa Thomsen Wisconsin Distinguished Graduate Fellowship from the College of Agricultural and Life Sciences (CALS). The year-long fellowship was established in 1999 by the estate of Elsa Thomsen to support CALS graduate students who demonstrate excellence in research.

Roschdi explores the structure and function of repeating sequences of RNA known as pUGs (poly-uridine-guanosine sequences). In a paper published last year, Roschdi, Butcher, and collaborators revealed a unique folding pattern formed by pUG RNA sequences. Using roundworms as a model organism, they confirmed that, when properly folded, pUGs function as part of a "silencing pathway" which

turns off certain genes, preventing those genes from being expressed.

Roschdi is spending his final year of graduate school diving deeper into the roles pUGs play in roundworms, as well as other species — including humans. "What's interesting about these repeats," says Roschdi, "is that they're highly abundant in humans but we don't fully understand their roles. Originally, many scientists thought that they weren't structured at all because it's such a simple repeat. Now, we've been able to solve the structure and we know that it is conserved across many species, which makes us think even though we don't know exactly what it's doing, more information will lead to important connections about their function."

He hopes his research will offer new insights into additional roles pUGs



Saeed Roschdi

may serve in humans. Roschdi says, "In the past year our paper was released, and there has been more understanding about the role this structure plays in regulation. And we think there will be more."

IPiB Degrees 2023



Alexander Duckworth (Keck) Ph.D., March 2023



Jonathan Tai (Pagliarini/ Henzler-Wildman) Ph.D., March 2023



Emma Goguen (Brow) Ph.D., April 2023



Nina Jocic Bonde (Cox & Keck) Ph.D., May 2023



Ahlan Sabah Ferdous (Kimble) Ph.D., May 2023



Thuong Ho (Merrins) Ph.D., May 2023



Anthony Meger (Raman) Ph.D., May 2023



Laura Steenberge (Pagliarini/Fan) Ph.D., May 2023



Yunyun Zhu (Coon) Ph.D., May 2023



Yu Bao (Landick) Ph.D., July 2023



Brian Carrick (Kimble & Wickens) Ph.D., July 2023



Anthony Meza (Buller) Ph.D., July 2023



Iryna Pustova (Audhya) Ph.D., July 2023



Debayan Chaudhury (B. Fox) M.S., Aug 2023



Raghav Jain (Simcox) Ph.D., Aug 2023



William Kasberg (Audhya) Ph.D., Aug 2023



Lillian Miller (Denu) Ph.D., Aug 2023



John Ahn (Coyle) Ph.D., Nov 2023



Hugo Lee (Engin) Ph.D., Nov 2023



Expery Omollo (Landick) Ph.D., Nov 2023

Degrees Dec. 1, 2022 - Nov. 30, 2023

Biochemistry Advisor Degrees

Hao-Che Wang (Record), Biophysics **Ph.D.**, August 2022 **Vicky Pappas** (Wright), Biophysics **M.S.**, May 2023

More Honors & Awards

Faculty

Scott Coyle 2023 NIH Director's New Innovator Award

Aaron Hoskins Elected to RNA Society Board of Directors

2022 Badger Challenge Award (with Christina Hull)

Judith Kimble Awarded Emeritus status at HHMI

James Ntambi Named ASBMB Fellow

John Ralph Lifetime Achievement Award at the 2023 International Symposium on Wood, Fiber & Pulping Chemistry

2023 Clarivate Analytics Highly Cited Researcher

2023 Royal Society of Chemistry highly-cited article award for: Guidelines for performing lignin-first

biorefining. Energy & Environmental Science 14: 262-292 (2021)

Vatsan Raman 2023 NSF CAREER Award
Philip Romero 2023 Research Forward Award

Judith Simcox Named HHMI Freeman Hrabowski Scholar

2023 Walter A. Shaw Young Investigator Award in Lipid Research from ASBMB

Ophelia Venturelli 2023 ACS Synthetic Biology Young Innovator Award

Amy Weeks Young Investigator Award by the International Proteolysis Society

Elizabeth Wright Named Vilas Associate

Andrew Buller (Biochemistry Affiliate) 2023 Sloan Research Fellow

Postdoctoral Staff

Collin Borcik Rienstra NIH Ruth L. Kirschstein Postdoctoral Fellowship

Mugagga Kalyesubula Ntambi Received an ASBMB travel award

Claire Palmer Venturelli National Institute of Food and Agriculture (NIFA) Fellowship

Daniel Parrell Wright GLBRC Outreach and Service Award

Graduate Student Awards

Bianca Chavez Lim Denton Award for Graduate Student Excellence in Teaching & Mentoring

Thomas Anderson Kirchdoerfer Sigrid Leirmo Memorial Award in Biochemistry

Roma Broadberry Grant Poster award at the 2023 IPiB Retreat

Alex DuckworthGrantPoster award at the Helicases and Nucleic Acid-Based Machines ConferencePeter DucosGrantWon the Raleigh and Clara Miller Memorial Scholarship scholar award

Max Frenkel Raman American Society of Human Genetics Conference Travel award

Qixiang He Lim Chinese Government Award for Outstanding Self-financed Students Abroad

Vanderbilt-Ingram Cancer Center Genome Maintenance Graduate Student Travel Award

Weill Institute Emerging Scholars Award

Joseph Y. Kim Wright Microscopy & Microanalysis Student Poster Award at Microscopy Society of America 2023

Guy Kunzmann Cantor Selected for Gibco Cell Culture Heroes Program

Silas Miller Raman Best poster award, RosettaCon, Aug 2023

Evelyn Okal Raman Poster award at the 2023 IPiB Retreat

Juan Sanchez Wright Outstanding poster award at Bacterial Locomotion and Signal Transduction

Graduate Student Fellowships

Thomas Anderson Kirchdoerfer William H. Peterson Fellowships in Biochemistry

Roma Broadberry Grant William R. & Dorothy E. Sullivan Wisconsin Distinguished Graduate Fellowship

Merissa Brousseau Henzler-Wildman William H. Peterson Fellowships in Biochemistry

Chih-Chia (Eden) Chang Coyle Dr. James Chieh-Hsia Mao Wisconsin Distinguished Graduate Fellowship

Bianca Chavez Lim Science & Medicine Graduate Research Scholars (SciMed GRS) Fellowship

Lauren Clark Attie NIH Predoctoral Fellowship

Jess DavidsonSimcoxNSF Graduate Research Fellowship ProgramJulie DuClosVenturelliNSF Graduate Research Fellowship Program

Kyle Flickinger Cantor Stephen Babcock Agricultural Chemistry Research Fellows

Clara FrazierWeeksWilliam H. Peterson Fellowships in BiochemistryBenjamin HardingRienstraWilliam H. Peterson Fellowships in BiochemistryQixiang HeLimWilliam H. Peterson Fellowships in Biochemistry

Kimberly Huggler Cantor Stephen Babcock Agricultural Chemistry Research Fellows
Andrea Hunger Cantor Stephen Babcock Agricultural Chemistry Research Fellows

Christine Hustmyer Landick NSF Graduate Research Fellowship Program

Aysiah Jaeke Cantor NSF Graduate Research Fellowship Program Honorable Mention
Isabella James Simcox Stephen Babcock Agricultural Chemistry Research Fellows

Karli Lipinski Hoskins William H. Peterson Fellowships in Biochemistry

Andres Lira Romero Science & Medicine Graduate Research Scholars (SciMed GRS) Fellowship

Expery Omollo Landick William H. Peterson Fellowships in Biochemistry

Riley Petersen Butcher Arthur B. Michael Fund

Rohith Rajasekaran Coyle Paul H. Phillips Biochemistry Scholarship

Saeed Roschdi Butcher CALS Louis & Elsa Thomsen Wisconsin Distinguished Graduate Fellowship

Johnson Saba Landick NIH Predoctoral Fellowship

Juan SanchezWrightSteenbock Predoctoral Fellowship in BiochemistrySarah Schmidt-DannertRamanWilliam H. Peterson Fellowships in BiochemistryRoss SoensCantorNSF Graduate Research Fellowship Program

Megan Taylor Romero NSF Graduate Research Fellowship Program Honorable Mention

Uzziah Urquiza IPiB Rotator Science & Medicine Graduate Research Scholars (SciMed GRS) Fellowship

Helaina Von Bank Simcox NSF Graduate Research Fellowship Program

Andrea Wegrzynowicz Henzler-Wildman NIH Predoctoral Fellowship

Xiao Lin (Casey) Wong Coyle Natural Sciences and Engineering Research Council of Canada (NSERC) Fellowship

Anna Zmich Buller Arnold E. & Catherine M. Denton Biochemistry Fellowship

Graduate Student Training Grants

Kaitlyn AbeLimMolecular Biophysics Training Program (MBTP)Ethan AubuchonHoskinsChemistry-Biology Interface Training Program (CBI)

Dennis BolshakovCoyleBiotechnology Training Program (BTP)Max FrenkelRamanGenomic Sciences Training Program (GSTP)Chase FreschlinRomeroGenomic Sciences Training Program (GSTP)Ashley HiettHenzler-WildmanMolecular Biophysics Training Program (MBTP)Hunter KrzysikHoskinsGenomic Sciences Training Program (GSTP)

William Leiter Weeks Chemistry-Biology Interface Training Program (CBI)

Robert MejiaFoxBiotechnology Training Program (BTP)Nathan NovyRamanBiotechnology Training Program (BTP)

Undergraduate Awards

Yara AL-Rayyan Alpha Helix Scholarship Award

Tommy GalateoCoyleHonorable mention at the 2023 ASBMB Undergraduate Poster SymposiumVictoria TholkesLim2023 SACNAS National Diversity in STEM Conference Travel Scholarship

Thi Van Tran Alpha Helix Scholarship Award

Biochemistry Mary Shine Peterson Award

Megan Berg Rienstra

Dev Desai

Jihyun Hwang Venturelli

Brad Li

Martin Olson Rienstra
Lars Schimmelpfennig Gellman
Victoria Tholkes Lim







Victoria Tholkes

Biochemistry Undergraduate Summer Research Award

Emma Cushman Senes

Joshua DeRuyter David Givand Sophie Grunder Allison Harris

Peter Hoferle Kirchdoerfer

Jacob Kunkel Niharika Patankar

Hailey Rude Record



Martin Olson

Undergraduate Fellowships

Hilldale Undergraduate Research Fellowship

Megan Berg Rienstra Erika Kay-Tsumagari

Aaron Brekken Hoskins Brad Li Dev Desai Ivy Lucier

Christine Glitchev Niharika Patankar Amory Griffin Easton Prazak

Sophie GrunderLars SchimmelpfennigGellmanPeter HoferleKirchdoerferVictoria TholkesLimAmogh KalyanamNatalie ZepsHoskins



Peter Hoferle

Sophomore Research Fellowship

Tyler Chang Hoskins

Jessica Fernandez John Clinton Merrick II

Mridula Srivathsan Cavagnero



Jihyun Hwang

The 2023 Biochemistry Undergraduate Summer Research Awards were made possible by: Stuart L. Feldman Biochemistry Scholarship Fund, Floyd C. McIntire Biochemistry Award Fund, E. W. Hopkins Fund, Dr. Shang-Chen Pan Fund in Biochemistry, Eric Bey & Amanda Boley Scholarships and Research Fund, Henry A. Lardy Undergraduate Research Fund, Dr. Arthur G. Saponara & Ms. Nijole Saponara. Awardees for whom a lab is not listed perform research in other departments on campus.

We Heard About You

Below are some updates we received from the faculty and other sources.

Have something you'd like to share with us? (You don't need to wait for someone else to tell us.)

Contact: alumninews@biochem.wisc.edu.

Ansari Lab

Devesh Bhimsaria an Assistant Professor at IIT-Roorkee, India.

Christopher Brandon is a research scientist with Clinical Genetics at the New York State Dept of Health Newborn Screening Program. Asuka Eguchi is an Assistant Professor at UC-Irvine.

Graham Erwin will start as an Assistant Professor at Baylor College Dept of Molecular & Human Genetics in Jan 2024.

Debostuti Ghoshdastidar is now an Assistant Professor at the Birla Institute of Technology (BITS-Pilani), India.

Matthew S. Grieshop is a former Hilldale and Biochem scholar now an MD-PhD student at Stanford.

Corey Nemec is a team leader at 10X Genomics.

Jose Rodriguez-Martinez has been granted tenure and is now an Associate Professor at the University of Puerto Rico.

Juan Rodriguez-Molina, is completing his postdoctoral training as the Clare Hall Fellow with Lori Passmore at University of Cambridge, UK.

Attie Lab

Sushant Bhatnagar was promoted to Associate Professor with tenure at the University of Alabama.

Melkam Kebede was also promoted to Associate Professor with tenure, at the University of Sydney, Australia.

Lauren Clark received an F31 Pre-doctoral Fellowship from the NIH.

Charles Opara, a graduate student in Genetics, joined our lab.

Cleland Lab via Ron Raines (Thank you Ron for letting us know!)

Gwen Sowa (Ph.D. 1997; M.D. 2000), Professor of Physical Medicine and Rehabilitation at the University of Pittsburgh School of Medicine, was elected to the National Academy of Medicine.

Covle Lab

Tommy Galateo (undergrad) recently graduated and is working in Amy Weeks' lab while he prepares to apply for graduate school.

Fox Lab

This year, our Dane County Youth Apprenticeship students became undergraduates at outstanding institutions: Ella Lodewyk (Duke University); Kaya Meyers (UC Santa Barbara), Daniel Lee (Johns Hopkins University), Hailey Sieren (UW–Madison).

Henzler-Wildman Lab

Chao Wu is now a Junior Principal Investigator at Shenzhen Bay Laboratory.

Peyton Spreacker successfully defended her thesis and is now a study director at Labcorp.

Kiessling Lab

Jason Gestwicki, Director of the Chemistry and Chemical Biology Graduate Program won the Emil Thomas Kaiser Award from the Protein Society.

Christine Isabella is a senior scientist at Apriori Bio.

Eric Underbakke was promoted to Associate Professor with tenure at Iowa State.

Laura Kiessling was elected to the National Academy of Medicine and received the Breslow Award from the American Chemical Society.

Kimble Lab

Brian Carrick (joint student with Marv Wickens) defended his PhD thesis in July 2023 and will be heading to Cambridge, England in early 2024 for a postdoc at the MRC Lab of Molecular Biology in the lab of Lori Passmore.

After completing her Ph.D. in August 2023, Ahlan Ferdous accepted a postdoctoral position in Seattle with Dr. Jeff Rasmussen, who focuses on understanding tissue plasticity using zebra fish.

After nearly 30 years in the Kimble lab, Peggy Kroll-Conner retired in June 2023 and was awarded emeritus status.

Lim Lab

Benjamin Lusk (a former biochemistry undergraduate and Mary Shine Peterson Awardee) graduated in Spring 2023 and is now a junior specialist researcher at Dave Toczyski lab at University of California San Francisco.

Joana Pashaj (a former biochemistry undergraduate and Hilldale Undergraduate Research Fellow) graduated in Spring 2023 and is now a research technician at the UW Department of Surgery.

Juliet Arzumanyan (a former biochemistry undergraduate) graduated in Spring 2022 and is now studying for her doctorate in dental medicine at the University of Louisville School of Dentistry.

Ntambi Lab

Ayrene McGahee: (former undergraduate) Associate Scientist at Pharmaceutical Product Development (PPD).

Luke Alan Leferes: (former undergraduate) PhD Student, Ohio State University.

Hailey Huff: (former undergraduate) Medical transcriptionist at Allergy & Asthma Associates of Southern California.

Raines Lab

Marcia Haigis (Ph.D. 2002), Professor of Cell Biology at the Harvard Medical School, won the 2023 Samsung Ho-Am Award in Medicine.

Brian Gold (postdoc) is now an Assistant Professor of Chemistry at New Mexico State University.

Brett VanVeller (postdoc) earned tenure in the chemistry department at Iowa State University.

Record Lab

Tom Record will be receiving the 2024 Ignacio Tinoco Award. Record, who retired earlier this year, will be honored at the Biophysical Society's 68th Annual Meeting in Philadelphia.

Simcox Lab

Mae Hurtado-Thiele is a postbaccalaureate with the National Cancer Institute after receiving Cancer Research Training Award.

Siwei Qian is a graduate student in the Biophysics Graduate Program at the University of Wisconsin-Madison.

Jenna Rogalinski was promoted to Technical Sales Representative at Ibidi, and is a cancer survivor after battling leiomyosarcoma.

Gisela Geoghegan accepted a position as a Senior Scientist at AstraZeneca.

Michael Gilpin accepted a Scientist position at Newcomer Supply.

Autumn Chevalier accepted a position as a Pathway Liaison for the Native American Center for Health Professionals.

Raghav Jain accepted a position as a postdoctoral fellow at Pacific Northwest National Laboratories.

Paula Gonzalez was promoted to Associate Scientist at PPD.

Wickens Lab

A very partial list of movements and positions follows, as space permits:

Marv retired at the end of last year, and as an emeritus professor continues to collaborate via discussions with Scott Kennedy and Sam Butcher on a project begun with the discovery of pUGylation by Melanie Preston, now at Promega.

Dave Zarkower and Vivian Bardwell have retired from the University of Minnesota.

Dave Bernstein is now Senior Director, Science and Strategy at Stand Up to Cancer.

Chris Lapointe recently assumed a faculty position at the Hutchinson Institute in Seattle.

Amy Cooke currently on sabbatical at Haverford, will be back in the RNA saddle when she returns.

Brian Kramer now studies neurodegenerative disease in the U Washington.

Jeff Coller moved to Johns Hopkins to become Distinguished Professor of RNA Biology and Therapeutics.

Niki Gray is Chair of Gene Regulation and RNA Biology at U Edinburgh.

Zak Campbell is now a professor at UW-Madison.

Marv would love to hear from any of you who were in the lab at any time. Know you are missed.

Wright Lab

Kai Cai, a former scientist with the Cryo-EM Research Center, is now a cryo-EM specialist in the Beckman Center for Cryo-EM at Johns Hopkins University.

Vicky Pappas, a Biophysics graduate student, has graduated with a master's degree and is working as a research specialist at Northwestern University.





Cross section (*left*) and close up (*above*) from the stately elm tree, Elmer. For more news about the beloved tree, <u>see inside front cover</u>.

In Memoriam

James Adkins

Ph.D. 1961 — Prof. Harper February 2023

Fredrick Anderson

B.S. 1973 May 2019

Dorothy (Lun Wu) Ballou

M.S. 1949 — Prof. Link June 2017

Matthew Bolland

B.S. 1982 March 2023

Valerian Brungardt

Ph.D. 1962 — Prof. Hoekstra January 2021

James Dallman

Generous Supporter Notified April 2023

Emily (Swan) DeLuca

M.S. 1954 — Prof. Anderson October 2023

Philip Erwin

M.S. 1998 — Prof. Reed December 2020

Michael Gilgan

Ph.D. 1965 — Prof. Stahmann August 2023 Michael Green

B.S. 1974 Notified February 2023

James Heath

Generous Supporter June 2017

Robert Janasik

Generous Supporter June 2013

Michael Lauer

B.S. 1977 June 2012

William Maxon

M.S. 1951, Ph.D. 1953 — Prof. Johnson Generous Supporter January 2023

Anthony Norman

M.S. 1961, Ph.D. 1963 — Prof. DeLuca June 2019

Brian Olson

B.S. 2004 March 2023

Leslie Partridge

Generous Supporter March 2022 Frank Reuter

Generous Supporter November 2020

Willis Riesen

Ph.D. 1949 — Prof. Elvehjem April 1998

LJ Sloup

Generous Supporter July 2015

Thomas Soulen

M.S. 1961, Ph.D. 1963 — Prof. Burris July 2015

Kazutosh Ueno

Generous Supporter December 2022

Priscilla Visek

Generous Supporter Notified January 2023

Harry Winter

M.S. 1964, Ph.D. 1967 — Prof. Burris January 2022

David Wisnefske

B.S. 1971 August 2023

Israel Zelitch

Ph.D. 1951 — Prof. Burris March 2023

Our thoughts are with the families of any others in the Biochemistry community who recently passed.

WHAT'S YOUR UW LEGACY?

Start shaping it today by giving from your IRA with a charitable rollover gift.

Giving directly from your IRA is a simple way to contribute for those aged 70½ or older, and can result in tax benefits, even if you don't itemize. As the new year begins, January is a great time to look at your financials for the year and plan charitable giving.

Go to <u>supportuw.org/how-to-give/give-from-ira</u> for more information regarding the Qualified Charitable Distribution, also sometimes referred to as an IRA charitable rollover gift. Be sure to note that it is for the Department of Biochemistry Fund.

If you have any questions regarding Qualified Charitable Distributions, please contact the Gift Processing Team at the University of Wisconsin Foundation by calling 1-800-443-6162 or emailing us at *giving@supportuw.org*.

Gifts can allow us to fund scholarships for undergraduate research and fellowships for graduate students, support international experiences for students, host seminars, build community with our annual retreat, further our research and innovation, and much more.

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Ms. Mary Pat P. Berry

Dr. Larry E. Bockstahler & Ms. Rotraut Z. Bockstahler

Dr. Roger E. Boldt

Dr. Landy E. Bonelli

Ms. Julie E. Brady & Mr. James E. Brady

Dr. Larry M. Brand & Mrs. Regina Brand

Mr. Steven D. Braun & Ms. Amy L. Pollock

Dr. Andrew M. Brugger &

Mrs. Kathleen A. Brugger

Dr. Charles F. Burant &

Ms. Mary K. Treutelaar

Mr. Gregory M. Campbell Dr. Carolyn A. Campen

Ms. Jamie Chermak

Dr. Marie F. Chiang

Mr. Edmund Cueny &

Mrs. Mary Louise Cueny

Dr. Melvin L. DePamphilis &

Ms. Margarete DePamphilis

Dr. Alan M. Easton

Dr. Roderick E. Echols &

Ms. Andrea C. Lewis-Echols

Ms. Marcia M. Elmer &

Dr. Larry C. Mattheakis

Professor David W. Emerich &

Ms. Nila J. Emerich

Mr. Stuart L. Feldman &

Ms. Rebecca R. Feldman

Mr. Marc A. Frahm & Ms. Rebecca A. Frahm

Dr. Charles A. Frolik & Ms. Barbara Frolik

Dr. Haian Fu & Ms. Guo-Hua Wang

Dr. Carl W. Gilbert & Dr. Linda C. Gilbert

Dr. Joshua J. Hamilton

Dr. Qunfang Hou

Dr. Cheryl A. Janson

Dr. Daniel F. Klessig &

Ms. Judith A. Hope-Klessig

Dr. Voula K. Kodoyianni &

Professor M. Thomas Record, Jr.

Mrs. Ann C. Kuo & Dr. Mei-Chang Kuo

Dr. Leon W. LeVan & Ms. Elizabeth C. LeVan

Ms. Jennifer M. Loeb

Mr. Brian C. Loeffler

Dr. Paul W. Ludden & Ms. Linda E. Ludden

Dr. John E. Mazuski &

Ms. Clemencia M. Mazuski

Dr. William L. McClements

Dr. Samuel T. Nadler

Dr. Yeh-Shan Peng & Mrs. Yei-Mei Peng

Mr. Robert G. Presler

Ms. Christine L. Schneider &

Mr. Russell L. Schneider

Professor James D. Shull &

Ms. Sara J. Smith-Shull

Dr. Margaret A. Shupnik

Dr. Charles W. Slife

Mr. Kevin M. Sokolowski

Ms. Dace E. Sprecher

Dr. Jiunn-Yann Tang

Ms. Margaret S. Walker

Dr. Theodore R. Watson &

Ms. Emma A. Watson

Ms. Joy R. Wideburg &

Mr. Norman E. Wideburg

Dr. Andrea R. Yoder

Dr. David W. Zhang

Ms. Yurun Zhang

Professor Maija V. Zile

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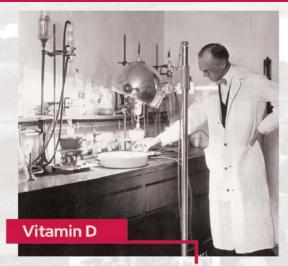
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Innovations



Harry Steenbock discovers how to enrich food and drugs with vitamin D, building off seminal vitamin research by Elmer McCollum, Marguerite Davis, and other UW biochemists. Revenue from this advancement helps to form the Wisconsin Alumni Research Foundation (WARF).



Har Gobind Khorana manipulates the chemical components of life itself by creating a synthetic gene in a test tube, building on his earlier Nobel-winning work synthesizing DNA.

DNA synthesis



The Hector F. DeLuca Biochemical Sciences Complex grows to encompass over 120,000 square feet of state-of-the-art research facilities.

1883

1923

1940

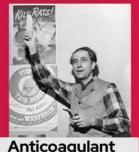
1970

2012

2023

The Department of Agricultural Chemistry is founded in 1883, with the first departmental building constructed in 1912 at 420 Henry Mall. The department's name is changed to Biochemistry in 1938 by faculty vote.





Anticoagulant

Karl Paul Link and his lab discover how a substance responsible for killing cows can be synthesized to save human lives, ultimately resulting in the creation of warfarin (named for WARF), now the most-prescribed blood thinner in the world.

140 Years

This year, UW-Madison celebrates its 175th anniversary and looks to the future. Learn about the university's history and research, and more events in the Department of Biochemistry's 140 years, by scanning the QR code or visiting 175.wisc.edu.

