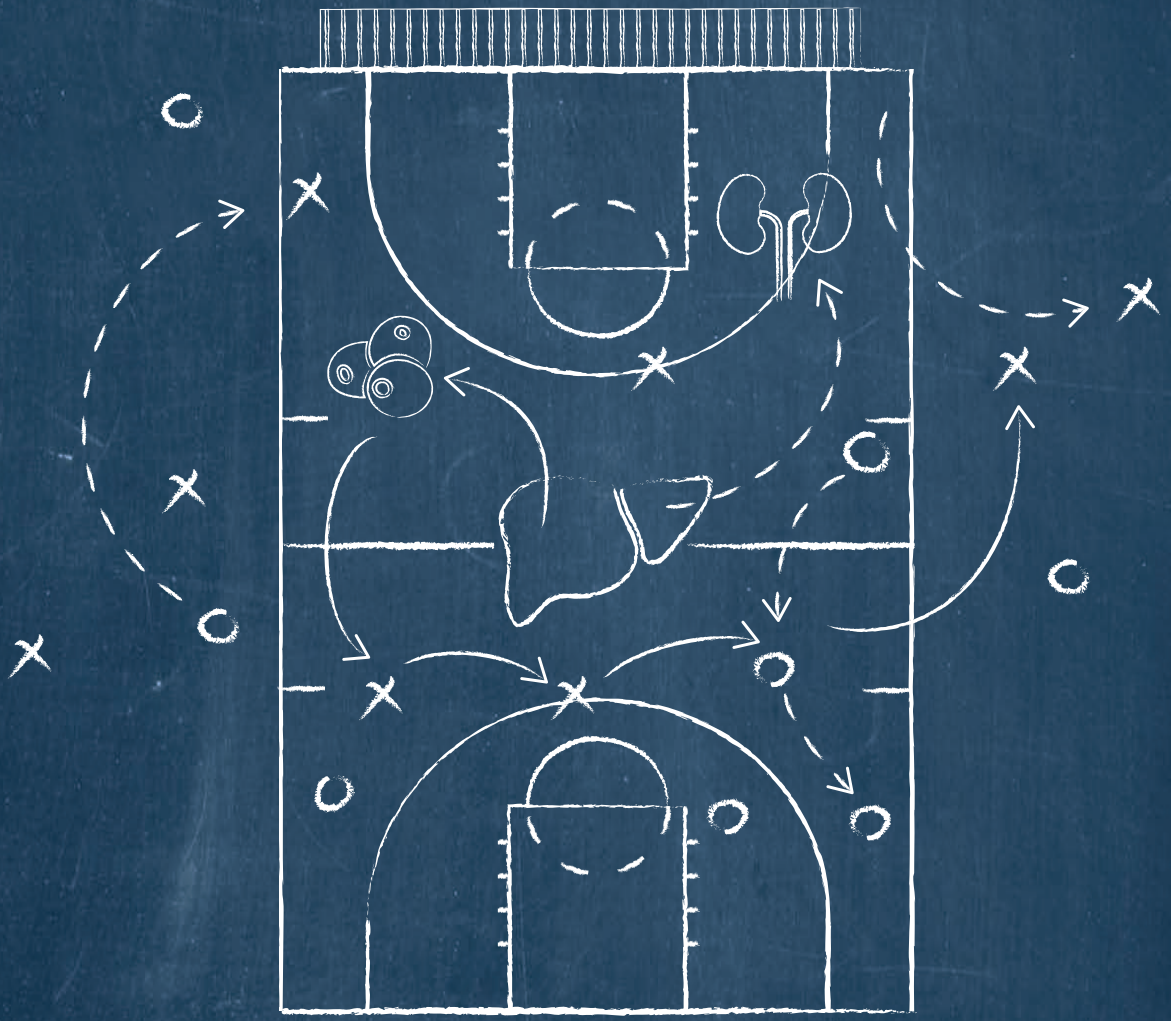
LIFE SCIENCES INSTITUTE
UNIVERSITY OF MICHIGAN
Spring 2026

METABOLIC MASH-UP

Combining their diverse expertise, LSI researchers are putting a full-court press on metabolic health and disease



OPEN GYM

This open-source software program is using AI to level the playing field in animal behavior research

TRAINING GROUND

In the LSI's collaborative environment, trainees build the skills to become team leaders

HOME FIELD ADVANTAGE

Director Roger Cone discusses how experts across disciplines tackle complex challenges together at the LSI, and how this collaborative spirit leads to scientific wins

From the Director

"The Team, The Team, The Team."

It's almost impossible to have any association with the University of Michigan and not know this quote from Bo Schembechler's famous 1983 speech. While originally used to define what differentiated that group of football players from their opponents — their ability to play, and win, as a team — the idea has since permeated U-M's entire culture.

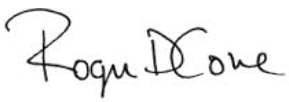
But how does it apply to fundamental scientific research and the Life Sciences Institute?

The phrase "team science" is often used to describe large, multi-institutional projects focused on tackling one specific health challenge. This is critical to discovery in many instances; but teams don't wake up in the middle of the night thinking, "I have got to figure out how to solve this. I'm going to solve this problem." Teams need champions because, as Billie Jean King said, "Champions keep playing until they get it right."

That is why the team science that we are creating at the LSI is really built around individuals, creating a team through the "best athlete" model. Our institute is intentionally structured around the concept of multidisciplinarity, with nationally leading scientists in a diversity of fields, from synthetic organic chemistry to human medical genetics and everything in between. We bring these individual players, each an expert in their own position, together in a single building where they break down the barriers between disciplines and work together to solve problems.

The results of our approach to team science are evident throughout this year's issue of the LSI Magazine, from the numerous research advances over the past year involving multiple LSI labs, through the feature article exploring how distinct labs at the LSI are, together and individually, advancing the field of metabolic health research. In the article "Training Ground," you'll learn how we are instilling this approach to scientific excellence and collaboration in LSI trainees, as they train at the bench today to become tomorrow's team leaders. In "Open Gym," you'll discover how one LSI lab's pursuit of a technological question is benefiting animal behavior research worldwide. And in a Q&A later in the magazine, I explain more about how this very approach has benefited my own lab's work within the LSI.

As is clear throughout this magazine, and throughout the halls of our building, the LSI's excellence stems from the combined effort of each community member who shows up every day for this team. In August, I will conclude my second and final term as the Mary Sue Coleman Director of the Life Sciences Institute. I am tremendously excited to see what the future holds for the LSI under our next coach and to once again put 110% of my effort into solving some difficult scientific questions as a rank-and-file member of this championship team.



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Back cover: Researchers in Jiandie Lin's lab investigate mechanisms that regulate nutrient and energy metabolism in cells, tissues and organisms. They have discovered that immune cells called TREM2+ macrophages in fat tissue, identified by Trem2 and Ms4a7 mRNA (red and yellow), contribute to dead cell clearance and fat tissue remodeling during obesity. Image credit: Linkang Zhou and Jiandie Lin.

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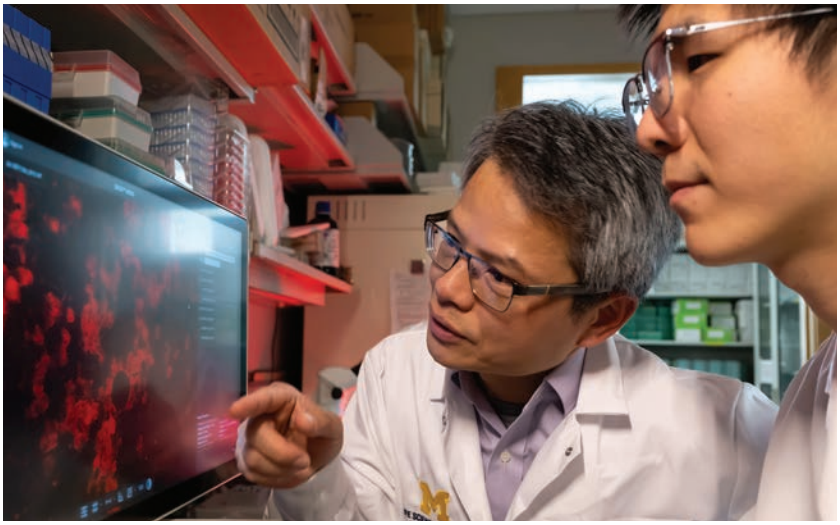
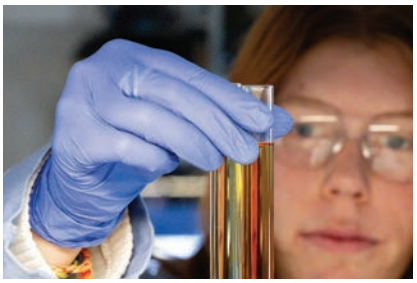




LIFE SCIENCES INSTITUTE
UNIVERSITY OF MICHIGAN

Photos by Leisa Thompson, Michigan Photography and Cédric Sueur (Open Gym)

Advances

Weisman & Cianfrocco labs
Journal of Cell Biology
May 2025

How cellular delivery trucks secure precious cargo

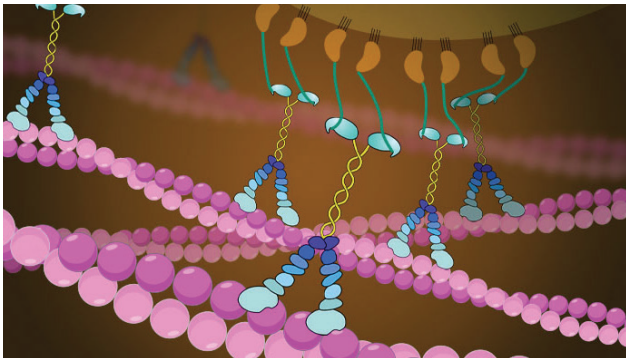
It's always rush hour inside your cells, with proteins constantly commuting to specific sites to perform their assigned tasks. Cells don't have subways to transport these subunits to work; rather, they rely on delivery trucks in the form of motor proteins to pick up cellular cargo and move it to its destination on time.

One such motor protein is myosin-V, which uses adaptor proteins to latch onto the cargo. Myosin-V proteins play an essential role in a wide range of cellular processes, and they can lead to life-threatening diseases when they malfunction.

"And so there's a lot of interest in how these myosin-V motors work," says LSI Professor Lois Weisman.

The flexible nature of these adaptor proteins makes them difficult to study, but two labs at the LSI decided to take on this challenge together. Using advanced microscopy techniques, researchers in the labs of Weisman and Michael Cianfrocco discovered that the latch's connection is more robust than the previously proposed models. The tighter, handhold connection would hold tight even in challenging environments, such as squeezing into a new emerging cell.

Lily Hahn, a former Weisman lab graduate student and the study's lead author, explains, "This new structural model of the binding mechanism offers important insights into how this crucial process is tightly regulated to support proper cell function."



Parent lab
Nature Cell Biology
May 2025

Inflammation 'off' switch

With media and doctors alike emphasizing the dangers of long-term inflammation, we often forget that inflammation, in moderation, sometimes is exactly what our body needs to stay healthy.

White blood cells called neutrophils, for example, initiate inflammation to start healing damaged tissue. When injury occurs, they rush to the injury site and begin clearing out harmful materials. Along the way, these first responder cells leave chemical cues to recruit more neutrophils to the job.

While this initial inflammation is beneficial, it needs an "off" switch to avoid developing into more harmful chronic inflammation, which can lead to issues like arthritis and auto-immune conditions.

LSI faculty member Carole Parent investigates how neutrophils migrate and communicate with each other to start and stop inflammatory responses. Her team recently discovered that, along with the recruitment cues, the neutrophils also release tiny pieces of their own DNA as they migrate.

When these DNA fragments were removed from their migration route, the neutrophils continued their inflammatory response much longer than necessary.

The secreted DNA, it turns out, sticks to the chemicals that recruit neutrophils in a way that holds them in place so the concentration spikes. When the concentration reaches a certain threshold, a switch is flipped and the neutrophils know their task is complete.

"In a way, neutrophils exist to die, so they don't need to preserve their DNA the way most cells in the body do," Parent says. "The way I view it is that these cells are programmed to use everything they have to defend the body, including their own DNA."

100–200 billion
The number of new neutrophils the human body produces each day; half of these cells will die within their first 24 hours

Weisman and Mosalaganti labs
Molecular Biology of the Cell
June 2025

Protein's 'star' power essential for cellular health

Cellular biologist Lois Weisman is an expert at measuring minute quantities. One of the molecules her lab studies, a signaling lipid called PI(3,5)P2, represents less than 0.01% of the components found in cellular membranes.

Though little more than a rounding error in a cell's composition, PI(3,5)P2 is critical to sustaining cellular health. Previous work from the Weisman lab showed that even slight reductions in PI(3,5)P2 levels can lead to neurodegeneration.

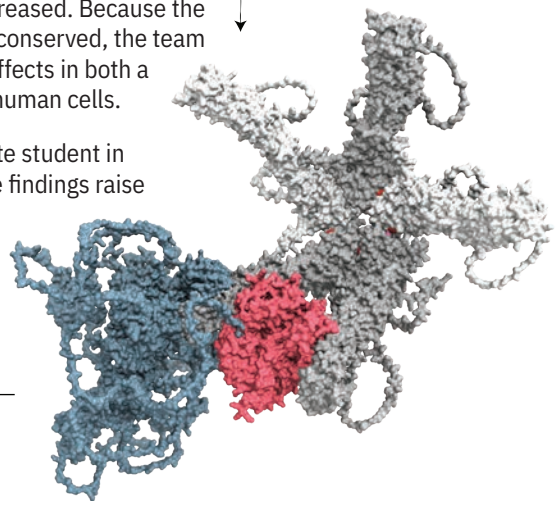
The building blocks of PI(3,5)P2 are no less vital. Mutations in the genetic code of VAC14, one of the proteins involved in the synthesis of PI(3,5)P2, have been found in patients with childhood-onset neurodegeneration.

"But no one knew what the mutations did at the molecular level and how they were causing damage," Weisman says.

Weisman teamed up with LSI structural biologist Shyamal Mosalaganti to predict how the mutated proteins were malfunctioning in their cellular environment. Using advanced microscopy, biochemistry and AI modeling tools, they determined the effect of the mutations.

In a normal cell, PI(3,5)P2 production begins when five VAC14 proteins connect in the shape of a star. The mutations Weisman's team was investigating turned out to disrupt these connections, causing the star complex to disintegrate. Without the VAC14 star, PI(3,5)P2 production decreased. Because the VAC14 star is genetically conserved, the team was able to verify these effects in both a yeast model system and human cells.

Tunahan Uygun, a graduate student in Weisman's lab, says, "The findings raise the possibility that strengthening the VAC14 connections could offer an avenue for targeting these diseases."



PIKfyve-VAC14-FIG4 complex. Image credit: Tunahan Uygun.

> *"Understanding how RNA-binding proteins interact with RNA under different conditions is key to understanding how genes are regulated and respond to changes.*
>
> — Jay Brito Querido, Ph.D.

Brito Querido lab
Cell
September 2025

This SPIDR spins a web of proteins and RNA

Ribonucleic acid (RNA) controls how our genetic code gets translated into the proteins that carry out the work of all cells. But what controls the RNA's activity?

Of the more than 100,000 unique proteins in the human body, up to 30% bind to RNA to regulate everything from the start of the translation process to the final degradation of the RNA. Mutations in these RNA-binding proteins (RBPs) are known to cause myriad diseases; yet the precise function of most of these proteins remains unknown, because scientists have not been able to map how they bind to RNA and what job they perform through that connection.

"Understanding how RNA-binding proteins interact with RNA under different conditions is key to understanding how genes are regulated and respond to changes," explains LSI faculty member Jay Brito Querido.

Existing tools map these relationships at a painstakingly slow rate — one RBP at a time — in a limited number of cell types, resulting in maps that may not be accurate in other cells or organisms.

A new protocol called SPIDR (short for "split-and-pool identification of RBP targets") aims to overcome these challenges. Developed by a team spanning the University of Michigan, Columbia University, the University of Southern California and the California Institute of Technology, this multiplexed method enables researchers to map dozens to hundreds of RBPs and RNAs in a single experiment, quickly spinning a web of connections.

Combining the method with advanced microscopy techniques, Brito Querido and colleagues have already identified new interactions that help explain how and when RNA is converted into new proteins.

Narayan lab
Nature
October 2025

Matchmaking for enzymes

"Do you have a biocatalyst that can run this reaction?" Chemist and LSI faculty member Alison Narayan says this may be the question she hears most frequently. So she and her collaborators built a tool to answer it.

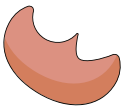
Biocatalysts, enzymes that initiate or speed up biochemical reactions, are proteins that have evolved to perform intricate chemical transformations with incredible efficiency. Unlike synthetic pipelines, enzymes often can perform reactions in water and at room temperature, reducing the need for toxic or expensive chemical reagents.

This efficiency comes with a trade-off, though: Biocatalysts have evolved to work very well with the specific starting materials, or substrates, that they interact with in their natural environment. To realize the full potential of biocatalysis in the lab, chemists need to know what other substrates a given enzyme can work with.

Narayan's team, in partnership with Gabe Gomes' group at Carnegie Mellon, has created a web-based tool that puts that knowledge — and biocatalysis — in reach for more chemists. Starting with a diverse dataset of potential matches between enzymes and substrates, the team developed an algorithm that predicts the relationship between enzyme space and substrate space.

The resulting open-access platform, called CATNIP, enables chemists to input a given substrate and receive a ranked list of enzymes that will enable a chemical transformation, and vice versa.

"It is a great starting model to enable synthetic campaigns using biocatalysts," says Alexandra Paton, a former postdoctoral researcher in Narayan's lab who led this work. "And there is already work underway to begin expanding the database."



<1%

The percentage of natural enzyme sequences whose chemical function is known

Nearly **15 billion** pounds of waste are produced by the chemical industry annually

Narayan lab
Nature
November 2025

Nature's key unlocks a molecular mirror

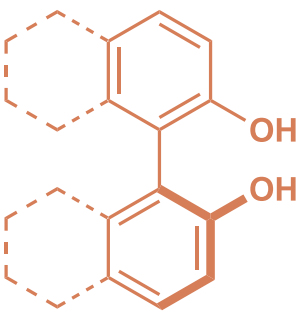
Hold your hands palm to palm, and they look the same. But, no matter how you rotate them, your left hand cannot convert into the exact arrangement of your right hand. Chemists call arrangements like this enantiomers: two substances that have the same composition, but are in fact non-superimposable mirror images of each other.

Enantiomers are a natural result of the reactions that produce chemical substances. While these reactions control which and how many molecules come together, they often lack specificity in their precise three-dimensional arrangement. This can result in a mixture of molecules that are mirror images of each other, which then have to be separated to isolate only the desired version.

Researchers in Alison Narayan's lab at the LSI wanted to see if they could engineer an enzyme that would produce only one enantiomer of a commonly used compound called a BINOL. Instead, they unlocked a new process for converting one enantiomer into its mirror image.

Because of their complex structure, BINOL enantiomers are locked in place around one bond and cannot rotate to convert into the other form. But that's exactly what was happening in the researchers' experiment. Five minutes into the reaction, the solution contained equal parts of both enantiomers. An hour later, the product was composed almost entirely of the desired enantiomer.

This discovery unlocks the potential of enzymes to selectively enrich chemical solutions for a single enantiomer. Building on this proof-of-principle could dramatically reduce chemical waste by removing the need to separate and discard unwanted enantiomers.



Sherman and Pereira labs
Communications Chemistry
December 2025

Bacterial boost for anti-malarial drug development

Even with existing treatments, malaria remains a global health crisis. The disease-causing parasite led to over 280 million infections and 600,000 deaths in 2024 alone. And as it continues to evolve new ways to survive treatments, another threat looms on the horizon: multidrug-resistant malaria.

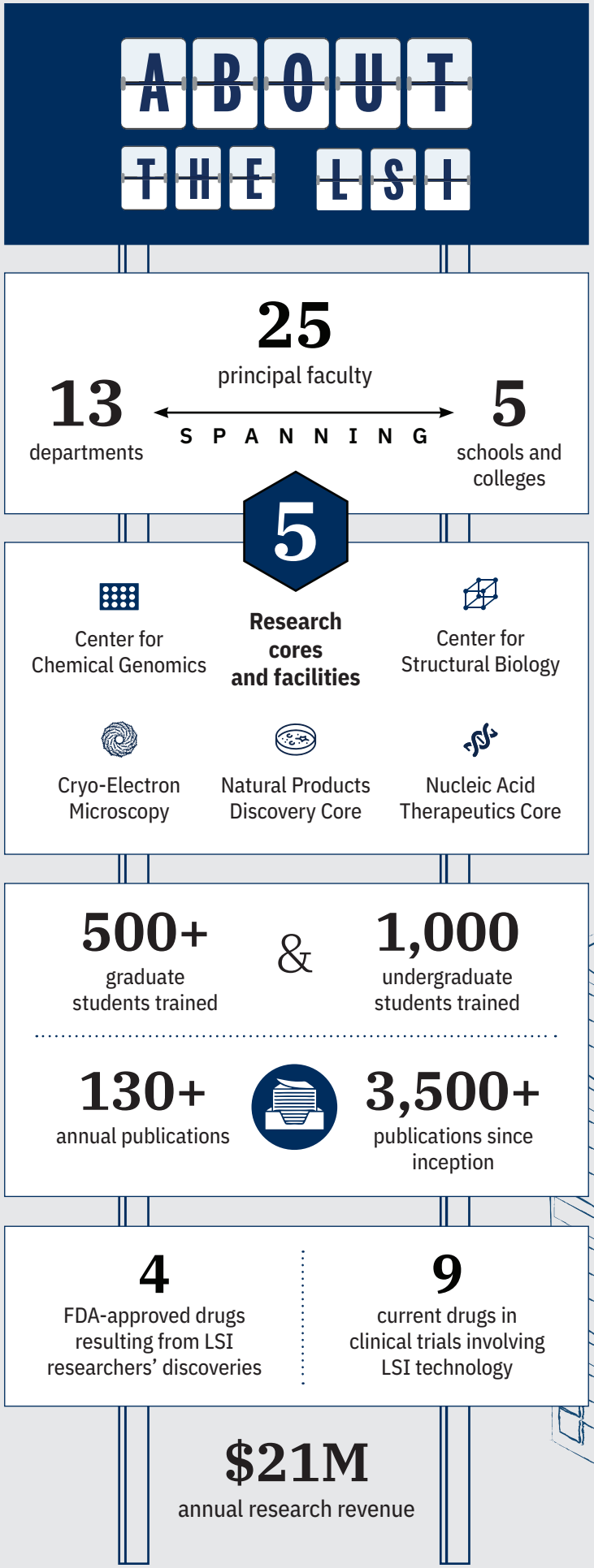
"The problem with any fast-replicating organism, like this parasite, is that it can develop resistance to current drug regimens if they are used over extended periods of time," says LSI faculty member David Sherman. "So it is imperative that we continue urgent efforts to stay a step ahead of the parasite."

The labs of Sherman and U-M bioengineer Filipa Pereira are pursuing such an effort, with the help of genetically modified bacteria.

Their approach centers on a chemical compound called premarineosin A, which is known to have anti-malarial properties but has remained understudied for a frustratingly simple reason: lack of supply. The bacteria that make the compound produce too little to be useful for research, and chemists have not found a way to manufacture it efficiently through total chemical synthesis.

The team noticed that a bacterial strain Sherman studies for its anti-HIV properties also had the genetic blueprints to make premarineosin A. Pereira found a way to augment the genetic "on" switch for the pathway that builds premarineosin, coaxing the bacteria to increase their production 150-fold.

With workable quantities of the compound in hand, the researchers have begun developing new versions by introducing specific edits to its chemical structure. So far, one version has demonstrated 20 times more activity against a drug-resistant strain of the malaria-causing parasite than the starting compound, with almost no toxicity to human cell cultures.

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LSI

Metabolic MASH-Up

COMBINING THEIR DIVERSE EXPERTISE, LSI RESEARCHERS ARE PUTTING A FULL-COURT PRESS ON METABOLIC HEALTH AND DISEASE

BY EMILY KAGEY

When Jiandie Lin opened his lab at the University of Michigan Life Sciences Institute in 2005, he was one of the first metabolism researchers to join the multidisciplinary faculty of cell biologists, geneticists, neurobiologists, chemists and structural biologists. That year, fewer than 100 studies were published about a liver disease that would shape his research program: non-alcoholic steatohepatitis (NASH).

Despite being defined by physicians 25 years earlier, NASH remained fairly unknown and understudied. But Lin foresaw the potential for a pending epidemic due to the disease's correlation with rising obesity rates. Early on, he set his sights on understanding the cellular environment that defends, or dooms, the body's largest internal organ.

"It's not only liver cells that maintain health, but the neighboring cell types that live alongside them," Lin explains. "They are just as important, and maybe more important in some respects, because different cells constantly communicate with their neighbors, and together they create a functional, healthy tissue."

Lin's study of liver disease has expanded as the LSI has grown and evolved, driven in large part by collaborations with faculty members studying different aspects of metabolism, genetics and even biomedical engineering.

Like the diverse cells in the liver's microenvironment, these scientists have their own unique research functions within the LSI. Yet they connect and communicate with each other — whether through formal collaborations or casual conversations — in ways that create novel advances in the field of metabolic health and disease.

1/3

The precursor to MASH is found in about one-third of U.S. adults.

Jiandie Lin (left) and graduate student Yuwei Tang

As of 2025, NASH — or MASH (metabolic dysfunction-associated steatohepatitis), as it is now called — was the second leading cause of liver transplants among U.S. adults, ahead of hepatitis C and only slightly behind alcohol-associated liver disease. In contrast to the publication output Lin's first year at the LSI, more than 1,000 new scientific papers referencing MASH or NASH were published in each of the past five years.

The precursor to MASH is found in about one-third of U.S. adults. It results from excess fat buildup in the liver, known as steatosis, which is relatively harmless. But in about one out of five cases, damage caused by persistent steatosis and other metabolic complications sets off a chain reaction leading to inflammation, cell death and eventually end-stage disease such as cirrhosis and cancer.

Lin wanted to understand what caused this switch from steatosis to MASH. He was especially curious about how other cell types in the liver could be influencing liver cells, or hepatocytes. About 60% of the 150 billion cells in a human liver are hepatocytes, and he wondered what was happening with the other 40%. What types of cells were there, and how were they communicating to promote or protect against this harmful chain reaction?

"When we began our liver work, we took a different path, focusing on inter-organ communication and on hormonal signals secreted by one cell type that act on another," recalls Lin, who is also a professor of cell and developmental biology in the U-M Medical School.

A discovery from his lab about 10 years ago brought the role of inter-organ communication in MASH into sharper focus. And it came not from liver tissue but from fat cells, or adipocytes.

Lin's lab revealed that adipocytes in fat tissue were releasing a hormone called NRG4, which seemed to help protect liver health. When NRG4 reaches and interacts with liver cells, it slows the conversion of sugars into lipids and reduces overall fat accumulation in the liver. In mice fed a high-fat diet, animals with higher NRG4 levels show less liver cell death, inflammation and fibrosis. Similar results have been found in human patients, where lower NRG4 correlates with more severe MASH.

"That early work demonstrated that these adipose hormones could have a big impact on liver metabolism and liver disease," Lin says. "But it also led us to wonder how other cell types in the liver work together to influence hepatocyte health and disease progression."

To answer that question, Lin's team turned to an emerging technology that made it possible to analyze the patterns of gene expression in thousands of individual cells at once. Performing single-cell analysis on healthy and diseased livers, the researchers revealed a high-definition blueprint of the cell types operating in the liver, the signals they produce and receive, and how those signals evolve into distress calls as the disease worsens.

"In that study, one of the most interesting changes we observed was in a type of white blood cells called

Photo by Leisa Thompson, Michigan Photography

Ken Inoki with lab members Swayam Srivastava (front) and Mihir Bharadwaj (back)

macrophages," Lin says. "Those findings led to a shift in the lab's focus to consider how immune cells may be involved with later stages of this disease, like inflammation and cancer. It opened several new research paths for us."

One of those paths led to a fellow LSI faculty member approaching metabolic health from a vantage point just south of the liver.

Ken Inoki started his scientific career as a practicing physician in Japan, specializing in diabetic kidney disease. There, he saw firsthand the life-threatening impacts of disrupted cell growth.

"In diabetes, the kidney enlarges and also has to filter more blood than a healthy kidney," explains Inoki, who joined the faculty at the LSI and the U-M Medical School in 2008. "So the cells that form part of this filtration system are forced to grow in size to cover the larger area."

That enlargement leads to diabetic nephropathy, the most common cause of kidney failure worldwide.

Frustrated by the lack of treatment options for his patients, Inoki turned to the lab bench to see whether he could identify the cellular processes behind the disease conditions. He and his colleagues discovered an essential cellular mechanism that was causing increased cell size in response to growth factors and nutrients in diabetic conditions.

"And that's how I started studying mTOR," Inoki recalls.

The mTOR (mechanistic target of rapamycin) pathway serves as a master regulator of cell growth. As a nutrient-sensing protein, mTOR triggers a multitude of cellular processes in response to signals from nutrient and energy sources outside the cell. In diabetic conditions, for example, overabundant nutrients such as glucose and amino acids can over-activate mTOR, leading to the harmful overgrowth of cells in the kidney's filtration system.

"So that's why we are continuously working on nutrient-sensing mechanisms, to understand this complicated pathway and ways we can prevent its disruption to maintain healthy cells in the kidney," Inoki says.

During an informal presentation to his fellow LSI faculty members a couple of years ago, Inoki mentioned a protein molecule that he was starting to analyze because it damages kidney cells under diabetic conditions. The name of the molecule, BASP1, immediately caught Lin's attention. Lin's single-cell analysis data had found the gene that encodes BASP1 highly expressed in macrophages in both mouse and human MASH livers.

"We had already developed a model and molecular tools for studying what this gene does in the kidneys, and it turned out Jiandie had been hoping to study the

Photo by Leisa Thompson, Michigan Photography

Connie Wu (left) with Jiandie Lin

same protein in livers," Inoki says. "So even before we had published any of our methods, we were able to share those tools to study the effect of this protein in the progression of MASH."

The team found that, in mice fed a high-fat diet, macrophages are reprogrammed to produce more BASP1; and switching mice from a high-fat diet to regular food reduced BASP1 levels in the liver. This aberrant increase in BASP1 plays a critical role in the inflammatory responses that drive the transition from steatosis to MASH. Reducing BASP1 levels in mice on a high-fat diet decreased both inflammation and the severity of MASH.

"We know that there is a lot of crosstalk between kidneys and livers, and our labs are also very complementary in terms of Ken's expertise in biochemical molecular analysis and our work with whole-organism models, so it's a great combination," Lin explains. "And it turns out we were able to uncover this very interesting pathway that is influencing the inflammatory response from macrophages, which in turn influences liver disease."

The BASP1 results provided new understandings of how macrophages participate in the onset and worsening of MASH. But Lin noticed that those same immune cells also seemed to be involved in one of the terminal stages of the disease's progression: hepatic hepatocellular carcinoma (HCC), the most common form of liver cancer.

"We observed some molecular changes within these macrophages that resembled the tumor microenvironment, but they were happening before any cancer was apparent," Lin explains. "It almost looked like the liver, once it developed MASH, was already preparing for cancer cells to thrive."

Photo by Leisa Thompson, Michigan Photography

> From a practical standpoint, the collaboration and proximity to Jiandie's lab allow us to do experiments that we had not previously envisioned within our own lab.

Now, Lin has teamed up with one of the LSI's newest faculty members to investigate how these immune cells might be promoting cancer development and whether the hormone his lab discovered almost a decade ago may help reverse course.

When Connie Wu joined the LSI faculty in 2023, Lin approached her about a joint project to more accurately measure NRG4 levels in circulation. His lab had recently shown that boosting NRG4 levels could slow down MASH-related HCC in mice. A major challenge in the field had been accurately measuring NRG4 levels in blood, during both disease progression and resolution, and Lin wanted to overcome that barrier to discern what NRG4 might be doing.

"But then I started to wonder if, besides trying to measure NRG4, we could make an mRNA [messenger RNA] therapeutic based on targeting this protein," Wu recalls. "Our collaboration has expanded from there."

Wu is a biomedical engineer by training. Her lab develops molecular tools with the dual goals of measuring low-abundance molecules (like the low levels of NRG4 in blood) for earlier disease detection and delivering new therapeutics for disease treatment.

Toward this second goal, Wu and Lin are developing an mRNA-based delivery platform for NRG4. Rather than injecting the purified hormone into mice, the tool would induce the liver to start producing more NRG4 on its own, in a way that is more scalable and refinable. The team is using this approach both to uncover the specific mechanisms of NRG4 in HCC and to pursue new methods for delivering the hormone as a treatment for the cancer.

“

There are so many types of collaborations that can emerge in an environment like the LSI, whether it’s through common scientific interests, or applying a shared technique, or just chance conversations.

Photo by Leisa Thompson, Michigan Photography

Jun Wu (left) with research investigator Shanshan Liu

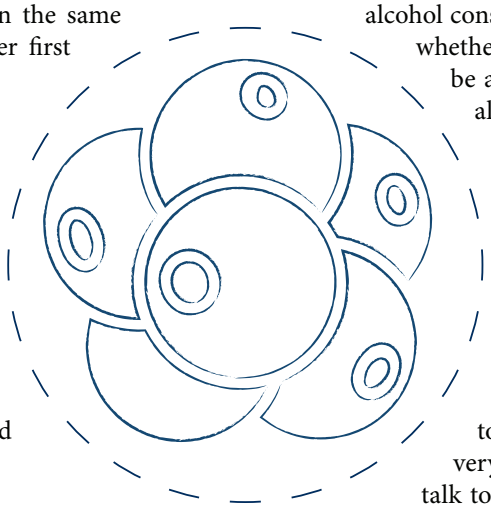
The collaboration with Lin has also created opportunities to expand her lab's playbook, developing strategies that she can quickly apply in Lin's model systems.

"From a practical standpoint, the collaboration and proximity to Jiandie's lab allow us to do experiments that we had not previously envisioned within our own lab," explains Wu, who is also an assistant professor of biomedical engineering in the College of Engineering. "But it also helps us scientifically. It gives us a context to focus our technology development efforts toward, and it's allowed us to extend our applications from cancer to liver disease."

She isn't the only LSI faculty member who has added liver disease to their research lineup through connections with Lin's team.

Jun Wu's collaborations with her fellow LSI researchers predate her role on the faculty, and even the institute itself. As a graduate student at U-M, her first mentor was Ken Inoki, who was at that time a postdoctoral fellow in the same lab where she was completing her first graduate lab rotation.

Five years after Inoki joined the LSI, and after completing her own postdoctoral research at Harvard, Wu was recruited back to U-M in 2013 as an assistant professor. As a new faculty member, she was paired with a faculty mentor at the LSI to help her as she set up her lab. That's when she first started working with Lin.



Jun Wu founded her lab on the study of a unique type of adipose tissue called thermogenic fat. Rather than storing fat, thermogenic adipocytes help maintain body heat by burning calories and fat stores.

Recently, she noticed a connection between the thermogenic process and liver disease. Her lab had previously discovered that a receptor protein called CHRNA2 can induce the energy-burning process in fat cells. They looked for other areas where this protein might be active, to better understand its various roles throughout the body, and found it was highly expressed in liver cells.

"The liver is tricky, much more complicated than adipose tissue, because a large number of various cell types are present in the tissue niche," Wu says. "But, partly because we are in this environment where we can connect through faculty talks and trainee presentations, and we knew Jiandie was an expert in this area, we decided to look into what's happening in the liver."

Her team found that CHRNA2 sets off a series of cellular programs that protect the liver against the development of MASH. They also found that an FDA-approved drug for treating neurodegeneration could boost CHRNA2 activity in mouse liver.

Expanding the field of metabolic research at the LSI, her team is now extending this research into alcohol-associated liver disease. They have found hints indicating that communication between the liver cells and fat tissue can defend against liver damage following alcohol consumption. They are now exploring whether the CHRNA2 pathway may also be a potential drug target for treating alcohol-associated liver disease.

"I would say my lab is about half liver research now, and I don't think that would have happened if I wasn't here at the LSI, with Jiandie on the team," Wu says. "We've had tangible collaborations, like publishing papers and submitting grants together. But then there are also very intangible things — our students talk to each other all the time, I go into his office just to talk about the bigger picture of our science. It could be something big or small that leads to a totally new direction."

"There are so many types of collaborations that can emerge in an environment like the LSI, whether it's through common scientific interests, or applying a shared technique, or just chance conversations," Lin adds. "Collaborations like this are hard to predict. They come ad hoc, and then they end up working out really well not just for the labs but for the science."■

OPEN GYM

This open-source software program is using AI to level the playing field in animal behavior research

By Emily Kagey

In February 2026, the internet turned its collective attention to Punch, a Japanese macaque whose only companion was an orangutan plushie from IKEA. As videos of Punch snuggling his stuffed animal flooded social media and major news outlets, the world saw an adorable young monkey struggling to find his place among the troop in Japan's Ichikawa City Zoo.

Bobby Tomlinson saw a chance to showcase the strength of LabGym.

Tomlinson is a computer specialist in Bing Ye's lab at the University of Michigan Life Sciences Institute, a lab that primarily studies neurobiology using fruit flies as a model. He joined the LSI in August 2025 to support the expansion of LabGym, an open-source software developed by Ye's team to analyze animal behavior.

"Outside of the lab, I don't really talk to very many people who are deeply familiar with behavior analysis, biological research and things like this," says Tomlinson, a computer scientist by training. "But I started seeing Punch just take storm on social media. And I thought this was a golden opportunity to put LabGym in front of more people, even people who maybe aren't as familiar with the field of behavior analysis, and really show what it can do."

PERSONAL TRAINING

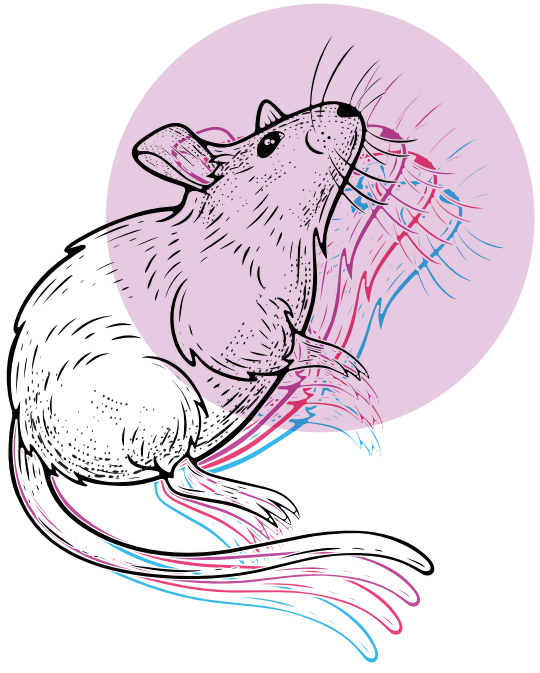
Since it first became publicly available in 2023, LabGym has been downloaded more than 70,000 times. Researchers across five continents have used it to analyze behavior in animals ranging from lab mice to wild jaguars. Its origins, though, arose from a much smaller need: measuring the activities of fruit fly larvae.

In 2019, Ye lab postdoctoral researcher Yujia Hu was studying how fruit fly larvae process harmful external stimuli to make behavioral decisions. The project required reviewing videos of the larvae and manually tabulating their activities. Hu estimates that it takes 30 to 60 minutes to analyze every 10-minute recording of larval behavior, and a typical study like this requires four to eight hours of recordings.

When Hu submitted his findings for publication, a reviewer suggested using automated tools for additional analyses of larval behavior.

"I tried a couple of tools, and at that time at least, they just were not useful or user-friendly," recalls Hu, who is now a research associate at the Cleveland Clinic. "They required more coding knowledge, and they couldn't classify behaviors at the level I needed."

Hu was able to publish the study without data from the automated tools, but he was left frustrated by the choice between time-consuming manual analysis or inadequate software options.



Yujia Hu leads a workshop at the annual LabGym Symposium

Then the COVID-19 pandemic hit. With most in-person research restricted at U-M, Hu was unable to come into the lab but still wanted to move his research forward in some way.

"And I had this idea: Why not just develop a tool?"

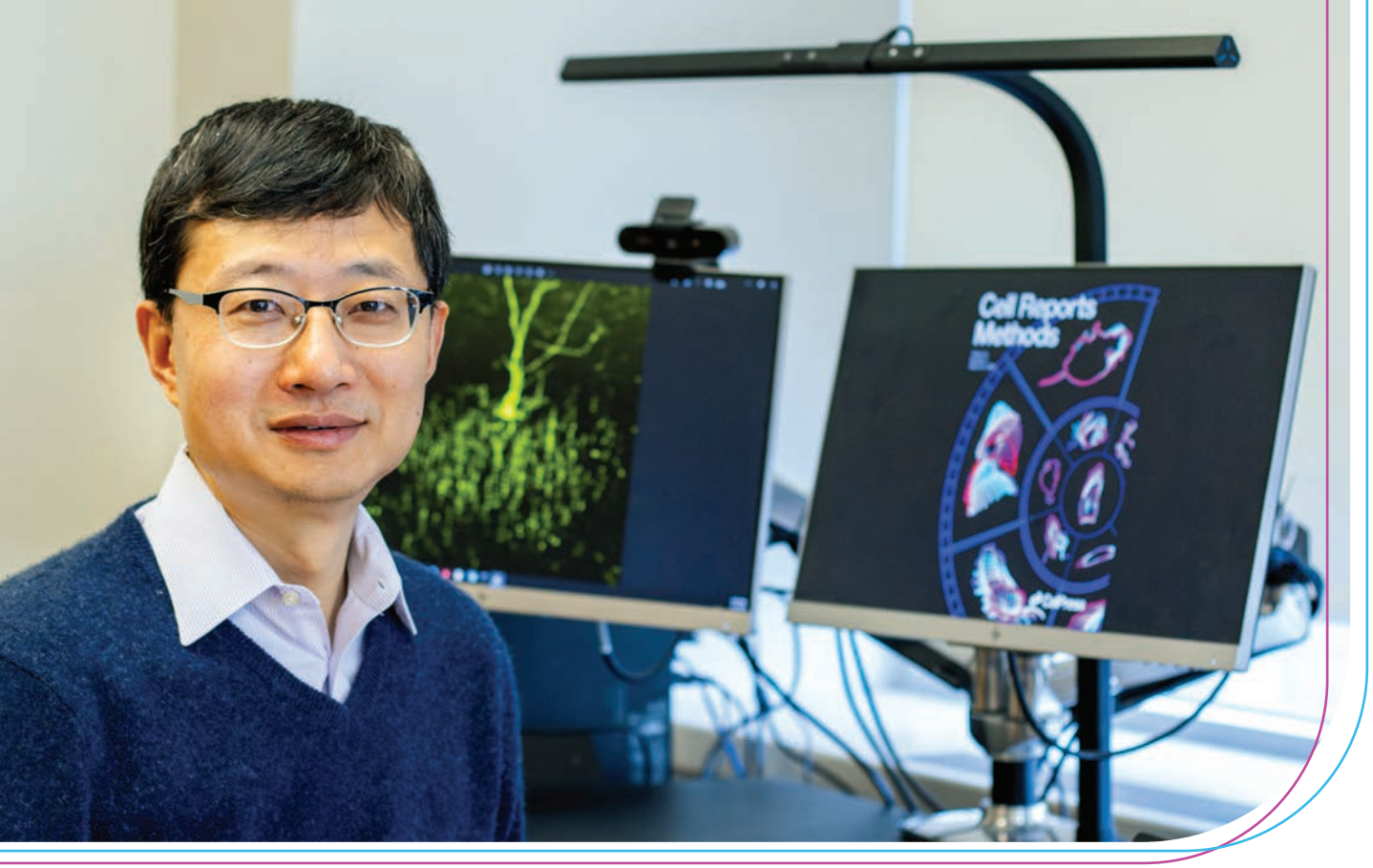
The neurobiologist taught himself to code using Python, a programming language, then collaborated with computer scientists to build LabGym.

At its core, LabGym is an artificial intelligence software tool that is designed to "think" like a human to identify and quantify animal behavior in videos fed into the program. Researchers can upload recordings and define the precise behaviors they want to measure, all without any coding expertise. The program then uses deep learning to improve its ability to recognize and quantify those behaviors.

"So, for example, a larva wouldn't have to roll a certain number of degrees for the program to decide it was a roll. As the user, I could tell the program 'these are examples of rolling,' and the program will teach itself to analyze all the features and details in these videos to accurately detect rolling," Hu explains.

Training LabGym for a new scenario — to analyze a new species or detect a new behavior — can take anywhere from a few hours to a few days of hands-on time from the researcher, depending on the complexity of the data. After that one-time training, the program can comb through video footage independently, analyzing and quantifying animal behavior while freeing researchers to continue other work.

Photo by Rajani Arora, LSI

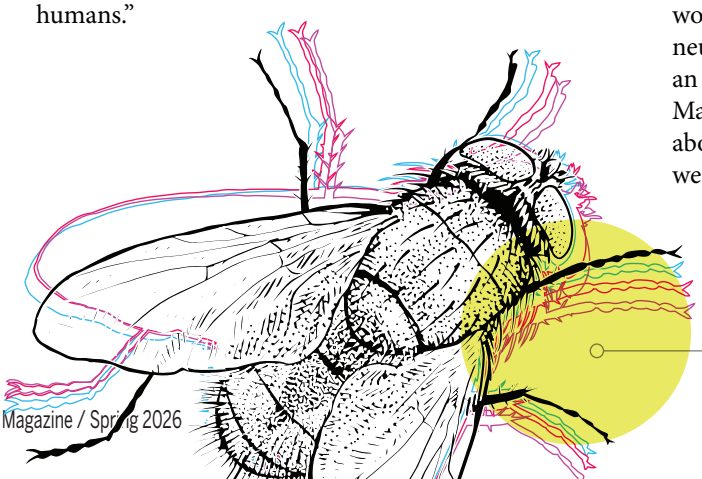


The first LabGym study from Bing Ye's lab was featured on the cover of *Cell Reports Methods* in 2023.

Once he could return to the lab full time, Hu began putting the program through various training trials with new fruit fly behavior scenarios. Around the same time, Carrie Ferrario, one of Ye's neuroscience colleagues at the Medical School, was looking for a tool to accurately analyze videos from her rodent behavior research.

Ye mentioned the program to Ferrario and Brendon Watson, another Medical School faculty member, and the three labs expanded their LabGym exercises to rats and mice. In February 2023, they published the first paper on LabGym, demonstrating that the program could efficiently detect and quantify behaviors across various animals.

"As the project evolved, I realized that, because we had built the tool around deep learning, it didn't have to be for just larva," Hu recalls. "It could be trained to analyze other species, like mice, rats, monkeys or maybe humans."



GROUP EXERCISE

About 200 yards from Ye's lab in the LSI, U-M School of Dentistry faculty member Joshua Emrick was encountering the same challenge that Hu had faced in 2019: the need to objectively assess animal behavior, without adequate automated systems to do so.

Emrick is a sensory biologist and dentist who launched his lab in 2021. His team explores how nerves within the mouth, neck and head process sensory information and contribute to normal tissue function and pain perception. They were developing their first major study, examining the role of specialized neurons within the tooth, when Elizabeth Ronan joined the group as a postdoctoral researcher.

"As the project came together, we had gotten some feedback that there was a lot of enthusiasm for this work, but also that, if we wanted to state that these neurons cause pain, we had to show it," recalls Emrick, an assistant professor in the Department of Biologic and Materials Sciences & Prosthodontics. "And thinking about pain sensation and behavior in animal models, we wanted to take a different approach."

Photo by Rajani Arora, LSI

> It's kind of an amazing illustration of both collaboration at U-M and the application of AI.

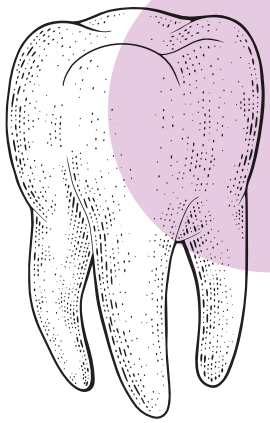
In this case, Ronan knew about a promising option. She had completed her Ph.D. in a lab just one floor up from Ye in the LSI. As fellow trainees at the LSI, she and Hu had frequently discussed the development of LabGym, and she realized it may be relevant to her new project.

Ronan contacted Hu and asked if he thought the program could be trained to detect and measure pain behavior. Together, the two groups began to define the specific postures and facial features that indicate pain, and then they started training LabGym.

The main output of this work was the discovery that these neurons don't just sense pain, they use that information to induce jaw movements that protect the tooth from further damage. But beyond those findings, the effort also resulted in a novel approach to detecting and quantifying pain sensation in animal models. The two labs are now collaborating to further develop this approach.

"It's kind of an amazing illustration of both collaboration at U-M and the application of AI," Emrick says. "The trouble with studying behavior is that it takes a really long time to evaluate, and there is still a high potential for individual bias. Here, we had ready access to LabGym, which addressed both challenges."

As more colleagues expressed interest in the program, Ye and his team began building more resources to support its adoption: user manuals, training videos, even an annual symposium with more than 150 participants each year. Now, what started as an effort to maximize efficiency in his own lab has helped Ye forge connections across a global network of animal behavior research powered by AI.



Josh Emrick (left), Kayla Moehn (middle) and Liz Ronan (right) in Emrick's lab at the U-M School of Dentistry

Photo by Rajan Jivora, LSI

Three years after LabGym opened:

70,000+ downloads

20 publications

>10 species tested

> LabGym is here to democratize the use of AI for behavior analysis.

FROM HOME GYM TO FIELD TRAINING

In March 2024, Ye got an email notification about a new publication that mentioned LabGym. It was the first LabGym study to come from outside of U-M, and its authors were, at the time, completely unknown to Ye.

The study's senior author, animal behavior researcher Cédric Sueur, found out about LabGym through a graduate student in his lab, Théo Ardoin. Sueur's research program at the University of Strasbourg in France aims to automate the recognition and analysis of complex behaviors in Japanese macaques using deep learning, with the dual goals of advancing fundamental primatology and developing accessible AI tools for behavioral research. After benchmarking available programs, Ardoin landed on LabGym.

Sueur and Ardoin trained the program using only materials and tutorials the developers had posted online. Their goal was to determine whether LabGym could be applied to primates in the field, without needing advanced programming modifications. They found the software could accurately detect the behaviors they aimed to study (specifically, stone-handling behaviors of macaques in the wild) while significantly reducing the hands-on time for researchers.

"Without AI assistance, analyzing continuous video data across individuals, seasons and years would require prohibitive human resources," Sueur explains. "LabGym enables us to envision large-scale, long-term automated behavioral monitoring in wild primates — something that would be unrealistic using manual annotation alone."

Sueur's publication led to a new international collaboration for Ye's group, as they evolve the software to accommodate new use cases. One of the newer features enables the program to analyze individuals interacting in a group, which Ye and Sueur are using to study social roles in groups of macaques.

It's a feature that has been particularly useful for other researchers who want to take LabGym out into the field. At the University of Aalborg in Denmark, for example, undergraduate students Laura Liv Nørgaard Larsen, Ninette Christensen and Trine Kristense used it to track the activity of three jaguars housed together in captivity. The students and their mentor then applied that training data to videos of jaguars in the wild, to see if LabGym could adapt its training to a new setting.

While LabGym did struggle a bit to accurately evaluate the animals in the wild, having never seen footage from that setting, the team was surprised by its ability to adjust to the new context without additional instruction.

Cédric Sueur studies social behavior and decision-making of Japanese macaques in the field

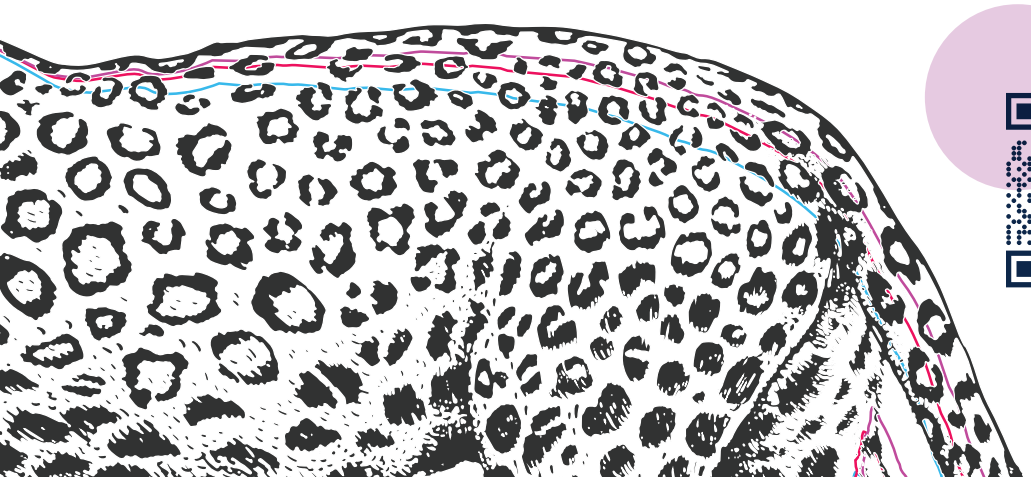
"It was very amazing that researchers and students like us, who have not been taught anything yet about data science or machine learning, were able to pick up this program so quickly and actually get meaningful scientific results out of it," Larsen says.

Ye, Tomlinson and Hu hope to expand this usability enough that perhaps even non-scientists will find a use for the program. That's where Punch comes in.

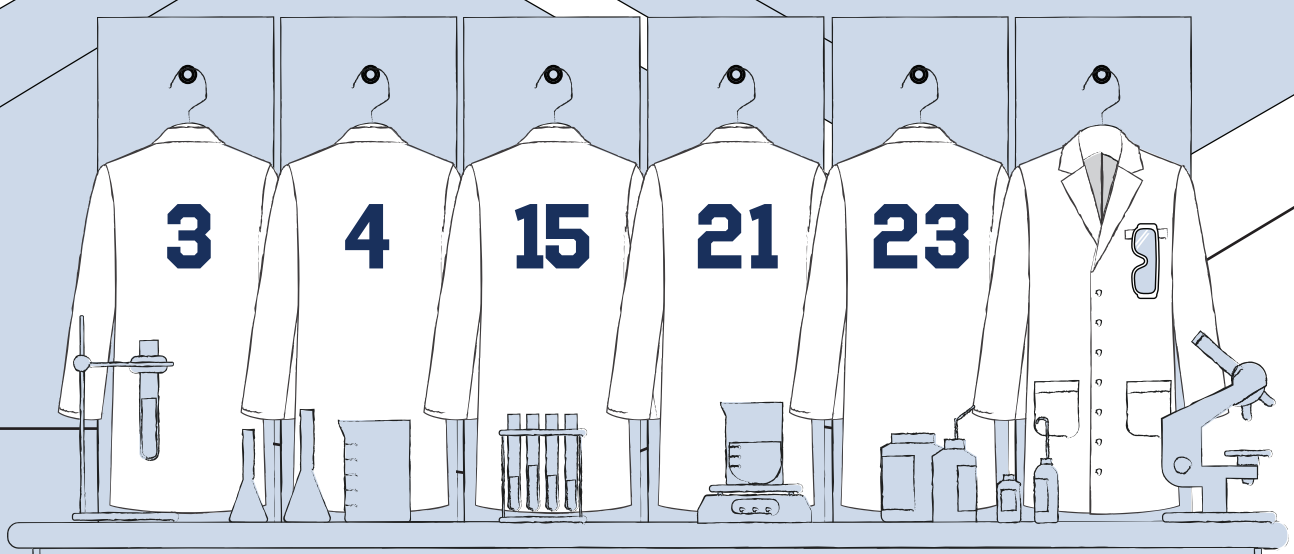
The team is now testing the program not on well-controlled videos recorded on stationary cameras, but on zoo visitors' videos posted on YouTube and other social media channels — with widely varying perspectives, filming angles, lighting and orientation. Beyond deriving new behavioral insights from analyses of Punch's interactions, they hope to extend the program's adoption outside of traditional scientific settings, envisioning its use by citizen scientists, high school students or even animal enthusiasts who want to learn more about animal behavior.

"We are optimizing its accessibility as well as its effectiveness for researchers," Tomlinson says. "We hope to unlock this pipeline in a very real way that makes it easier for our current users to use it within research, but also apply it to new context and to new types of users."

"We have always thought that LabGym could have that kind of broad use because, after all, LabGym is here to democratize the use of AI for behavior analysis. And we're really excited about that," Ye adds. "At the end of the day, we have to ask ourselves: 'Why are we doing this work?' It's because we love it, and we believe it can help the whole field of science." ■



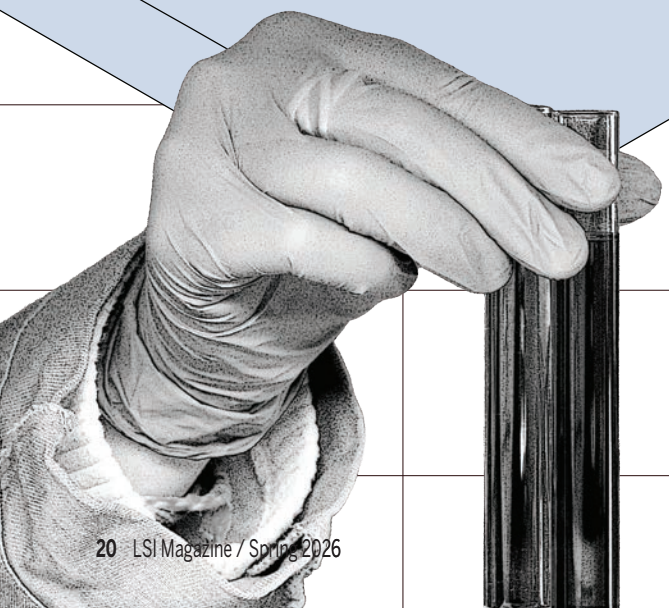
Learn more about LabGym and Punch research

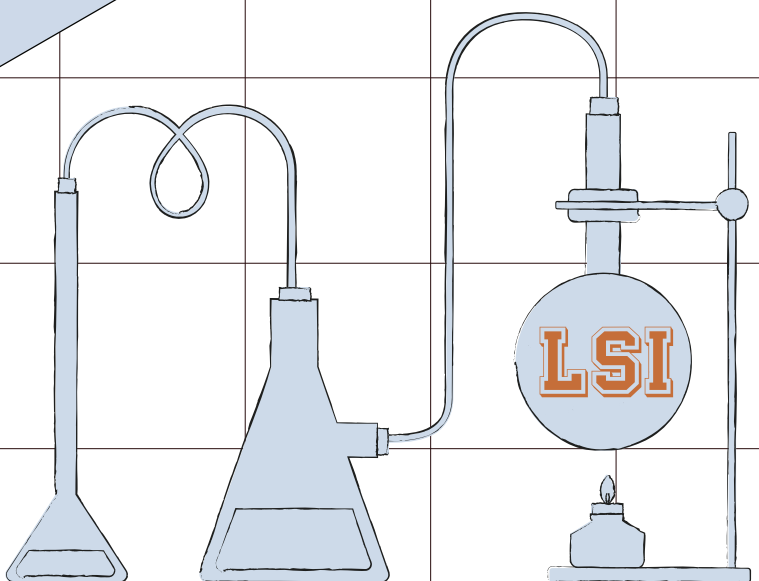


TRAINING GROUND

IN THE LSI'S COLLABORATIVE ENVIRONMENT, TRAINEES BUILD THE SKILLS TO BECOME TEAM LEADERS

BY APRIL SCHOONOVER





When we watch professional athletes performing at the height of their careers, it's not always easy to remember their origin stories. While some catapult to instant fame and recognition, the more common narrative is one of methodical development, with years spent on training squads, patiently working toward the spotlight.

As an athlete evolves, their training environment plays a critical role in their eventual success. They thrive under the guidance of insightful coaches, hone their skills by training with talented teammates and discover their own signature style of play.

Training a professional scientist is no different. The skills and expertise necessary to advance the forefront of the field cannot be acquired overnight — they are the result of a steady progression toward a goal. A developing scientist needs supportive mentors, collaborative colleagues and the freedom to pursue training that aligns with their scientific interests.

At the Life Sciences Institute, the principles of mentorship, peer-to-peer learning and scientific agency are foundational to trainee maturation. Researchers ranging from undergraduate students through graduate students and postdoctoral fellows come here to train, to gain the guidance, experience and expertise that prepare future scientific leaders.

Christina McBride (left) and Chloe Warrell

COACHING A SCIENTIFIC MINDSET

Chloe Warrell first learned about natural products in her high school chemistry class and was intrigued by the science behind how the indigenous use of natural products resulted in healing properties. Her desire to better understand the science behind these products led her to David Sherman's lab at the LSI. Now, as an undergraduate researcher in the Sherman lab, she is learning to harness nature's chemistry to produce important molecules.

Warrell, a junior biochemistry major, works on a joint project between the Sherman and Filipa Pereira Labs, led by graduate student Christina McBride. This team approach allows her to seek guidance from multiple mentors. She credits the multi-tiered mentorship she receives as key to her evolution as a researcher.

McBride specializes in creating "bacteria factories." Some molecules are incredibly complicated to produce in the lab and use a lot of resources, making their synthetic production harmful for the environment. McBride's research focuses on genetically altering bacteria to manufacture these molecules, increasing production efficiency and reducing environmental impact. With enough of the molecule in hand, the lab can begin experimenting with different chemical modifications to try to increase the compound's medicinal properties.

Warrell focuses on purifying the molecules produced by the bacteria and analyzing their purity, yield and

> I've really built my scientific intuition at the LSI. I see patterns of what will and won't work, and why.

Photo by Leisa Thompson, Michigan Photography

chemical structures. To improve production, she also experiments with various growth conditions to see what will have the highest yield of the desired molecule. She is now using a similar system to produce another molecule, which is equally laborious to make synthetically.

"At first, I helped Christina with her project and grew my scientific problem-solving mentality," she says. "But I eventually gained the skills to be able to branch out to my own project."

Long term, Warrell is eager to use the research skills she began developing at the LSI to explore how natural products can make the agricultural industry more environmentally friendly.

"My mentors have helped me figure out how to move on when a result isn't what I expected or wanted, and how we can shift a poor result into a positive product," she says. "I've really built my scientific intuition at the LSI. I see patterns of what will and won't work, and why."

FREE AGENT

One of the most challenging and rewarding aspects of Romie Azur's thesis work was the agency he was given while designing his experiments. While some graduate students are assigned to planned projects, LSI faculty member Tzumin Lee allowed Azur more autonomy.

"If it aligned with his lab's goals, Tzumin was supportive," says Azur, a fourth-year student in the Molecular, Cellular, and Developmental Biology Ph.D. program. "I had to think hard and critically about where I wanted my project to go, but I was able to design a project that satisfied my curiosity."

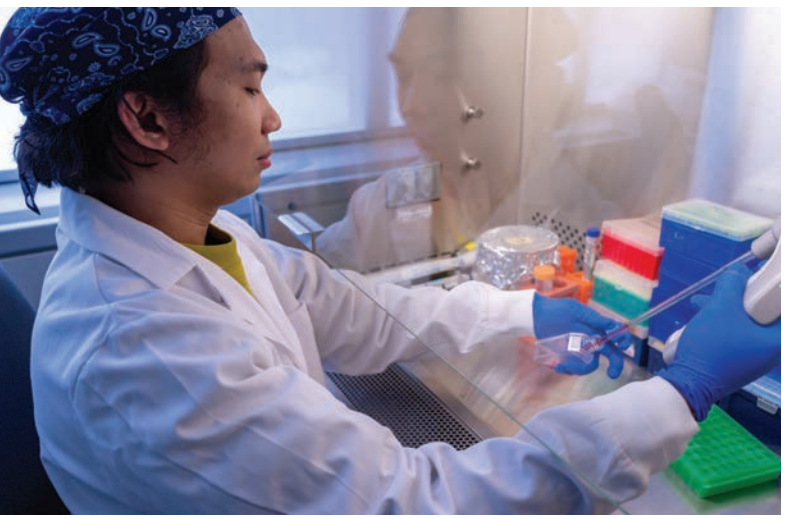


Photo by Leisa Thompson, Michigan Photography

Romie Azur

And Azur was curious about what controls neuronal fate in the developing brain.

During brain formation, neurons go through a series of iterative cell divisions, resulting in neurons that are born at different points on the developmental time scale. The timing of a neuron's genesis helps dictate its neuronal fate, or what type of cell it will become.

Based on previous work, Azur suspected that a gene called Imp1 influenced neuronal fate. He wanted to use a tool invented by the Lee lab, called TEMPO, to test this hypothesis. This genetic tool uses fluorescent colors to label neurons as they divide, revealing the birth order of neurons in relation to each other.

For that approach to work, however, TEMPO needed to be surgically delivered to early-stage embryos — a procedure that only a few people in the world know how to do. For the initial Imp1 experiments, Azur was able to leverage an existing Lee lab collaboration; but he knew that his future research goals necessitated that he become proficient in the technique himself.

Lee connected with a collaborator in Japan who knew the technique and was willing to train Azur. He traveled to Japan for 10 days of specialized training, in part with support from the LSI's David and Michelle Kroin Graduate Student Professional Development Program. This donor-funded program supports LSI graduate students pursuing external professional development opportunities.

"The LSI's Kroin Program helped a lot in terms of having the financial support to go somewhere and train for more than a week," Azur says.

The effective administration of TEMPO confirmed Azur's hypothesis that Imp1 regulates neuronal fate. In the longer term, Azur and the Lee lab are interested in using his training to perturb other genes that are predicted to influence brain development, to uncover greater insights into how these genes influence cell type production, division and location.

"My time at the LSI and Tzumin's style of mentorship helped me to grow into a more independent researcher, a better advocate for my own science," Azur says. "It comes with time, and here I think you get all the time you need."

A DEEP BENCH: THE BENEFITS OF DIVERSE EXPERTISE

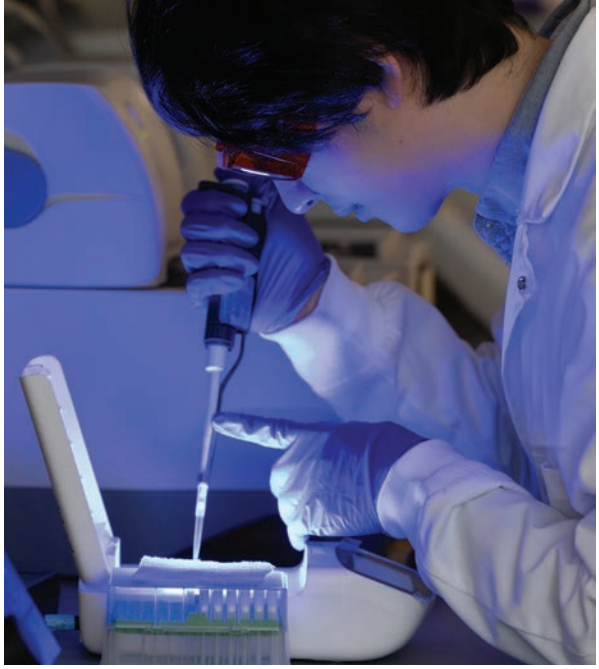
Postdoctoral fellow Jingcheng Wang came to the LSI looking to expand his scientific playbook. As the May-Walt fellow in the Michigan Pioneer Fellows Program, which aims to support exceptional early-career scientists on their journey to independent leadership, he wanted an opportunity to rapidly gain a variety of skills that could prepare him to one day lead his own lab.

Wang's graduate research had focused on using traditional biochemistry and cell biology to study how lipids change the shape and function of proteins. A desire to augment his research approach with new skills in next-generation genetic tools led him to David Ginsburg's lab at the LSI.

"There are quite a few different interests and specializations in the lab," he says. "There was one senior investigator who specializes in evolutionary biology and another with a lot of expertise in the assay I'm performing. They helped me get started."

This variety of expertise has proved critical to the success of Wang's research into the movement of a key regulator of cholesterol in our blood, a protein called PCSK9. Extending some of the lab's previous research on PCSK9, Wang is investigating how a carrier protein called SURF4 transports the PCSK9 where it needs to go within the cell to support healthy cholesterol levels.

This project requires not only the knowledge Wang brought from his graduate training but also quite a few new skills, fostering opportunities for him to learn some trick plays from his teammates.



Jingcheng Wang

The expertise of fellow lab members Laura Haynes and Matthew Holding, in particular, was critical to advancing his project, Wang says. Each detail of the experiment needed to be carefully planned, including the preparation of the samples that would be sent for sequencing and how the results would be analyzed. Haynes' experience with screening experiments and Holding's specialization in bioinformatics helped guide Wang's strategy for executing initial experiments.

Within months of his start date, a few other postdoctoral scholars joined the lab. "The new hires help each other out, and if there is something we all need, we work together to get it," Wang says.

The synergy within the Ginsburg lab has allowed Wang to identify additional mutations for further investigation, and he considers this synergy a defining feature of the culture of the LSI.

"The science here at the LSI is very collaborative, and we all care about each other," he says. "It's an ideal atmosphere to learn new skill sets and build beneficial connections." ■

> It's an ideal atmosphere to learn new skill sets and build beneficial connections.

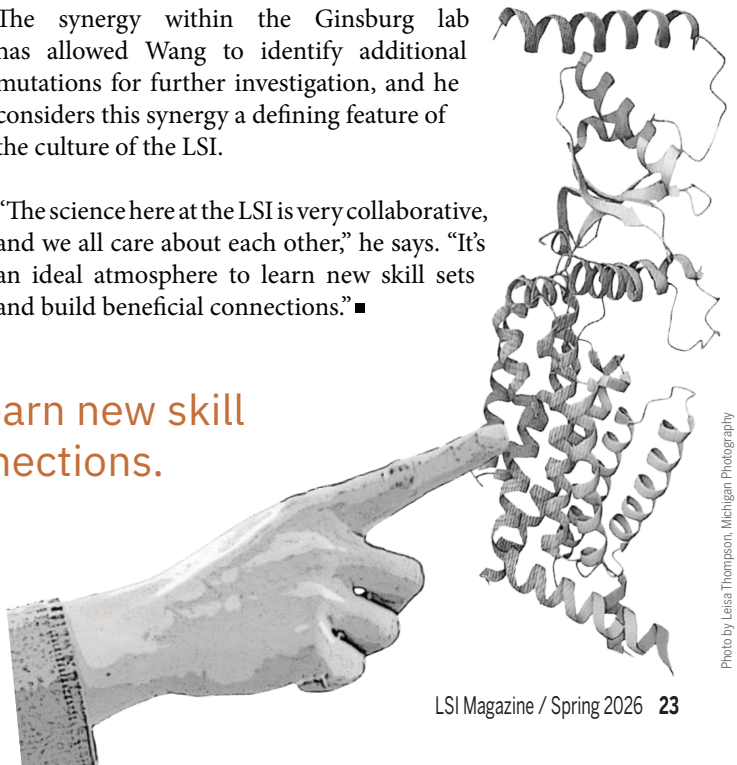


Photo by Leisa Thompson, Michigan Photography

HOME FIELD ADVANTAGE

Director Roger Cone discusses how experts across disciplines tackle complex challenges together at the LSI, and how this collaborative spirit leads to scientific wins

New GLP-1 drugs such as Ozempic and Wegovy have rapidly become household names, hailed by many patients and physicians for their effectiveness in treating obesity and diabetes. These drugs are not a perfect solution for everyone, though; studies estimate that 10% to 20% of patients see little or no weight loss, and half of patients stop taking GLP-1s within a year of starting the medication, many in response to negative side effects.

For more than two decades, Roger Cone, Mary Sue Coleman Director of the Life Sciences Institute, has studied the brain circuitry that regulates energy balances and food intake. Recently, his lab uncovered biological mechanisms that could be leveraged to refine the effectiveness of GLP-1 drugs.

The discovery comes at a time when Cone is concluding his decade-long tenure as the LSI's director to return to research full time. He has guided the LSI as it expanded its scientific discovery cores, recruited 11 new faculty members, launched new educational programs for both high school and postdoctoral researchers, and navigated a national pandemic and changing federal funding landscape.

Here, Cone reflects on what attracted him to the LSI, how the institute's unique atmosphere has influenced his own research and what's next for his lab as he transitions into the role of a full-time faculty member.

Photo by Leisa Thompson Photography

Anna Mapp (left) with Roger Cone

> In my decade as director, I've focused on recruiting world-class scientists, keeping our discovery technology at the cutting edge and making these resources accessible to all.

Q: What do you think makes the LSI unique?

A: The LSI intentionally recruits people who internalize diversity, who are comfortable talking, thinking and working with people that do very different things to solve big problems.

We have people here doing everything from synthetic organic chemistry to human medical genetics, from the smallest molecules to whole organisms. We have scientists across all different disciplines who are regularly engaging. We can go get a chemical compound to use in our research. We can determine a structure. We can talk to a physician scientist about human genetics and how that is relevant to the process that we're studying.

To me, that's what makes the LSI great.

Q: You've referred to this method of recruiting LSI scientists as the "best athletes" approach. How does the LSI cultivate an atmosphere where independently successful individuals want to invest in collaborative efforts?

A: There are two major things that we try to do. One is the type of person that we recruit. We don't want to just hire the best person in cryo-EM; we want to hire the best person in cryo-EM who wants to collaborate widely, bringing in skills from other areas of expertise to solve difficult problems within their field.

Secondly, we try to create a small, collegial environment. For example, we have regular workshops where faculty members share their research ideas with each other. We create a comfortable environment for them to discuss new, potentially high-risk ideas, and get feedback from a chemist, a geneticist, a medical doctor. That doesn't happen in a lot of discipline-specific departments. You don't often have people in widely divergent fields together in one room, focused on your specific question and commenting on how you could better solve this problem using another technique or area of expertise.

Q: Has this approach impacted research within your own lab at the LSI?

A: Yes, in many ways. For example, I had spent a lot of time working to understand one specific receptor protein in the brain called the melanocortin 3 (MC3) receptor. When looking at receptor function, pharmacology is a great tool, since you can block a receptor and an hour later ask what the effect is.

A colleague of mine had published a study describing the only credible molecule that could bind to the MC3 receptor and block its activity. I contacted her and asked if she could send us some, but she did not have any of it and had no plans to make more because it had been so challenging to synthesize.

I walked down two floors and showed the structure to Anna Mapp, a faculty member here who is an expert in synthesizing complex molecules. She looked at it and said, "Oh, yeah, we can make that." Her lab not only succeeded in making the molecule, but also developed a more efficient route to making it than the published method.

That is just one of many examples of what makes the LSI unique. Someone like me, who has zero chemistry

Photo by Leisa Thompson, Michigan Photography

expertise but needs a chemical to solve a problem, can just go down the hall and talk to a chemist, and they'll collaborate with me because they love to work in different areas.

Q: Why are the melanocortin receptors important to understand?

A: Mutations in the melanocortin 4 (MC4) receptor were discovered to be the most common genetic cause of obesity in humans. Leptin is a signal that tells the brain how much energy you have in the form of fat, and it depends on MC4 receptor signaling. A mutation in even one copy of the MC4R gene produced early-onset severe obesity.

In contrast, turning off the MC3 receptor did not provide a satisfying hypothesis as to its role in energy regulation. The animals did show some late-onset modest obesity; but, on the other hand, the animals showed heightened sensitivity to multiple weight loss stimuli. Overall, the animals showed an inability to maintain a proper energy balance. We realized, partially through experiments with the molecule from Anna's lab, that the MC3 receptor acts as an energy regulator, but in a more complex manner than the MC4 receptors.

If you think about a thermostat, it doesn't really keep the temperature constant. When the temperature hits a lower boundary, the furnace comes on and raises it. When the temperature hits an upper boundary, the furnace goes off and the temperature starts going back down. As a result, the temperature fluctuates between upper and lower boundaries. We demonstrated that the MC3 receptor functions in much the same way, regulating the upper and lower boundaries of energy balances, in part by blocking the activity of MC4 receptor neurons.

Understanding how the MC3 and MC4 receptors interact to influence the body's regulation of energy, including the desire to eat and how energy is stored, is essential for addressing a range of metabolic disorders, from obesity to anorexia.

Q: How do the melanocortin receptors interface with the rapid emergence of GLP-1 drugs, such as Ozempic?

A: GLP-1 is a gut peptide, and its normal role is to signal satiety, or fullness, to the brain. At high levels of GLP-1, nausea occurs. At low levels, nothing occurs. The trick was to figure out how to ramp up GLP-1 levels to inhibit food intake without terrible nausea occurring. They cause a pre-satiation effect. You feel full, you eat less, you lose weight.

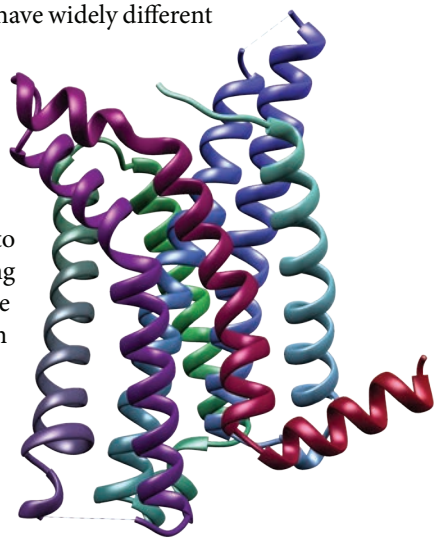
The GLP-1 inhibition of food intake requires the melanocortin circuits to work. If you block the melanocortin circuits, you can reduce GLP-1-induced inhibition of feeding. We hypothesized that if we sensitize the melanocortin system, either by removing the inhibitory effects of MC3 or by partially activating MC4 neurons, we can sensitize animals to the weight loss effects of the GLP-1 drugs, making the GLP-1 drugs more effective.

Q: What's next for your research program as you transition from the directorship back into the role of a full-time faculty member?

A: We have made several findings over the last few years that I'm really fascinated by and want to solve, and now I will have more time and intellectual energy to do that. I want to understand how sensitizing the melanocortin system can improve the activity of obesity therapeutics. In addition, the activity of the MC4 receptor appears to be linearly related to body weight. We don't yet understand the mechanism that drives that relationship, and I have a few theories to test. I also hope to further advance our understanding of anorexia, cachexia and other disorders of inadequate nutritional intake, and determine if regulation of the melanocortin circuits can be used to treat some of these disorders.

In my decade as director, I've focused on recruiting world-class scientists, keeping our discovery technology at the cutting edge and making these resources accessible to all. Our faculty have widely different areas of expertise and skills, and they come together in a single building, breaking down barriers to cross-disciplinary work and collaborating to solve problems. That's why I came to the LSI, and I'm really looking forward to spending more time pursuing my research in this amazing environment. ■

Interview by April Schoonover. Responses have been edited for clarity and length.



Structure of the melanocortin 4 receptor. Image credit: Luis Diaz Gimenez.

Image courtesy of Paul Bruno

Embracing risk, from the bench to the boardroom

By April Schoonover

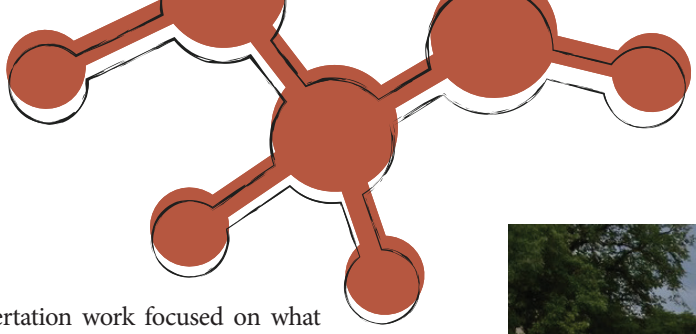
Paul Bruno (Ph.D., ’15) has a high threshold when it comes to the fear of failure. His dissertation focused on “undruggable” drug targets, he co-founded a start-up in an area outside his expertise while still in graduate school and he has seamlessly navigated high-level strategy roles for several biotechnology start-ups.

Bruno, a U-M Life Sciences Institute alum and chief business officer at Atavistik Bio, traces his interest in science to his time at Santa Clara University. An undergraduate research experience in Amelia Fuller’s lab, which focused on creating molecules that mimic peptides, inspired him to turn his ambitions into a career in research.

His graduate school aspirations led him to the lab of Anna Mapp, a faculty member at the LSI and Fuller’s former graduate school mentor. The common research threads between the Mapp and Fuller labs, and Bruno’s chemistry experience designing molecules inspired by biology, enabled him to begin his dissertation research with unusual momentum, Mapp says.

> “By the time I left the LSI, I had great confidence that I could solve hard problems.

“Paul was an absolute delight as a graduate student,” she recalls. “He was incredibly bright, he always asked good questions, and when he faced headwinds in his projects, he was great about both figuring out new experiments and pivoting to go in a different direction.”



Bruno's dissertation work focused on what were then known as "undruggable targets" — proteins that were difficult to drug because little was known about their structure and mechanism, and because many were characterized by attributes like large surface areas that resulted in weak interactions.

Bruno credits Mapp and the LSI for developing his problem-solving ability. Mapp's research program includes multiple disciplines, including biophysics, biology and chemistry, and Bruno liked the multi-dimensionality of the problems the lab was looking to address.

"There wasn't an expectation that you were a chemistry expert or a biology expert," he explains. "It was more, 'We are going to take learnings from all of these different individual disciplines and pull them together to create something interesting.' By the time I left the LSI, I had great confidence that I could solve hard problems."

With this combination of different scientific disciplines and problem-solving approach, Bruno was able to successfully explore new applications of small molecule combinations and even help uncover new biologically active natural products during his graduate research.

While working on these undruggable targets at the LSI, Bruno also had his first exposure to entrepreneurship. He and his sister, Ariana Bruno, raised seed funding and co-founded a company based on a novel, patented polymer that they co-developed for helmets and other protective sports equipment. While the company ultimately did not succeed, Bruno found it a highly valuable experience.

"We got exposure to raising money, running a business and doing market research. It was a great experience for us," he says.

After completing his Ph.D., Bruno's entrepreneurial bent led him to the lab of Stuart Orkin, a professor of pediatrics at Harvard Medical School and a member of the LSI Scientific Advisory Board. Orkin was looking for someone with expertise in both chemical biology and entrepreneurship, with the hope of commercializing novel therapies for sickle cell disease.

During his postdoctoral experience, Bruno realized that he was ready to leave the bench and find a field where he could more directly combine his business acumen with his scientific expertise.

LSI Mapp lab, 2012 (Paul Bruno, fifth from the left in the front row, next to Anna Mapp)

"While I couldn't imagine doing anything outside the life sciences, I knew that being at the bench setting up reactions wasn't for me," he recalls. "I liked the business side of things."

He joined Clearview Healthcare Partners, a boutique life sciences consulting firm, where he says his scientific training played a key role in operating as a successful consultant. Before long, he had the opportunity to join Fulcrum Therapeutics, a small biotechnology company whose scientific area of focus aligned with Bruno's expertise. Bruno saw Fulcrum as an opportunity to continue strategic advising in a domain of strong scientific fit. The company developed two therapeutics during Bruno's tenure. One, a sickle cell disease candidate, is currently in clinical trials.

In 2024, Bruno transitioned to his current role at Atavistik, where he leads efforts to establish the overall corporate strategy and finance the company for long-term success. He leverages both his consulting expertise and life sciences acumen to communicate a thoughtful, compelling vision of the company to stakeholders.

This vision has culminated in Atavistik raising $160 million to advance from a series A company to a series B company, a significant milestone in its developmental trajectory.

With each career change, Bruno has deliberately considered his potential for impact.

"For each move, the question that excited me enough to make the move was, 'Can I add value to this?' If the answer was yes, I always felt comfortable taking that leap, even knowing things may not pan out the way I envisioned." ■

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

Michael Marletta Collegiate Professor in the Life Sciences; 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

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 Assistant Professor of Biophysics, **College of Literature, Science, and the Arts**

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

LSI LSA 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; 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

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 Associate Professor

J. Bernard Machen Collegiate Professor in the Life Sciences; Associate Professor of Biologic and Materials Sciences, **Dental School**; Associate 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

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

Photos by Leisa Thompson Photography

Awards

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

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

Roger Cone received a Lundbeck Foundation Visiting Professorship

Janet Smith was elected to the American Academy of Arts and Sciences

David Ginsburg was named the University of Michigan's 2026 Henry Russel Lecturer

Received the Outstanding Mentor Award from the International Society of Thrombosis and Haemostasis

Connie Wu received the NSF Faculty Early Career Development (CAREER) award

Melanie Ohi received the Biophysical Society's June Almeida Award

Photos by Leisa Thompson Photography and Michigan Photography. Leisa Thompson

Year in Photos

All photos by Rajani Arora, LSI, unless otherwise noted

Undergraduate scientists presented their research at the summer undergraduate poster session.

Faculty, staff and trainees gathered to welcome the LSI's summer researchers with a smoothie party.

Research!America President and CEO Mary Woolley talked with trainees about roles for scientists in advocacy and civic engagement.

U-M President Emerita Mary Sue Coleman and legislative staff toured the LSI.

Photo by Savannah Williams, LSI

Aspirnaut interns learned lab safety skills before stepping into the LSI labs.

Summer interns celebrated after receiving their white coats.

Alex Johnson, LSI

Aspirnauts had the opportunity to present science projects to the community at U-M's Museum of Natural History.

The LSI hosted the Center for ChemoEnzymatic Synthesis 2025 Biocatalysis Workshop.

LSI faculty, staff and leadership board members toured the Big House.

LSI community members enjoyed snacks and made friendship bracelets at the Fall Welcome Back event.

Michigan Pioneer Fellows discussed research and lab experiences at one of their monthly gatherings.

At the fall 2025 LSI SciComm Series lecture, author Kate Zernike discussed what the next generation of scientists can learn from the experience of the women described in her book, ***The Exceptions: Nancy Hopkins, MIT, and the Fight for Women in Science.***

LSI Seminar Series speaker Huda Akil discussed the neurobiology of stress and resilience.

Photo by Michigan Photography

U-M President Domenico Grasso (right) awarded LSI Professor David Ginsburg the Henry Russel Lectureship, the university's highest honor for senior faculty members.

LSI members competed in the annual Halloween costume contest.

LSI community members celebrate the Lunar New Year.

Laura Haynes (center) was the inaugural recipient of the LSI's Marilyn Kroin Beck Mentorship Award.

for transformative discoveries that launch tomorrow's translations

for the next generation of scientific leaders

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

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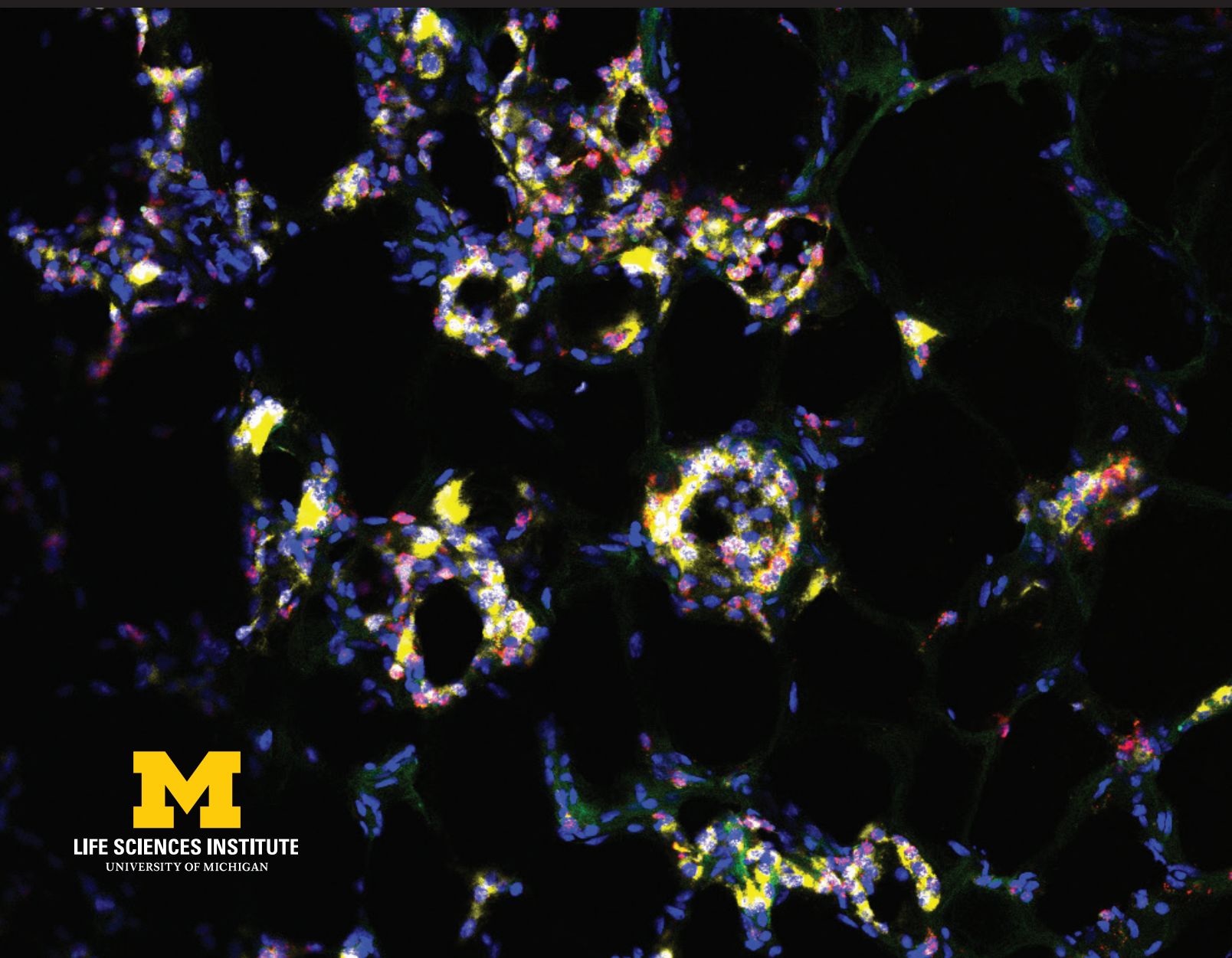

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