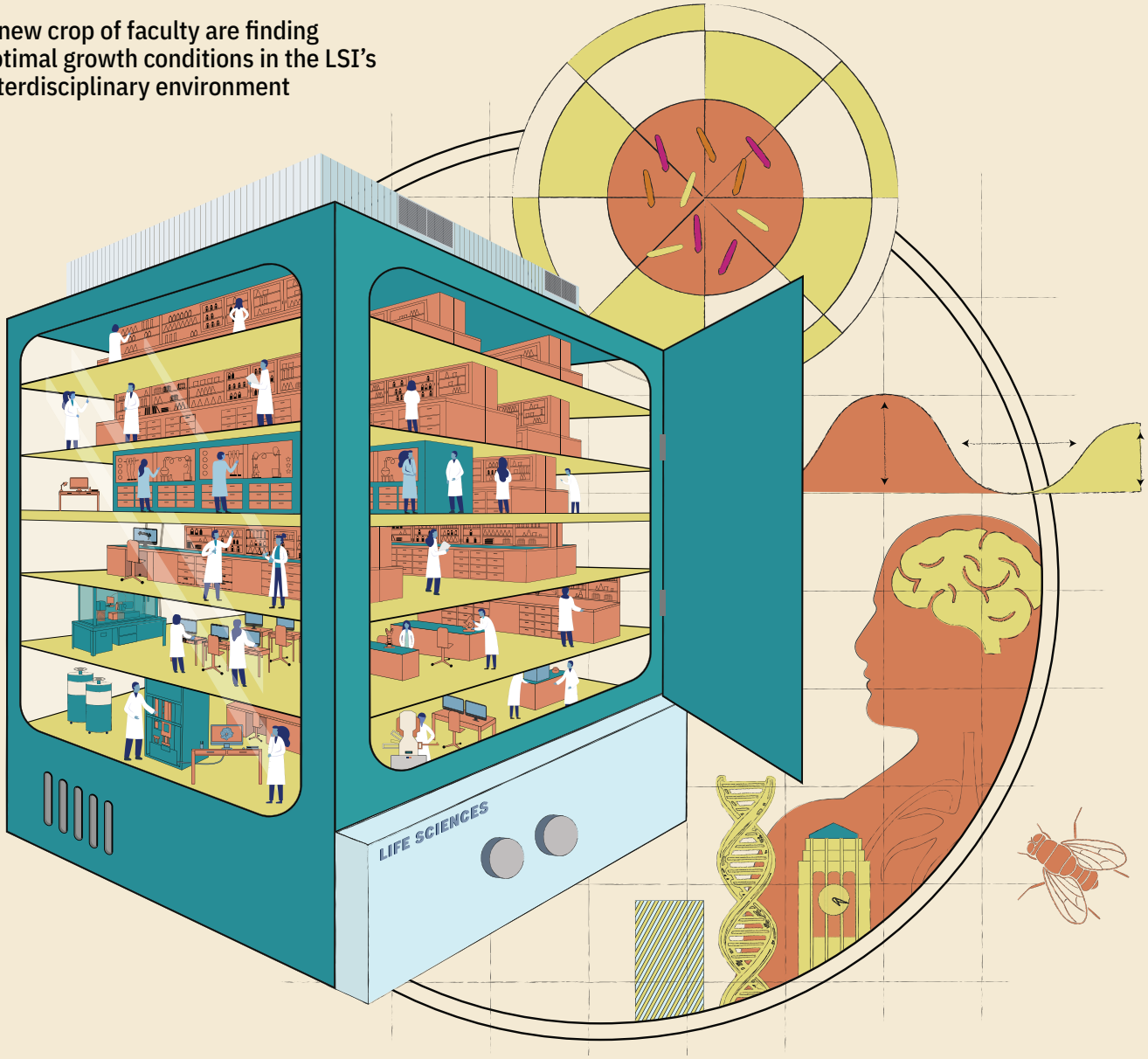
LIFE SCIENCES INSTITUTE
UNIVERSITY OF MICHIGAN
Spring 2025

INCUBATOR FOR INNOVATION

A new crop of faculty are finding optimal growth conditions in the LSI's interdisciplinary environment



CORE STRENGTH

The experts in the LSI's cores don't just advance research projects — they pioneer new science

BROADENING THE RESEARCH LENS

In the Aspirnaut Program at U-M, high school scientists see the full picture of their futures in STEM

'AMAZINGLY FERTILE GROUND'

Two LSI faculty members discuss how their long-standing cross-discipline collaboration has helped their research flourish

From the Director

While exploring the origins of the COVID-19 vaccine, author and journalist Malcolm Gladwell observed that progress does not come from ideas alone. Rather, "it comes from places where smart people have the time and freedom to wander around and make mistakes and pursue interesting ideas that one day may end up saving your life."*

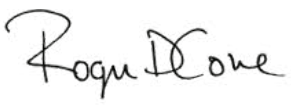
The following pages demonstrate how the LSI strives to be such a place — how our multidisciplinarity, research excellence and training for future generations combine to create a powerful incubator for innovation.

On the most basic level, simply having 26 spectacular faculty leading labs in the same compact building amplifies the opportunity for outstanding collaborations. Our toughest scientific questions need answers from diverse perspectives. The LSI brings those perspectives together in one environment, housing scientists with expertise in fields ranging from synthetic organic chemistry to human genetics. In this issue's cover story, you will see how our newest faculty are capitalizing on that environment to tackle tough questions and build tools that can open new paths of discovery across the life sciences.

Then, of course, come the results of the very intentional multidisciplinary nature of the LSI. Our scientists share not only a building but also a culture of collaboration that encourages connections across labs and across disciplines. A colleague of mine once commented that "collaboration is like radiation: It falls off by the distance squared!" In this issue's "Perspectives" article, you will see how proximity combats this challenge in our institute — fostering a 20-year collaboration through which a chemist and a structural biologist solve problems that neither could have solved on their own.

The state-of-the-art discovery tools found in our scientific cores support LSI investigators with cutting-edge technologies; but more than that, the LSI cores also bring hundreds of investigators into our building, further increasing opportunities for collaboration. And, as you'll learn on page 14, the expert scientists within these cores are advancing their own novel projects and working together to unleash new scientific pursuits.

Most important, however, are the LSI investigators themselves. Throughout this issue, you will read how researchers at every level — from high school scientists through senior faculty — continuously seek out opportunities for exploration, growth, collaboration and innovation. Bringing investigators like this into the LSI, at a university like U-M with its excellence at scale, keeps me excited for the future.



*"Bonus Episode: Druid Hills." *Revisionist History*. December 10, 2020.

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Cover art and magazine illustrations by Rajani Arora

Back cover: Using advanced cryo-electron microscopy techniques, researchers in Shyamal Mosalaganti's lab are able to peer into cells, creating 3D visualizations of individual cellular components in their environment to reveal how they contribute to the cell's function and health. Image credit: Renaldo Sutanto.

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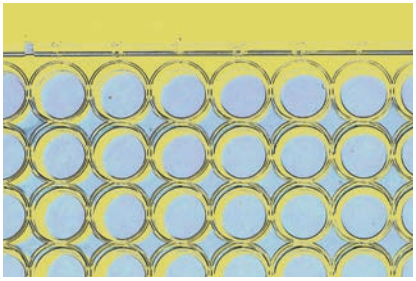

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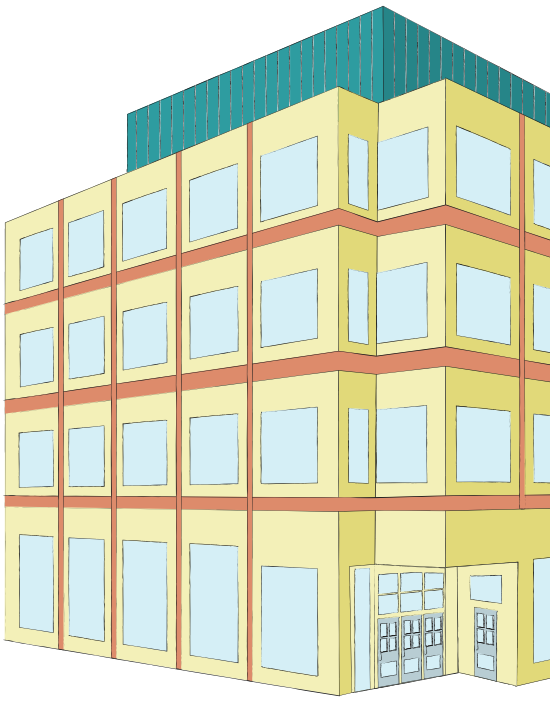

LIFE SCIENCES INSTITUTE
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Advances

Herman Fung, Ph.D.

New faculty member aims to unravel DNA's dynamic organization

Structural biologist Herman Fung, Ph.D., has joined the University of Michigan as an assistant professor of cell and developmental biology and biological chemistry in the Medical School and a research assistant professor at the LSI.

Fung specializes in a technique called cryo-electron tomography (cryo-ET), which allows researchers to determine the structures of molecules within the context of their cellular environment. His newly launched research program will combine cryo-ET with other structural and cellular biology techniques to understand the 3D arrangement of the genome within cells and how that organization impacts gene regulation.

"My research sits at the interface of structural biology and developmental biology," Fung says. "So with the strength of the electron microscopy program at the LSI and the biological breadth of both departments at the Medical School, this is the perfect home for me to do this research."

"When we analyze behavior types, we often actually are based on the experimenters' judgment of the behavior type, rather than mathematical clustering.

—Bing Ye, *Popular Science*

Ye's team has developed an open-source software suite, LabGym, that capitalizes on artificial intelligence and supervised machine learning to efficiently analyze animal behavior for a range of species both in the lab and in the field.

Basic science discovery moves from bench to bedside

In late 2023, the U.S. Food and Drug Administration approved the first pharmaceutical treatment for congenital thrombotic thrombocytopenic purpura (TTP), a rare but potentially lethal genetic blood disorder.

The new drug, TAK-755 (commercial name Adzynma), arose from research that started more than two decades ago in the lab of LSI faculty member and physician-scientist David Ginsburg.

Patients with TTP develop small blood clots throughout their body, blocking blood flow to essential organs. Ginsburg and his colleagues were able to track down the faulty gene underlying the disorder and discovered that patients were missing a protein called ADAMST13, which prevents such clots in healthy conditions.

That discovery formed the basis of TAK-755. The treatment provides patients with purified ADAMST13 (also called the recombinant protein) instead of plasma from healthy human donors, which was the only treatment option previously available.

"The big advantage of the recombinant protein over human plasma is that you're just getting this pure, clean protein," Ginsburg explains. "With this new treatment, we know exactly what is going into the patient, and at exactly what dose, and we don't risk exposing the patient to anything else that may be in human plasma."

Visit the QR code to watch a video about the scientists behind this discovery:

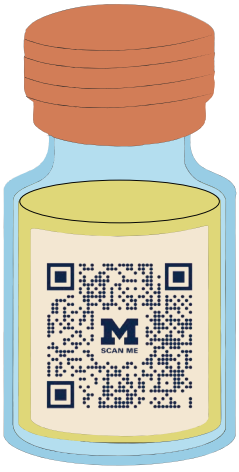


Photo by Leisa Thompson, Michigan Photography

Xu lab
Nature Neuroscience
March 2024

Maybe it's cold outside — this protein is how we know

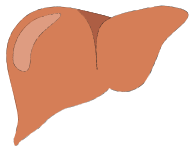
"Clearly, our skin can sense cold. When you step outside and you sense it's too cold, you're going to take action to get back to a warmer environment. But exactly how do you know it's cold?"

It's a question that nagged neuroscientist Shawn Xu for years — and one that has remained unanswered in the field of sensory biology. Researchers have pinpointed which proteins across the nervous system enable mammals to sense hot, warm and even cool temperatures in their environments, but not temperatures below about 60° Fahrenheit.

A recent study from Xu's team filled that long-standing gap, identifying the mammalian cold-sensing protein.

It's called GluK2, and it's unrelated to most other temperature-sensing proteins. Instead, it's best known for transmitting chemical signals within the brain. But it is also found on sensory neurons outside the brain and spinal cord. There, it's tuned to pick up temperature cues rather than chemical ones, the new study found.

"Knowing how we sense cold opens new paths to better understand why humans experience cold differently under various disease conditions," Xu says. "And it potentially offers a starting point for thinking about how to treat pain in patients whose cold sensation is overstimulated."



Cases of metabolic dysfunction-associated steatotic liver disease have ballooned over the past three decades. Now affecting **25% to 30%** of the world's population, MASLD is the leading cause of chronic liver disease.

Lin lab
Science Translational Medicine
March 2024

J. Wu lab
PLOS Biology
July 2024

Pursuing MASH extinction

It starts out simply as accumulation of fat in the liver, and it's relatively benign. But when metabolic dysfunction-associated steatotic liver disease (MASLD) develops into its more severe form — which it does in about 20% of cases — it causes liver damage leading to cirrhosis, cancer and end-stage liver disease.

Researchers in Jiandie Lin's lab and Jun Wu's lab at the LSI want to determine what molecular and cellular mechanisms drive this progression from MASLD to the more harmful metabolic-associated steatohepatitis (MASH). Their goal is to identify cellular checkpoints that could be harnessed to stop or reverse the disease's progression.

Working with a mouse model of MASLD, Lin's team recently discovered how the damaged liver cells themselves set off a chain reaction that ultimately snowballs into MASH by recruiting immune cells called TREM2+ macrophages. They also observed that these macrophages were producing elevated levels of a protein called MS4A7 and that blocking this protein was protective against MASH.

"This same protein is found elevated in humans with MASH," Lin explains. "By specifically targeting MS4A7, we may be able to unlock a new therapeutic avenue to alleviate MASH."

Wu's lab concurrently uncovered a naturally occurring signaling pathway that serves as a self-defense mechanism against MASH. Boosting this signal in mouse livers protected the animals from disease progression, while silencing it accelerated disease onset.

"We also found that a family of drugs used to treat dementia in humans showed beneficial effects against MASH in mice," Wu says. "It is conceivable that these drugs can be evaluated and repurposed for treating human MASH in the future."

Wang and Li labs
Proceedings of the National Academy of Sciences
April 2024

SPOTting chemicals across the brain

On the surface of every cell, various forms of proteins stand ready to detect signals transmitting outside the cell and activate cellular processes in response.

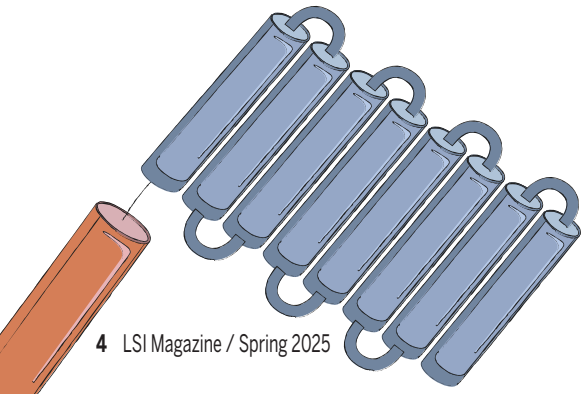
The most ubiquitous of these are the large family of proteins known as G protein-coupled receptors (GPCRs). They are highly conserved across species and found in every human cell, processing signals ranging from light and odors to hormones, sugars and other proteins.

LSI faculty member Wenjing Wang is particularly interested in how these proteins function in the brain to process dopamine, epinephrine, opioids and other chemicals that modulate neuronal activity.

"To get a comprehensive understanding of how these various molecules interact with GPCRs, though, we need to be able to see them interacting at a detailed, cellular level and at a larger scale across the whole brain," Wang explains. "The challenge in our field has been achieving the right balance of these competing scales."

Working with Peng Li's lab at the LSI, her team has now developed a chemical tool that could overcome this challenge. The tool, SPOTall, creates a permanent fluorescent mark in the cells when a specific molecule is detected. Thus, researchers can see the individual cells that are highlighted, as well as the whole picture of activated cells across the brain.

The group has already demonstrated the tool's efficacy with opioids and epinephrine in cultured neurons and in mouse models. They ultimately aim to create a brain-wide map for multiple neuromodulators concurrently.



The human genome encodes more than **800 G** protein-coupled receptors. More than one-third of FDA-approved drugs target members of this large protein family.

Ohi and Mosalaganti labs
Journal of Molecular Biology
April 2024

Toxin's technique revealed in 3D

The bacteria *Helicobacter pylori* can be found thriving in the stomach lining of more than half the world's population.

Although the bacteria cause no discernible harm to their hosts in most cases, they can lead to peptic ulcers and even gastric cancer in many people. They do this by forming biological machines that secrete toxins and inject a harmful protein directly into gastric cells.

LSI professor Melanie Ohi investigates the structures of these machines and the secreted toxins to understand how they cause such damage in some cases, and to expose weaknesses that could be exploited to block infection.

Her team recently partnered with Shyamal Mosalaganti's lab at the LSI to examine how one of these toxins — a pore-forming protein called VacA — interacts with host cell membranes to cause harm.

Using a combination of advanced electron microscopy techniques, they were able to examine the protein in the context of a lipid membrane and observe how VacA rearranges itself to form a pore. Their findings offered new understandings of this essential step for the protein's contribution to gastric disease.

"Our work combining biochemistry, single particle cryo-electron microscopy and cryo-electron tomography allowed us to visualize the structure of this toxin in a way that creates a new model for its ability to lead to ulcer formation," Ohi says. "The expertise and resources at the LSI make these types of multidisciplinary studies possible and lead to paradigm-shifting discoveries."

Cone lab
Journal of Clinical Investigation
July 2024

Fine-tuning GLP-1 drug effects

The use of GLP-1 agonists such as Ozempic and Mounjaro has skyrocketed in recent years, driven in large part by their effectiveness in treating obesity and obesity-related disorders.

But these medications, originally designed as Type 2 diabetes treatments, don't work for everyone. About 10% to 15% of patients do not achieve their desired results, and up to half experience adverse gastrointestinal side effects.

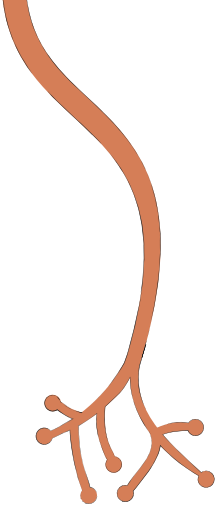
Recent findings from the lab of LSI Director Roger Cone may point to a solution to both of these challenges: a pair of proteins in the central nervous system called the melanocortin 3 and melanocortin 4 receptors (MC3R and MC4R).

"The MC3R and MC4R impact everything from sensing long-term energy stores to processing signals from the gut regarding short-term fullness, or satiety," says Cone, whose lab has studied the melanocortin system for decades. "So the obvious question for us was: How do these GLP-1 drugs, which work by manipulating satiety signals, function when we prime the melanocortin system?"

Cone and his colleagues tested the effects of several hormones that reduce food intake in mice with altered MC3R or MC4R activity. In all cases, the mice showed stronger responses to GLP-1 drugs and other hormones that affect feeding behavior.

The researchers also measured activity in parts of the mouse brain thought to trigger nausea in response to GLP-1 drugs, and they observed no increased activation when GLP-1 drugs were combined with alterations to the melanocortin system.

The findings indicate that pairing the existing GLP-1 drugs with an MC4R agonist could improve responses to the desired effects of the drugs by up to five-fold, without increasing unwanted side effects.



Since the FDA approved a GLP-1 agonist specifically for weight loss in 2021, GLP-1 drug prescriptions have nearly tripled. In just the fourth quarter of 2023, more than **9 million** patients in the U.S. were prescribed a GLP-1 drug.

Li lab
Nature Neuroscience
September 2024

If you give a mouse capsaicin ...

It will probably start to cough. And that little cough has big implications for understanding one of the most common medical complaints among human patients.

"In the research field, people have generally thought that mice do not cough," says LSI faculty member Peng Li, whose team has now shown not only that mice cough but also which neurons are involved in the behavior.

The discovery began almost by accident. Li's lab uses mice as a model to understand the molecular mechanisms that coordinate different forms of breathing.

When they activated a group of neurons called tachykinin 1 neurons, the researchers noticed an unfamiliar breathing pattern in the animal — and it looked exactly like the coughing pattern observed in other species.

To confirm that this pattern was in fact a cough, the team exposed mice to small doses of capsaicin, which is known to induce coughing in humans, and then ran a series of experiments to measure the animals' responses. They also mapped the neural circuit responsible for producing this behavior, providing a route to study coughing at the genetic and molecular level.

"With the advanced genetic tools available for studying mouse models, this opens a lot of opportunities across the field," Li says. "We now have a new model for studying the specific mechanisms underlying chronic coughing and even potentially identifying new targets for developing better anti-coughing treatments."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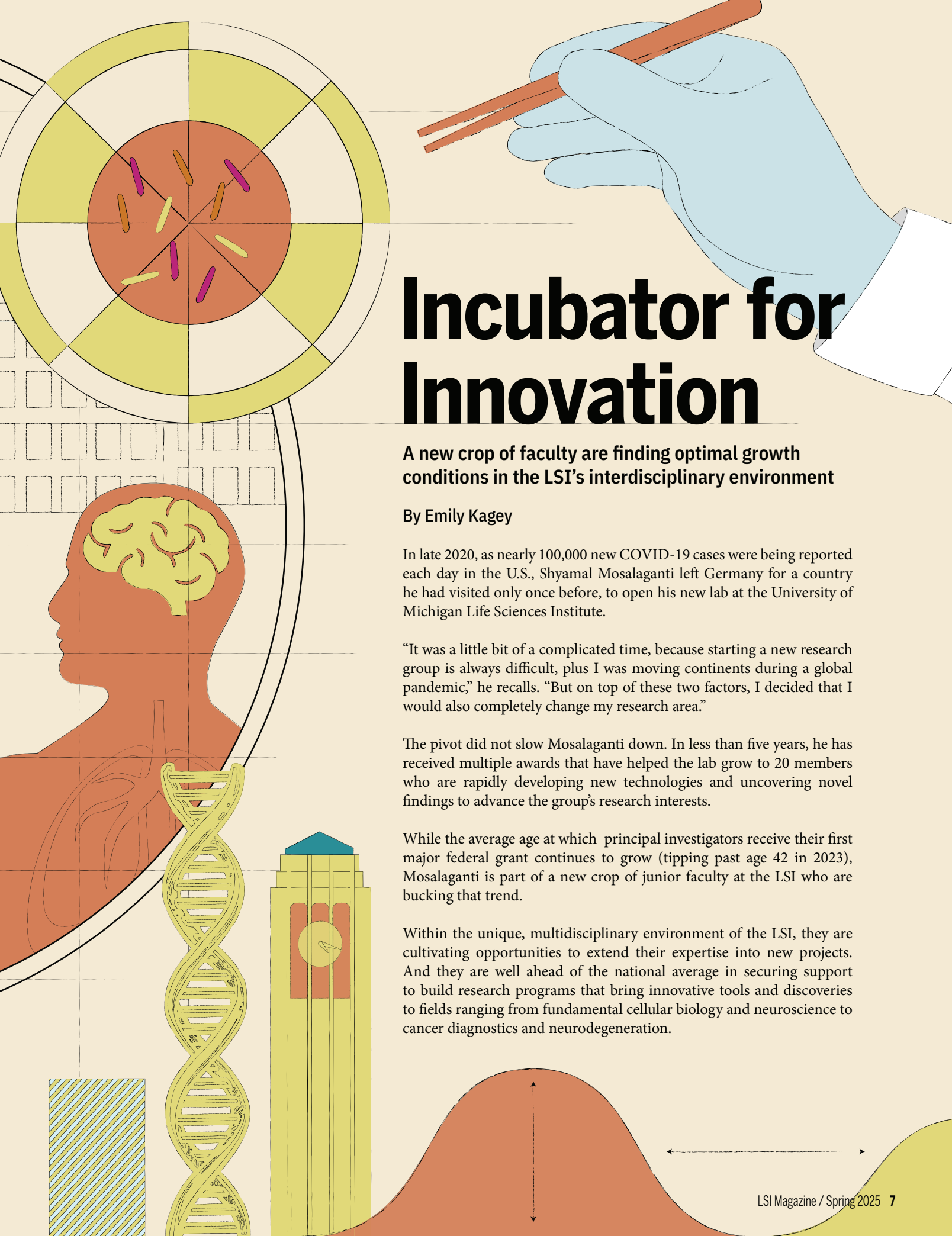


Incubator for Innovation

A new crop of faculty are finding optimal growth conditions in the LSI's interdisciplinary environment

By Emily Kagey

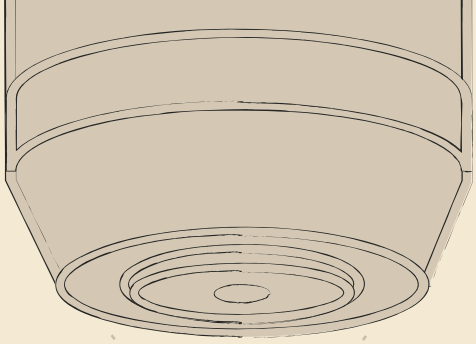
In late 2020, as nearly 100,000 new COVID-19 cases were being reported each day in the U.S., Shyamal Mosalaganti left Germany for a country he had visited only once before, to open his new lab at the University of Michigan Life Sciences Institute.

"It was a little bit of a complicated time, because starting a new research group is always difficult, plus I was moving continents during a global pandemic," he recalls. "But on top of these two factors, I decided that I would also completely change my research area."

The pivot did not slow Mosalaganti down. In less than five years, he has received multiple awards that have helped the lab grow to 20 members who are rapidly developing new technologies and uncovering novel findings to advance the group's research interests.

While the average age at which principal investigators receive their first major federal grant continues to grow (tipping past age 42 in 2023), Mosalaganti is part of a new crop of junior faculty at the LSI who are bucking that trend.

Within the unique, multidisciplinary environment of the LSI, they are cultivating opportunities to extend their expertise into new projects. And they are well ahead of the national average in securing support to build research programs that bring innovative tools and discoveries to fields ranging from fundamental cellular biology and neuroscience to cancer diagnostics and neurodegeneration.



As a postdoctoral fellow at the European Molecular Biology Laboratory, Mosalaganti honed his expertise in the burgeoning field of cryo-electron tomography (cryo-ET). This technique involves flash-freezing cells and then using specialized microscopes that beam electrons at the sample to reveal the three-dimensional structure of complex biological machines in their native cellular environment.

As he began planning for his own lab, Mosalaganti got the itch to expand beyond the types of protein complexes he'd studied as a postdoctoral fellow. Instead, he wanted to use cryo-ET to investigate organelles — specialized compartments of the cell that perform specific tasks. He was particularly interested in lysosomes, organelles that break down unnecessary and malfunctioning biomolecules to be recycled or removed from the cell.

"Changing research topics like that is a bit of a risk when launching a lab, because the larger funding agencies want to see that you already have some experience or preliminary data," says Mosalaganti, who is now an assistant professor at the U-M Medical School and College of Literature, Science, and the Arts, in addition to his LSI appointment. "But with the advanced instrumentation and connections across disciplines, the LSI just felt like a place where I could already see my research growing and being successful."

By October 2022, Mosalaganti had secured his first major funding award to advance his research program: the highly competitive NIH Director's New Innovator Award (or DP2 Award), which supports early-career investigators to pursue bold, creative research projects.

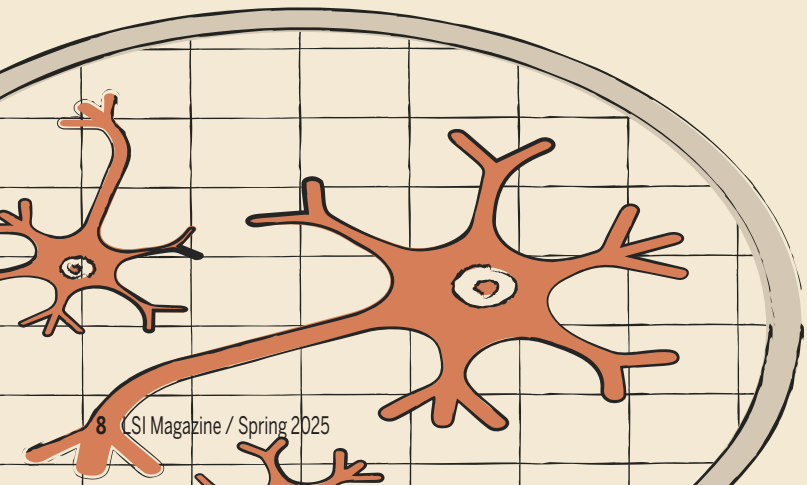
Shyamal Mosalaganti (left) discusses data with graduate student Renaldo Sutanto.

With the five-year award, he hopes to figure out how various organelles, including lysosomes, connect with each other to regulate processes that are essential for the life of all cells.

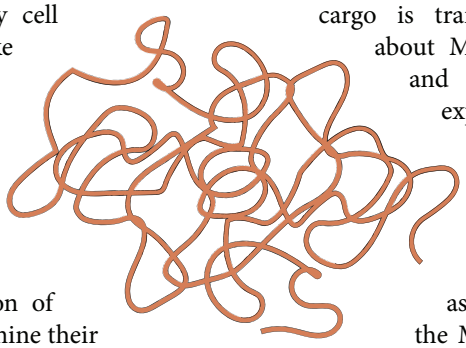
In the initial phase of this project, Mosalaganti first had to develop a pipeline of microscopes, software and data analysis tools that could capture dynamic organelles coming together, in high resolution. With all the pieces in place now, Mosalaganti says the pipeline can swiftly be adapted for a range of projects while also moving the DP2 work forward.

"It's a good platform for asking new questions, or asking questions differently, because we can look inside cells and see what's happening in unprecedented detail," he says. "Already we're finding evidence that contradicts some long-held beliefs in the field."

That platform also serves as the foundation for other projects in his lab, including a collaboration to unearth new understandings of neurodegeneration.



A common feature across neurodegenerative disorders — Alzheimer's disease, Parkinson's disease, frontotemporal dementia and others — is abnormal protein aggregation, primarily within neurons. These are proteins that a healthy cell would normally clear out, like taking out the garbage. Genetic abnormalities, risk factors and aging can slow or halt the clearing processes, allowing the garbage to pile up until it eventually chokes the cell.



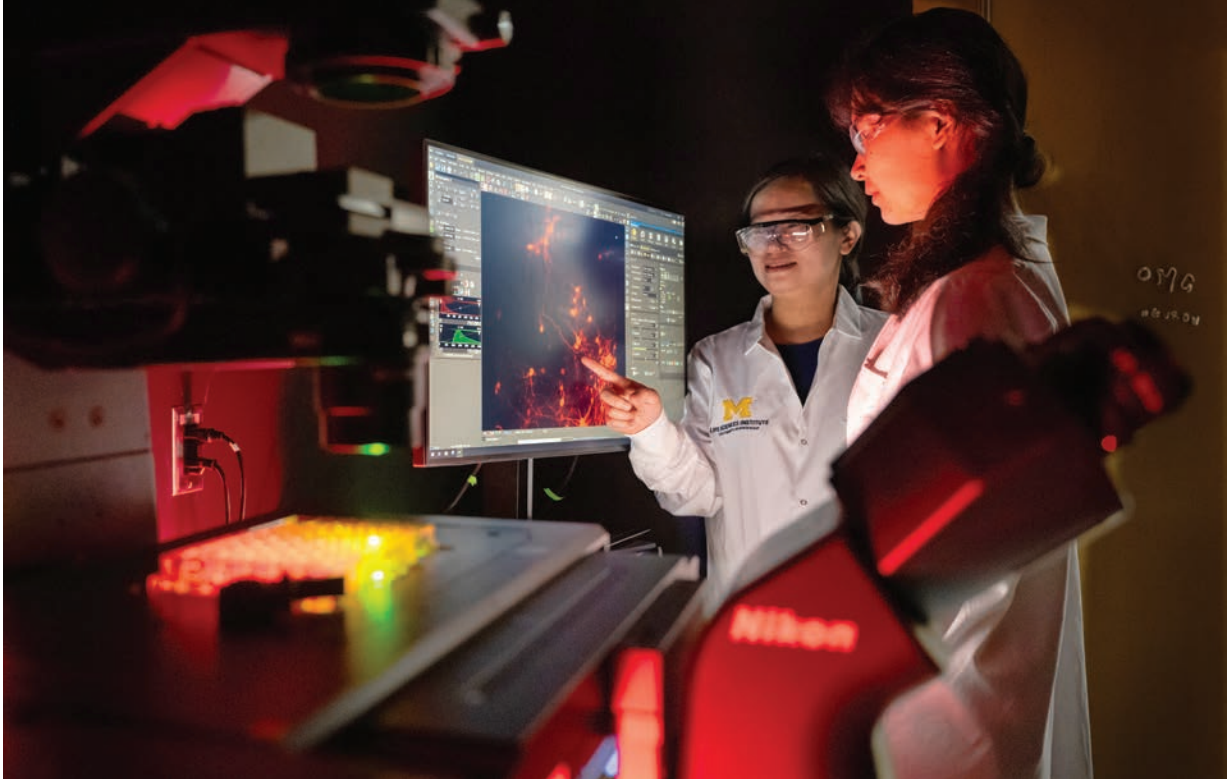
"One way to inhibit the formation of these aggregates would be to determine their structure so you can target them," Mosalaganti explains. "But neither conventional microscopy nor patient tissues can show us where within the cell these proteins are aggregating and what they look like during the formation process, before it's too late to intervene."

He hypothesized that cryo-ET could uncover what the aggregates look like within patient-derived neurons in various stages of aggregation. Even before he arrived in Ann Arbor, one of Mosalaganti's soon-to-be colleagues connected him with a neurologist on campus who could help him test this theory.

LSI professor Lois Weisman, who studies how cellular cargo is transported within neurons, heard about Mosalaganti's postdoctoral research and thought his structural biology expertise would be a good addition to a consortium of U-M faculty who study protein folding and trafficking. That's where Mosalaganti met physician-scientist Sami Barmada, an associate professor of neurology in the Medical School and the director of the Michigan Brain Bank.

He and Mosalaganti quickly hatched a plan to use cryo-ET to peer directly into neurons and determine where and how these proteins were aggregating. To get started, they applied for seed funding from the LSI's Klatskin-Sutker Discovery Fund. This philanthropic award supports early-stage research that has high potential to positively impact human health. That funding allowed them to visualize the protein aggregates directly in

Photo by Leisa Thompson, Michigan Photography



Wenjing Wang (left) and postdoctoral fellow Jiahui Ding analyze neurons labeled by the lab's dopamine reporter (red).

patient-derived neurons, providing enough data to demonstrate their proof of concept.

Less than four years after their first meeting, the team now has a grant from the Kissick Family Foundation and Milken Institute, and the project is expanding in scope and detail. They next plan to apply their approach to neurons that carry specific genetic mutations associated with frontotemporal dementia. They will also use patient tissue to map the detailed structure and location of the proteins in unprecedented detail.

The research has the potential to identify more effective therapeutic avenues for frontotemporal dementia. The team has already uncovered data indicating that one prominent strategy others are using to develop treatments is unlikely to work, based on where they are finding the protein aggregates within the cell.

"I think, in retrospect, this project would have taken much longer if Lois had not introduced me to this consortium — and now we already have a full team working on this with exciting new discoveries," Mosalaganti says.

"That's the benefit of being somewhere like the LSI. As scientists, we each have a finite amount of time to make an everlasting impact and address outstanding, difficult-to-tackle questions in biology. It really helps to be at a place like the LSI, where you have access to excellent resources and connections across disciplines that allow you to address these big questions."

Mosalaganti was one of two U-M faculty members to receive the NIH Director's New Innovator Award in 2022. (Prior to that, no U-M faculty had received the award since 2016, and only five had received it in the past decade.) The second recipient was his colleague and upstairs neighbor at the LSI, Wenjing Wang.

Wang joined the LSI faculty as an assistant professor in 2018 with a plan to engineer cellular proteins for studying cell activity. Her lab develops specific types of genetically encoded tools called chemogenetic and optogenetic tools.

In general, genetically encoded tools work by delivering a small sequence of extra DNA to the nucleus,

"As scientists, we each have a finite amount of time to make an everlasting impact and address outstanding, difficult-to-tackle questions in biology. It really helps to be at a place like the LSI, where you have access to excellent resources and connections across disciplines that allow you to address these big questions.

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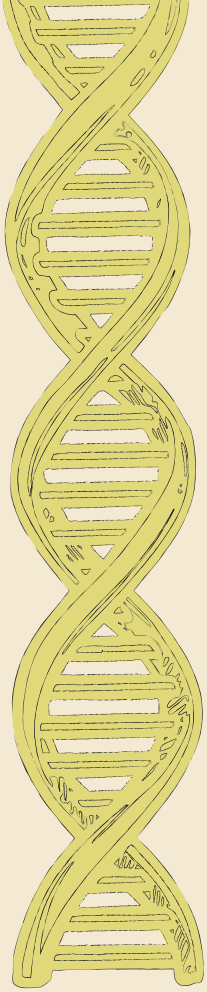


prompting the cell to produce the protein encoded in the DNA — like sending a factory a new set of instructions to build one extra type of machine part, with the thousands of parts it's already building. Once that new protein is built, it begins performing the job it was designed for, such as activating a cellular process, targeting an unwanted protein or even silencing the whole cell. But Wang's tools also incorporate an extra on/off switch.

"With chemogenetics and optogenetics, we're basically adding another layer of control," says Wang, now an associate research professor at the LSI and associate professor of chemistry in the College of Literature, Science, and the Arts. "Instead of becoming active as soon as they are built, these proteins do not turn on until we add a chemical or light to the cell. So we can remotely control when they start or stop the function we want to see."

The tools are a powerful platform for fundamental discovery science, allowing researchers to uncover how specific cellular functions contribute to health and disease. With the DP2 Award, for example, Wang hopes to create tools that will unlock new understandings of G protein-coupled receptors (GPCRs) — a large family of proteins that sit on the surface of every cell to receive messages and inform cellular behavior.

While Wang is developing these tools to help advance her own research questions, her lab is certainly not the only one benefiting. Other LSI labs are now implementing these tools to investigate how different neurons control breathing and how proteins found in one brain region can regulate food intake in mice. And recently, she's partnered with LSI faculty member Bing Ye to customize her tools for fruit flies.

Drosophila melanogaster, or common fruit flies, share about 75% of their genome with humans, and their nervous system has been carefully mapped down to the level of individual neurons. These factors make them a popular model organism for studying neurobiology. Ye wanted a way to mark neurons that were active during a particular learning process and then manipulate those neurons later to determine their role in cognition and sensory perception.

"But there was basically no such tool for *Drosophila*," says Ye, a research professor at the LSI and professor of cell and developmental biology in the U-M Medical School. "I reached out to Wenjing about my need for the tool, and she saw an opportunity to use flies as an efficient testing ground for new tools."

Adapting a tool Wang began developing as a postdoctoral fellow, the team has now validated a new framework for studying cognition and behavior in *Drosophila*, while also demonstrating the power of this model organism for characterizing genetically encoded tools.

The collaborations are mutually beneficial: Wang's team of biological chemists specializes in building these tools, but they need a platform for testing them. By working with labs that have established research projects in model organisms, Wang gains access to such platforms while opening new research possibilities for her colleagues.

"It's very natural for our lab to collaborate, because we design these tools, but they need to be validated and tested in animal models," Wang says. "Being at the LSI just makes that collaboration much more accessible. It's a great place for tool-builders, like my lab."

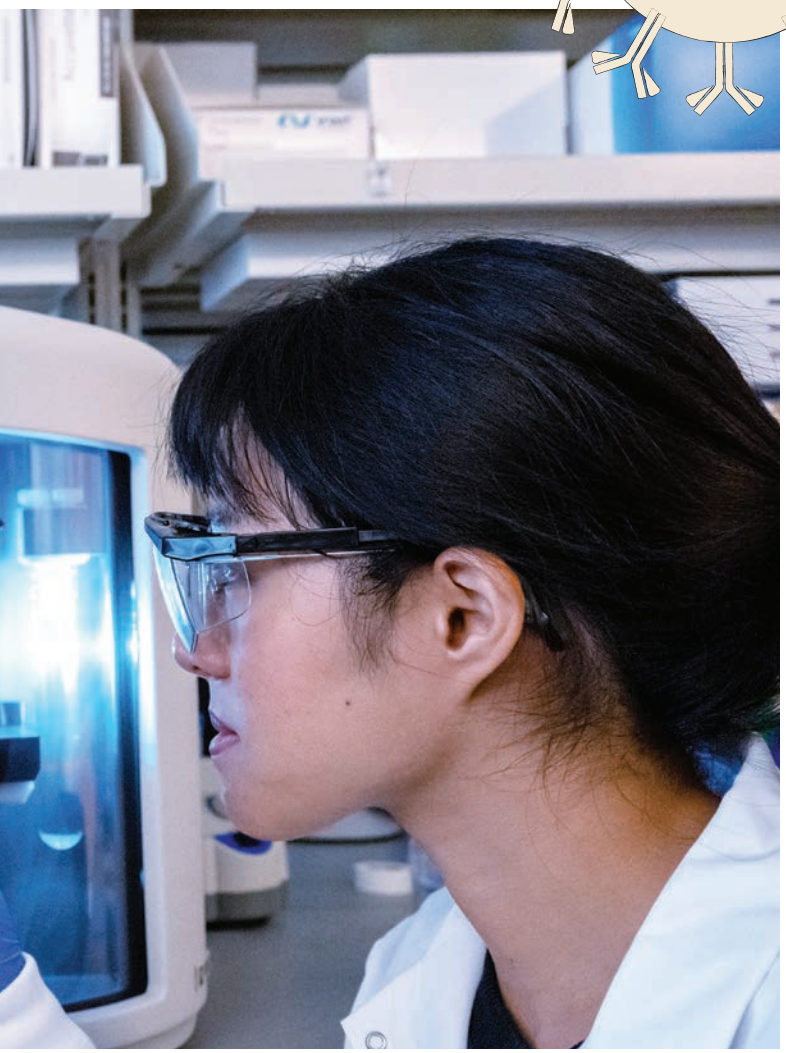
Biomedical engineer Connie Wu, another self-described tool-builder and one of the LSI's newest faculty members, similarly has already experienced how connections across disciplines can help budding research programs thrive.

Wu joined U-M in January 2023 as the first joint recruit between the LSI and the College of Engineering. In her first two years, she has secured multiple grants — including a five-year MIRA (Maximizing Investigators' Research Award), which funds "the nation's highly talented and promising investigators" — and added several postdoctoral fellows, graduate students and undergrads to her lab.

The growing group is using RNA as a scaffold to build molecular tools for two distinct purposes. One objective is to develop new drug-delivery approaches. The second

Connie Wu (left) works with graduate student Chi-Chia Wang.

> Being in this collaborative environment where everyone has such different areas of expertise makes it really easy to delve into new areas.



is to detect proteins and other biomolecules that are present in our bodies at levels too low to be spotted by existing methods — molecules that could be used to diagnose diseases earlier.

"Being able to detect even small differences in the profiles of these low-abundance biomolecules could help us better understand and diagnose disease," explains Wu, who is a research assistant professor at the LSI and an assistant professor of biomedical engineering in the College of Engineering. "But right now there is just so much unknown because we don't have the tools to find the biomolecules that we might want to measure."

Her ultimate goal is to use such tools to address diagnostic and therapeutic challenges related to cancer and other diseases. But she also envisions extending their application for a variety of basic discovery and clinical questions that other LSI labs investigate.

"From a basic science approach, having a tool that can measure extremely low levels of biomolecules could be quite useful for studying a range of fundamental cellular processes, and we're already expanding into new sub-directions," Wu says. "Being in this collaborative environment where everyone has such different areas of expertise makes it really easy to delve into new areas."

One of those new areas is a collaboration with her LSI faculty mentor, Jiandie Lin, which draws on both the diagnostic and the therapeutic aims of the Wu lab.

Lin's lab investigates how metabolic processes become reprogrammed in disease, particularly in the context of steatotic liver disease (formerly called fatty liver disease). He initially wondered whether Wu's detection techniques could help measure a molecule his lab studies called NRG4. This hormone is secreted primarily by fat cells but has important roles in protecting against liver injury, fibrosis and cancer. As Wu began reviewing Lin's published research, she saw an opportunity to add another dimension to the project.

"I noticed that they had developed a purified version of this hormone that had therapeutic efficacy," Wu says. "We began to wonder whether we could build an RNA-based platform for more effective delivery of this potential therapeutic. Now we're working toward improving both the detection and the delivery approaches."

The collaboration has provided Lin with new areas of exploration for his lab, while also giving Wu access to expertise in techniques and model systems that complement her lab's focus — access that she has found crucial for the rapid growth of her research program.

"As an early-career scientist getting ready to transition to a faculty role and set up an independent lab, I think we often hear a lot about how stressful that move can be," Wu says. "But with all the resources and support here, and the ease of forming new collaborations, after two years I honestly feel it's actually going much better than I could have anticipated."■

Photo by Leisa Thompson, Michigan Photography

Core Strength

The experts in the LSI's cores don't just advance research projects — they pioneer new science

By April Schoonover

Even before many of the faculty lab spaces were occupied, the nascent Life Sciences Institute was investing in its scientific cores — research centers with specialized expertise and technologies that could advance faculty and industry projects. Its first two cores, the Center for Chemical Genomics (CCG) and the Center for Structural Biology (CSB), launched in 2004, less than a year after the institute opened.

In early 2019, with support from the University of Michigan's Bioscience Initiative, the institute established the Cryo-Electron Microscopy Facility and the Natural Products Discovery Core (NPDC) to expand its strengths in structural biology and drug discovery technologies.

The cores provide research services in their respective domains to support projects from labs across and outside the university. They encapsulate the concept of normalized excellence, routinely completing complex experiments with enough frequency that they have become second nature.

"Researchers typically engage the cores for things that they aren't capable of doing in-house, and the cores provide our technologies and experience to make those experiments successful," explains Aaron Robida, a scientist in the CCG.

In the last decade alone, more than 400 scientists (both internal and external to U-M) have capitalized on the expertise and technologies within the cores — and that expertise has helped bring 16 drugs to pre-clinical and clinical development and supported 313 publications.

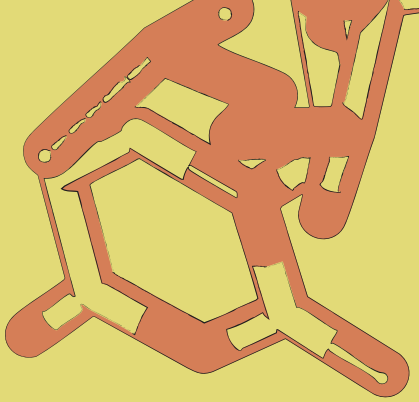
As instrumental as the cores have been in projects from other labs, the experts who manage the cores' daily activities also originate their own novel projects. Center for Structural Biology Managing Director Jeanne Stuckey, for example, has contributed significantly to the development of three anti-cancer drugs that are now in clinical trials.

Now a new project initiated by NPDC Managing Director Ashu Tripathi has brought three of the cores together to reimagine how one common analytical tool, mass spectrometry, can aid drug discovery.

Weighty changes

Mass spectrometry works by breaking a compound into different pieces based on weight and charge, allowing scientists to understand what the original compound was made of.

"I began to wonder: Can we use high-throughput mass spectrometry as a screening tool to identify new drugs that work against specific disease targets?" Tripathi recalls. His idea was to use mass spectrometry to screen



The **four research cores** at the LSI create a comprehensive suite of services and expertise to support drug discovery and basic science research projects.

The **CCG** specializes in using high-throughput screening, or efficiently running many experiments at once, to search their library of over 300,000 compounds for molecules with specific properties or biological activity.

The **CSB** focuses on engineering, purifying and crystallizing proteins to better understand how their structure dictates their biological function.

Using cryogenic temperatures and state-of-the-art microscopy, the **Cryo-electron Microscopy Facility** allows researchers to determine the structure of proteins and macromolecular machines at atomic resolution.

The **NPDC** provides access to a unique library of 55,000 microbial extracts to support the discovery of natural products that may be developed for new therapeutic, agricultural or industrial applications.

Ashu Tripathi (left) and postdoctoral fellow Mohamed Mohyeldin work with the NPDC's high-throughput mass spectrometry system.

hundreds of molecules to see if they interfered with the function of a disease-causing protein.

To test the idea, Tripathi needed a protein that would yield an observable change in mass when working properly — specifically, one capable of modifying its target molecule by adding or removing a part of it. Ideally, the protein would also be relevant to a disease with high therapeutic demand and limited drug options. The SARS-CoV-2 M^{pro} protein, essential for viral replication in COVID-19, met both criteria.

"M^{pro} is a protease, which means it is a protein that cleaves peptides, or small chains of amino acids," Tripathi explains. "When a peptide is cleaved into two pieces by M^{pro}, the molecular weight of the individual components provides an observable difference in a mass spectrometry experiment. So, we can use the cleaving of a peptide as our reporter of enzyme activity."

When Tripathi began formulating this project in 2022, SARS-CoV-2 was a high-priority disease. Additionally, the only on-market drug that targets the SARS-CoV-2 M^{pro} protein, Paxlovid, has a significant side-effect profile, making an alternative drug choice desirable.

Tripathi wanted to use his high-throughput mass spectrometry screening experiment to assess whether any of the natural product extracts in the NPDC could successfully combat the activity of the M^{pro} protein.

To validate this experimental system, Tripathi needed a lot of M^{pro} proteins. For that, he turned to another LSI core: the CSB.

"The CSB is a frequent entry point for working with the other LSI cores," Stuckey says. "We are the first stop for people that want to do drug development and want to study a protein on the bench. People come here, get their protein, and can move very easily to the other cores."

The production of M^{pro} was a critical step in allowing Tripathi to move forward to the screening phase of the project. Collaborating with the CCG, the team created a system of test plates to efficiently evaluate the activity of 7,500 natural product extracts.

"Each plate contains 320 wells," Tripathi explains. "In each well, prepared by the CCG, we include

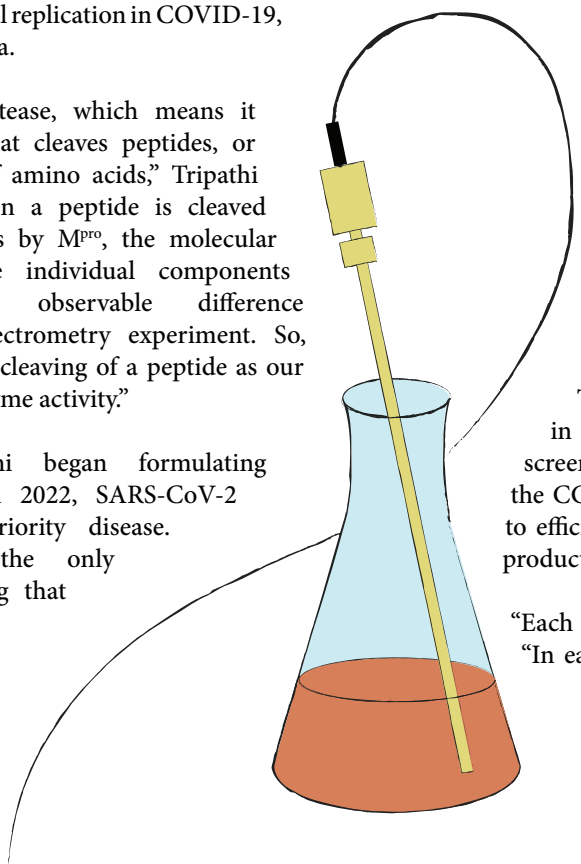


Photo by Leisa Thompson, Michigan Photography

Jeanne Stuckey (left), Aaron Robida (middle) and Ashu Tripathi discuss new data arising from their collaboration.

M^{pro} protein sourced from the CSB, a reporter peptide designed to be cleaved by M^{pro}, and a natural product extract from the NPDC."

Using high-throughput mass spectrometry, Tripathi identified wells where the peptide remained uncleaved, signaling that the natural product inhibited M^{pro} activity and potentially exhibited antiviral properties.

An exercise in optimization

After using mass spectrometry to identify compounds that showed potential, Tripathi partnered with Christiane Wobus, a virologist at Michigan Medicine, to test the compound against the real virus.

"Our lab is one of a few at Michigan that had access and clearance to work with the infectious virus. So, when someone wanted to test if their compounds impacted the infectivity of the virus, they reached out to us," Wobus says.

Wobus and members of her lab assessed the toxicity of the compounds to determine what concentration would harm healthy cells. Then they compared that with the concentrations of compounds needed to show antiviral activity against the SARS-CoV-2 infection in cells.

The anti-viral molecule identified by the initial screening provided a crucial starting point for further development, and the team has been able to design a natural product mimic with enhanced antiviral activity, surpassing the efficacy of Paxlovid.

> When everyone's interests align, there's almost no science we cannot do here at Michigan.

While the optimization process is ongoing, these advancements highlight the potential of natural product-inspired drug discovery in addressing critical therapeutic challenges. And the project itself offers a promising example of what can be accomplished through the LSI's comprehensive suite of research services.

"Each of the cores has its own forte, and most researchers leverage only one or two of these specialties. Since I started the NPDC, I always thought we should have a flagship project involving all the cores," Tripathi says. "When everyone's interests align, there's almost no science we cannot do here at Michigan." ■

Photo by Leisa Thompson, Michigan Photography

Broadening the Research Lens

In the Aspirnaut Program at U-M, high school scientists see the full picture of their futures in STEM

By Emily Kagey

It's 9 a.m. on a Monday in July, and Olises Perez is suited up in his lab gear, preparing his experiments for the day. As he loads DNA samples into a gel for analysis, he describes his research in Donald Zak's lab at the University of Michigan School for Environment and Sustainability (SEAS).

"We're analyzing DNA from samples of mature red oak root tips to see if AMF [arbuscular mycorrhizal fungi] are present. In the past, it's been known that mature red oaks only form associations with ectomycorrhizal fungi; but AMF are mycorrhizal fungi, and we're finding that both of them can live on the roots," he explains.

Unlike most students at work in U-M labs during the summer, Perez is not a graduate student or even an undergrad. He is one of 10 rising high school seniors spending their summer conducting research at the university as part of the Aspirnaut Summer Research Internship Program.

High school students from over 30 Michigan cities and towns have participated in the Aspirnaut Program at U-M.

> Prior to my Aspirnaut experience, I genuinely didn't even know what that world looked like, or that research was a career I could pursue.

Photo by Jessi Thompson, Michigan Photography

Olises Perez, Aspirnaut '24

Photo by Rajani Arora, LSI

Hailey Fiel, Aspirnaut '19 & '22

Aspirnaut at U-M is a six-week paid summer internship that provides promising high school scientists from across Michigan with a hands-on scientific research experience in a university lab.

While living in dorms on U-M's Ann Arbor campus, Aspirnaut students immerse themselves in the role of a full-time scientist, working side-by-side with their mentors to complete their own research projects. When not in the lab, the students participate in college-preparation workshops, engage in social activities and explore the campus and Ann Arbor.

By focusing recruitment efforts particularly on under-resourced areas throughout Michigan — including socioeconomically disadvantaged communities and areas that are geographically distant from a large research university — the program aims to broaden access to cutting-edge scientific resources and expand the pipeline of students pursuing STEM (science, technology, engineering and math) careers. To date, the program has drawn students from more than 30 Michigan communities.

The Life Sciences Institute launched the program at U-M in 2018, modeling it after a program LSI Director Roger Cone was involved with during his time at Vanderbilt University, prior to joining U-M.

"We know there are talented young scientists in every corner of this state. The goal of this program is to help them realize their potential and to connect them to their futures in STEM," Cone says. "Now, several years in, we are really seeing the impact this program can have on long-term outcomes for these students."

Over three-fourths of the 44 students who participated in the program between 2018 and 2023* were first-generation college students. To date, 100% have matriculated to a postsecondary institution — almost half of them to U-M — with 70% majoring in a STEM field.

"It was my first exposure to the world of research," says Hailey Fiel, who participated in the 2019 cohort,

*Data exclude the 2024 cohort, who are in their senior year of high school at the time of this publication.

conducting research in Wenjing Wang's lab at the LSI. "Prior to my Aspirnaut experience, I genuinely didn't even know what that world looked like, or that research was a career I could pursue."

Fiel was accepted at U-M and enrolled in the fall of 2020. After a brief hiatus from research (in part due to COVID-related restrictions for students working in labs), she decided to return to the Aspirnaut program — and to the Wang lab — as a resident assistant in summer 2022.

"I had a desire to give back to the community that the Aspirnaut program serves, and being an RA also gave me a chance to get back to research," she says. "My mentor and I made a lot of progress in the lab that summer. I think that's when I decided for myself that I wanted to keep pursuing research."

Fiel continued to conduct research in the Wang lab until she graduated from U-M in May 2024, contributing to two published manuscripts along the way. This fall, after being accepted to eight graduate schools, she enrolled in the Biological and Biomedical Sciences Ph.D. program at Yale University.

"I wouldn't have had that idea to go back to the program as an RA, and get back into the lab, if I hadn't had my Aspirnaut experience in high school," Fiel says. "That experience ended up being, I would say, the very first step in the progression to where I am now."

By immersing students in authentic research experiences, the Aspirnaut program can shift not just long-term outcomes but even shorter-term goals and perceptions for participants.

"My idea of biology totally changed during the program," says Aissatou Diallo, a 2024 Aspirnaut intern. "Before, I thought of biology as mostly memorizing stuff but not really putting it into practice. And then, being in the lab and doing the hands-on experiments, it just started to feel different."

Diallo came into the program already passionate about a career in STEM, particularly chemistry and drug discovery. In the lab of cell biologist Lois Weisman, though, she began to explore the inner workings of the cell. She learned how to introduce specific mutations to bacteria, investigating how slight modifications in what she calls "a sort of GPS inside the cell" can lead to disease.

Working in the multidisciplinary institute also gave Diallo access to researchers from other life sciences fields who could help her chart a path leading to her career goals — including LSI faculty member and chemical biologist Anna Mapp.

"I had been planning to study chemical engineering, but then I talked with Dr. Mapp and she gave me some ideas for how to get more directly into drug discovery," Diallo says. "Now I'm thinking I want to study chemical biology or biochemistry."

In the years since it launched, the program has grown in both cohort size and campus reach. With eight to 10 undergrads attending each summer (up from the original cohort of six), the LSI has begun to partner with other schools and colleges to place students in labs that align with their goals.

That's how Perez found himself in SEAS over the summer, analyzing samples from 120-year-old oak trees. He had expressed an interest in environmental science on his Aspirnaut application, so the program administrators reached out to colleagues in SEAS to see if they could match him with a lab there.

"I have always been a huge proponent of teaching and mentoring, but I haven't had much opportunity to mentor as a postdoc," says Morgan McPherson, a postdoctoral researcher in SEAS who mentored Perez. "So when the request came in, I said, 'Absolutely, let's go.'"

> being able to educate and support the next generation of scientists ...that is unbeatable

McPherson admits she was a bit unsure about what to expect when the program began, having not worked with high school researchers before. She had a project ready for Perez to begin as soon as he arrived; but only a few days into their work together, contamination issues with the samples put a halt to their progress. Even so, Perez quickly surpassed her expectations, she says, overcoming challenges and helping to move the lab's research forward.

"The whole experience was honestly so worthwhile," she reflects. "Doing the research is great, publishing your findings is great. But being able to educate and support the next generation of scientists — to help Olises get to where he wants to go — that is unbeatable."■

Photo by Rajani Arora, LSI

Olises Perez with mentor Morgan McPherson

Photo by Rajani Arora, LSI

Photo by Sophie Gabrysiak, LSI

Photo by Rajani Arora, LSI

Learn more in this video about Aspirnaut at U-M:

SCAN ME

‘AMAZINGLY FERTILE GROUND’

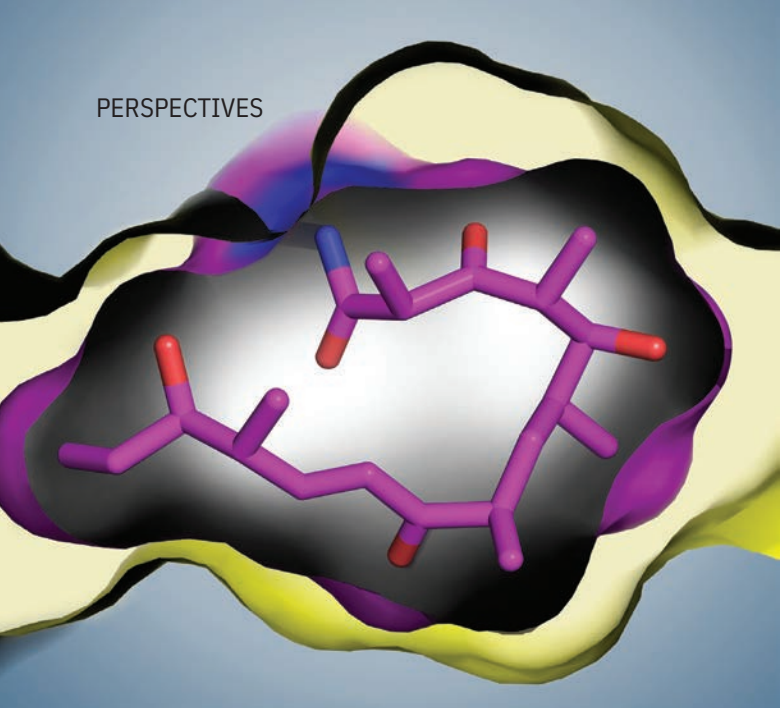
Two LSI faculty members discuss how their long-standing cross-discipline collaboration has helped their research flourish

Since its doors opened in 2003, the Life Sciences Institute has operated under the conviction that unexpected and transformational discoveries lie at the intersection of disparate disciplines — and the best way to unearth these new discoveries is to convene scientists from across scientific fields in a building where they can take on complex scientific challenges together.

David Sherman joined the budding experiment of the LSI in July 2004, and Janet Smith arrived in January 2005. Before their labs were fully unpacked, the chemist and structural biologist had begun to envision a collaboration that could open new avenues for both of their research programs.

Two decades (and 40 joint publications) later, the two professors reflect on the unique conditions that have enabled their transdisciplinary collaboration to flourish and expand, driving their labs and their scientific fields forward.

Photo by Leisa Thompson, Michigan Photography



In their most recent joint publication, the Smith and Sherman labs revealed how one biological machine completes the production of an important class of antibiotics (magenta).

You arrived at the LSI within six months of each other, and in less than two years you had published your first scientific paper together. How did this whole collaboration form and become fruitful so quickly?

Janet Smith: I had always been fascinated by the molecular systems that David works on, but I was not familiar with him or his work before joining the LSI. And when I was recruited here, I looked up his work and I thought, "Wow, this is fantastic. I've been really interested in these." I knew there was a lot of structural biology to be done — very few structures were known at the time. I reached out to David before I moved to Ann Arbor, and we met up to chat about the potential. Just in that initial conversation, we realized that this was amazingly fertile ground.

David Sherman: I have the exact memory of our meeting, and just having an electrifying discussion and feeling like this was going to be incredible. Even before I came to Michigan, I had been thinking about the evolution of the field of natural products discovery and how the piece that was still really missing was structural biology. I was confident that I would find someone at Michigan and a great partnership could start, and that's what happened with Janet. And we quickly launched into a theme that has driven our collaboration for the last 20 years.

How would you describe that theme? What lies at the core of this collaboration?

DS: Well, we study these amazing bacteria that produce complex natural product molecules. Many of them have become FDA-approved drugs. And the way they're constructed is with these biochemical machines inside microorganisms. These machines have many working parts, like a car engine, and they all have to work together in synchrony. So at a high level, we want to essentially understand the different moving parts in the machine that built the molecule and to understand the details of how the construction occurs. At that time we had the ability to determine what the machine was doing, but we had no structural insights to tell us how it was working.

JS: And it turns out there are a lot of machines that are very similar to each other, but they all make different molecules. So, from my perspective as a lover of protein function and how a protein's structure enables its function, I've been really fascinated by how enzymes that have some standard function get slightly adapted in nature to do some truly unusual chemistry that doesn't happen elsewhere.

We want to uncover how these reactions take place and how the enzymes can be tweaked to achieve other outcomes. They could be used as tools to do chemistry that is really challenging at the bench, or to create new molecules with important uses — so there's an application aspect to it. But we're also interested in it from a fundamental, "how does this protein work?" perspective.

You've sustained this work for almost 20 years now. What do you think has contributed to the productivity and longevity of the collaboration?

JS: I think it has a lot to do with how we think about problems. I do have a degree in chemistry, but I think in terms of the 3D structure of the enzymes that build these compounds. I approach it from a very protein-centric perspective: How does this protein perform its function, where did it come from, who are its ancestors? Whereas I think David thinks of it from a much more chemical perspective and the discovery of natural products.

DS: Yes, the fundamentals for me are driven by the architecture of the molecules. I can just look at a compound and get an instant sense that there is something unique and exciting happening, and I'll want to study it. I'm interested in the organic chemistry and the mechanisms of how it all comes together. But the way it comes together is through the enzymes that catalyze these reactions, which Janet studies. You can do all the chemistry without knowing anything about the enzymes, but ultimately you need to actually find

the enzymes and run the experiments to assess if they're working in the way that you're predicting. That's what structural biology has enabled.

So our interests fit together in a really important and complementary way. And I think one of the reasons we've had such a long, successful period of collaboration is because we can each contribute to the work in unique ways, but we're also both really interested in the whole picture. And that's really, in my view, where you want to be with a collaboration.

How has your focus evolved over the past two decades? Has it impacted the direction of your research programs or even the broader scientific field?

DS: Our work together has stimulated a lot of further integration of innovative methods that I think other people in the field have really adopted. What Janet's lab does gives us an amazing snapshot of how a substrate is actually held in an active site and offers insights into the potential mechanism for the reaction. We have this pipeline now: We isolate the molecule and select it as something we're really interested in, we figure out what the biosynthetic enzymes do, and then we get the structural biology information. And that's helped us to move into engineering proteins — to coax them to do things they can't do in nature, to expand their ability to accept unnatural compounds and diversify molecule structures — which is a field that is really exploding now.

JS: And more recently, there have been a lot of advances in computational biology that help us get a much deeper understanding of what we see in the structures. For example, in the paper we just published, we were able to draw on some of the computational work David had previously developed with another collaborator. That combination of calculations, biochemical data and what we saw in the structure allows us to tell a much richer story than we could if we lacked any one of those pieces.

You each collaborate with labs outside of the LSI and even outside the University of Michigan. Do you find that being in the same building makes a difference in the case of this collaboration?

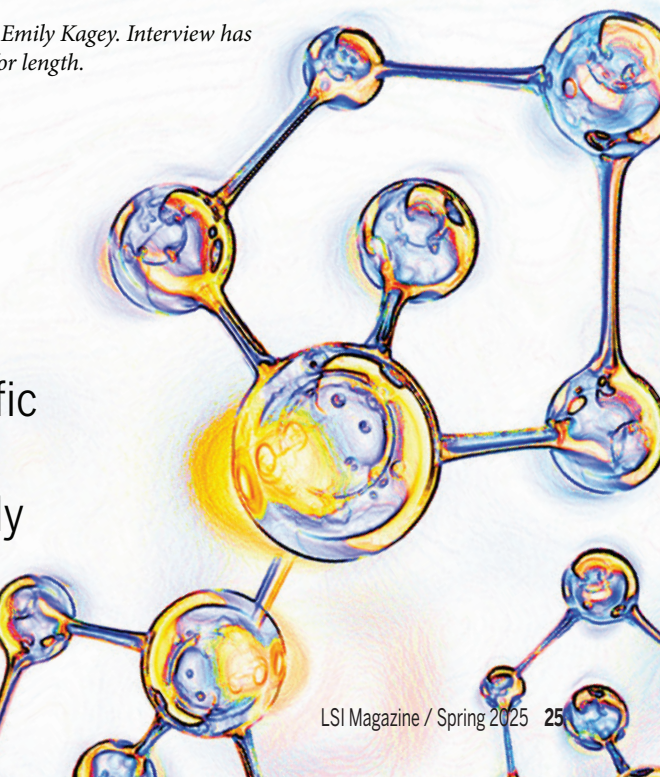
JS: I think the physical proximity of our labs has been extremely helpful. I don't believe we would've gotten as far as we have if we were on opposite sides of the same campus. It would have still worked; but there's just an easy exchange of expertise between the labs that we all benefit from by being right here. And for me, I love having people in the institute who have very, very different scientific backgrounds. The cross-fertilization and ability to learn from them is really wonderful.

DS: There are just endless opportunities to develop projects and push them forward, and the in-person aspect is such an important element for that. There is an osmosis when people get together from different fields and they can learn just by listening, watching, going into the lab, seeing what's happening. And it stimulates new interests and new ideas. It's really very special. ■

David Sherman is a Research Professor at the LSI; the Hans W. Vahlteich Professor of Medicinal Chemistry at the College of Pharmacy; a Professor of Microbiology and Immunology at the Medical School; and a Professor of Chemistry in the College of Literature, Science, and the Arts.

Janet Smith is the Associate Institute Director and Rita Willis Professor of the Life Sciences at the LSI; the Martha L. Ludwig Distinguished University Professor of Biological Chemistry at the Medical School; and a Professor of Biophysics, College of Literature, Science, and the Arts.

Interview by Emily Kagey. Interview has been edited for length.



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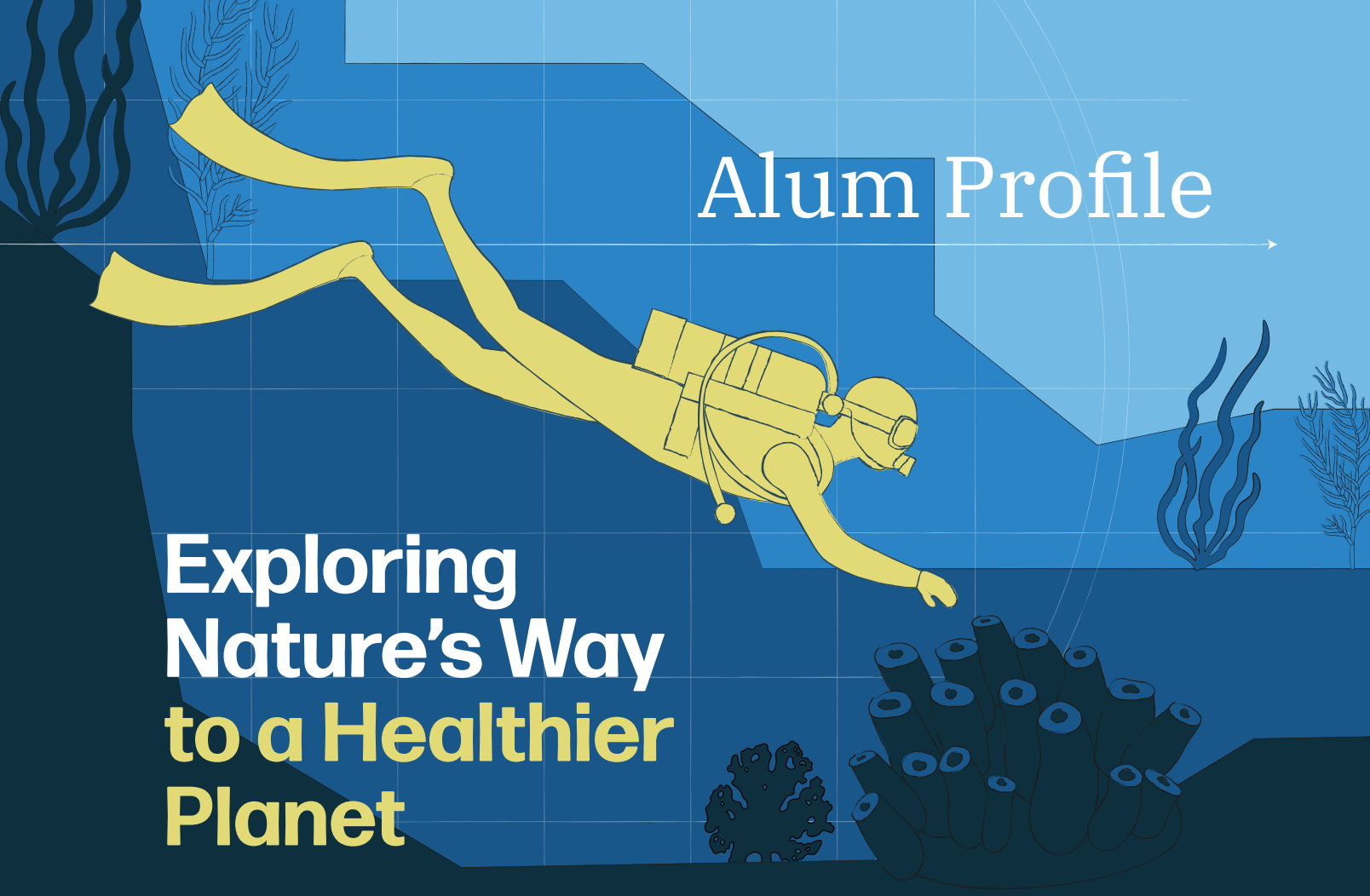

Alum Profile

Exploring Nature's Way to a Healthier Planet

By Staci Vernick

Inspired by her engineer father, teacher mother and environmental scientist aunt, Amy Fraley has charted a unique career path to the juncture of natural product chemistry, pharmaceutical sciences and environmental sustainability, with a core focus on educating the next generation of scientists.

Fraley is an assistant professor of medicinal chemistry at ETH Zürich, the Swiss Federal Institute of Technology and one of the top universities in continental Europe. At ETH, she leads a research group centered on bioactive natural products — generating enzymes and synthetic biology platforms that can be used to develop new medicines and better understand disease mechanisms. (Think of the powerful cancer drug paclitaxel, for example, bioengineered from yew trees.) The lab is also interested in how the natural defenses in plants and invertebrates could be harnessed to address the health of our planet.

This focus carries into the classroom, too, where Fraley teaches pharmaceutical biology with an emphasis on natural products derived from plants. Bioactive extracts and supplements are widely sold in pharmacies in Switzerland; she trains pharmacy students in the science of distinguishing fact from fiction regarding bioactive molecules in these preparations.

For Fraley, it all started with marine sponges.

As an undergraduate studying marine biology at Millersville University of Pennsylvania, she was fascinated by a section in her organic chemistry textbook about anti-cancer molecules isolated from sponges. The realization that complex chemistry occurs in natural systems spurred her decision to change her academic major and move to the Department of Chemistry.

In 2013 she made her way to the University of Michigan's Life Sciences Institute for a 10-week summer study program in the lab of chemist David Sherman, whose research focuses on the biosynthesis of natural products from microbes from both marine and terrestrial organisms.

Fraley saw the potential of natural product biochemistry to facilitate production of molecules with the potential to improve both human and environmental health.

"This was really a pivotal point in my career," Fraley recalls. "I realized after this experience in David's lab that this was the direction I wanted to go with my career and I, too, had the potential to obtain a doctorate in this field."

After completing her bachelor's degree in chemistry, she returned to U-M to pursue her Ph.D. in pharmacy, again joining the Sherman lab and adding LSI faculty member Janet Smith as a co-mentor. Fraley says co-mentoring made perfect sense for pursuing her academic interests.

"I could do the whole span of natural products research in their groups, both of them in the LSI, one floor apart," she explains. "It exemplified the kind of collaboration that's fostered in the LSI."

When it came time to begin her postdoctoral research, Fraley's initial fascination with sponges lured her to work in the lab of Jörn Piel at ETH Zürich.

Piel had discovered that, many times, it's not the sponge that makes the anti-cancer molecules — it's actually a microbe living inside it, Fraley says. In the Piel lab she studied *Mycale hentscheli*, a marine sponge species known to be a prolific source of anti-cancer polyketides.

"For a while it's been unknown how these compounds were made. I'm figuring that out, what organism is making them and how they do it," Fraley says. "The final results aren't published yet, but it's an exciting story."

> I could do the whole span of natural products research in their groups, both of them in the LSI, one floor apart.

Amy Fraley, Ph.D.

Fraley finished her postdoctoral fellowship in December 2023. During her time abroad, she found she really liked Switzerland and the excellence of research at ETH, she says. She landed her tenure-track position at ETH Zürich in January 2024 and launched her research program. Now the group is combining synthetic chemistry with biochemistry to produce complex molecules that can be used to understand disease mechanisms in humans and plants.

One challenge for the field, she says, is the sustainable production of natural products — not over-farming plants and sponges with bioactive properties. To that end, one of the first projects in her group involves the laboratory cultivation of bioactive Swiss alpine plants.

"That brings us to the next challenge, which is using our knowledge in natural product chemistry and medicinal chemistry to give back to nature," Fraley says. "Instead of just taking from nature to develop medicines, how can we use similar methodologies to ultimately protect biodiversity? With our laboratory cultures, we are generating microcosms, studying their metabolic reactions to environmental changes and ultimately using these data to understand the resilience of protected plants under climate change conditions.

"It's caring for the planet and caring for human health at the same time." ■

Photo by Michael Ruepp

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for technologies and expertise that accelerate scientific possibilities

for fundamental discoveries with global impact ▸

Look to the Life Sciences Institute at the University of Michigan

SCAN ME

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LIFE SCIENCES INSTITUTE
UNIVERSITY OF MICHIGAN

Awards

WENJING WANG
NSF Faculty Early Career Development (CAREER) Award, 2024 Sloan Research Fellow

DAVID SHERMAN
American Society of Pharmacognosy Norman R. Farnsworth Research Achievement Award

ROGER CONE
Named the Tadataka Yamada Distinguished University Professor of Molecular and Integrative Physiology

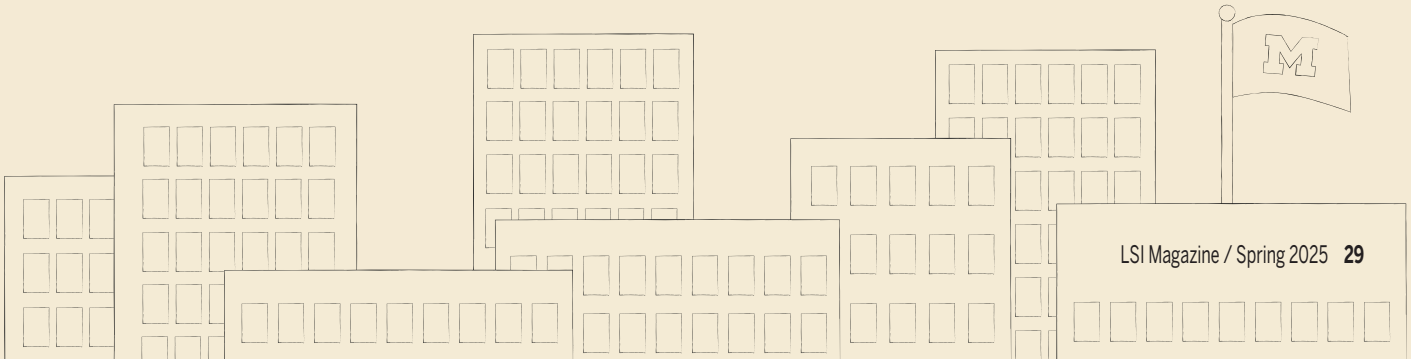
Promotions

MICHAEL CIANFROCCO
Promoted to associate professor with tenure

ALISON NARAYAN
Promoted to professor

JEANNE STUCKEY
Promoted to research professor

WENJING WANG
Promoted to associate professor with tenure



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LSI Faculty

Jay Brito Querido, Ph.D.
Research Assistant Professor

Assistant Professor of Biological Chemistry, **Medical School;** Faculty Scholar, Center for RNA Biomedicine

Research areas: cryo-electron microscopy, mRNA translation, RNA helicases, biochemistry

LSI MED

Michael Cianfrocco, Ph.D.
Research Associate Professor

Associate Professor of Biological Chemistry, **Medical School**

Research areas: cryo-electron microscopy, single molecule methods, biochemistry, intracellular transport

LSI MED

Roger D. Cone, Ph.D.
Mary Sue Coleman Director
Research Professor

Vice Provost and Director, **U-M Biosciences Initiative**; Tadataka Yamada Distinguished University Professor of Molecular and Integrative Physiology, **Medical School**; Professor of Molecular, Cellular, and Developmental Biology, **College of Literature, Science, and the Arts**

Research areas: neurobiology of obesity, energy homeostasis, cachexia, anorexia nervosa

LSI LSA MED

Herman Fung, Ph.D.
Research Assistant Professor

Assistant Professor of Cell and Developmental Biology, Assistant Professor of Biological Chemistry, **Medical School**

Research areas: cryo-correlative light and electron microscopy, cryo-electron tomography, chromatin structure

LSI MED

David Ginsburg, M.D.
Research Professor

James V. Neel Distinguished University Professor of Internal Medicine and Human Genetics, Warner-Lambert/Parke-Davis Professor of Medicine, Professor of Pediatrics, **Medical School**

Research areas: hematology, blood clotting, genetics, intracellular transport

LSI MED

Ken Inoki, M.D., Ph.D.
Research Associate Professor

Roger C. Wiggins Collegiate Professor of the Life Sciences; Associate Professor of Internal Medicine and Molecular and Integrative Physiology, **Medical School**

Research areas: nutrient sensing, mTOR/AMPK signaling, diabetic complications, cancer

LSI MED

Daniel J. Klionsky, Ph.D.
Research Professor

Alexander G. Ruthven Professor of Life Sciences; Professor of Molecular, Cellular, and Developmental Biology, **College of Literature, Science, and the Arts**

Research areas: autophagy, cell biology

LSI LSA

Cheng-Yu Lee, Ph.D.
Research Associate Professor

Robert H. Bartlett Collegiate Professor of the Life Sciences; Associate Professor of Internal Medicine and Cell and Developmental Biology, **Medical School**

Research areas: stem cells, neurological disease

LSI MED

Tools and Model Systems

Cell culture · Cryo-EM/ET · *Drosophila* · Mice · Yeast · Zebrafish

Photos by Leisa Thompson Photography and Michigan Photography; Leisa Thompson

LSI Faculty

Tzumin Lee, M.D., Ph.D.
Research Professor

Peter D. Meister Professor of the Life Sciences; Professor of Molecular, Cellular, and Developmental Biology, **College of Literature, Science, and the Arts**; Howard Hughes Medical Institute Investigator

Research areas: cell lineage, brain development, neural stem cell fate, neural regeneration, single-cell genomics

LSI | LSA | HHMI

Peng Li, Ph.D.
Research Assistant Professor

Assistant Professor of Biologic and Materials Sciences, **Dental School**; Assistant Professor of Molecular and Integrative Physiology, **Medical School**

Research areas: molecular neuroscience, breathing and sighing

LSI | DENT | MED

Jiandie Lin, Ph.D.
Research Professor

Bradley M. Patten Collegiate Professor of the Life Sciences; Professor of Cell and Developmental Biology, **Medical School**

Research areas: obesity-associated metabolic disease, signaling and gene transcription, metabolic tissue development

LSI | MED

Anna Mapp, Ph.D.
Research Professor

Associate Dean for Academic Programs and Initiatives, **Horace H. Rackham School of Graduate Studies**; Edwin Vedejs Collegiate Professor of Chemistry, **College of Literature, Science, and the Arts**

Research areas: synthetic organic chemistry, chemical biology, molecular biology

LSI | LSA

Rowena Matthews, Ph.D.
Research Professor Emerita

G. Robert Greenberg Distinguished University Professor Emerita of Biological Chemistry, **Medical School**; Professor Emerita of Chemistry and Research Professor Emerita of Biophysics, **College of Literature, Science, and the Arts**

Research areas: vitamin-derived cofactors in the catalysis of complex chemical reactions

LSI | LSA | MED

Shyamal Mosalaganti, Ph.D.
Research Assistant Professor

Assistant Professor of Cell and Developmental Biology, Assistant Professor of Biological Chemistry, **Medical School;** Assistant Professor of Biophysics, **College of Literature, Science, and the Arts**

Research areas: cryo-electron tomography, cryo-electron microscopy, organelles

LSI | LSA | MED

Alison Narayan, Ph.D.
Research Professor

Mary Sue Coleman Collegiate Professor of the Life Sciences; Professor of Chemistry, **College of Literature, Science, and the Arts;** Director, Program in Chemical Biology

Research areas: biocatalysis, complex molecule synthesis, natural products

LSI | LSA

Melanie Ohi, Ph.D.
Research Professor

Rowena G. Matthews Collegiate Professor of the Life Sciences; Professor of Cell and Developmental Biology, **Medical School**

Research areas: cryo-electron microscopy, biochemistry, genetics, bacterial pathogenesis

LSI | MED

Tools and Model Systems

Cryo-EM/ET | *Drosophila* | Mice | Natural products | Yeast | Zebrafish

Photos by Leisa Thompson Photography and Michigan Photography, Leisa Thompson

LSI Faculty

Carole Parent, Ph.D.
Research Professor

Raymond and Lynne Ruddon Collegiate Professor of Cancer Biology and Pharmacology, Professor of Cell and Developmental Biology, **Medical School**

Research areas: cancer biology, cell biology, pharmacology, chemotactic signaling

LSI | MED

David H. Sherman, Ph.D.
Research Professor

Hans W. Vahlteich Professor of Medicinal Chemistry, **College of Pharmacy**; Professor of Microbiology and Immunology, **Medical School**; Professor of Chemistry, **College of Literature, Science, and the Arts**

Research areas: natural product biosynthesis, synthetic organic chemistry, marine microorganisms, drug discovery

LSI | LSA | MED | PHARM

Janet L. Smith, Ph.D.
Associate Director
Research Professor

Martha L. Ludwig Distinguished University Professor of Biological Chemistry, **Medical School**; Rita Willis Professor of the Life Sciences; Professor of Biophysics, **College of Literature, Science, and the Arts**

Research areas: structural biology of viral and antiviral proteins and enzymes of natural product biosynthesis

LSI | LSA | MED

Chelsey Spriggs, Ph.D.
Research Assistant Professor

Assistant Professor of Cell and Developmental Biology, Assistant Professor of Microbiology and Immunology, **Medical School**

Research areas: viral-host interactions, oncolytic and oncogenic viruses, cell biology

LSI | MED

Wenjing Wang, Ph.D.
Research Associate Professor

William R. Roush Associate Professor of Chemistry, **College of Literature, Science, and the Arts**

Research areas: chemical biology, protein engineering, neuroscience, optogenetics, nanobody design

LSI | LSA

Lois Weisman, Ph.D.
Research Professor

Sarah Winans Newman Collegiate Professor of the Life Sciences; Professor of Cell and Developmental Biology, **Medical School**

Research areas: organelle inheritance, phosphoinositide signaling, cancer, neuroscience

LSI | MED

Stephen J. Weiss, M.D.
Research Professor

E. Gifford and Love Barnett Upjohn Professor of Internal Medicine and Oncology, **Medical School**

Research areas: cancer, metastasis, stem cell functions, angiogenesis, inflammation

LSI | MED

Connie Wu, Ph.D.
Research Assistant Professor

Assistant Professor, Biomedical Engineering, **College of Engineering**; Assistant Professor of Pharmaceutical Sciences, **College of Pharmacy**

Research areas: biomolecular engineering, single-molecule detection, RNA therapeutics, clinical diagnostics

LSI | ENG | PHARM

Tools and Model Systems

Cell culture | Mice | Natural products | X-ray crystallography | Yeast

Photos by Leisa Thompson Photography

LSI Faculty

Jun Wu, Ph.D.
Research Associate Professor

Jessica Schwartz Collegiate Professor of the Life Sciences; Associate Professor of Molecular and Integrative Physiology and Internal Medicine, **Medical School**

Research areas: "beige" thermogenic fat cells, metabolism, alcoholic liver disease, nonalcoholic steatohepatitis

LSI MED

X.Z. Shawn Xu, Ph.D.
Research Professor

Bernard W. Agranoff Collegiate Professor in the Life Sciences; Professor of Molecular and Integrative Physiology, **Medical School**

Research areas: sensory transduction, synaptic mechanisms underlying behavior and addiction, aging and longevity

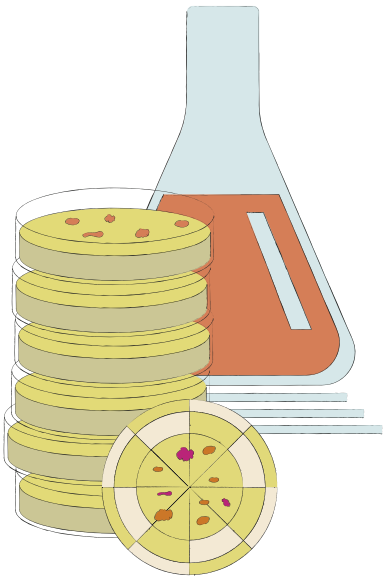
LSI MED

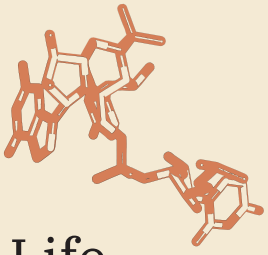
Bing Ye, Ph.D.
Research Associate Dean
Research Professor

Burton L. Baker Collegiate Professor of the Life Sciences; Professor of Cell and Developmental Biology, **Medical School**

Research areas: neuronal development, neurodevelopmental diseases

LSI MED





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LSI

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Research Professor

Center for Structural Biology Director and Research Professor, **Life Sciences Institute**; Research Professor, Biological Chemistry, **Medical School**; Research Professor, Biophysics, **College of Literature, Science, and the Arts**

LSI LSA MED

Ashootosh Tripathi, Ph.D.
Associate Research Scientist

Natural Products Discovery Core Director and Associate Research Scientist, **Life Sciences Institute**; Research Associate Professor of Medicinal Chemistry, **College of Pharmacy**

LSI PHARM

Tools and Model Systems

C. elegans Cell culture *Drosophila* Mice

Photos by Leisa Thompson Photography

Year in Photos

All photos by Rajani Arora, LSI, unless otherwise noted

LSI community members gathered to celebrate the Lunar New Year.

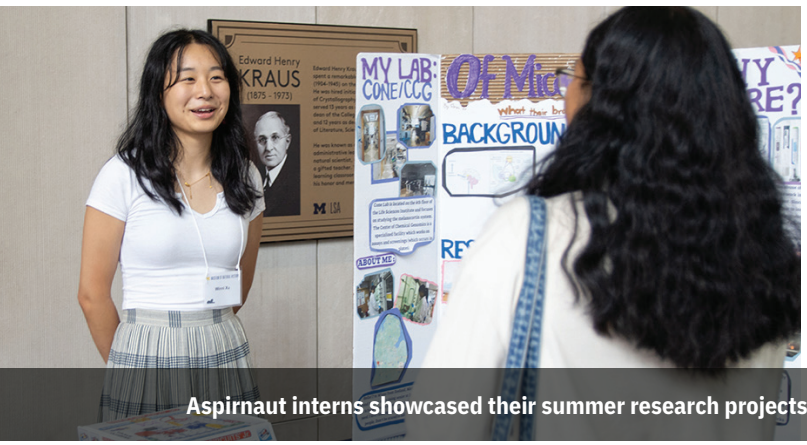
Kareem Abouilhosn, PCB

PCB students stepped away from the lab to volunteer at the Veterans Memorial Park.

At the 2024 LSI SciComm Series lecture, Sophie Bushwick discussed the promises and pitfalls of AI for science communication.

The LSI hosted a pie baking competition in honor of Pi Day.

Trainees presented posters to share their current projects and findings with the LSI community.



Aspirnaut photos by Sophie Gabrysiak

Aspirnaut interns showcased their summer research projects at U-M's Museum of Natural History with a variety of interactive activities.

The LSI community celebrated the launch of LSI CONNECTS, a new community initiative that brings people together through shared hobbies and interests.

Scientists came from across the country to gain experience in data processing at the cryo-ET summer workshop.

Bing Ye hosted a symposium to showcase his team's new AI-based software suite, LabGym, used for automating video analysis and quantification of animal behavior.

Scott Summers, Ph.D., from the University of Utah presented the first LSI Seminar Series of 2024.

U-M President Santa Ono met with LSI leaders and advisory board members at their fall meeting.

The Program in Chemical Biology hosted its annual fall retreat.

The Michigan Pioneer Fellows hosted their annual symposium featuring fellow talks, a poster session and keynote speaker Catherine Drennan, Ph.D.

LSI members competed in the institute's annual Halloween costume contest.

LSI faculty gathered for a Cryo-EM retreat at the U-M observatory.


LSI
20
IMPACT


20
CELEBRATING 20 YEARS OF IMPACT
Saltiel Life Sciences Symposium
May 20 and 21, 2024
Kahn Auditorium,
Taubman Biomedical Science Research Building
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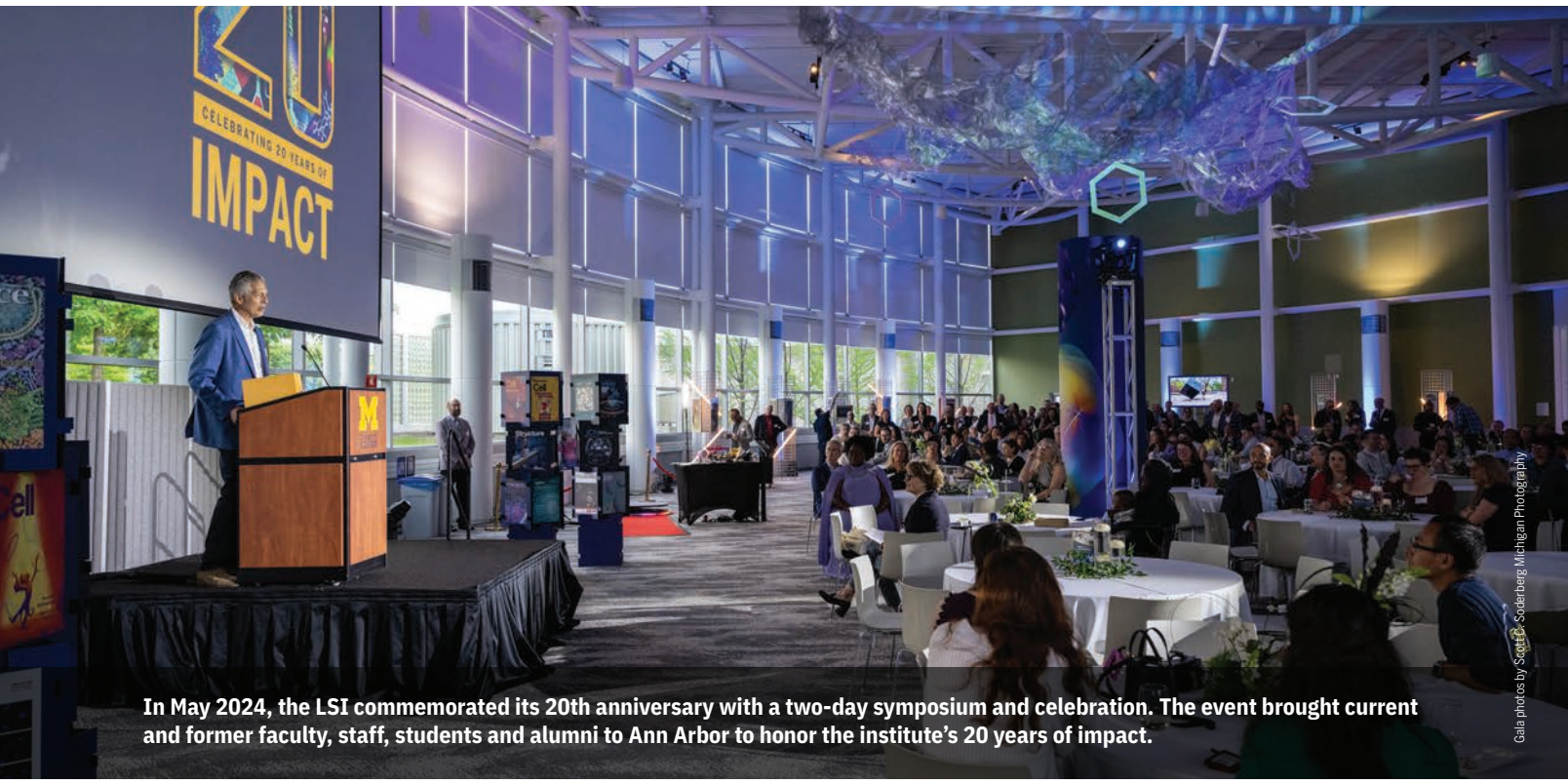
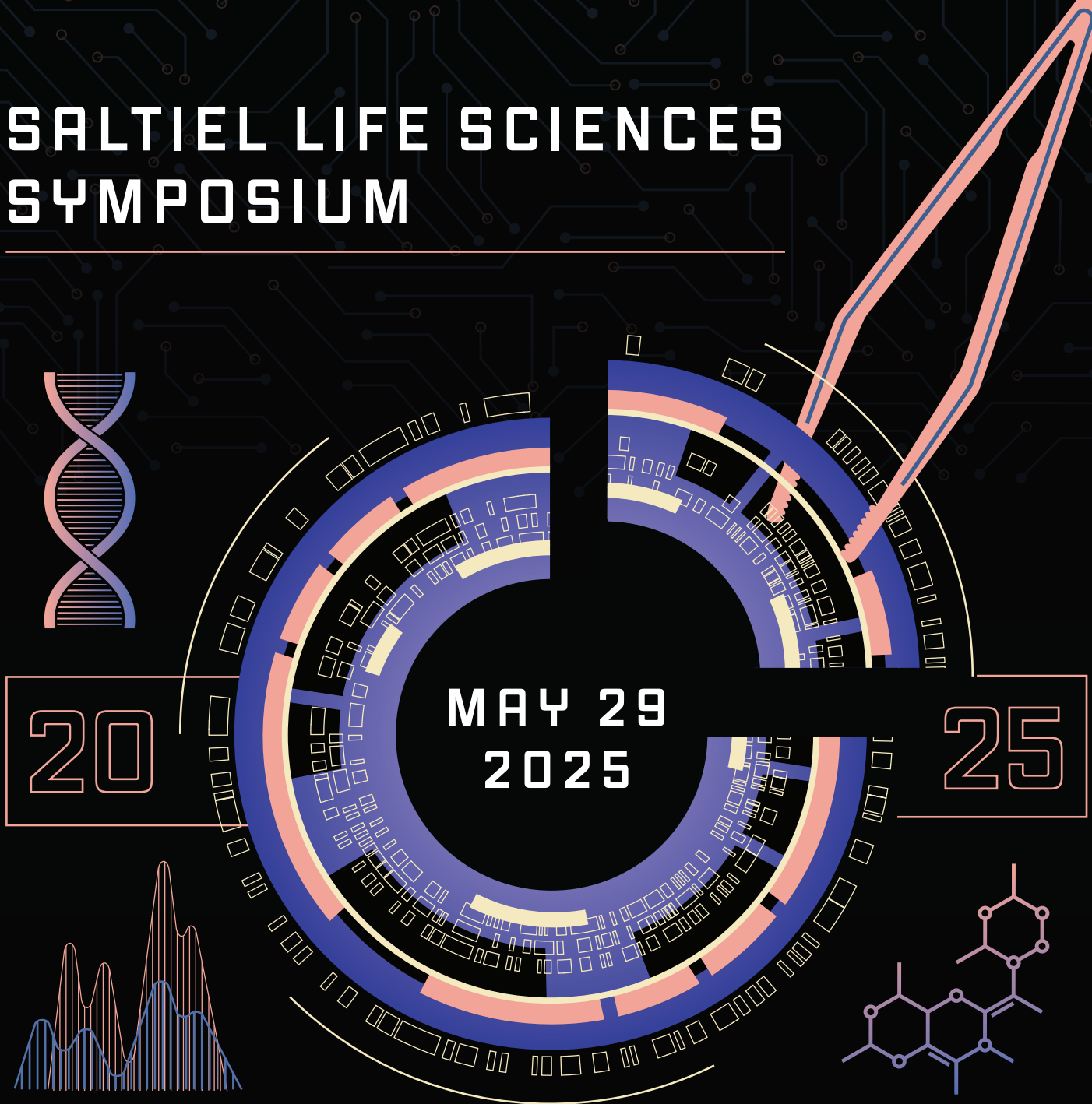
LIFE SCIENCES INSTITUTE



In May 2024, the LSI commemorated its 20th anniversary with a two-day symposium and celebration. The event brought current and former faculty, staff, students and alumni to Ann Arbor to honor the institute's 20 years of impact.

Gala photos by Scott C. Soderberg Michigan Photography

SALTIEL LIFE SCIENCES SYMPOSIUM



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