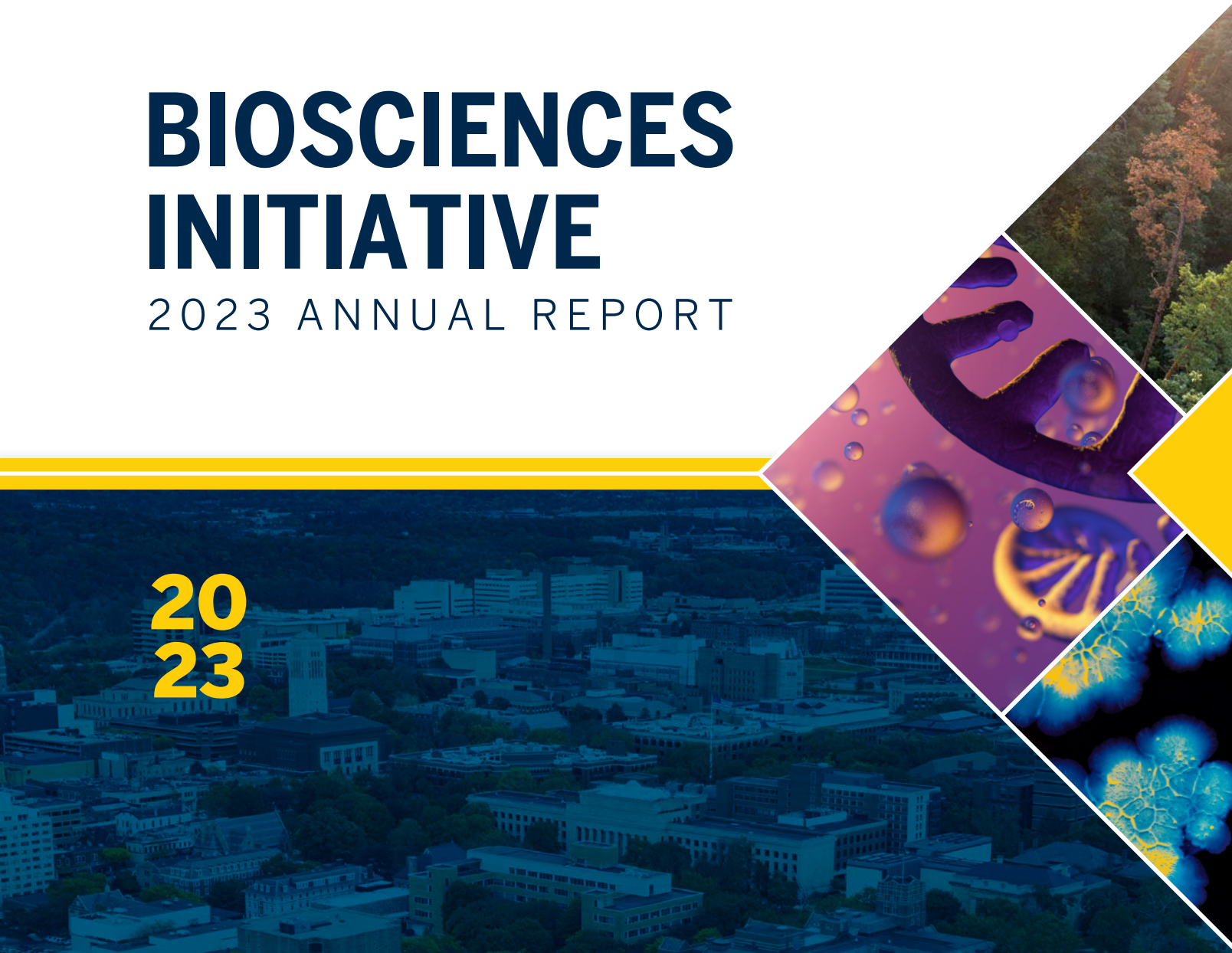
BIOSCIENCES INITIATIVE

2023 ANNUAL REPORT



2023

BIOSCIENCES
UNIVERSITY OF MICHIGAN

Established in 2017, the Biosciences Initiative Coordinating Committee (BICC) received a mandate to enhance biosciences research across the University of Michigan, focusing on strategic leadership, coordination and alignment across the campus. We are delighted to reflect on our significant achievements. Our commitment to fostering innovation and interdisciplinary collaboration has been instrumental in these accomplishments.

To date, we have invested $139 million in a focused set of strategies and programs, with significant funding directed toward developing bioscience research enterprises in emerging areas, positioning U-M as a leader in these fields. We have created nine scientific research initiatives (SRIs) spanning multiple schools and colleges, covering fields from brain cancer to RNA-based therapeutics and natural products drug discovery.

The strategic recruitment of world-renowned experts has been a cornerstone of the BICC's efforts. Over the past several years, this has been a primary focus of the research initiatives and other Biosciences Initiative (BSI) endeavors. For example, Peter Reich, Ph.D., a leading forest ecologist and National Academy of Sciences member, was recruited to Michigan to lead the new Institute of Global Change Biology. The BSI also helped fund the recruitment of Ravi Allada, M.D., a prominent expert in neuroscience, to direct the Michigan Neuroscience Institute. The BSI scientific research initiatives have now recruited a total of 19 outstanding junior faculty as well, who are already being recognized for their groundbreaking work. As just one example of their calibur, both U-M winners of the prestigious 2022 NIH Director's New Innovator Award were young faculty members recruited through BSI programs.

The BSI's hiring efforts extend beyond adding experts to the SRIs. The initiative has supported the recruitment of 18 high-flying junior scholars to our campus through the Biological Scholars Science Program (BSSP), nine of whom are also members of our research initiatives, significantly enriching our academic landscape. Another nine faculty have also received the Mid-career Biosciences Faculty Achievement Recognition (MBioFAR) to pursue high-risk, high-reward research endeavors, with projects ranging from developing technologies capable of training our immune systems to fight against disease to the use of synthetic biology and bioengineering to advance our understanding of early human development.

Other strategies developed by the BICC include the Ideas Lab events, conceived to facilitate interdisciplinary collaboration and high-risk, high-reward research, particularly for young faculty at U-M. This year's participants were tasked with devising nature-based solutions for climate mitigation, with an eye toward social justice and biodiversity. Our investment in shareable discovery resources — such as cutting-edge equipment, technologies and educational tools — has furthered our research capabilities and paved the way for more groundbreaking advancements, with 14 research cores created or enhanced.

In the following sections, this report delves into these achievements in greater detail, illustrating the transformative impact of our work. Our hope is that these collective efforts continue to advance the biosciences at U-M for years to come.

Sincerely,

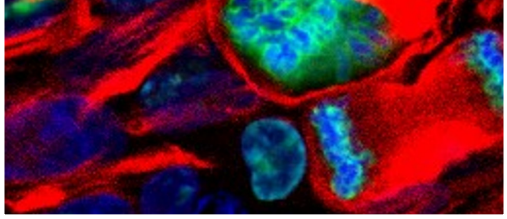
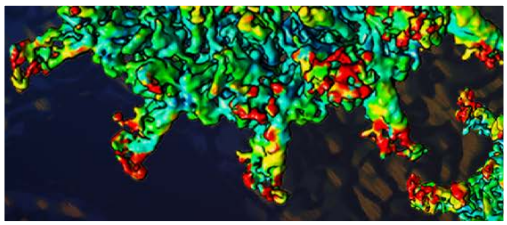
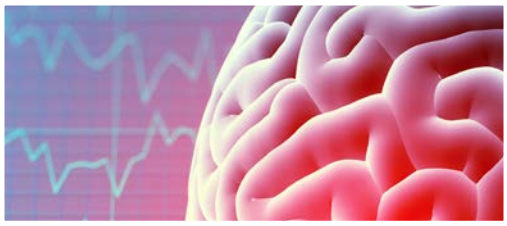
Laurie K. McCauley, DDS, MS, Ph.D.
Provost and Executive Vice President for Academic Affairs; William K. and Mary Anne Najjar Professor

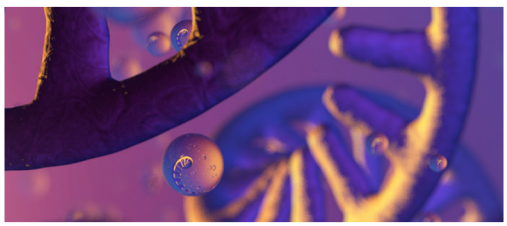
Roger D. Cone, Ph.D.
Vice Provost and Director of the Biosciences Initiative; Mary Sue Coleman Director, Life Sciences Institute

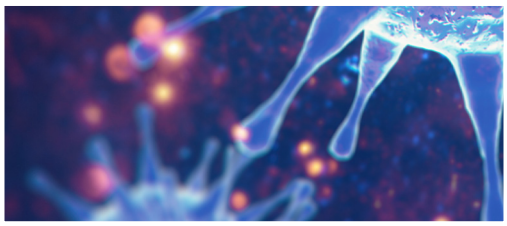
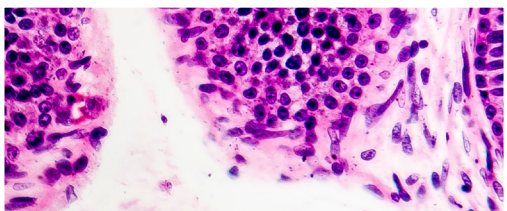
McCauley: Leisa Thompson Photography; Cone: Rajani Arora, LSI

Table of Contents


AUG 2017
DATE LAUNCHED
2
4
5
3
1
COMPETITIVE FUNDING PROGRAMS CREATED
14
CORES CREATED OR ENHANCED
BSI: BY THE NUMBERS
9
MBioFAR AWARDEES
9
SCIENTIFIC RESEARCH INITIATIVES CREATED
19
FACULTY HIRED
HIRES/HIRES SUPPORTED
18
BSSP
$139M ALLOCATED
$150M FUNDING TOTAL



Behind the Breakthroughs:

Chronicles of the BSI's Research Endeavors

Central to the Biosciences Initiative's steadfast commitment to elevating cutting-edge interdisciplinary research is our goal to find and fund visionary, high-impact projects in the biological sciences and convergent disciplines. In pursuit of this goal, the initiative launched a funding competition to foster world-leading programs focused on tackling crucial challenges.

Based on these competitions, the BSI has allocated $132.7 million and 30 tenure lines to fund nine Scientific Research Initiatives (SRIs) and to participate in the launch of the Michigan Neuroscience Institute. Conceived through a rigorous selection process conducted by the Biosciences Initiative Coordinating Committee, these SRIs are a foundational component of the BSI's strategy for fostering groundbreaking research at U-M.

The following sections spotlight the stories of these remarkable initiatives. They trace the journey from their inception and ambitious visions through to the progress they have made and what lies ahead. Whether advancing our understanding of the molecular machines inside our cells, developing new approaches to treat brain cancer or addressing the impact of climate change on biological systems, these initiatives have become pinnacles of excellence and innovation.

BioInnovations in Brain Cancer

Cryo-EM at U-M

Engineering Cell Programmable Biomaterials

Institute for Global Change Biology

Michigan Center for Infectious Disease Threats

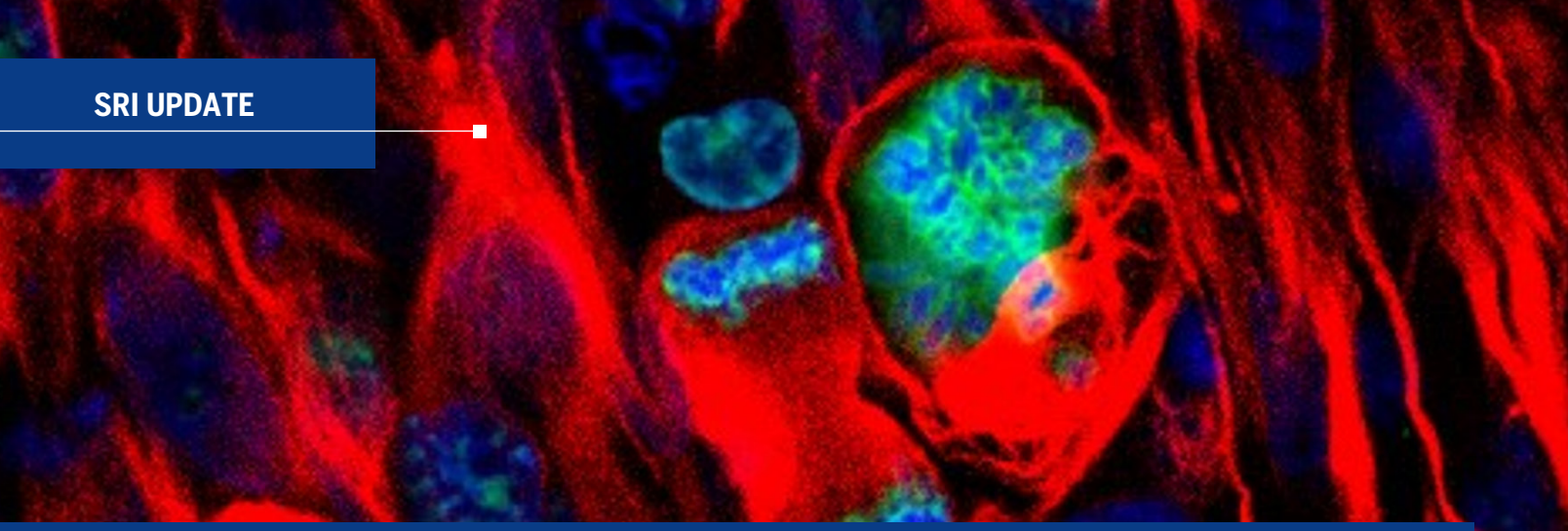
Michigan Concussion Center

Michigan Neuroscience Institute

Natural Product Drug Discovery at U-M

RNA Biomedicine

Single Cell Spatial Analysis Program



BioInnovations in Brain Cancer (BIBC)

Brainstorming Breakthroughs: How the BIBC is Revolutionizing Brain Cancer Research

Brain cancer research, particularly on the treatment of gliomas, has long been mired in challenges that have stymied progress. Traditional approaches have proven insufficient, and the barriers — both biological and technological — have been formidable.

In this context of stagnant progress and unmet clinical needs, the BioInnovations in Brain Cancer (BIBC) initiative, backed by the Biosciences Initiative, aims to break new ground.

Birth of the BIBC

The inception of the BIBC can be traced back to a modest but impactful challenge grant.

"The challenge was to investigate how we can get therapeutics past the blood-brain barrier and into the brain," recalls Maria Castro, Ph.D., co-director of the BIBC. "A lot of the drugs developed for other cancers could be implemented for brain cancer if only we could get them into the brain."

The seed grant united a multidisciplinary team of experts, including Steven Schwendeman, Ph.D., the BIBC's other co-director, who felt they could significantly enhance their research and expedite their impact on brain cancer with the BSI's support.

Maria Castro, Ph.D.

"With the BSI's help, we ended up with this great platform and the power to grow our group, becoming a critical force in the field," Schwendeman emphasizes. "The BSI served as a catalyst they needed to leverage the university's collaborative environment and infrastructure and elevate their work to the next level."

Their strategy is broken down into two sub-goals: use basic biology to identify new therapy targets, and develop medicine based on these discoveries.

"We take a dual approach, with one group that can develop new, actionable targets and an army

Top image: Marianela Candolfi and Maria Castro; Castro headshot: Courtesy of Maria Castro

of technologists who can turn these findings into better treatments," Schwendeman says.

Steven Schwendeman, Ph.D.

Tooling up for breakthroughs:

With the BSI funding, the BIBC is creating and acquiring state-of-the-art research tools and technologies critical to advancing new understandings of how to treat brain cancer.

One key advancement has been the development of their purpose-built animal models used to test hypotheses and treatments prior to human experiments.

"Our group has genetically engineered animal models that mimic brain cancer in humans," says Castro. "We are using these models to test several therapeutics, one of which is close to publication."

The initiative also focuses on specialized equipment for cellular analysis.

"We've developed a tool that enables us to identify and analyze specific cells within the tumor microenvironments, which is crucial for understanding the interactions between tumors and neighboring brain tissue, such as how they impact tumor growth or predict responses to medications."

A critical component of the BIBC's approach is the rigorous evaluation of potential treatments, enabling the team to prioritize the most promising avenues for further research and clinical trials.

"We have advanced chromatographic instruments that help us determine the stability and molecular weight of special biologics and the materials we use to deliver them," Schwendeman explains. "This greatly expedites the process of translating discoveries in basic science to new medical interventions."

To successfully test a new drug, the team says, researchers need to be able to take precise measurements of biological samples across multiple tissues to determine whether it's reaching the target area and to assess proper dosing. To improve this process, the team acquired a Triple Quad liquid chromatography-mass spectrometry (LC-MS) machine, which allows for increased sensitivity and specificity when analyzing complex mixtures including drug formulations and biological tissues.

Through its targeted investments in innovative technologies and research tools, the BIBC is elevating the quality, efficiency and reliability of its research, streamlining research and drug development.

Strengthening the team

Castro and Schwendeman realized early on that assembling the right team was as vital as enhancing their toolkit.

Schwendeman identified a need in the area of drug delivery for nucleic acid-based drugs. Julian Zhu, Ph.D., a specialist in nucleic acid technologies and immunology, was recruited to advance the team's work in this domain.

Castro emphasizes the importance of having expertise in the tumor microenvironment, noting how Toshiro Hara, Ph.D., assistant professor of neurological surgery, was the perfect hire to bring this knowledge to the team.

Julian Zhu, Ph.D.

"Hara specializes in tumor microenvironment interactions, focusing on cellular communication," Castro explains. "His work allows for the targeted delivery of therapeutic molecules into brain tumor models."

Toshiro Hara, Ph.D.

These strategic hires fill essential gaps and synergize with the team's strengths, enhancing the BIBC's overall capabilities.

Innovations and interventions: progress in brain cancer research and treatments

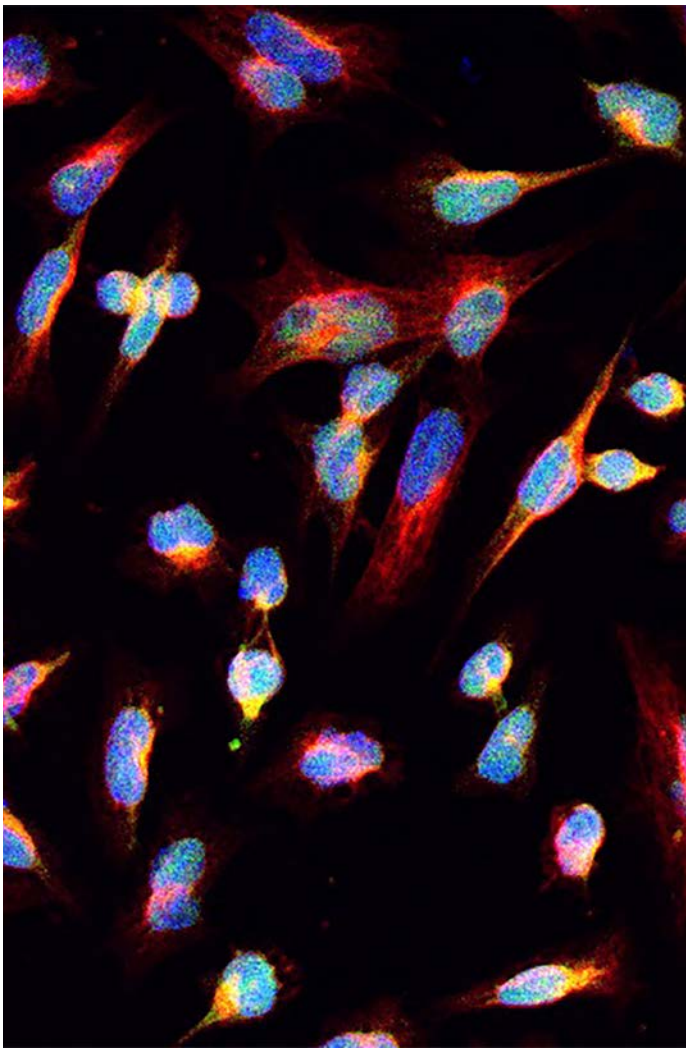
Armed with specialized tools and a well-rounded team, the BIBC is making significant strides in both scientific discovery and technological innovation.

Headshots courtesy of Steven Schwendeman, Julian Zhu, and Toshiro Hara

"We've made considerable inroads identifying targetable pathways," Castro says. "This research has led to R01s funded by the NIH and even to a clinical trial involving gene therapy."

This groundbreaking trial utilized viral vectors engineered to carry therapeutic agents to genetic targets. The viral vectors do two things: one viral vector (plus a systemically administered prodrug Valtrex) kills some tumor cells; the second recruits immune system cells that are typically absent from the brain. In combination, they stimulate a systemic immune response against brain tumors.

The therapy showed exciting early results, including improved survival. Six of the 18 patients enrolled in the trial survived more than two years, three survived more than three years, and one has survived more than five years.



The team is also pioneering diagnostic tools, such as platforms to measure circulating tumor cells in the blood, a capability unique to their initiative, which is crucial for assessing the efficacy of a drug, determining when one is in remission and catching a resurgence early on.

And they have developed several medicines and technologies to solve the blood-brain barrier dilemma.

"We're working to deliver drugs that block the epidermal growth factor receptor (EGFR), which is overexpressed in glioma cells," Castro states. "These drugs are normally incapable of crossing the blood-brain barrier, so we're delivering an antibody that is genetically engineered to make this possible."

Schwendeman highlights a novel route for getting monoclonal antibodies past the brain's bodyguard. Unlike chemotherapy and other systemic interventions, this treatment can specifically target cancer cells while leaving different cell types alone.

Future directions

Looking ahead, the BIBC anticipates continued innovation with a focus on recruitment and collaborative enterprises. They are seeking to add another member to the team and are open to a wide range of backgrounds and specialties, from basic research to drug development.

The research group is also organizing several events to promote scientific collaboration. These include the BIBC Challenge and National Symposium, which will gather experts in the field, facilitating the development and integration of diverse ideas and perspectives.

By bringing together biological discoveries and technological advancements with key recruitments and efforts to facilitate collaboration, the BIBC is accelerating progress in a field that has long faced challenges in innovation, offering a new hope for those affected by brain cancer.

Image credit: Castro Lab, Michigan Medicine, Ann Arbor; National Institute of Health.

Cryo-Electron Microscopy at U-M

Shaping the Future of Structural Biology: U-M's Pioneering Role in Cryo-Electron Microscopy

Ask any biologist why structure is so important, and they'll tell you it's because structure guides function. The implication of this is that by understanding the complex shapes and designs of biological molecules, we can unlock insights into their roles and behaviors.

Rise of cryo-EM

Cryo-electron microscopy, or cryo-EM, has emerged as a pivotal tool in this endeavor. The technique, which uses electron beams to "photograph" frozen biological molecules, allows researchers to learn about the structure of a wide range of organic matter that is not amenable to other popular technologies.

Janet Smith, Ph.D., founding member of the Cryo-EM Scientific Research Initiative, was instrumental in its early integration at the University of Michigan.

"U-M has been at the leading edge of cryo-EM due to her vision and foresight," says the program's director, Melanie Ohi, Ph.D., reflecting on this legacy. "Her work demonstrated to U-M the value of the technology."

Janet Smith, Ph.D.

Further bolstering U-M's leadership in cryo-EM is Michael Cianfrocco, Ph.D., one of the program's co-principal investigators. His groundbreaking work in building cloud computation infrastructure has helped the field overcome a host of computational barriers.

These individual contributions have been part of a larger wave of innovation. Dramatic advances have continued to shift the cutting edge of cryo-EM and greatly expanded its utility. As an early adopter of this novel tool, U-M was uniquely positioned to tap into its expertise and shape the future of cryo-EM research. Recognizing this potential, the Biosciences Initiative funded the cryo-EM program in 2019 to help the team achieve two key goals: make cryo-EM more accessible to the broader U-M community, and launch a new technology, cryo-electron tomography (cryo-ET).

Top image: Rajani Arora, LSI; Smith headshot: Leisa Thompson Photography

Democratizing access

Historically, the nuances and expense of cryo-EM meant that only a select few could harness its potential.

Melanie Ohi, Ph.D.

Michael Cianfrocco, Ph.D.

"Before the program, many researchers wanted access to this technique," says Ohi. "But the rapid evolution of the field made it challenging."

For many at U-M and beyond, this technique remained just out of reach, a powerful tool they didn't have the knowledge or means to utilize.

The program leaders have taken a multi-pronged approach to bridge this gap. First, they expanded the Life Sciences Institute's cryo-EM facility, adding new instruments to enable more scientists across the university to incorporate the technology into their research.

Access to the equipment is a good start, but on its own, it's not enough to spread the use of cryo-EM throughout the U-M research community because the technology can be difficult to implement successfully.

"It's a field that's in its infancy. So it's still very time-consuming, and there's no cookie-cutter method for every application," Ohi explains.

To combat this challenge, the group also provides training for researchers who are new to the technology. A notable example is the annual cryo-EM data processing workshop, run with the help of Cianfrocco. Partially funded by the BSI, this workshop has become a global attraction, bringing in researchers from all over the world.

The results of these efforts have been transformative, with scientists from diverse departments tapping into the potential of cryo-EM. A fascinating illustration of this comes from a study led by Tobias Giessen, Ph.D., an assistant professor of biological chemistry. Giessen had previously developed a technology for disassembling and reassembling protein nanocages. Found naturally in a variety of biomolecules, such as viruses and bacteria, these microscopic protein shells have been used as biomolecular tools for applications in biocatalysis, drug delivery, and bionanotechnology. Leveraging the training and resources provided by cryo-EM, his team was able to create high-resolution images of the resulting engineered nanocage and validate its ability to disassemble and reassemble on demand.

Talent and technology: Advancing cryo-EM

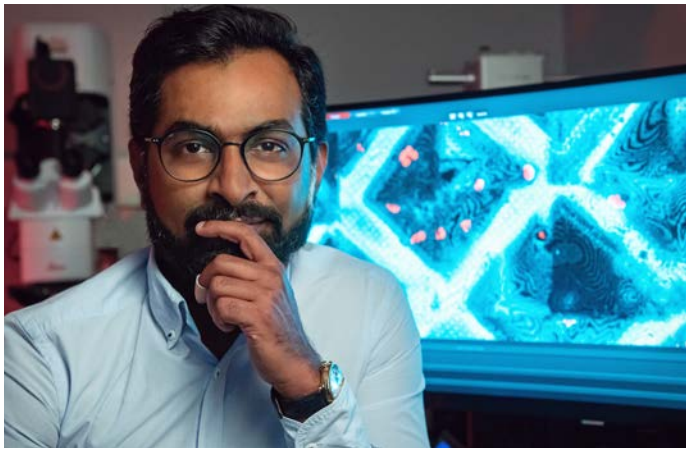
In addition to facilitating the use of currently available cryo-EM technologies and techniques, the initiative has been expanding into cryo-ET.

Achieving this aim meant bringing in key experts to the team, but Ohi notes that finding expertise in such a burgeoning field can be challenging.

"There are so few people in this specialized area, competing for them can be intense given the short supply of faculty focusing on it," she says.

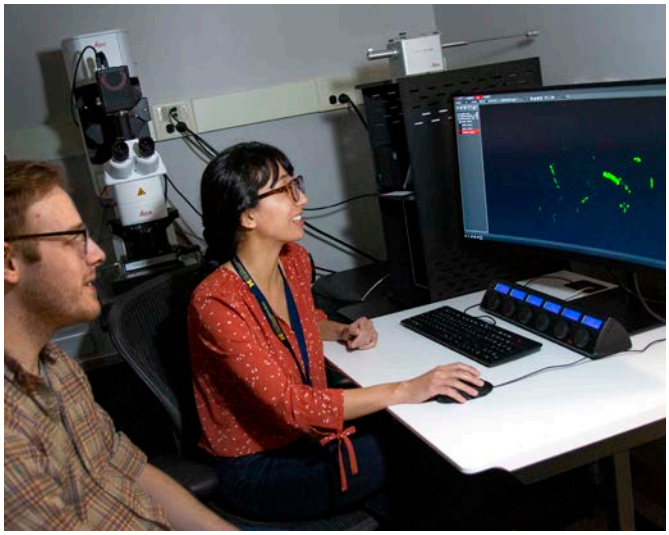
One of the critical hires made by the initiative is Shyamal Mosalaganti, Ph.D., an assistant professor of biological chemistry and cell and developmental biology, who has made significant strides in his first three years with the group.

Mosalaganti's expertise in cryo-ET has been a major asset to the initiative. This technique allows investigators to determine the high-resolution structure of molecular machines in their native environments, offering a deeper dive into the cellular world and allowing researchers



Shyamal Mosalaganti, Ph.D.; Leisa Thompson Photography

Ohi and Cianfrocco headshots: Leisa Thompson Photography



Titan Krios (left). Tyler Brant and Amanda Erwin, Ph.D. (top). Image credit: Rajani Arora, Life Sciences Institute.

to visualize the intricate details of cellular components in a 3-D context.

"With support from the BSI, we began acquiring the necessary equipment for this advanced form of cryo-EM," Ohi explains. "Shyamal's presence and knowledge have been instrumental in ensuring we harness the full potential of cryo-ET."

Looking ahead

Drawing from its achievements, the program is setting its sights on the horizon, with plans to further enhance the accessibility of this technology and continue pioneering new frontiers in the field.

"Our focus is on training as many individuals as possible, enabling them to determine structures that can deepen their grasp of biological questions," Ohi says.

In addition to this endeavor, the initiative is expanding into correlative light and electron microscopy (CLEM), a technique that combines fluorescence imaging and electron microscopy, allowing investigators to pinpoint specific areas within cells to focus on imaging. Herman Fung, Ph.D., a new faculty member with expertise in this area, will join the team in June 2024.

Importantly, the team is continuing its efforts to develop cryo-ET, a pursuit for which they recently received a prestigious Beckham Foundation Grant, along with only six other sites in the United States.

Ohi highlights how investment in this advanced microscopy has profound implications for health and medicine. These techniques allow researchers to determine structures at such a resolution that they can build molecular models, which is key when trying to grasp the mechanisms of disease.

"We are building a team of investigators using cryo-EM and cryo-ET to understand the functions in the cell at a whole new level," Ohi explains. "This work will revolutionize our understanding of the cellular basis of diseases."

With these ambitious objectives, the Cryo-EM initiative at U-M is well-positioned to be at the forefront of cryo-electron-based imaging, techniques and research. ■

Engineering Cell Programmable Biomaterials for Dental and Musculoskeletal Health

Transforming Tissue Engineering: Inside the Programmable Biomaterials Initiative

Our bodies have the remarkable ability to regenerate tissue. This can be observed in skin healing from a small cut or bone mending after a fracture. Yet, this regenerative capability has its boundaries. In some cases, especially when it comes to more complex tissues or injuries, the body struggles to restore what's been lost or damaged with age or disease. This is where the field of regenerative medicine steps in, aiming to provide solutions that can either kickstart or supplement the body's natural healing processes.

U-M's unique potential

In 2019, the University of Michigan stood at a distinct juncture in the world of regenerative medicine. David Kohn, Ph.D., now the director of the Engineering Cell Programmable Biomaterials for Dental and Musculoskeletal Health initiative, noted that unlike institutions that had historically focused either on a stem cell approach within medical centers or a technology-driven approach within engineering faculties, U-M was well-positioned to attack the issue from both sides.

The expertise for advancing regenerative medicine existed across various departments and facilities within the university, and individual researchers and teams had already made some significant advances. What was missing, though, was a coordinated effort to maximize the impact of this varied expertise.

The Biosciences Initiative answered the call and helped provide the funding and organization needed to foster the connections required to make U-M a maverick in the field.

Integrating cellular insights for personalized therapies

Under Kohn's guidance, the Programmable Biomaterials Scientific Research Initiative embarked on a journey to synergize the strengths of biology and engineering in regenerative medicine.

Top image: Koldunova, Adobe Stock

David Kohn, Ph.D.

Central to the program's mission was the aspiration to develop materials rooted in a comprehensive understanding of cellular organization and tissue formation dynamics.

"One of the primary things we want to accomplish is providing a rational basis for developing materials," Kohn explains. "And that basis really comes from understanding how cells organize, and how tissues are formed in time and space."

While the development of new biomaterials is crucial, Kohn's vision goes beyond just their fabrication. He envisaged a new generation of novel materials that aren't merely passive structures introduced into the body but actively interact with their environment, possessing the ability to sense, respond and adapt, seamlessly integrating therapeutic, diagnostic and sensing functionalities.

One of the primary benefits of this novel approach to regenerative biomaterials is its potential to advance personalized medicine.

"If the technology is using signals from an individual, which will differ from one person to another, then it opens the door for a personalized approach as opposed to a one-size-fits-all therapy," Kohn says.

Innovation through interdisciplinary synergy

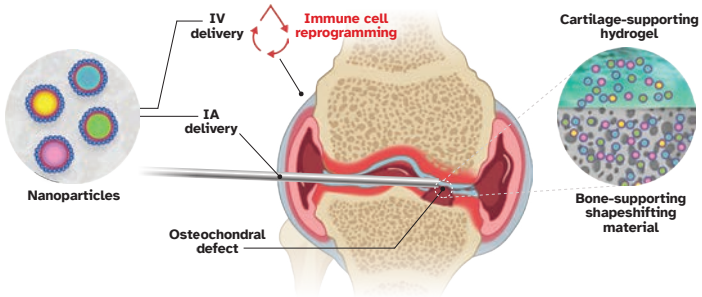
"Many of our activities are based on team building and creating some glue around our vast campus," Kohn says.

The depth of collaboration within the initiative is evident in its close ties with the Single-Cell Spatial Analysis Program (SCSAP). Working together, the two programs aim to span the basic discovery, technology and clinical domains, bridging dimensional scales from the single-cell level up to the whole body.

Central to the program's collaborative efforts is its Grand Challenge workshop, a competitive event created by the Programmable Biomaterials Initiative to stimulate innovative research by funding teams that propose groundbreaking solutions.

In 2022, the inaugural Grand Challenge bore fruit, funding several new teams that came together to address pressing problems. One such team led by Aaron Morris, Ph.D., an assistant professor of biomedical engineering, developed cell-based sensors with the potential to discern between beneficial tissue regeneration and harmful inflammation.

A week before their second Grand Challenge, the team had to quickly reorient to respond to a recent call for proposals from the Advanced Research Projects Agency for Health's NITRO Program. The call sought solutions to help those suffering from osteoarthritis through novel approaches to tissue regeneration. Kohn says, the request "was right in our wheelhouse," presenting an unmissable opportunity.



Graphic for the NITRO program. Image created by Steve Alvey for Kurt Hankenson

Leveraging the collaborative infrastructure already established by the BSI, they convened a team of 15 experts. In less than a month, they crafted a proposal emphasizing therapies that can be delivered locally or systemically to target inflammatory responses and promote joint regeneration, with the goal of starting in-human studies within five years.

"It would have been difficult, if not impossible, to hash out those ideas from scratch," says Kohn. "The BSI's support enabled us to leap out of the gate with a solid foundation of ideas, a strong team framework and the ability to swiftly bring together additional expertise, both internal and external to U-M, to propose innovative solutions."

Through events like the Grand Challenge and partnerships such as with the SCSAP, the initiative has built a responsive and collaborative network ready to tackle complex challenges in regenerative medicine.

Kohn headshot: Courtesy of David Kohn

Tools of the trade: Mass spectrometry and AI

In biomaterials research, tools and tech are paramount. Spatial mass spectrometry stands out as a pivotal instrument for the team. Unlike its traditional counterpart, which is destructive, spatial mass spectrometry allows for a detailed mapping of proteins on tissue surfaces without compromising the tissue's integrity.

This technology produces lots of data, which requires time and skills to unpack.

"The challenge lies in analyzing this information," Kohn notes. "What exactly are we aiming to measure? Once we've collected the data, how do we interpret it to inform our material designs or to evaluate the performance of a material or tissue?"

This is where artificial intelligence and machine learning come into play, helping the team find the needle in a haystack of data.

Leveraging spatial mass spectrometry and AI analytics, the initiative is enhancing its research capabilities, ensuring more precise and informed material designs for targeted applications.

New faces, focused goals

When asked about the direction the initiative is headed in the next year few years, Kohn emphasizes key hires, collaboration and integration:

"A big direction falls under the umbrella of continued efforts to weave the right people together."

Maria Coronel, Ph.D., an assistant professor of biomedical engineering, was the program's first hire. Her expertise lies in "smart materials"

Maria Coronel, Ph.D.

that can modulate immune responses and sense and treat diseases. The program is also conducting a joint search for the next two hires to further bolster its capabilities.

One of the key technological goals is to refine the signals used for monitoring cellular conditions, an ability which is crucial both for enabling biomaterials to effectively assess and promote tissue regeneration and inform the development of new and improved designs. Basic indicators like pH and temperature, while informative, can be influenced by numerous external factors. A pH change might arise from inflammation or just from consuming a beverage, for example, making it a less than fully reliable guide to tissue health. To enhance the precision of their work, the team aims to move beyond these general measurements. The objective is to develop unambiguous signals that provide clear and specific insights tailored to particular diseases or therapeutic responses.

Kohn also touched upon the importance of clarifying conceptual issues.

"We want to tailor the conceptualization of programmable materials to solving a clinical problem," he says. "It's not about creating materials for the sake of innovation but to address real-world clinical challenges."

This conceptual clarity is achieved by ensuring that different groups of experts from basic life sciences to engineering technologies clinicians are constantly communicating and collaborating.

With strategic hires, continued collaboration and a commitment to refining sensing technologies, the initiative is leading the way in personalized biomaterials for clinical solutions. ■

> *"The BSI's support enabled us to leap out of the gate with a solid foundation of ideas, a strong team framework and the ability to swiftly bring together additional expertise.*

Coronel headshot: Courtesy of Maria Coronel

Institute for Global Change Biology (IGCB)

Bridging Science and Solutions: The IGCB's Collaborative Drive for Global Change Mitigation

The Earth and its myriad life forms are under mounting pressure from a range of human-mediated changes, including climate change, biodiversity loss, pollution and altered land use. The result is a planet out of balance, with increasingly devastating consequences.

"Unless we swiftly change our attitudes and behaviors toward anthropogenic-induced change, we won't be able to realize the rest of our collective endeavors," warns Peter Reich, Ph.D., director of the Institute for Global Change Biology (IGCB).

Formed in 2019 with the support of the Biosciences Initiative, the IGCB was developed with the aim of generating a comprehensive understanding of the interactive effects of global change on organisms and the systems they are a part of, and assisting in the development of environmental policy and decision-making.

Brought on board as the director in 2021, Reich builds on the institute's mission, with a strong emphasis on actively addressing global change drivers instead of merely responding to their effects.

Peter Reich, Ph.D.

"All sorts of programs within science or government and agencies are focused solely on adapting to climate change, not mitigating it," Reich points out. "But we're never going to be able to build enough sea walls or change how we do agriculture in a way that makes us safe from the mounting effects of global change."

Viewing his role as a catalyst for this broader, mitigation-based change, Reich sets the stage for the IGCB as a transformative force in global change biology.

Collaboration in action

Under Reich's leadership, the program has become a hub for interdisciplinary research, bringing together experts from diverse fields to tackle the complex challenges of global change.

Top image: Maykal, Adobe Stock; Reich headshot: Anne Reich

"I saw a chance to build a community of people who focus on global change biology research, but whose interests were more interdisciplinary and who are interested in solutions that bridge across campus," Reich explains.

This bridge-building cooperative tactic has resulted in a host of remarkable achievements and discoveries.

One such example is a collaboration between Reich and Xinli Chen, Ph.D., an IGCB Exchange Fellow whose main appointment is at the University of Alberta. Chen, Reich and his team of colleagues worked together to investigate the impact of forest diversity on soil carbon storage. Through a partnership with the Canadian government, the team utilized existing data to discover that forests with greater biodiversity can store soil carbon faster than less diverse forests, offering actionable insights for mitigating climate change through enhanced carbon storage practices.

The collaborative mindset extends throughout the IGCB. Tsung Fung Au, Ph.D., an IGCB postdoctoral research fellow, collaborated with experts across a host of different fields, including ecology, climatology, geography and the social sciences, at institutions spanning several continents. Their work, which has received international attention, demonstrated the importance of maintaining a diverse age structure in forests to withstand future climate extremes.

In another intercontinental effort, Thiago Gonçalves-Souza, Ph.D., a visiting professor and IGCB research scientist, and ecologist Nate Sanders, Ph.D., professor in ecology and evolutionary biology, collaborated with graduate students from multiple Brazilian universities to investigate the interplay between animal biodiversity and global change. They reviewed 1,655 articles on trait-based animal ecology, uncovering significant gaps and biases in existing research. Left unchecked, these shortcomings have limited our ability to investigate how global change drivers, such as climate change and habitat loss, affect trait variation.

Building a multidisciplinary team

As part of its integrated approach, the IGCB saw the importance of creating a diverse and multifaceted team of experts, and is working on multiple joint hires with different U-M schools and colleges.

Kai Zhu, Ph.D.

Kai Zhu, Ph.D., the initiative's second hire, holds a joint appointment with the School for Environment and Sustainability and the Department of Ecology and Evolutionary Biology in the College of Literature, Science, and the Arts. With a focus on understanding how plants and soil respond to environmental changes, Zhu brings a unique perspective that combines ecology, statistics and computer science.

Jennifer Head, Ph.D.

Jennifer Head, Ph.D., recently joined the IGCB and Department of Epidemiology in the School of Public Health. She studies the impact of public health policies, climate, animal hosts and individual behaviors on infectious diseases. Head's research adds a crucial perspective to the team, uncovering some of the more unexpected but equally significant health effects of the drivers of global change.

Reinforcing the impact of these multidisciplinary hires is the support of nearly 30 postdocs and exchange researchers with backgrounds in areas ranging from evolutionary biology to biogeochemistry, social policy and behavioral health.

> *"I saw a chance to build a community of people who focus on global change biology research, but whose interests were more interdisciplinary and who are interested in solutions that bridge across campus.*

Zhu headshot: Melissa Alice De Witte; Head headshot: Michigan Photography, courtesy of Jennifer Head

With this well-rounded team, the IGCB is not only expanding its research capabilities but also solidifying its commitment to a comprehensive, integrative approach.

From research to real-world solutions: What's next for the IGCB

"We're not just generating knowledge for the sake of it," Reich emphasizes. "Our work must drive action and address pressing global issues."

Two years into his leadership, this vision of turning discovery into real-world impact is beginning to come to life.

Reich highlights how the IGCB team is increasingly consulted for their expertise in managing ecosystems like forests, savannas and grasslands in the face of climate change, biodiversity loss and invasive species. In a recent example, a forest manager in Quebec sought the team's advice on optimizing tree species mix for productivity gains and carbon storage in new forests that would replace spruce monoculture plantations.

"It would be great if in five or 10 years our institute helped build a center that's the world's go-to place for having the best information possible on how to keep carbon in ecosystems," Reich notes.

The institute is also building partnerships to tackle complex ecological challenges. Their collaboration with the Berkeley National Lab aims to improve our understanding of soil carbon cycling. This project has the potential to influence both global carbon cycle models and policies around carbon offsets.

"Given that carbon offsets are a billion-dollar industry based on assumptions with a lot of uncertainties, the need for reliable information is critical," says Reich. "The hope is to link the science directly to the industry, ensuring that carbon offset initiatives are grounded in solid research."

The IGCB is eager to continue fostering collaborations among scientists at U-M and across the globe, enabling them to address questions collectively that might not otherwise have been possible.

In the 2023 Ideas lab led by Reich and funded by the BSI, two dozen professors and scientists from a wide range of disciplines coalesced into groups to devise projects aimed at the implementation of nature-based solutions to climate change, with a focus on storing more carbon in plants and soils while also preserving biodiversity and acting towards social justice.

As for what's on the immediate horizon, Reich is pragmatic yet ambitious: "We've really just started. The question is: Can we catalyze our existing projects to be more holistic, larger and address bigger questions and issues?"

The IGCB demonstrates what interdisciplinary, mitigation-oriented research can accomplish in global change biology. Through targeted collaborations and a focus on tangible impact, the institute is becoming a global leader in scientific understanding and actionable solutions for diminishing drivers of global change.

Michigan Center for Infectious Disease Threats (MCIDT)

MCIDT: A New Paradigm in Infectious Disease Research

From an early age, epidemiologist Aubree Gordon, Ph.D., held a keen interest in communicable diseases. Films like "Outbreak" piqued her curiosity as a teenager, but it wasn't until her undergraduate years that she discovered the field of epidemiology.

"I spent a lot of my teenage years reading books like *The Hot Zone*," she recalls, "but didn't learn about epidemiology until I was in college."

For Gordon, now the director of the Michigan Center for Infectious Disease Threats (MCIDT), epidemiology offered a unique opportunity to combine her interest in lab work with a broader study of disease patterns in populations.

MCIDT: A pandemic response with lasting aspirations

As the COVID-19 pandemic emerged, the University of Michigan recognized the importance of infectious disease research, and faculty were eager to use their varied expertise to help.

"During the early days of the pandemic, people from all over campus were saying, 'I'm here, I have the skill set, what can I do?'" says Gordon. "As the urgent importance of infectious disease research became even clearer to the university, we realized that there wasn't a good mechanism for getting everybody together and interacting."

Aubree Gordon, Ph.D.

In response, the Biosciences Initiative funded the formation of the MCIDT. Its vision is both local and broad. The center aims to bring together infectious disease researchers and develop critical resources that facilitate collaboration.

The program's aspirations extend beyond the university's boundaries. Recognizing U-M's role as a public institution, the MCIDT has sought to help the state and surrounding region by increasing capacity in various sectors, from public health departments to laboratories and hospitals.

Making an impact: Research and public outreach

Reflecting on the ultimate purpose of her work, Gordon highlights the importance she attributes to ensuring her research leads to real-time tangible benefits.

Top image: Thaut Images, Adobe Stock; Gordon headshot: Courtesy of Aubree Gordon

COVID research lab in Nicaragua. Image credit: Marc-Grégor Campredon.

"I think that knowledge is really valuable," she explains. "But of course, I'm doing this because I want to see our discoveries contribute to interventions and improve health."

A prime example is the MCIDT's involvement in the National Institute for Health (NIH) Immunity Associated with SARS-CoV-2 (IASO) cohort study. By offering assistance through its tools and research, the team helped the inter-institutional research groups working on the project rapidly characterize and assess new COVID-19 variants.

The team's efforts also heavily inform policy.

"We provide real-time information to the U.S. Government through the SARS-CoV-2 to variant evolution (SAVE) program," Gordon shares.

This collaboration is pivotal, involving extensive data collection to decipher how virus variants might be evading immunity and providing evidence for what to put in the next boosters. In a recent study, they concluded that boosting with the bivalent mRNA vaccines is not better than boosting with the original monovalent vaccine. Their findings and suggestions resonated with the FDA when they met to discuss the next generation of vaccines.

"When the FDA convened, they heavily reviewed and cited our data in determining how to formulate it," Gordon highlights.

In addition to research and policy-making, the MCIDT formed Public Health Prepared to translate findings into actionable strategies for building the skills and capacities of the public health workforce. For example, they collaborated with neighboring schools to team up with One-Health ECHO, a discussion-based learning series that provides events focusing on how to leverage human, animal and environmental health partners to keep Michigan healthy.

The MCIDT's work showcases the power of research that extends beyond the academy to influence public health and policy. Whether contributing to risk assessment for new SARS-CoV-2 variants or informing the FDA's decisions on vaccine boosters, the team is making a real-world impact. Their commitment to public health preparedness further underscores MCIDT's dual role as researchers and active contributors to community well-being.

> *"I see the MCIDT as a resource available to researchers across the U.S. and beyond, helping us identify potential threats and, hopefully, prevent pandemics.*

Critical facilities for infectious disease research

The MCIDT's research facilities are instrumental in understanding and responding to infectious diseases. Central to these discovery cores are the Biosafety Level 3 (BSL3) labs. These labs are funded in part with investments from the BSI, designed for working on higher-risk pathogens that need containment.

"Without BSL3 facilities, there were many things we could not do to respond to the SARS-CoV-2 pandemic," Gordon explains. "If we want to grow that virus and evaluate its risk, especially with the mutations we see in the community, we depend on these research centers due to their ability to protect both investigators and the public from the diseases we study."

Kelly Speer, Ph.D.

Another essential facility for MCIDT is the Michigan Pathogen Biorepository, which archives infectious disease specimens that can be made available for genetic and molecular analysis. Kelly Speer, Ph.D., a recent hire who specializes in ecology and evolutionary biology, is now the director of the biorepository. Her work revolves around the concept that these collections can also be used to study pathogens that may threaten human health.

Additionally, the Life Sciences Institute's protein production facility housed in the Center for Structural Biology has been pivotal in the global response to the pandemic.

"It provides a great service to the campus and multiple countries," Gordon shares. "For example, prior to the commercial rapid antigen tests, they were producing SARS-CoV-2 antigen for serology, which was sent to several low- and middle-income countries to help them respond to the pandemic."

The core facilities are necessary ingredients in the MCIDT's recipe for addressing SARS-CoV-2 and other infectious diseases. They have enabled critical research with direct effects on how we respond to and manage the pandemic.

Pathogen pathways: Upcoming plans and directions

Gordon shared her vision for the coming years, emphasizing the sustained commitment to encouraging interdisciplinary collaboration.

"We aim to continue bringing faculty together from across schools and institutes to do cutting-edge science and public health work," she says. "The MCIDT will help Michigan and the nation be better prepared for any future pandemics that arrive."

A particularly exciting avenue for the MCIDT is the potential expansion of the Pathogen Biorepository. Gordon envisions this as a pivotal asset, not just for U-M but for the broader scientific community.

The program is also exploring proactive measures against future infectious threats, such as building up the knowledge required to help other groups create prototype vaccines for yet-to-emerge pathogens. With organizations like the NIH showing keen interest in such endeavors, the MCIDT is ready to play a significant role in these efforts.

Gordon concludes, "I see the MCIDT as a resource available to researchers across the U.S. and beyond, helping us identify potential threats and, hopefully, prevent pandemics." ■

Jennifer Meagher, Ph.D., Center for Structural Biology at the Life Sciences Institute. Image credit: Rajani Arora, Life Sciences Institute.

Speer headshot: Camille Walker, courtesy of Kelly Speer.

Michigan Concussion Center

Michigan Concussion Center: A Triad of Research, Clinical Care and Outreach

Concussions are a prevalent form of traumatic brain injury, with an estimated 5.3 million people living with a permanent TBI-related disability in the U.S. today, according to the Centers for Disease Control and Prevention (CDC).

Despite this widespread impact, many people affected by concussions don't receive treatment.

"It is widely believed that up to 50 percent of concussions go unreported," explains Steven Broglio, Ph.D., the director of the Michigan Concussion Center.

Unfortunately, even when medical care is sought, diagnostic and treatment protocols for concussions are still inconsistent. This gap in medical practice affects individual health and carries a significant economic burden, estimated at $76.5 billion annually in the U.S.

And although researchers have made substantial progress in understanding concussions, there is much left to know — from immediate and long-term impacts, to who is most vulnerable, to how to prevent and reduce harm.

Steven Broglio, Ph.D.

To close gaps in public knowledge, treatment protocols and research, there is an urgent need for an interdisciplinary, integrated approach to concussion research and care.

Michigan Concussion Center: Origins, goals and strategy

When Broglio arrived at the University of Michigan in 2011, he was part of a small but dedicated group focused on concussion research. A turning point came when the Biosciences Initiative launched.

"We saw it as an opportunity to start a center that would give us the ability to bring everybody on campus together in a very collaborative way, all while attracting new minds who can broaden our capacities," Broglio recalls.

Top image: Iaremenko, Adobe Stock; Broglio headshot: Michigan Photography, courtesy of Steven Broglio

With the BSI's support, the center focused on improving the concussion crisis from three angles: research, clinical treatment and outreach. Brogilo notes that this tripartite strategy is unique among concussion programs.

"While there are other centers across the country that are really good at research, amazing at clinical practice, or do fantastic outreach work, I don't see anybody that does all three the way that we do it," he says.

In addition to allowing the center to be a one-stop-shop for concussion work, each component benefits the other, Brioglio explains, making the whole greater than the sum of its parts.

Bench to bedside to broader community

From a small group of dedicated researchers to a pioneering center redefining approaches to concussion science and treatment, Broglio's vision has been realized in ways that exceed traditional academic boundaries. The center's innovative structure allows the team to tackle the multi-faceted issue of concussions in unique ways, with countless accomplishments from the lab to policy.

Starting with its research endeavors, the center houses the country's two largest sport concussion studies — the Ivy League Big Ten Epidemiology of Concussion Study and the CARE Consortium — each of which has produced critical discoveries. Findings from the CARE Consortium redefined typical concussion recovery from 14 days to up to one month. The center also found through these studies that the pre-season poses the highest risk for concussion to athletes, more than when the competition begins.

On top of improving understanding of concussion risk, these results informed changes in the National Collegiate Athletic Association's concussion policies guidelines. The center has also advised the CDC on concussion educational materials and collaborated with sports non-governmental organizations like U.S. Soccer and USA Cycling to shape concussion policies.

In support of its research and policy influence, the center engages in various forms of public outreach to further mitigate concussion risk and severity in key groups. A notable example is the Pop-up Safety Town events, led by Andrew Hashikawa, M.D., a clinical professor in the Department of Emergency Medicine and Pediatrics. These injury prevention and education programs provide free helmet fittings and basic concussion information to youth and families in underserved communities.

Broglio emphasized the fulfilling nature of these events: "The gratitude people express makes it one of the most fun and rewarding elements of my job."

Although these efforts can reduce the prevalence of concussions, medical care will continue to be essential when they occur, which is why the center includes a comprehensive clinical core. Spearheaded by the Michigan NeuroSport

Pop-up Safety Town event. Image credit: Sacred, Moon Reflections Photography & Videography.

> *"While there are other centers across the country that are really good at research, amazing at clinical practice, or do fantastic outreach work, I don't see anybody that does all three the way that we do it.*

NeuroSport Clinical Team; image courtesy of Tina Chen.

team, which treats sports-related concussions and sees nearly 2,000 unique patients annually, the Michigan Concussion Center's clinical practice was recognized for ranking in the 99th percentile for patient satisfaction by Michigan Medicine's Office of Patient Experience.

This synergistic quality of the center's three pillars is exemplified by an ongoing project called the Concussion Learning Health System (C-LHS).

"The C-LHS is set up to enable researchers to explore a wide range of questions, without having to gather new data," Broglio explains. "In turn, research findings guide our clinicians in their practice, whose experiences are fed back to investigators, further informing their questions, facilitating discoveries, and so on."

Space for innovation

The program's innovative three-core approach has not only led to groundbreaking discoveries but also necessitated a dedicated space to foster further collaboration and the seamless sharing of information and insights.

Supported by the School of Kinesiology, this specialized environment serves as the primary meeting space for all center members. It's strategically located adjacent to the Kinesiology Neurosuite research space, which houses a range of cutting-edge equipment and tools, all available for concussion research.

"This dedicated space adds legitimacy to the program and allows us to think on a bigger scale, which has been key to our success," Broglio says.

Looking ahead: Future of concussion research and care

The center's future vision is as ambitious and impactful as its current work. Broglio is particularly excited about the longitudinal nature of the CARE Consortium.

"That will hopefully go on for 40 more years," he says. "This type of multi-decade project is vital for understanding the long-term consequences of brain injuries."

The center is also in early conversations about developing its own brain bank, aiming to study individuals whose injuries have been well-documented from their college years onward by examining anatomical abnormalities and looking for informative correlations with their concussion-induced behavioral and cognitive changes.

Broglio also hopes his team will conduct a comprehensive evaluation of former Michigan athletes. While still in the conceptual stage, this study would provide detailed assessments involving magnetic resonance imaging (MRI), full clinical exams and blood draws, targeting individuals potentially in their 60s and 70s to offer a better understanding of the long-term effects of concussions.

Public outreach will remain a vital component of the center's strategy, as well.

"We want to expand the Safety Town effort into the tribal communities and up into the northern parts of the state where access to healthcare is more limited," Broglio says.

To facilitate this, the center is developing a mobile app to map out all the clinics in the state that provide concussion care, with a focus on underserved communities, which is set to be ready by springtime.

With ambitious research plans and a continued emphasis on translating discovery, the center is ready not only to deepen our understanding of concussions but to turn knowledge into tangible benefits for communities near and far. ■

Natural Products Drug Discovery (NPDD)

Unlocking Nature's Pharmacy: U-M's Natural Products Drug Discovery Initiative

From the life-saving antibiotic penicillin discovered in 1928 to modern anti-cancer drugs derived from microorganisms, natural products have long been a cornerstone in drug discovery and development.

David Sherman, Ph.D.

"The original drugs for use in humans have always been natural products," says David Sherman, Ph.D., director of the Natural Products Drug Discovery (NPDD) initiative at the University of Michigan. "This rich history underscores the immense potential that nature holds for medicinal breakthroughs, even in the era of synthetic chemistry."

Formation, vision and goals

When the Biosciences Initiative was formed, Sherman realized there was an opportunity to take his work to the next level and accomplish his aims for natural products research in ways he would not otherwise have been able to.

"I saw a great opportunity when this BSI came about," says Sherman. "With their support, we aim to become a global authority in natural products research and development."

In particular, the BSI's backing has allowed the Sherman and co-principle investigator Ashu Tripathi, Ph.D., to broaden and streamline basic research, refining the transition from fundamental discovery to translation into publicly available medicines.

Natural Products Discovery Core

Ashu Tripathi, Ph.D.

To facilitate the ambitious goals of the NPDD program, the team created a specialized facility called the Natural Products Discovery Core (NPDC). Led by Tripathi, the core's most significant asset is the ability to swiftly identify compounds that exhibit biological effects from extensive collections of microbial small molecule extracts. They use this capacity to advance both their own work and that of other researchers at U-M and in industry.

"The core's primary function is to employ a distinctive, state-of-the-art high-throughput

Top image: Sinhyu, Adobe Stock; Sherman headshot: Leisa Thompson Photography; Tripathi headshot: Stephanie King, LSI

method for pinpointing biologically active natural product entities within complex extracts, a capability few institutions can match on such a large scale," Tripathi says. "Our data-intensive, cheminformatic platform enhances our capacity to identify molecules quickly and reproducibly."

While identifying active compounds is a crucial step, the NPDC's journey doesn't end there. Understanding the structure of these compounds is vital for the entire development process, from optimizing their effects to scaling up manufacturing for public use.

"Consider a substance with known anti-cancer properties," Tripathi says. "To produce it consistently on a mass scale, perform medicinal chemistry and pharmacokinetic analysis, and conduct further downstream development, you must first know its complete structure."

To expedite workflows and reduce the time and effort required to complete various stages of the natural products drug discovery and development process, the NPDC has added several state-of-the-art robotics.

"By minimizing the need for mundane personnel efforts, faculty can conserve energy and time for other critical and analytical aspects of their research," Tripathi explains, highlighting the efficiency gains made possible by automation.

The NPDC has established significant impact and utility within U-M and among other academic institutions and industry partners.

To date, the NPDC has undertaken 51 external projects with outside groups. Of these, 23 were in collaboration with researchers at U-M. Additionally, 16 projects were conducted with external academic institutions and 12 with industry partners. This diverse project distribution underscores the NPDC's wide appeal and its robust capacity to support a varied spectrum of research endeavors in the field of natural product discovery.

Assembling a team of experts

Recognizing the complexity of natural products drug discovery, the NPDD initiative strategically convened a multidisciplinary team of experts. So far, they've hired two new faculty and plan to add a third. Each brings a unique set of skills and knowledge to the table.

Roland Kersten, Ph.D.

Their first hire was Roland Kersten, Ph.D., a plant scientist and medicinal chemistry professor. His expertise in genome sequencing, in particular, is crucial for the team, enabling the exploration of complex genetic information within plants. This path of investigation is revealing novel biosynthetic pathways for drug discovery that were previously only understood in microorganisms, thus expanding the scope of plant-based natural product research.

Marcy Balunas, Ph.D.

Marcy Balunas, Ph.D., joins the initiative as the second key hire, contributing her extensive knowledge in microbiology and immunology. Her research is centered on the intricate ecosystems of microbiomes, which are complex assemblies of microorganisms coexisting within various habitats, ranging from the human gut to the microenvironments of cancerous tumors. Balunas's investigations are crucial for uncovering previously unrecognized natural products.

Research highlights: Advancements and innovations

From pioneering computational methods to innovative microbiome studies, the research emerging from the NPDD initiative spans a broad spectrum of impactful science.

Top image: Rajani Arora, LSI; Headshots courtesy of Roland Kersten and Marcy Balunas

In collaboration with Carnegie Mellon University, Tripathi has created a predictive model that determines the structure and activity of molecules directly from genome sequences. This approach facilitated the discovery of a potent antifungal compound, which, after successful toxicity assays, has now entered mass production to perform pre-clinical studies in collaboration with the National Institute of Allergy and Infectious Diseases.

With access to U-M plant repositories, Kersten discovered bioactive molecules in some of its oldest samples, opening up a new age range and category of plants that can be studied for active natural products. He also identified a new class of plant-based peptide molecules that have the potential to be utilized for many therapeutic and biological applications.

Balunas has secured funding from the NIH for her innovative work on the human gut microbiome in relation to cancer tumors. She's also exploring the marine microbiome, particularly the interactions between bacteria and invertebrates, expanding our understanding of microbiomes' potential applications in drug discovery.

Collaborating with U-M's own Kathleen Collins, M.D., Ph.D., a professor of internal medicine and microbiology and immunology, Sherman developed an anti-HIV drug targeting the nef gene product — a key element that helps HIV-infected cells hide from our immune systems. Using bephyllomycin and concanamycin A, essential natural products discovered in their lab, they now have a sustainable process to manufacture a molecule that might revolutionize HIV treatment. Patents filed on their research indicate that they are establishing substantial intellectual property to aid their drug discovery.

In oncology, Sherman's team worked to create natural product-based toxins that can be conjugated to monoclonal antibodies targeting tumor-specific antigens to destroy cancer cells more effectively. Together with a pharmaceutical partner, they have developed promising drug candidates and even begun tests on their first new antibody-drug conjugate.

These projects situate the natural products team at the heart of critical breakthroughs in drug discovery, pushing the NPDD initiative towards more effective, sustainable and impactful treatments.

Future directions

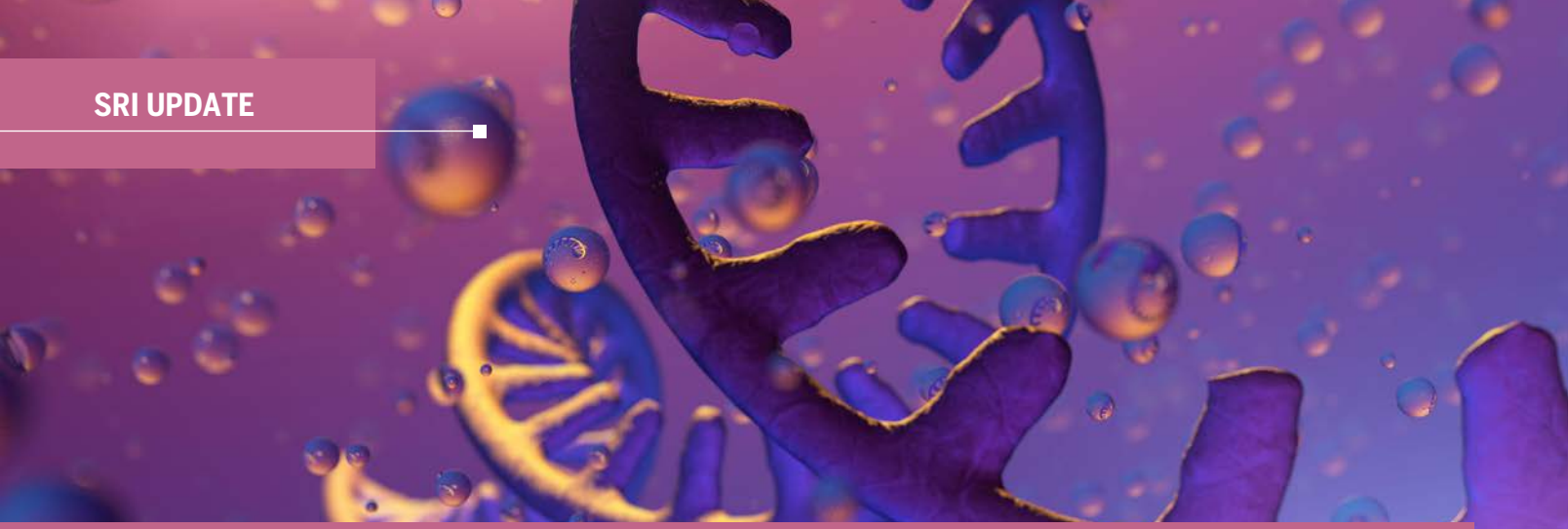
As the NPDD initiative continues to grow, the team highlighted several goals, from securing their final hire to creating interdisciplinary training for students to continuing to form partnerships with industry.

Natural product research generates massive amounts of data, which can be difficult and time-consuming to extract insights from. Because of this, the NPDD initiative is looking to round out its team by recruiting an expert in computer science, synthetic biology and engineering. The goal is to enable the team to use artificial intelligence and machine learning to accelerate the discovery of new natural products.

From an educational standpoint, Sherman advocates for developing a robust, interdisciplinary training program in natural products that will draw on faculty in medicinal chemistry, environmental science, engineering and computer science. This program will serve as a pipeline for students passionate about bio-catalysis, computational methods for drug discovery, fermentation and pathway engineering.

The program also plans to continue bridging the gap between academia and industry. Sherman highlights how pharmaceutical and biotech firms increasingly recognize the importance of biocatalysis, the process of using natural substances that include enzymes or whole cells to speed up chemical reactions in drug development and manufacturing. He suggests building a consortium with these industries, capitalizing on this opportunity by having companies contribute financially to the training and mentorship program. In this symbiotic relationship, U-M can secure funding for its programs, and the companies ensure a steady stream of highly skilled personnel.

The work of the NPDD initiative has the potential to revolutionize treatment for diseases worldwide, from cancer to HIV, marking a new era in natural product-based therapies.



RNA Biomedicine

Beyond the Genome: Michigan's Dive into RNA Therapeutics

In the wake of the COVID-19 pandemic, the world witnessed the transformative power of ribonucleic acid (RNA)-based medicines. Vaccines developed in record time showcased the potential of RNA technology, offering a beacon of hope in challenging times.

Yet, the exploration of RNA's vast potential began much earlier at the University of Michigan with the establishment of the Center for RNA Biomedicine in 2016. This early commitment to understanding the intricacies of RNA laid the foundation for many critical advancements in this field.

Although it was making great progress, RNA research is an expensive enterprise, a fact which made it challenging for the center to achieve its full potential.

"Sustaining the requisite level of funding to support our research and achieve our vision was quite difficult," explains Nils Walter, Ph.D., founder and director of the Center for RNA Biomedicine."We needed support to take what was already there and bring it to the next level to make the University of Michigan a leader in RNA biomedicine."

Nils Walter, Ph.D.

In 2019, with the support of the Biosciences Initiative, the RNA Biomedicine Scientific Research Initiative was launched. With the BSI's financial backing and Walter's leadership, the Center for RNA Biomedicine was ready to accelerate research uncovering the nuances of RNA and focus on translating these discoveries into tangible medical advancements for the betterment of human health.

Science of RNA

RNA stands as a cornerstone in the realm of molecular biology. Unlike its counterpart, deoxyribonucleic acid (DNA), RNA plays a multifaceted role, both conveying and regulating genetic information.

"RNA is the only molecule that can both encode information in its sequence just like DNA does in the genome, but also execute functions based on that sequence by folding just like proteins do into very complex three-dimensional structures," Walter explains.

Top image: Crocothery, Adobe Stock; Walter headshot: Courtesy of Nils Walter

This complexity and varied functionality make RNA a powerful tool for applications in medicine and beyond.

RNA therapeutics

Michelle Hastings, Ph.D.

The field of RNA therapeutics aims to build on the foundational understanding of RNA's diverse roles in our cells to enable the treatment and prevention of diseases using RNA-based molecules.

Led by Michelle Hastings, Ph.D., the program's most recent hire and director of "M"-RNA Therapeutics, translating basic discoveries into RNA-based treatments is now a primary focus.

"With the hire of Hastings, we hope to build what we refer to as M-RNA therapeutics ("M" for Michigan)," Walter says. "This program will accelerate the process of going from patient to scientist and back to patient, making precision medicines based on diverse RNA modalities."

The scope of RNA therapeutics extends far beyond the vaccines we are all now familiar with. Hastings has been at the forefront of another RNA-based medicine built from antisense oligonucleotides (ASOs), single-stranded RNA molecules that offer novel therapeutic avenues for modulating protein synthesis.

Hastings' early involvement in pioneering work developing ASOs for spinal muscular atrophy, which became the first successful ASO drug, set the trajectory for her future endeavors. Inspired by the potential of ASOs, her lab has since focused on utilizing them for various neurological diseases.

One of the factors that makes RNA-based treatments so significant is that they can be readily designed on a computer and quickly adapted as needed. This means they are particularly valuable when it comes to conditions that pharmaceutical companies might not deem economically viable to address.

"RNA's cost-effectiveness and the potential to rapidly develop treatments mean that even patients with extremely rare conditions might receive therapy within a year of diagnosis and before their conditions worsen," Hastings says.

In addition to paving the way for the rapid and cost-effective development of interventions for rare conditions, RNA therapeutics offer a fresh perspective on existing treatments for more common diseases and illnesses. Instead of broad-spectrum drugs that might cause a range of side effects, RNA allows for the creation of "smarter" drugs, targeting specific issues without unwanted collateral damage.

"The promise of RNA therapeutics is immense, and while we're still in the early stages, the strides we're making could one day radically alter the treatment landscape for a wide array of medical conditions," Walter says.

Advancements and milestones: The journey of RNA biomedicine at Michigan

The RNA Biomedicine initiative has become a nexus of innovation and discovery.

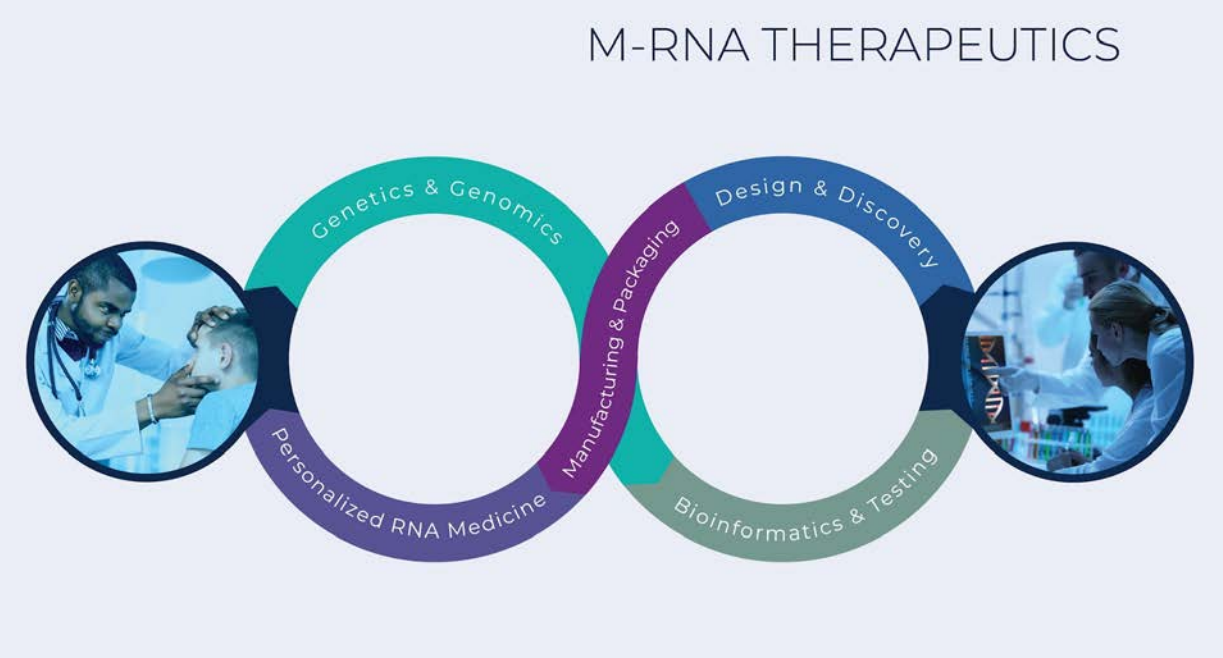
Hastings' lab has made significant strides in the realm of RNA therapeutics. One of her standout projects zeroes in on ceroid-lipofuscinosis (CLN) 3-Batten disease, a rare pediatric neurodegenerative condition. Using specialized RNA therapeutic platforms, her team is not only targeting the specific genetic mutations responsible for the illness but also tailoring treatments to individual needs. They've managed to craft highly personalized interventions in under a year.

At the same time, Walter has been engrossed in understanding bacterial gene regulation. In a recent advancement in this endeavor, he and his colleagues identified the workings of a bacterial RNA riboswitch, a promising new target for antibiotics, using cryo-electron microscopy (cryo-EM) to create high-resolution images.

"Now we understand the whole process of riboswitch regulation and can use that knowledge to specifically target these critical parts of bacterial life, hopefully averting a pandemic of multidrug-resistant bacteria."

Another noteworthy endeavor comes from Arul Chinnaiyan, M.D., Ph.D., the director of the Michigan Center for Translational Pathology. Embracing the "bed-to-bench-to-bed"

Hastings headshot: Marcus Norman Photography



RNA Biomedicine's ultimate goal is to deliver personalized bed-to-bench-to-bed RNA-based treatments.
Image Credit: Paul Avedisian, RNA Biomedicine

approach, Chinnaiyan collaborated with Ionis Pharmaceuticals to develop ASOs for cancer treatment. The method involves taking real-world clinical problems to the research bench and translating the findings into patient care. His efforts resulted in the project progressing through clinical trials, exemplifying the initiative's commitment to translating research into tangible solutions.

Aside from facilitating discoveries, the BSI enabled the Center for RNA Biomedicine to accomplish its mission of hiring five key experts to strengthen underexplored areas of RNA research at U-M, such as RNA drug testing and structural biology of RNA nanomachines. Hastings was the capstone hire, making the RNA Biomedicine program the first of the SRIs to complete its hiring goals.

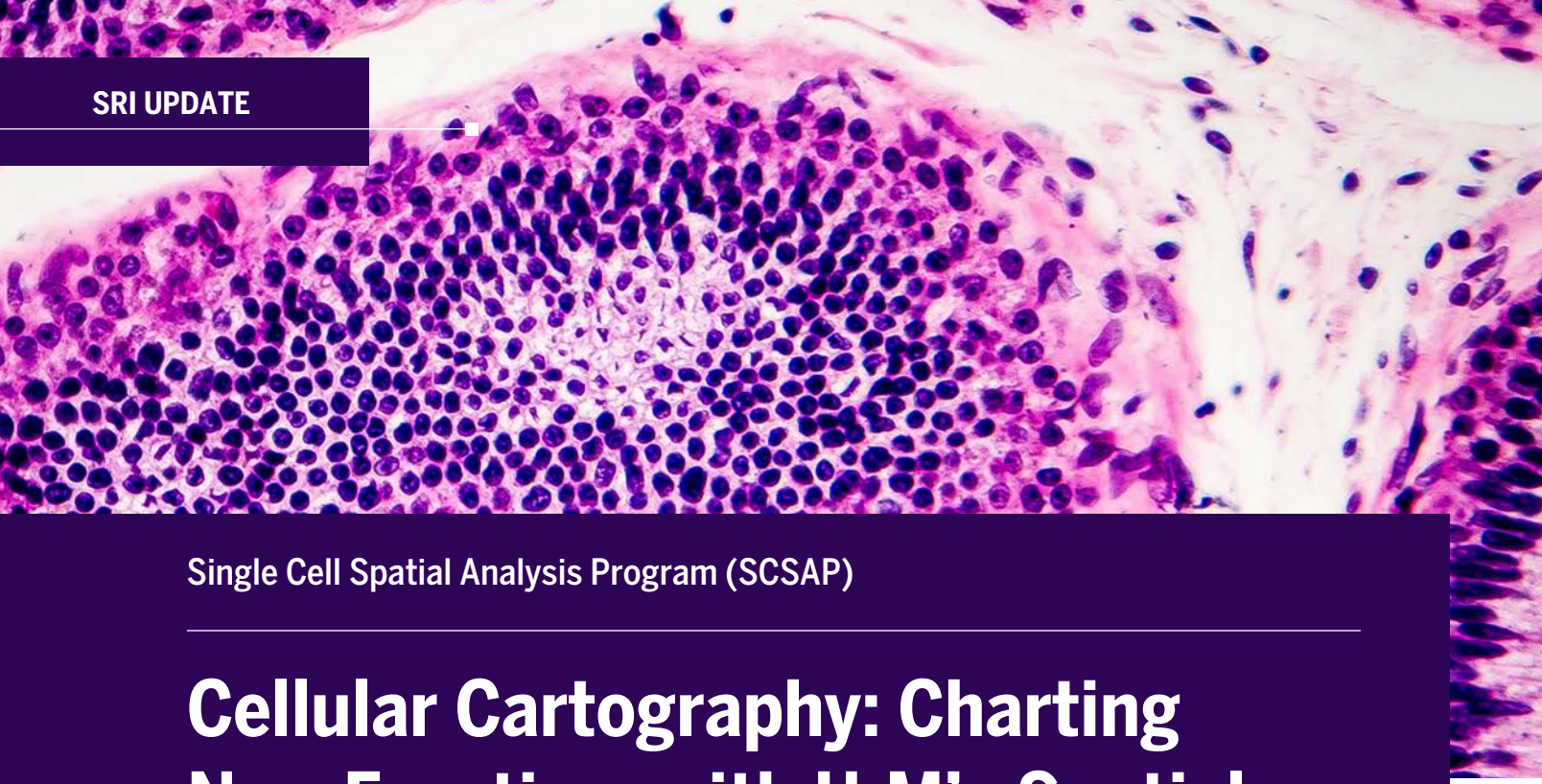
The next strand of innovation

Peering into what the future holds for M-RNA research, the center is eager to foster deeper collaborations and attract investments to further its mission.

A significant part of this forward momentum is the recognition of the interconnectedness of the SRIs funded by the BSI. Walter envisions a future where these programs — whether they're about single-cell transcriptomics, brain cancer, or infectious diseases — can synergize to create a holistic understanding of RNA's role in health and disease.

To further amplify its impact, RNA Biomedicine has set its sights on the broader biomedical landscape. With continued emphasis on RNA therapeutics, the team aims to become a magnet for pharmaceutical and biotech companies. By attracting both industry giants and small biotech startups, the group hopes to accelerate the translation of their research into treatments for patients worldwide.

As the program sets its sights on the future, its focus on RNA therapeutics and industry collaboration promises to usher in a new era of personalized and precise RNA-based medical solutions.



Single Cell Spatial Analysis Program (SCSAP)

Cellular Cartography: Charting New Frontiers with U-M's Spatial Analysis Initiative

More than a decade ago, Evan Keller, Ph.D., started working on understanding the microenvironment of tumors. He focused on the crosstalk between cancer cells and their surrounding non-cancerous counterparts. As he delved into this complex world, Keller realized that the tools at his disposal were often inadequate for the level of detail he sought and that a new approach was essential for deeper insights.

Key technological advancements

Recognizing the limitations of existing methods, Keller embraced the advent of single-cell technologies, which allow for a more precise examination of individual cells.

"The technology for single-cell analyses came about," says Keller, now the director of the Single Cell Spatial Analysis Program (SCSAP) at the University of Michigan. "I swiftly got an equipment grant and started a single cell core through U-M's Cancer Center."

From there, spatial analysis technology emerged, bringing further benefits.

Evan Keller, Ph.D.

"Spatial analysis retains the cellular positioning within tissues," Keller explains. "With spatial analysis, we can now start to see relationships between cells and how they are talking to and influencing each other based on their spatial context."

This technological leap not only enhanced Keller's research but also opened new avenues for understanding the complex interactions that govern cellular behavior, setting the stage for the transformative work that would follow.

Building bridges with BSI

When the opportunity arose to launch new large-scale programs through the Biosciences Initiative, Keller realized that with the initiative's support, he could bring single-cell and spatial technologies to the next level and make U-M a leader in the field.

Top image: Dr_Microbe, Adobe Stock; Keller headshot: University of Michigan Medicine

To fully capitalize on this opportunity, Keller assembled a leadership team for the SCSAP — Justin Colacino, Ph.D.; Jun Li, Ph.D.; Sunitha Nagrath, Ph.D.; Arvind Rao, Ph.D.; and Tom Wilson, Ph.D. — setting the stage for transformative advances.

"The BSI provided the essential support we needed to advance single-cell and spatial analysis research at the university," Keller notes. "Their backing allowed us to expand our team and unite researchers across disciplines, fostering collaboration and pushing the boundaries of single-cell and spatial analysis."

From cells to solutions: Advancing bioscience discoveries at U-M

While single-cell and spatial technologies are exciting in their own right, what is equally tantalizing is the transformative research it's facilitating.

In one notable study, SCSAP members Rao and Tim Frankel, Ph.D., used spatial analysis to examine the tumor-microenvironment of lung cancer patients and look for factors associated with non-response to a class of anti-cancer drugs called immune checkpoint inhibitors (ICIs). This research revealed that the spatial relationship between immune cells and tumors distinguished responders from non-responders. In another fascinating case with significant clinical implications, Nisha D'Silva, Ph.D., used spatial analysis to investigate how the distance between tumors and their surrounding nerves impacts the survivability of perineural invasion (PNI), a common occurrence in oral squamous cell carcinomas. The team found patients with close nerve-tumor distance have significantly worse outcomes.

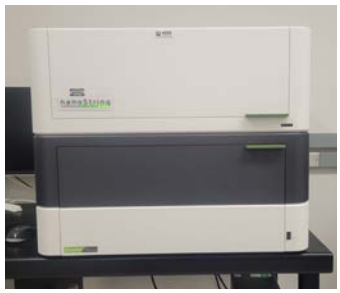
Such studies underscore the therapeutic potential of single-cell spatial analysis.

Tools of the trade

Although all single-cell and spatial technologies share in common the ability to look at individual cells, either on their own or in various contexts, their particular benefits and drawbacks make each technology suitable for some types of projects but not others.

"Some of the technologies may be able to look at 5,000 RNAs or maybe 100 proteins at a time," Keller notes. "That's great for what we would call discovery work, or trying to identify targets that may be important. But when we want to move forward in an experiment, we can only practically look at so many cells in each case."

The right tools make all the difference in SCSAP's research. One key piece of equipment is the 10x Nanostring GeoMx platform, which the team uses to examine tissues and groups of cells, about 100 to 200 at a time. Other newly acquired equipment includes the 10x Genomics Visium and Genomics Xenium systems.



Though the team mostly looks at RNA, Keller points out the unmatched clarity of focusing on proteins.

"Proteins are the biomolecules that actually do the work," he explains. "So looking at the proteins gives us more confidence in what we're seeing."

Because of this advantage, the team is looking to acquire a single-cell tool focused on extracting protein data.

From examining large groups of cells to zeroing in on proteins, each piece of equipment serves a unique purpose. As the team eyes protein data

> *"Their backing allowed us to expand our team and unite researchers across disciplines, fostering collaboration and pushing the boundaries of single-cell and spatial analysis.*

Image: Courtesy of Evan Keller

extraction, it's clear that their toolkit is ever-evolving, just like the science they're exploring.

Empowering the U-M research community

Leveraging its state-of-the-art equipment and deep expertise, the SCSAP has been catalyzing single-cell investigations across U-M.

"Our goal has always been to help all researchers at the university move forward with single-cell and spatial analysis," Keller notes, underscoring the importance of this mission.

The SCSAP has rolled out a multi-pronged strategy to achieve this aim. A key component is their comprehensive membership program, which invites everyone from experimentalists to data scientists to be part of a dynamic community of researchers interested in utilizing single-cell technology.

Beyond fostering community, the program ensures tangible support by offering access to specialized research cores and providing both pilot funding and technical assistance, helping researchers become equipped to explore the intricacies of single-cell and spatial analysis.

In progress and on deck: Methodologies and team expansion

One of the remaining challenges for the SCSAP is the need to expand and advance research methodologies.

"Currently, most research focuses on just one aspect, like RNA or proteins," Keller explains. "What can be more informative is multi-omics, which involves examining multiple types of molecules simultaneously, providing a richer, more integrated understanding of cellular dynamics."

In addition to pursuing methods that allow researchers to assess multiple parts of individual cells at once, the team is also exploring strategies for moving from 2-D to 3-D images. This approach would offer a more comprehensive and readily interpretable view of cellular interactions.

Temporal spatial analysis is another area of interest. The goal is to understand tissues not as just a one-time static shot but as a dynamic system evolving over time. Changyang Linghu, Ph.D., a recent SCSAP hire whose research focuses on developing and applying technologies to observe and decode complex biological dynamics,such as those in the brain, is at the forefront of these methods.

Jun Hee Lee, Ph.D., another SCSAP member who works on understanding stress, aging and metabolism, is developing a technique called Seq-Scope, a spatial barcoding technology that can reveal the spatial organization of cell types in ever more complex tissues, such as tumors or organoids.

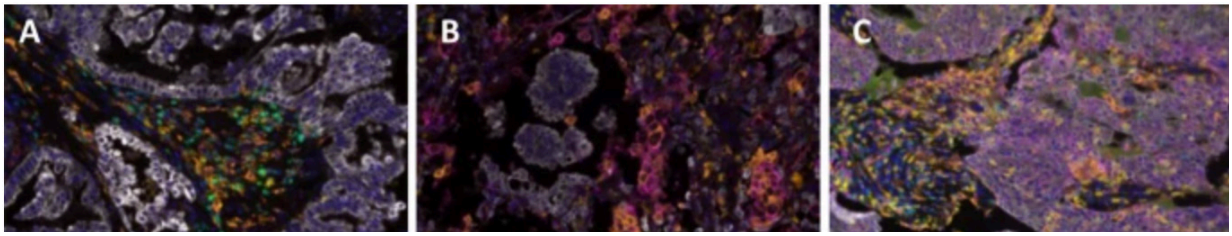
The recent applications of artificial intelligence in enabling the rapid processing of large amounts of complex data are particularly noteworthy, Keller says.

"AI offers a powerful lens to examine tissues, analyzing myriad parameters from the size and shape of nuclei to detailed cellular spatial relationships," he explains. "As it learns, especially when informed by disease outcomes, it can provide profound insights."

By continually improving technologies and methodologies, and by fostering a collaborative research environment, the program is setting new standards for what's possible in single-cell and spatial analysis. ■

Changyang Linghu, Ph.D.

Jun Hee Lee, Ph.D.



PD-L1 staining patterns on tumor cells and antigen presenting cells, showing (A) no PD-L1 expression, (B) primary expression on APCs (magenta) and (C) primary expression on tumor cells (light purple). Image from *Scientific Reports*, DOI: 10.1038/s41598-022-13236-8. CC BY 4.0.

Linghu headshot: Corbain Swain Photography; Lee headshot: Courtesy of Jun Hee Lee

A New Chapter for Neuroscience at U-M

The Michigan Neuroscience Institute (MNI) has long been a powerhouse in neuroscience research. Huda Akil, Ph.D., and Stan Watson, M.D., Ph.D., co-directors of the formerly named Molecular and Behavioral Neuroscience Institute (MBNI), led the program for 25 years, during which it produced countless impactful medical breakthroughs and scientific discoveries.

In 2020, after more than two decades of outstanding stewardship and continued scientific contributions, Akil and Watson announced they would be stepping down from their roles. Looking to build on the incredible foundation and campus-wide strengths built by the institute's former leaders, the Biosciences Initiative committed $20 million to help the MNI further elevate its reach and round out the team's collective neuroscientific prowess through strategic hires, including a new director to foster synergy between the MNI's 11 different schools and programs.

"The BSI's support was motivated by the need to find a collaborative leader who could synchronize expertise from diverse academic fields and strategically recruit talent to cover essential gaps," says BSI Director Roger Cone.

After an intensive national search, the MNI welcomed Ravi Allada, M.D., renowned neuroscientist and U-M alumnus, as its new director in Sepetember 2023.

"Dr. Allada has the perfect combination of scientific expertise, leadership experience, national stature and vision to direct and synchronize our diverse U-M neuroscience community in research, graduate training, public outreach and philanthropy," says Lori Isom, Ph.D., professor of pharmacology and co-chair of the search committee.

Tasked with aligning the expansive range of neuroscience expertise across the educational landscape at U-M, Allada is well-positioned to make an indelible mark.

Charting a synergistic path to neuroscience leadership

Allada has planned a multi-tiered approach to making U-M a world leader in the field.

A crucial part of his plan is identifying the broad categories of neuroscience research the MNI should focus on. Setting out on a 'listening tour,' Allada aims to accomplish this by speaking with neuroscience faculty, learning about what they focus on, and uncovering areas of excellence and key research topics.

The next challenge is to expand faculty members' connections with potential collaborators on campus.

"The University of Michigan is great in so many different areas," he says. "One of my main goals is to take all of the great U-M scientists, both in and outside of strictly neuroscience-focused areas, help them connect, and identify how they can combine their expertise to tackle the most urgent and difficult problems in the field."

To jumpstart this, Allada is eyeing interdisciplinary grant programs and targeted workshops to organically build a network of problem-solvers across the university.

Doing world-leading research will, in some cases, require the help of new experts — and BSI funds will be critical for bringing these neuroscience authorities to U-M.

"At the core of all of it is the people who make up the institute," Allada says. "The ability to recruit the leading innovative investigators may be the single most important thing it does, and the BSI's support will be absolutely central to that, helping make the MNI a world leader in neuroscience research."

Under the visionary guidance of Allada and supported by the BSI's substantial investment, the MNI is set to foster unprecedented collaborations and drive breakthroughs in neuroscience, elevating U-M as a hub of excellence in the discipline.

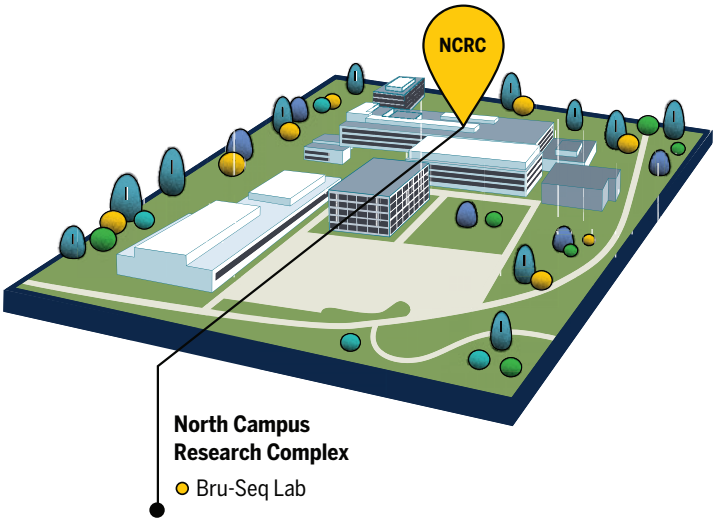
Allada headshot: Courtesy of Ravi Allada

BSI Discovery Cores & Resources

Empowering exploration through discovery resources

Cutting-edge bioscience research requires the latest and most advanced discovery resources: the tools, technologies and training that enable investigators to work at the frontiers of their field.

To facilitate such pioneering research, the Biosciences Initiative (BSI) focused on three key areas of investment: creating a single, unified platform for finding exceptional resources already available across U-M's vast research enterprise; allocating funds for new cores or discovery resource facilities containing a collection of top-of-the-line tools; and supporting the acquisition of new technologies for existing cores.



Michigan Research Cores website

The University of Michigan has an expansive collection of bioscience discovery resources. What the community lacked, however, was a centralized and publicly accessible website for identifying what was available to campus researchers.

BSI partnered with the Medical School to create the Michigan Research Cores website to improve awareness and maximize utilization of campus tools and resources. With a user-friendly search function that allows filtering by services, equipment and locations, the website helps researchers quickly identify the best campus resources available for their specific needs.

Tools, technologies and trainings

As the biosciences rapidly evolve, so do researchers' equipment needs. New technologies are constantly being released, which can improve current research and open new lines of inquiry.

Consequently, the BSI has allocated over $25 million to its nine Scientific Research Initiatives (SRI) and the broader biosciences community to help create new shareable and self-contained discovery centers with a collection of resources, from specialized equipment to computational software to one-on-one training sessions. In total, 14 discovery resources and facilities have been created or enhanced (see map for details).

Our SRIs have made their own contributions to this endeavor, collaborating with other departments and schools to acquire discovery resources that will foster next-level research. For example, the Single Cell-Spatial Analysis Program contributed to the purchase of advanced tools like the 10x Genomics and Visium Systems.

Collectively, these efforts have filled critical gaps in the availability and usability of top-of-the-line biosciences research resources at U-M.

Faculty Recruitment and Development

The Biosciences Initiative (BSI) is committed to attracting and nurturing top-tier faculty. The program achieves this through targeted recruitment to its nine Scientific Research Initiatives (SRIs), supporting the Biological Sciences Scholars Program (BSSP) awardees and recognizing excellence through the Mid-Career Biosciences Faculty Achievement Recognition (MBioFAR) award. These efforts serve as catalysts for bringing in new talent and retaining world-leading experts at the University of Michigan.

New Faculty

Learn about the bioscience faculty we've helped bring to U-M.

Faculty hired under SRIs

BSSP

Ravi Allada, M.D.
Theophile Raphael M.D. Collegiate Professor of Neurosciences, Executive Director, Michigan Neuroscience Institute and Professor of Anesthesiology, Medical School

Marcy Balunas, Ph.D.
Associate Professor of Microbiology & Immunology, Medical School; Associate Professor of Medicinal Chemistry, College of Pharmacy

Jailson Brito Querido, Ph.D.
Research Assistant Professor, Life Sciences Institute; Assistant Professor of Biological Chemistry, Medical School

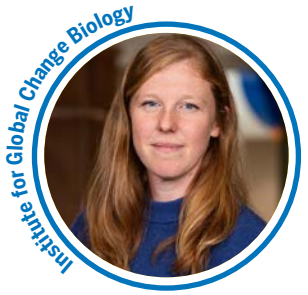
Maria Coronel, Ph.D.
Assistant Professor of Biomedical Engineering, College of Engineering

Morgan DeSantis, Ph.D.
Affiliate Faculty of Biological Chemistry, Medical School; Assistant Professor of Molecular, Cellular, and Developmental Biology, College of Literature, Science, and the Arts

Joshua Emrick, DDS, Ph.D.
Assistant Professor of Dentistry, School of Dentistry

Toshiro Hara, Ph.D.
Assistant Professor of Neurosurgery, Medical School

Michelle Hastings, Ph.D.
Professor of Pharmacology, Pfizer Upjohn Research Professor of Pharmacology, Medical School; Professor of Medicinal Chemistry, College of Pharmacy



Jennifer Head, Ph.D.
Assistant Professor of Epidemiology, School of Public Health

Sarah Hill, Ph.D.
Assistant Professor of Molecular, Cellular, and Developmental Biology, College of Literature, Science, and the Arts

Roland Kersten, Ph.D.
Assistant Professor of Medicinal Chemistry, College of Pharmacy

Paul Kramer, Ph.D.
Assistant Professor of Molecular, Cellular, and Developmental Biology, College of Literature, Science, and the Arts

Changyang Linghu, Ph.D.
Assistant Professor of Cell and Developmental Biology, Medical School

Claudia Loebel, Ph.D.
Assistant Professor of Materials Science and Engineering, Chemical Engineering, and Macromolecular Science and Engineering, College of Engineering; Assistant Professor of Dentistry, School of Dentistry

Alex Marand, Ph.D.
Assistant Professor of Molecular, Cellular, and Developmental Biology, College of Literature, Science, and the Arts

Stephanie Moon, Ph.D.
Affiliate Faculty of Biological Chemistry, Assistant Professor of Human Genetics, Michigan Medicine

Shyamal Mosalanganti, Ph.D.
Research Assistant Professor, Life Sciences Institute; Assistant Professor of Biophysics, Assistant Professor of Cell and Developmental Biology, Medical School

Rachel Niederer, Ph.D.
Assistant Professor of Biological Chemistry, Medical School

Peter Reich, Ph.D.
Program Director and Professor of Environment and Sustainability, School for Environment and Sustainability

Kelly Speer, Ph.D.
Assistant Professor of Ecology and Evolutionary Biology, College of Literature, Science, and the Arts

Lauren Surface, Ph.D.
Assistant Professor of Dentistry, School of Dentistry

Eleanna Varangis, Ph.D.
Assistant Professor of Kinesiology, School of Kinesiology

Wenjing Wang, Ph.D.
Research Assistant Professor, Life Sciences Institute; Assistant Professor of Chemistry, College of Literature, Science, and the Arts

Chase Weidmann, Ph.D.
Assistant Professor of Biological Chemistry, Medical School

Connie Wu, Ph.D.
Research Assistant Professor, Life Sciences Institute; Assistant Professor of Biomedical Engineering, College of Engineering; Assistant Professor of Pharmaceutical Sciences, College of Pharmacy

Guizhi (Julian) Zhu, Ph.D.
Ara Garo Paul Professor and Associate Professor of Pharmaceutical Sciences, College of Pharmacy

Kai Zhu, Ph.D.
Associate Professor of Environment and Sustainability, School of Environment and Sustainability; Associate Professor of Ecology and Evolutionary Biology, College of Literature, Science, and the Arts

Joining us in 2024

Herman Fung, Ph.D.
Research Assistant Professor, Life Sciences Institute; Assistant Professor of Cell and Developmental Biology, Medical School

BSI Award Boosts Research Capabilities for Top Mid-Career Faculty

The MBioFAR award is a prestigious recognition program developed by the BSI to celebrate and empower mid-career biosciences faculty at U-M with substantial discretionary resources, fostering innovative and high-risk research.

"The award serves not just as recognition but as an investment in the pursuit of novel boundary-pushing research that can address major challenges in the biological sciences," says Roger Cone, Ph.D., the director of the BSI.

The MBioFAR program functions similarly to an internal MacArthur award, where faculty members are confidentially nominated rather than applying themselves. The highly selective award underscores the extraordinary productivity and impact of the university's most outstanding faculty during their prime career phase.

2022 MBioFAR Awardees

In 2022, the BSI continued to highlight the university's commitment to groundbreaking research, with six outstanding faculty members being recognized with the MBioFAR award for their significant contributions to the biosciences.

Reflecting on the work and accomplishments of these awardees, President Santa Ono expressed his excitement over how they are shaping their fields and using their research to improve well-being.

"At the University of Michigan, we share an ethos of excellence, innovation and research impact. Our MBioFAR awardees are doing more than creating knowledge and opening new horizons in an array of fields – from synthetic chemistry and gastroenterology to pharmaceutics and oncology to neurology and synthetic embryology – ultimately, they are transforming lives. Thanks to their efforts, our research is bolder, our faculty is stronger, and our impact is greater."

Daryl Marshke, Michigan Photography

SAMI BARMADA, PH.D.
Associate Professor of Neurology

Barmada focuses on RNA and protein metabolism in neurodegenerative conditions such as amyotrophic lateral sclerosis and frontotemporal dementia. He is also a key advocate for community awareness.

"The MBioFar award, and the cutting-edge equipment it helped support, is a crucial step towards a unique program centered on frontotemporal dementia," says Barmada. "We are in the process of establishing a comprehensive combination of basic research, disease modeling, and therapeutic investigation that interfaces with patient care and clinical research efforts."

JIANPING FU, PH.D.
Professor of Mechanical and Biomedical Engineering, and Cell and Developmental Biology

Fu is a notable pioneer in synthetic embryology. His work at the crossroads of stem cell, developmental, and synthetic biology and bioengineering opens new possibilities in creating artificial embryos.

"The support from this award has enabled my lab to pursue exciting research using human pluripotent stem cells to model early human development in a dish," Fu explains. "This research represents the most exciting frontier of stem cell and developmental biology. With the backing of MBioFAR, we can maintain our pioneering role in this field."

COSTAS LYSSIOTIS, PH.D.
Associate Professor of Molecular and Integrative Physiology

Lyssiotis probes the intricate biochemical pathways and metabolic requirements that facilitate tumor growth and survival. His commitment to cultivating future scientists reinforces his in-depth exploration of cancer biology.

"I am extremely grateful for the recognition of the MBioFar award," he says. "The financial backing allowed my team to pursue those high-risk, high-reward ideas that have the potential to be the next breakthroughs in cancer medicine."

JAMES MOON, PH.D.
Professor of Pharmaceutical Sciences and Biomedical Engineering

Moon is an expert in developing novel biomaterials-based strategies to understand the immune system, aiming to develop vaccines against cancer and autoimmune diseases. His innovative approach is reflected in 20 pending and approved patents and the founding of three startups.

"With this award, we will develop new technologies that can train our immune system to fight against human diseases, including cancer and inflammation, transforming how we treat patients and improve outcomes," Moon says.

ALISON NARAYAN, PH.D.
Associate Professor of Chemistry

Narayan specializes in increasing the efficiency and sustainability of chemical synthesis, with a focus on harnessing enzymes to make new molecules that can't be produced by conventional organic synthesis. The MBioFAR award has allowed her team to combine this expertise with bioinformatics and data science.

"The generous support from the MBioFAR award has enabled bold, interdisciplinary directions in my research group," Narayan explains. "Specifically, we have paired our established expertise in biocatalysis for innovation in chemical synthesis with bioinformatics and data science. These efforts have proven to be extremely fruitful and provide a roadmap for developing predictive models and expanding the impact and accessibility of biocatalysis in chemical synthesis."

ELIZABETH SPELIOTES, M.D., PH.D.
Professor of Gastroenterology and Computational Medicine and Bioinformatics

Speliotes' contribution to the medical sciences extends beyond her role as a gastroenterologist and bioinformatician. She is working to unveil gene variants connected to nonalcoholic fatty liver disease and building a biobank of resources for precision medicine.

"The MBioFar award has helped us complete a critical study on dysfunction-associated steatotic liver disease genetics and phenotypes," Speilotes says. "It has also facilitated new projects in the genetics of metabolic syndrome and genome-wide screens for genes that affect hepatic steatosis."

Barmada: Courtesy of Sami Barmada; Fu: Megan Ocelnik/Michigan Engineering; Lyssiotis: Courtesy of Costas Lyssiotis; Moon and Narayan: Leisa Thompson Photography; Speliotes: Michigan Photography

Insights from the BSI Ideas Labs

Inspired by the National Science Foundation's Ideas Lab model, the Biosciences Initiative's Ideas Labs are dedicated to stimulating interdisciplinary, collaborative research, resulting in groundbreaking ideas that address large-scale challenges in the biosciences.

The Ideas Lab culminates in a three-day workshop that unites scholars from various academic spheres. Attendees collaborate to conceptualize innovative solutions to a well-defined research question. This engaging atmosphere promotes teamwork and creativity, forging connections between faculty with the shared goal of using their collective expertise to conduct game-changing biosciences investigations.

2019 Ideas Lab: Predicting Human Performance

The inaugural 2019 Ideas Lab set out to unravel the complexities of human performance, with a focus on predicting and influencing it. The BSI allocated up to $3 million for projects conceived by the interdisciplinary teams formed during the lab.

You-M: Personalizing Student Performance at the University of Michigan

The You-M project utilizes wearable tracking technology and custom mobile apps to measure and enhance student wellness and academic performance. Preliminary data suggest that depression and anxiety, both known to negatively impact performance, tend to worsen across the fall semester. The team is currently working on recruiting their next cohort of study participants.

Toward a Neurobiological Understanding of Creative Traits and Creative States: A Cross-Domain Approach

This project uses wearable electroencephalogram (EEG) devices, machine learning and a custom app to probe the neural underpinnings of creativity. The team is close to launching its first round of data collection from participants. This new phase will cross-reference smartwatch data with sleep EEG measurements.

Enhancing Mechanisms of Human Resilience for Student Success and Well-Being

This group focuses on the metrics of human resilience, aiming to craft individualized, resilience-boosting interventions. They have undertaken a comprehensive study of resilience factors and are currently working on wearable sensors and a mobile app.

Predicting Human Connectivity

This team investigates the biological and psychological aspects of human connections. Their first step has been to use specialized BIOPAC systems to quantify physical synchrony: spontaneous rhythmic coordination of processes across time between two or more individuals. Next, they aim to understand the precursors of human connections and their implications for enhancing team performance and interpersonal relationships.

2INSPIRE: Optimizing Breathing for Exceptional Musical Performance

The 2INSPIRE project explores the relationship between breathing quality and musical performance. Using Hexoskin Smart Shirts, the team has captured and visualized performers' breathing data, correlating it with audio recordings and scores. They are currently developing an app to provide real-time multisensory feedback based on Hexoskin breathing data to improve musicians' execution of compositions.

Ideas lab images: Cody Abramson, BSI

2023 Ideas Lab: Biological Systems on the Edge

In the fall of 2023, the second Ideas Lab convened to address the pressing challenge of climate change. The workshop, titled "Biological Systems on the Edge," tasked participants with conceiving nature-based solutions for climate mitigation. These solutions, whether focused on reforestation or green urban development, seek to achieve scalable carbon capture while concurrently addressing the co-benefits of biodiversity and environmental justice.

Twenty participants from seven schools and colleges formed interdisciplinary teams proposing several ambitious projects to address this challenge. Several groups emerged that will work to advance their ideas into fundable research projects. Their interdisciplinary, high-risk, high-reward approaches to tackling drivers of global change provide a promising blueprint for future scientific endeavors to mitigate the impacts of climate change.

Fostering Progress in the Biosciences Through Strategic Communication

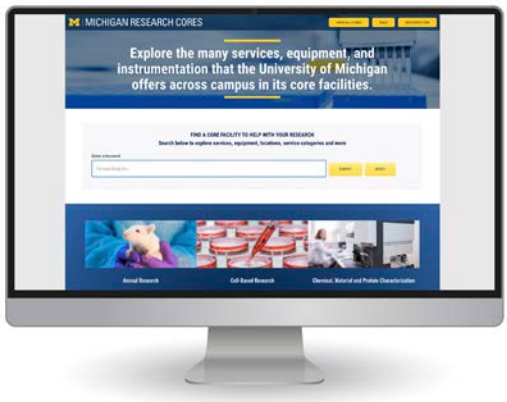
The Biosciences Initiative has sought to advance the biosciences at the University of Michigan through communications efforts to benefit its nine Scientific Research Initiatives (SRIs) and the university's bioscience-focused faculty, schools, colleges and institutes. This is achieved with a focus on improving:

- **Visibility and recognition: Amplifying the impact and profile of research and accomplishments**
- **Information accessibility: Centralizing and disseminating critical research and educational resources**
- **Community building: Fostering a sense of cohesion and interdisciplinary collaboration**
- **Skill and knowledge enhancement: Providing platforms for continuous professional and academic growth**

Guided by these goals, the BSI has employed a range of tactical communication methods and media.

BSI website: Connecting the biosciences community at U-M

Our BSI website serves as a central resource for information about both our initiative and the broader biosciences community at U-M. It consolidates a range of data, including SRI milestones, upcoming events and job opportunities, into a single, accessible platform.



Michigan Research Cores website: Streamlining resource discovery

In partnership with the Medical School, the BSI launched a dedicated research cores website to simplify access to U-M's extensive collection of discovery resource facilities with critical tools for cutting-edge research. With a user-friendly search function that allows for filtering by services, equipment and locations, the website helps researchers quickly identify the best equipment available on campus for their specific needs.

In the news: Partnerships that amplify impact

The BSI works with Michigan News and the University Record to broadcast the accomplishments and innovative research emerging from its SRIs to a larger audience.

BSI-hosted events: Catalysts for collaboration and recognition

Coming together in person (or virtually, as circumstances dictate) has an unparalleled power to inspire, celebrate and facilitate connections. The BSI taps into these benefits through two yearly events.

During the Annual Biosciences Community Celebration, the BSI showcases the excellence within our field. In the most recent installment, we recognized six researchers who received the BSI's Mid-career Biosciences Faculty Achievement Recognition (MBioFAR) award in 2022.

The BSI's Ideas Lab offers an immersive environment for innovators from various disciplines to tackle predefined challenge topics collaboratively and to form interdisciplinary connections that have the potential to inspire world-changing work. The most recent edition focused on nature-based solutions for mitigating climate change, focusing on biodiversity and social justice.

BSI Weekly: A hub for community updates

The BSI Weekly email curates a wealth of information, from upcoming speaker events and departmental seminars to job opportunities, funding possibilities and avenues for professional development.

This resource has been redesigned for enhanced clarity and engagement, with an intuitive layout that makes information more accessible. We also added several sections to better inform, educate, promote and engage the U-M bioscience community, such as the Bioscience Question of the Week. Here, we tap into the community's insights on topics from the future of bioscience research to grant writing strategies and laboratory management to publication tactics — all aimed at understanding and enhancing our collective research efficacy.

Upcoming endeavors: New avenues for community engagement

Recognizing the need for more in-depth coverage of our community's ongoing work, we are relaunching our newsletter. This publication will highlight SRI publications, new hires and interactions with the media, among other content that enriches our collective understanding of the biosciences at U-M.

We invite all members of the U-M biosciences community to join us on this journey of discovery and innovation. Your contributions, ideas and feedback are pivotal to shaping our shared future in the biosciences. Stay connected, stay informed, and let's advance the frontiers of science together.

Cody Abramson, BSI

Appendix

Annual Budget Narrative

The implementation of the Biosciences Initiative (BSI) programs, particularly faculty recruitment, was delayed by two years due to the challenges brought on by COVID-19 pandemic.

Consequently, former President Mary Sue Coleman extended the initiative's spending timeline through FY25. Following our first full recruiting year in FY23, the BSI has now filled 19 of its 30 tenure-line positions.

The initiative's bioscience project awards, varying from one to five years in duration, predominantly follow a milestone-based expense reimbursement model. Under these terms, principal investigators and award executors agree to submit annual and end-of-year reports for review by the Biosciences Initiative Coordinating Committee (BICC). Based on an evaluation of project metrics, financial justifications and budget assessments, the committee decides on the continuation of subsequent work and scientific goals.

Of the $150 million investment the BSI received at launch, approximately $139 million has already been put to work. The BICC plans to distribute the remaining funds over the next 18 months.

Explore the table below for more details and financial updates.

Category	Category Budgets	Allocated	Remaining
Administration	**1,885,359**	**1,885,359**	**0**
Scientific Initiatives	**85,711,608**	**85,711,608**	**0**
Precision Health	**10,000,000**	**10,000,000**	**0**
Biological Sciences Scholars Program	**3,000,000**	**2,901,011**	**98,989**
Scientific Core Resources	**9,000,000**	**7,019,781**	**1,980,219**
Educational Programs	**1,003,500**	**535,502**	**467,998**
Mid-Career Program (MBioFAR)	**7,399,534**	**4,500,000**	**2,899,534**
Ideas Lab	**9,000,000**	**3,045,385**	**5,954,615**
Michigan Neuroscience Institute	**20,000,000**	**20,000,000**	**0**
M-PACT Support	**3,000,000**	**3,000,000**	**0**
TOTALS	**150,000,000**	**138,598,646**	**11,401,355**

Biosciences Initiative Coordinating Committee

Under the leadership of Vice Provost and Director of the BSI Roger Cone, Ph.D., the Biosciences Initiative Coordinating Committee plays a central role in fostering collaborative, high-risk, high-reward innovation in the biosciences, establishing the University of Michigan as a leader in the field. With its rotating roster of members, each bringing diverse expertise and perspectives, the committee shapes the BSI's practices, policies and investments.

ARUL CHINNAIYAN, M.D., PH.D.
S.P. Hicks Endowed Professor of Pathology; Section Head, Michigan Center for Translational Pathology; Professor of Pathology and Professor of Urology, Medical School

LOLA ENIOLA-ADEFESO, PH.D.
Vennema Professor of Chemical Engineering, University Diversity and Social Transformation Professor, Associate Dean for Graduate and Professional Education, Professor of Chemical Engineering, Professor of Macromolecular Science and Engineering and Professor of Biomedical Engineering, College of Engineering

DANIEL FORGER, PH.D.
Robert W. and Lynn H. Browne Professor of Science, Professor of Mathematics, Director Academic Program, Mathematics, College of Literature, Science, and the Arts; Research Professor, Computational Medicine and Bioinformatics, Medical School

BETSY FOXMAN, PH.D.
Hunein F. and Hilda Maassab Endowed Professor of Epidemiology and Professor of Epidemiology, School of Public Health

MICHELLE HASTINGS, PH.D.
Pfizer Upjohn Research Professor of Pharmacology, Professor of Pharmacology, Medical School; Professor of Medicinal Chemistry, College of Pharmacy

URSULA JAKOB, PH.D.
Patricia S. Yaeger Collegiate Professor of Molecular, Cellular and Developmental Biology, Professor of Molecular, Cellular and Developmental Biology, College of Literature, Science, and the Arts; Professor of Biological Chemistry, Medical School

JON KINSEY, M.B.A
Chief of Staff, Office of the President

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Executive Vice Dean for Research; Peter A. Ward Distinguished University Professor of Pathology, Endowed Professor of Pathology Research and Professor of Pathology, Medical School

JUN LI, PH.D.
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YUJI MISHINA, PH.D.
William R. Mann Professor of Dentistry and Professor of Dentistry, Department of Biologic and Materials Sciences, School of Dentistry

JAMES MOON, PH.D.
Acting Chief Scientific Officer, Michigan Medicine; Senior Associate Dean for Research, Endowed Professor of Pathology Research, Department of Pathology, Medical School

LISA PROSSER, PH.D.
Marilyn Fisher Blanch Research Professor of Pediatrics, Associate Vice President for Research-Health Sciences, U-M Office of Research; Professor of Pediatrics, Medical School; Professor of Health Management and Policy, School of Public Health

DAN RABOSKY, PH.D.
Professor of Ecology and Evolutionary Biology and Curator, Ecology and Evolutionary Biology, College of Literature, Science, and the Arts

JANET SMITH, PH.D.
Martha L. Ludwig Distinguished University Professor of Biological Chemistry, Professor of Biological Chemistry, Medical School; Rita Willis Professor of the Life Sciences and Associate Director, Life Sciences Institute; Professor of Biophysics, College of Literature, Science, and the Arts

ELIZABETH SPELIOTES, M.D., PH.D.
Keith S, Henley M.D. Collegiate Professor of Gastroenterology, Professor of Internal Medicine, Professor of Computational Medicine and Bioinformatics, Associate Director, Medical Scientist Training Program (MSTP) and Program Director, Precision Medicine Program, Medical School

Former BICC Members

Huda Akil, Ph.D.
Elizabeth Barry, J.D.
Michael Boehnke, Ph.D.
Rebecca Cunningham, M.D.
Nisha D'Silva, Ph.D.
Eric Fearon, M.D., Ph.D.
David Ginsburg, M.D.
Richard Gonzalez, Ph.D.
Srijan Sen, M.D., Ph.D.
Joerg Lahann, Ph.D.
Anna Mapp, Ph.D.
Thomas Schmidt, Ph.D.
Patricia Wittkopp, Ph.D.
Donald Zak, Ph.D.

Management and Communications Team

Meet the dynamic duo driving operational excellence and strategic communication for the BSI.

Jennifer Ohren
Managing Director

Cody Abramson
Marketing and Communications Specialist

Consultants

Emily Kagey: Director of LSI Marketing and Communications
Rajani Arora: LSI Multimedia and Social Media Specialist
Cathy Andrews: Director of LSI Operations

Ohren headshot: Wahid Safdari; Abramson headshot: Rajani Arora, LSI

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