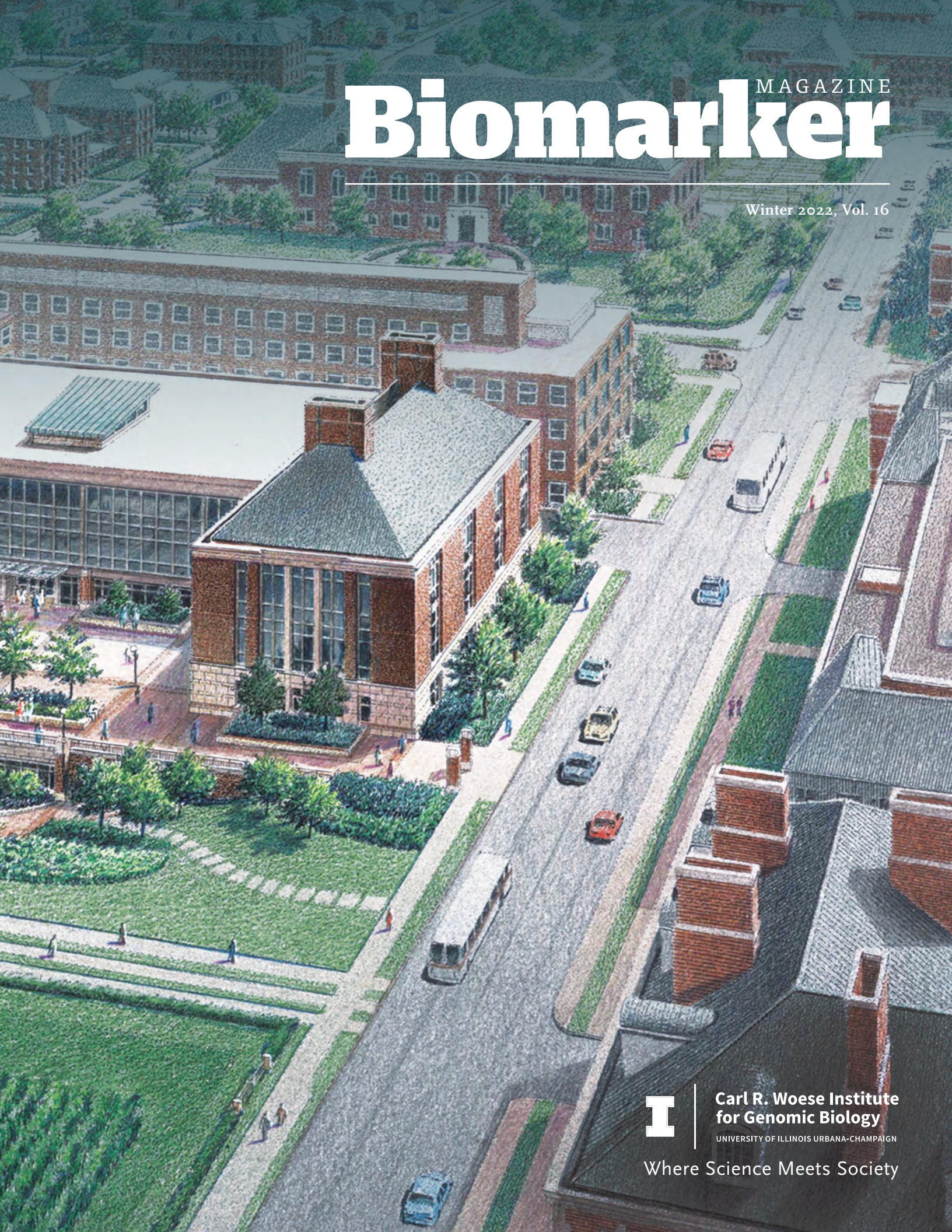
✦ The illustrations of the IGB building on the cover page and throughout this issue of the Biomarker were made before the IGB was built.

University of Illinois Urbana-Champaign
Carl R. Woese Institute for Genomic Biology

1206 West Gregory Drive
Urbana, IL 61801
www.igb.illinois.edu

@IGBIllinois



Biomarker MAGAZINE

Winter 2022, Vol. 16

Carl R. Woese Institute for Genomic Biology
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN

Where Science Meets Society

The IGB, with its amalgamation of eight interdisciplinary Research Themes (all problem based, and connected by the common language of genomics) is poised to shape the new "century of biology."

—Harris Lewin

FOUNDING IGB DIRECTOR, 2007

Winter 2022, Vol.16

IGB Themes

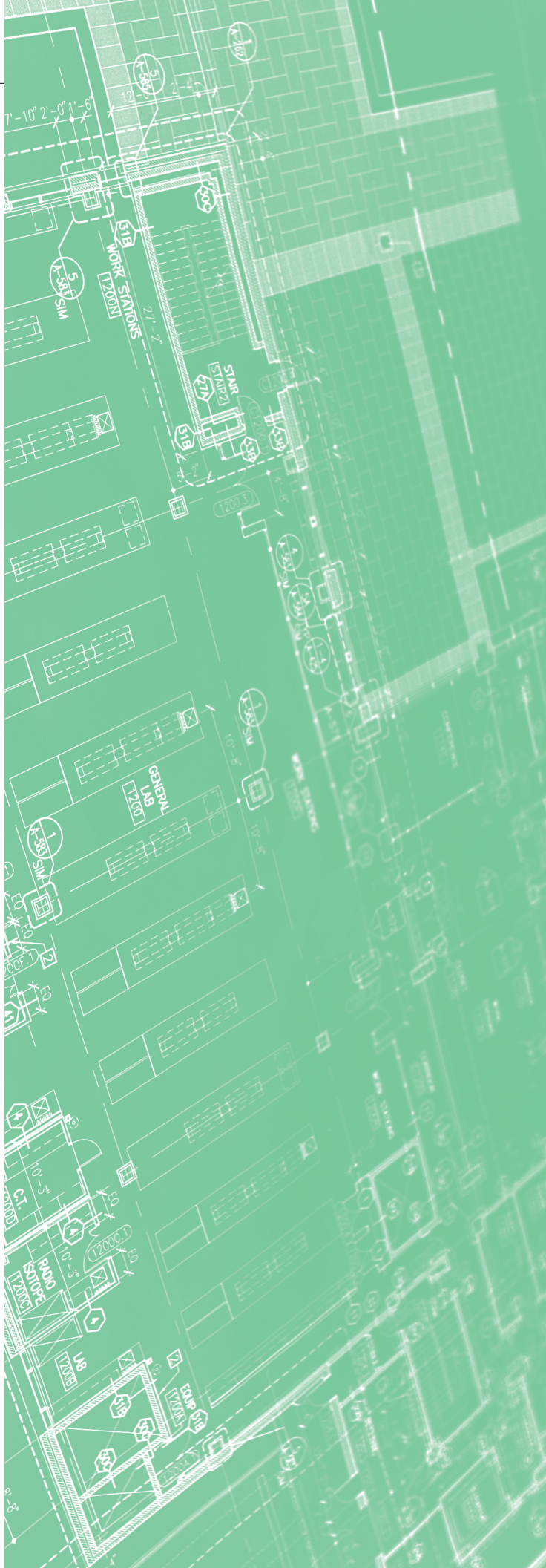
ACPP	Anticancer Discovery from Pets to People
BSD	Biosystems Design
CGD	Center for Genomic Diagnostics
EIRH	Environmental Impact on Reproductive Health
GEGC	Genomic Ecology of Global Change
GNDP	Gene Networks in Neural & Developmental Plasticity
GSE	Genomic Scale Engineering Center
GSP	Genomic Security and Privacy
IGOH	Infection Genomics for One Health
M-CELS	Multi-Cellular Engineered Living Systems
MME	Microbiome Metabolic Engineering
MMG	Mining Microbial Genomes
RBTE	Regenerative Biology & Tissue Engineering

IGB Strategic Partnerships

CABBI	Center for Advanced Bioenergy and Bioproducts Innovation
HPCBio	High-performance Biological Computing
MSI	Microbial Systems Initiative
MMLI	Molecule Maker Lab Institute
PNI	Personalized Nutrition Initiative

IGB Funding Agencies

DOE	United States Department of Energy
HHMI	Howard Hughes Medical Institute
NASA	National Aeronautics and Space Administration
NCSA	National Center for Supercomputing Applications
NIH	National Institutes of Health
NSF	National Science Foundation
USDA	United States Department of Agriculture
BioMADE	Bioindustrial Manufacturing and Design Ecosystem



CONTENTS

Winter 2022, Vol.16

Biomarker

Director: Gene Robinson
Associate Director: Subha Srinivasan
Director of Communications & Engagement: Nicholas Vasi

Writers

Allie Arp
Jenny Applequist
Claire Benjamin
Cancer Center at Illinois
Phil Ciciora
Tracy Crane
Dave Evensen
Grainger College of Engineering
Alisa King-Klemperer
Shelby Lawson
Susan McKenna
Amanda Nguyen
Lauren Quinn
Aaron Seidlitz
Ananya Sen
Kyle Shelton
Huan Song
Liz Ahlberg Touchstone
April Wendling
Julie Wurth
Diana Yates
Lois Yoksoulian

Design

Mirhee Lee

Images

Beckman Imaging Technology Group, Claire Benjamin, Eric Carlson, Andrew Dou, Kathryn Faith, Thomas Gaj, Cynthia Goldsmith (CDC), Don Hamerman, Michelle Hassel, Illinois State Police, Mirhee Lee, Colin Lim, Anna Longworth, Amanda Nguyen, Jillian Nickell, Julia Pollack, Alex David Jerez Roman, L. Brian Stauffer, Grace Darby Tan, Laura Troyer, Jim Vattano, Yanyu Xiong, Zhao Lab, Fred Zwicky

Biomarker is published by the Carl R. Woese Institute for Genomic Biology, University of Illinois Urbana-Champaign 1206 West Gregory Drive, Urbana, IL 61801

Research Articles

Director's Message

Features

Briefs

Honors

Director's Message

> "In these pages we recognize the scientific contributions of themes present and past, as well as the people whose efforts have made the IGB a beacon of innovative, transdisciplinary, and collaborative research."

Gene Robinson

DIRECTOR,
CARL R. WOESE
INSTITUTE FOR GENOMIC BIOLOGY

ANNIVERSARIES ARE A TIME FOR CELEBRATION, TO REFLECT on where we've been, and look forward to where we're heading. This year marks the 15th anniversary since the establishment of the Carl R. Woese Institute for Genomic Biology. Thanks to the efforts of our researchers, staff, faculty, and students, this year we have been able to safely reintroduce in-person classes, work, and activities across campus. Truly this demonstrates just how much is possible when science and society come together to work towards our goals. I am filled with pride with how far we have come, and I'm eager to see what the future holds.

It is my pleasure to introduce this year's edition of Biomarker, where we highlight the strides in science, diversity, and community that the IGB has created since its inception 15 years ago. In these pages we recognize the scientific contributions of themes present and past, as well as the people whose efforts have made the IGB a beacon of innovative, transdisciplinary, and collaborative research. You will read of great advances by the IGB in the last 15 years that have had impacts in our community and far beyond, including the treatment of diseases, the development of sustainable biofuels, and the invention of cutting-edge technology.

As the IGB has changed and grown over these years, so have the issues we face in the world around us. Rising temperatures, a growing population, a global pandemic, and increasing social injustice are but a few of the challenges we as a society face. In this edition you will read of the remarkable efforts made by the IGB through the years to tackle these issues in society, from improving photosynthesis, new cancer therapies, and increased DEI initiatives, to the creation of SHIELD, a program that was critical for curbing the spread of COVID-19 on our campus and in our community during the pandemic.

I'm also pleased to announce the creation of two new centers at the IGB. The first, Center for Artificial Intelligence and Modeling, will help connect biologists with people from more computational areas, such as computer science, furthering IGB's goal for transdisciplinary science and campus-wide collaborations. The second is the Center for Indigenous Science, created with the goal of lifting underrepresented voices and incorporating alternative models into current scientific practices that are collaborative, community-based, and inclusive. Although we have increased our efforts to create and foster an inclusive environment at the IGB, there is still more work to be done to ensure all voices are heard and supported. Diversity, equity, and interconnectivity between science and the public continue to be central elements of the IGB's mission. As we move into the future, I am thrilled to see how the IGB evolves, pushing the limits of what is possible, to create a better, brighter world. ■

Illinois General Assembly recognizes IGB's 15th anniversary

ON FEBRUARY 25TH 2022, THE ILLINOIS General Assembly adopted House Resolution 0690, commending the IGB on its 15th year of societal, scientific, and scholarly contributions at the intersection of science and society.

The IGB was established in 2007 with the goal of advancing life science research and stimulating bioeconomic development in Illinois through genomics. The state-of-the-art research facility has a unique structure that is designed to promote communication and collaboration among its members.

Over the past 15 years, the IGB has grown to include more than 200 faculty and affiliate members and more than 700 research staff and students, all from 40 departments across the University of Illinois Urbana-Champaign. With over $520 million in funding and the establishment of more than 20 start-up and small companies, the institute has carried out its mission to address grand societal challenges in the areas of agriculture and environment, health and wellness, technology, and society. The IGB has also established critical relationships with major industry partners such as Abbott, Bayer, BP, Dow AgroSciences, Illumina, IBM Systems, Intel Corp., and ZEISS Microscopy, as well as federal agencies including the Department of Defense, DOE, NIH, NSF, and USDA.

As part of its commitment to advancing public engagement with scientific progress, the IGB also hosts a broad variety of outreach and education programs to promote awareness of the field of genomic research. Opportunities are offered for a variety of groups and age levels and include structured workshops for judges, CEOs, physicians and other professionals, summer camps for children, travelling art exhibits, and museum learning stations.

"The IGB has been at the forefront of genomics since its launch in 2007," said Gene Robinson (GNDP), the IGB Director and Swanlund Chair, Entomology. "During the ensuing 15 years we have made great strides in this emergent field, expanding to become the most comprehensive genomics institute in the country through a research portfolio spanning medicine, agriculture, energy, and technology. In that same timeframe we have also directed significant effort towards the critical goal of furthering public understanding and engagement with the life sciences."

On June 14th, the IGB welcomed State Representative Carol Ammons, who serves the Illinois 103rd district. Ammons presented Robinson a copy of the resolution as a symbol of the General Assembly's respect and esteem.

"It is important to understand the role that genomic biology plays in solving today's pressing problems," Ammons said. "Without the IGB and SHIELD, COVID-19 would have been much more difficult to handle. We depend on the research you provide and recognize this institute and its ability to solve humanity's problems."

After accepting a copy of the resolution, Robinson highlighted two programs that exemplify the benefit of addressing scientific and societal goals in concert: Science, Technology, Engineering, Arts and Mathematics Transdisciplinary Research Across Institutional Near-peers or STEAM TRAIN and Illinois Biological Foundry for Advanced Biomanufacturing or iBioFAB.

The former grew out of partnerships with Franklin STEAM Academy Middle School in Champaign and University Laboratory High School in Urbana. STEAM TRAIN empowers middle school students to conduct independent research projects, over the course of a school year, in consultation with near-peer mentors from Uni High and researcher volunteers from the IGB.

Zanne Newman, teacher and Franklin Magnet Site Coordinator, and IGB researchers Ed Lochocki and Facundo Fernandez-Duque shared their experiences with the effort. "We can teach kids how to be a scientist in real life: how to come up with a hypothesis, how to communicate, and how to explain why the project is important," Lochocki said. "After working with them, I can say that the future of research is in great hands."

"As I think about the IGB's goal to promote an open dialogue between science and society, I am reminded of the achievements of Alice Ball," said Ammons. "Alice Ball was an African American chemist who developed an injectable oil extract that was the most effective treatment for leprosy until the 1940s. The solutions to humanity's various problems can emerge from untraditional places. Having different voices and perspectives be a part of the scientific community is so important."

Robinson also described iBioFAB, which was developed under the leadership of Huimin Zhao (BSD/GSE leader/CABBI/CGD/MMG), Steven L. Miller Chair in Chemical Engineering. iBioFAB is a precisely engineered set of robotic components combined with a highly adaptable software platform. It can reliably perform what would otherwise be those countless hours of error-prone labwork: handling reagents, incubating reactions or living cells, synthesizing products, applying treatments, and monitoring outcomes. The platform can support a broad array of research goals, from developing microbes that can sustainably produce vital bioproducts, strains of yeast that can make better biodiesel, fabricating biological molecules that could become new medical therapeutics, to rearing honey bees in a controlled environment for agricultural research.

"The solutions to humanity's various problems can emerge from untraditional places. Having different voices and perspectives be a part of the scientific community is so important."

"iBioFAB highlights the potential of team-based research to achieve goals that would be unreachable for the individual, as well as the power of genomics to effect positive societal change over diverse arenas," Robinson said. "Only in an interdisciplinary environment such as the IGB could such a system be not only conceived, but successfully constructed, implemented, and used to the realization of its full potential." ■

State Representative Carol Ammons (right) presented Gene Robinson a copy of House Resolution 0690.

15 Years of IGB: The RIPE Project

SCIENTISTS HAVING BEEN BREEDING plants for over a century with the goal of feeding hungry people across the world. To that end, the Green Revolution in the 1960s used new technologies to increase food production in scale with the population growth. But those advances have reached their biological limits, and new innovations from the RIPE project and other efforts will be crucial to keep pace with this century's growing population: 8.5 billion by 2030, 9.7 billion by 2050, and 11.2 billion by 2100.

"The UN Food and Agricultural Organization predicts that the world will need to increase staple crop yields 70 percent by 2050," said Stephen Long (BSD/CABBI/GEGC), the Ikenberry Endowed University Chair of Crop Sciences and Plant Biology. "The rapid advances that were achieved during the Green Revolution have slowed and will not meet this target."

To catch up, the international Realizing Increased Photosynthetic Efficiency project was started in 2012 with the Illinois research efforts based at the IGB. The goal of the project is to produce staple food crops that can efficiently convert sunlight into food and have increased productivity with fewer inputs.

RIPE primarily focuses on five crops: cassava, cowpea, maize, rice, and soybean, which are vital for sustaining the livelihood of people all over the world. "This project represents a huge effort to determine and apply the mechanisms of photosynthesis that can contribute to the challenge of this century—food security for all," said Long.

Even though significant progress has been made, it is likely that RIPE's technologies will not reach farmers until 2030, at which point the world's population will have grown by more than a billion people. To expedite the scientific process, the project has nine research objectives that broadly fall into three categories: understanding the nuances of photosynthesis, improving its efficiency by manipulating a model crop, and transforming the target food crops to boost their yields.

"Our rich knowledge from a half-century of photosynthesis research, coupled with modeling, has enabled us to re-engineer this complex process in staple food crops. Our models predict that we could achieve a 50 percent yield increase, which will go a long way to meeting the demands of this century," Long said.

The researcher's efforts have resulted in more than 80 research papers in the last 10 years and cover a wide range of topics including figuring out which of the 170 steps in photosynthesis can be tweaked to make the process more efficient; helping plants photosynthesize more efficiently even though sunlight intensity fluctuates throughout the day; modifying Rubisco—the main enzyme that captures carbon dioxide and converts it to sugars; optimizing crop canopies to allow better light penetration; and ensuring the modified crops are safe for the environment and consumption.

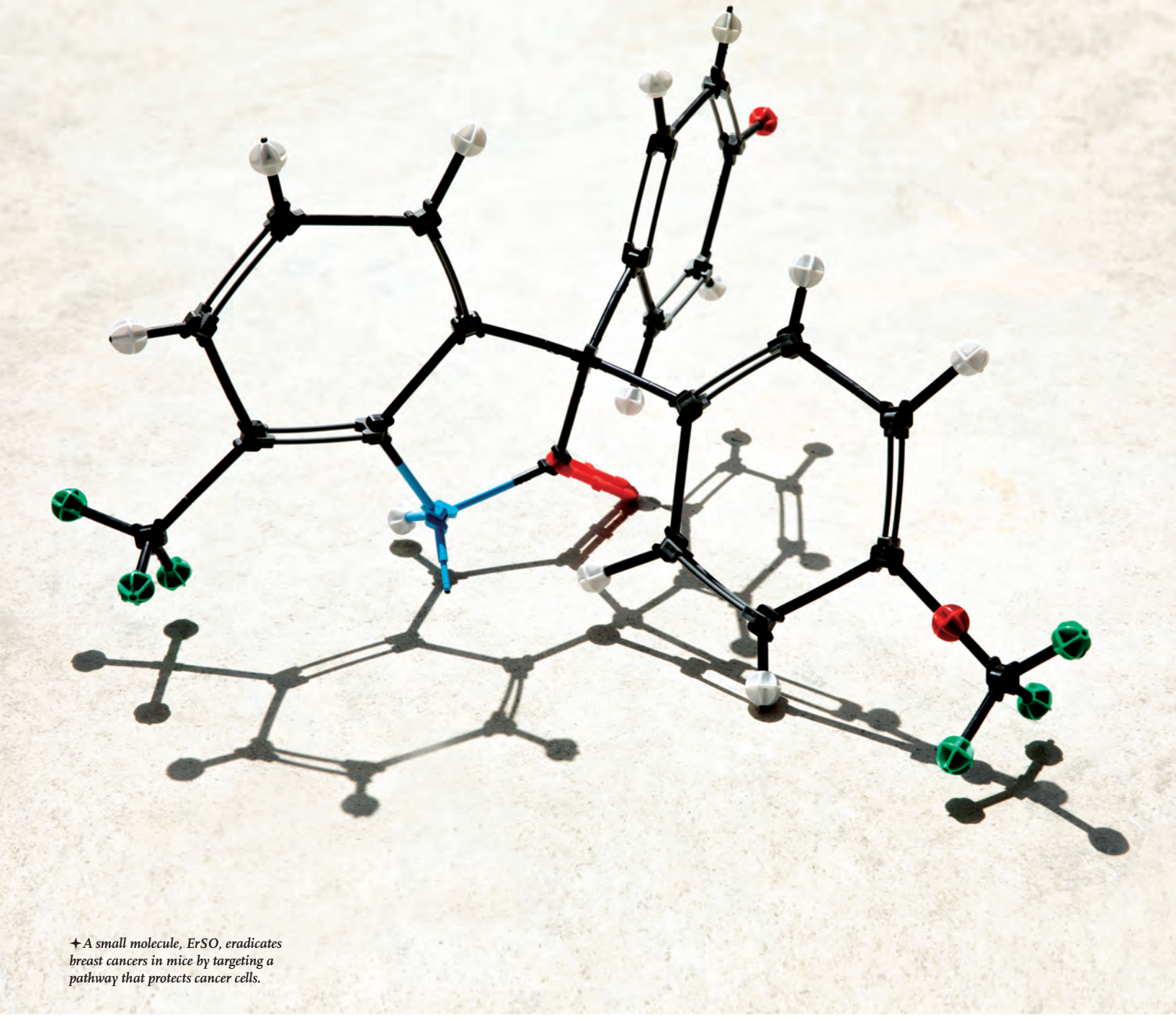
RIPE has several state-of-the-art facilities that help its researchers improve the complex process of photosynthesis to increase crop production. The Crop Transformation Facility was built and completed in August 2020, and was designed to provide lab and office space for researchers and crop technicians. In 2021, RIPE opened a High-Throughput Phenotyping Facility, which includes an 8,000 square foot greenhouse, allowing researchers to speed up gene editing in all of RIPE's crops of interest. The HTPF currently has 242 Elixia Heliospectra LED grow lights with four different LEDs to output in the near-red, red, white, and blue spectral regions. Simultaneously, an imaging system called the "plant eye" runs over the plants on a mobile gantry overhead, capturing the height, leaf area, and 3D volume of the plants in just 45 minutes. RIPE also installed a large-scale cable-driven camera system, which is the largest system of this kind used for research in the US. The RIPE Aerial Plant Phenotyping System, or Spidercam, allows the researchers to collect more sensing data and imagery than ever before.

RIPE and its sponsors are also focused on making the technologies available to the farmers who need them the most. "We are committed to ensuring that the literal fruits of our labor are globally available and royalty free for smallholder farmers, particularly in sub-Saharan Africa and Southeast Asia, to help meet the huge challenge of feeding the future," Long said. "While no single strategy will overcome the hurdles facing the industry, our success in RIPE and our sponsors' continued support give me hope that the future of agriculture is bright."

"This project represents a huge effort to determine and apply the mechanisms of photosynthesis that can contribute to the challenge of this century—food security for all."

RIPE was established with the help of a five-year, $25-million grant from the Bill & Melinda Gates Foundation. In 2017, the project received another five-year grant for $45 million from the Gates Foundation, the Foundation for Food and Agricultural Research, and the Foreign, Commonwealth & Development Office (formerly the U.K. Government's Department for International Development). Additionally, the Gates foundation funded a $13 million supplemental investment in 2018 to accelerate the translation of the project's successes into food crops.

The RIPE project is led by the University of Illinois Urbana-Champaign in partnership with the Australian National University, the University of Cambridge, the Chinese Academy of Sciences, the Commonwealth Scientific and Industrial Research Organization, Lancaster University, Louisiana State University, the University of California Berkeley, the University of Essex, and the USDA Agricultural Research Service. ■



✦A small molecule, ErSO, eradicates breast cancers in mice by targeting a pathway that protects cancer cells.

15 Years of IGB: Developing new drugs to battle cancer

FIGURING OUT WHICH DRUGS CAN HELP cure cancer is a laborious process, often requiring decades of careful research and multiple phases of clinical trials. To this end, the "Anticancer Discovery from Pets to People" research theme at the IGB has painstakingly worked on getting two drugs into clinical trials: PAC-1 and ErSO to treat brain and breast cancer, respectively. PAC-1 is currently in phase I clinical trials in humans and has been granted orphan drug status by the U.S. Food and Drug Administration for the treatment of glioblastoma, a deadly brain cancer. ErSO has been licensed by the pharmaceutical company Bayer AG and is currently being tested for human clinical trials.

One of the first steps in drug design includes testing them on animals that serve as a proxy for humans. Although researchers tested ErSO in mice models, they used a different animal for PAC-1: dogs with certain naturally occurring cancers. According to Timothy Fan (ACPP/CGD), a professor of veterinary clinical medicine, dogs may be better than rodents in many cancer drug-testing models because the latter need to be implanted with human cancer cells to mimic specific types of tumors. Additionally, certain cancers in dogs are genetically similar to those in humans and respond to the same medications. Dogs are also more similar in size to humans and are, therefore, better models to test how well the drugs work on larger tumors.

Researchers discovered PAC-1's anti-cancer capabilities in 2006 in the Hergenrother lab. "One of the unusual features of this drug is that unlike most cancer drugs, PAC-1 gets into the brain. We wanted to embrace that and try to address the unmet clinical need of brain cancer," said Paul Hergenrother (ACPP leader/MMG), a professor of chemistry.

PAC-1 activates the cellular enzyme procaspase-3, which triggers a series of reactions that causes only cancer cells to self-destruct, sparing healthy cells. "Even though they have elevated levels of procaspase-3, cancer cells never turn the enzyme on. They keep growing and become tumors," Hergenrother said. "PAC-1 restores the enzyme activity and because it is elevated in cancer cells, it targets cancer cells over non-cancerous cells."

In 2013, a $4 million investment, informed by the trials in dogs, helped PAC-1 on the road to human clinical trials. In 2016, the same anonymous donor contributed $7 million to help the studies progress in the drug-approval pipeline. Moreover, the funding also helped many veterinary patients that would not have received treatments for their cancer. PAC-1 is still in clinical trials in dogs with osteosarcoma, the most common type of bone cancer.

Fan and his colleagues are also looking at PAC-1 in combination with radiation and in combination with temozolomide, a brain cancer drug used in humans and dogs. "One of PAC-1's greatest strengths is that it synergizes with other drugs, increasing the anti-cancer effects of many compounds that are out there," Fan said. The three dogs in the trial tolerated the combination treatment well and responded well to the therapy. Fan said that a much larger study will be needed to quantify how much PAC-1 contributed to the positive results.

Currently in the human trials, PAC-1 has been cleared for use in a clinical trial of patients with anaplastic astrocytoma, a rare malignant brain tumor, and glioblastoma multiforme, an aggressive late-stage cancer of the brain. So far, there have been no significant side effects. The phase I trial will also determine if PAC-1 can be used safely with temozolomide. "We've been at this now for more than 10 years, and we're excited to be able to continue down this road," Hergenrother said. "It takes a lot of time, effort, and money to do human clinical trials. To expand access to PAC-1 from a dozen patients to, we hope, hundreds, is very exciting. That will allow us to get some definitive data on the drug."

The precursor to ErSO was first discovered in 2014 in the laboratories of Hergenrother and biochemistry professor David Shapiro. Although the original compound prevented breast cancer cells from growing, it did not rapidly kill them and had undesirable side effects. In 2021, the researchers discovered the small molecule ErSO that had powerful anticancer effects without side effects in mice. When they tested the drug in mice models of human estrogen-receptor-positive breast cancers and their metastases in the bone, brain, liver, and lungs, the drug killed 95-100% of the cancer cells and shrank large tumors to undetectable levels. The compound was also well tolerated in mice, rats, and dogs.

"Many of these breast cancers shrunk by more than 99% in just three days. ErSO is fast-acting and its effects on breast cancers in mice are large and dramatic."

ErSO works by binding to the estrogen receptor, upregulating the anticipatory Unfolded Protein Response or a-UPR, which kills cancer cells. About 75% of breast cancers are estrogen-receptor positive, making ErSO a potent drug. "Since the process is estrogen-receptor dependent, ErSO doesn't touch the cells that lack the receptor, and it also doesn't affect healthy cells—whether or not they have an estrogen receptor," Hergenrother said.

Impressively, within a week of exposure to ErSO, advanced, human-derived breast cancers in mice shrank to undetectable levels. "Many of these breast cancers shrunk by more than 99% in just three days," Shapiro said. "ErSO is fast-acting and its effects on breast cancers in mice are large and dramatic."

In the past 250 years, researchers have made several discoveries that have helped in the battle against cancer, a disease that has been afflicting humanity for thousands of years. Unfortunately, patients with metastatic estrogen-receptor-positive breast cancers or glioblastoma eventually succumb to the disease, even with treatment. Although PAC-1 and ErSO may not be the silver bullet we are looking for, the studies so far have all pointed to a favorable outcome. Hopefully, as we learn more about these drugs, we will get closer to finding better weapons that can help us treat cancer. ■

✦ *University of Illinois Urbana-Champaign SHIELD team members process saliva samples, testing for COVID-19 as they run the university testing program in labs housed at the Veterinary Diagnostic Laboratory.*

15 Years of IGB: SHIELDing the Illinois community against COVID-19

DURING THE EARLIEST MONTHS OF 2020, COVID-19 seemed like an innocuous event that was too geographically distant to affect the Illinois community. In fact, by March 10th there were only 19 confirmed cases. Nevertheless, Nigel Goldenfeld (BCXT leader/GNDP), former Swanlund Endowed Chair and professor of physics, and Sergei Maslov (BCXT/CABBI), a professor of bioengineering and Bliss Faculty Scholar, were worried. The news from China and Italy was concerning and in four days a significant portion of students, faculty, and staff were going to leave for spring break. They decided to build a simple mathematical model of Urbana and Champaign to predict what would happen to the community.

Goldenfeld and Maslov divided the population into four categories: susceptible, exposed, infected, and recovered. They were stunned by the results. The model predicted that if the students were allowed to return to campus, there would be a huge wave of infections. They immediately contacted the university provost, and on March 11th the students were told that their classes would be online after spring break. The model also convinced Governor J.B. Pritzker to issue a statewide stay-at-home order. The decision helped Illinois avoid the situation in New York, which implemented the same order a day later, yet at this point had ten times as many confirmed cases.

The model was just the first of many steps that were taken to protect the Illinois community from the devastating spread of COVID-19. The second was implementing SHIELD Illinois—a COVID-19 testing program designed to safely open schools, protect workplaces, and save lives. The developers came up with the name to evoke the concept of putting a protective shield around the University of Illinois campus. The team included experts in modeling, which emphasized the importance of regular testing; biochemistry and immunology experts who helped develop the saliva test; and community members who worked with the Illinois Department of Public Health and the CU Public Health District to develop safety guidelines.

The saliva-based testing procedure is simple, non-invasive and, most importantly, the results are available within 24 hours. The test targets three highly conserved regions of the viral genome and can pick up the virus as early as two to three days after exposure, making testing extremely accurate and reliable, regardless of variants.

The saliva test has been coupled with a digital app to establish a rapid-alert system where the individuals are directly notified within 30 minutes if they have tested positive, ensuring that they immediately isolate and reduce any spread of infection. Additionally, the supercomputing resources at the university was used to create real-time models to quickly identify and contain emerging outbreaks before they got out of control.

During the Fall 2020 semester, the university conducted about 10,000 tests each weekday and half that number during the weekends. "At the beginning of the semester, we worked 12-hour shifts to make sure everything was running smoothly," said Diana Ranoa, an IGB postdoctoral fellow who was instrumental in developing the saliva test. "The volume of samples we had to process was overwhelming and our team grew from four people to about forty, all working around the clock." Due to the rapid system, along with universal masking on campus, small in-person class sizes, and the availability of remote learning, the case positivity rate was usually well below 0.5% with zero COVID-19-related hospitalizations or death in the university community.

By December 2020, the university had administered one million tests, a milestone and a reflection of the creative spirit and tireless collaborations across the campus. "The SHIELD team made many innovations in a very short period of time that allowed to achieve fast, frequent testing that defends against COVID-19 transmission," said Martin Burke (MMG), a professor of chemistry and the leader of the SHIELD team. "At Illinois we love to innovate and we love working together. Failure was not an option and our entire campus rallied together to succeed."

The SHIELD team also developed a new resource—the K-12 Shield Playbook—to help guide teachers and school administrators as they reopened schools during the pandemic. It contains modules on cleaning, distancing, health data, masking, testing, and ventilation.

"The developers came up with the name to evoke the concept of putting a protective shield around the University of Illinois campus."

"The K-12 Playbook provides all of the resources that a school would need in one place," said Rebecca Smith (IGOH), a professor of pathobiology. "There are a lot of resources out there, but they're scattered. We brought it all together as a resource repository for schools, with a guide to making all the decisions necessary to reopen a K-12 school."

In recognition of SHIELD's efforts, Tim Killeen, the President of the University of Illinois, honored 28 key leaders of the system's COVID-19 response with the Presidential Medallion in August 2021. The IGB recipients included Nigel Goldenfeld; Sergei Maslov; Diana Ranoa; Martin Burke; Rebecca Smith (IGOH), associate professor of epidemiology; Fadi Alnaji, a post-doctoral researcher; Christopher Brooke (IGOH), associate professor of microbiology; Timothy Fan (ACPP/CGD), a professor of veterinary clinical medicine; Kelsie Green, a laboratory technician; and Paul Hergenrother (ACPP leader/MMG), Kenneth L. Rinehart Jr. Endowed Chair in natural products chemistry.

"In our fight against COVID-19, the efforts of the University of Illinois System have been a real asset to millions of Illinoisans," Pritzker said at the ceremony. "That begins with the successful effort last year to keep campuses open to the more than 90,000 students enrolled at U of I System universities. But it extends to the tens of thousands of people who found access to life-saving vaccines in the Chicago area, students at universities and community colleges who have been protected by the SHIELD test, and this Fall to students at more than 1,000 K-12 schools around the state who will be protected by access to SHIELD." ■

15 Years of IGB: Welcoming increased representation through DEI efforts

SCIENTIFIC PURSUITS OFTEN REQUIRE examining a problem from different angles in order to gain a complete understanding. Such an undertaking often requires multiple researchers, each with a unique skill set. But what happens when certain voices are ignored over and over, in favor of others? It breeds inequality that weakens our science and our sense of community.

Diversity, equity, and inclusion have always been valued at the IGB. We recognize that investigators, students, and staff from diverse backgrounds bring their lived experiences and unique perspectives together, improving our ability to solve problems and be responsive to societal needs. To this end, the IGB Committee on Diversity was established in 2018 with the goal of creating a more inclusive, diverse, and welcoming environment within our community. The COD is comprised of community members spanning the breadth of the IGB, including theme leaders, faculty, staff, and postdoctoral researchers.

In 2020 the world faced a summer of unrest. Several horrific events in our nation, including the murders of George Floyd, Ahmaud Arbery, and Breonna Taylor, victims in our Asian-American communities, and all too many others left us outraged. Black Lives Matter and other protests against racism, police brutality, and the targeting of specific nationalities continued and gained strength. Yet, after all those efforts, institutional racism persists.

Spurred by concern over these events in our community, the COD Task Force was formed in 2020 to use the COD's ideas, take action, and bring new initiatives to light. Guided by the COD, the Task Force has since accelerated initiatives that increase dialogue with the aim of creating a more inclusive environment. Their efforts include developing additional programs to diversify the practice and practitioners of science; increasing dialogues through workshops, panels, and hiring practices; funding new initiatives to help eliminate institutional racism and other inequities at the IGB; and working with campus units in strengthening intercultural relationships focused on DEI.

The initiatives of the Task Force fall under three broad categories: providing resources, creating new partnerships with the community, and providing support for the ongoing outreach efforts at the IGB.

DEI resources

The Task Force has created a dedicated webspace that houses DEI event information and resources, which include reading material, toolkits, podcast recommendations, and links to campus facilities including counseling services, all gender restrooms, and lactation rooms. Several workshops have also been organized that focus on creating an inclusive and supportive environment both within the IGB and in our community. Through these workshops, the participants can learn skills for promoting fairness in the workplace and becoming allies to those who need support.

Creating new partnerships

In 2014, the University of Illinois Urbana-Champaign was granted one of the Big Data to Knowledge grants from NIH. This grant, which aimed to enhance and accelerate analysis of complex data related to biomedical sciences, allowed us to forge a collaboration with Fisk University, a minority-serving institution, with the overall goal of increasing diversity on campus. Under the guidance of Founder Professor of Physics Jun Song (ACPP), both the IGB and Illinois Department of Physics provided administrative and technological support to host students each year. Based on the Fisk-Illinois partnership, the FUTURE-MINDS-QB bridge program was also established and in 2021 it was awarded a $1.3M 5-year T-32 training grant by the National Institute of General Medical Sciences, a member organization of the NIH. FUTURE-MINDS-QB will help streamline a path from a master's degree at Fisk University, to a doctoral degree at Illinois.

In 2021, the Task Force established the Lunchbox seminar series with the sponsorship of the Office of the Vice Chancellor for Diversity, Equity, and Inclusion. Through the Lunchbox, members from across the campus talked to the participants about the interconnectivity between food, science, and culture, and how food shapes our individual experiences. In partnership with Bevier Café, the seminar series also featured a dish for every talk. The organizers wanted to create stronger bonds across the campus and the local community and provide opportunities for open dialogue between the researchers and members of the public, adding increased familiarity with others' perspectives and worldviews, in addition to the educational value.

Supporting ongoing outreach efforts

In many schools, lessons about Indigenous Peoples are often presented only through social studies, ignoring their contributions to STEM. To address this issue, Ripan Malhi (GNDP/GSP/IGOH), a professor of anthropology, launched the Summer Internship for Indigenous People in Genomics program in 2011. The workshop brings together Indigenous scientists and community members every year for a week of hands-on training in genomics. The discussions also address the uses, misuses, and limitations of genomics as a tool for Indigenous peoples' communities and how Indigenous communities can use genomics as a tool for community interest. SING trains Indigenous peoples in the concepts and methods currently used in genomics, strengthening the trust between researchers and Indigenous peoples. Since its launch, SING USA has had more than 120 participants receive hands-on training in genomics.

> **"SING trains Indigenous peoples in the concepts and methods currently used in genomics, strengthening the trust between researchers and Indigenous peoples."**

Among the several outreach efforts at the IGB, the Pollen Power camp, which started in 2013, always excites the mentors and the students. The camp offers a unique blend of plant science, technological exploration, and summer fun. Middle school children, especially from underrepresented populations, are introduced to the world of plant biology research. The highlights of the camp's activities include imaging, modeling, and 3D printing representations of individual grains of pollen; pollinating research plants in the field; and constructing an evolutionary timeline of Earth's flora.

Although our ongoing efforts to create programs to diversify science and increase participation from members of minority groups in genomics has helped further our DEI goals, it is important to realize that we can and should do more to diminish racism and other inequities. Such efforts can include joining the Task Force, helping with outreach efforts across the campus, or even being an active member in the community and providing a voice for those who have been ignored for far too long. ■

✦ Sorghum in rows at the EBI Energy Farm, with Setaria growing as a weed between the rows.

15 Years of IGB: Using biology to solve energy problems

OVER THE PAST FEW DECADES, IT HAS become increasingly obvious that fossil fuels, such as coal, oil, and gas, are the biggest contributors to global climate change, accounting for over 75% of greenhouse emissions. If we want to avoid the catastrophic impacts of climate change, these emissions need to be reduced by almost half by 2030 and reach net zero by 2050. This goal can only be achieved if we invest in alternative sources of energy that are sustainable and reliable, a realization that led to the establishment of the Energy Biosciences Institute.

In 2006, BP issued an international call for proposals to engage in a research partnership with researchers who could use their expertise in basic biological sciences to solve problems in the energy sector. Following a competition involving 20 major research universities, in 2007 BP selected a consortium consisting of the University of California, Berkeley, Lawrence Berkeley National Laboratory, and the University of Illinois Urbana-Champaign to host the EBI.

"The projected effects on climate of relentlessly accelerating combustion of fossil fuels are alarming," said Chris Somerville, a professor of plant and microbial biology at Berkeley and the Director of EBI from 2007-2016. "The use of fossil fuels is so obviously unsustainable, and yet so hard to replace with alternatives that can reach the scale of fossil fuel consumption, that there is some urgency to explore alternatives."

The EBI had several overarching goals in their quest to develop alternative sources of energy: finding and improving plant sources that could serve as biofuels; efficiently extracting fuel from these crops; assessing the environmental, social, and economic impacts of developing biofuels; and improving the energy yields from fossil fuels.

Improving biofuel production

The most important aspect of biofuel production begins in the fields—finding sustainable, high-yielding plants. The ideal plant, which differs by region, will yield the most biomass with the lowest use of land, water, and energy. Researchers predict that with highly productive plants, such as Miscanthus, it is possible to produce about half of all transportation fuels by growing it on about 1% of the terrestrial surface area.

"The EBI established itself as the global leader for understanding Miscanthus, while also making significant advances with prairie grasses, including switchgrass, and laying the foundations for leading crops including energy cane, sugarcane, and miscane," said Stephen Long (BSD/CABBI/GEGC), the Ikenberry Endowed University Chair of Crop Sciences and Plant Biology and a former Deputy Director of the EBI.

After these plants are harvested, they must be reduced to their component elements. However, the sugars inside are chemically locked up in long polymers that must be broken down first. This deconstruction process, called biomass depolymerization, is one of the keys to economical biofuel production.

To tackle this challenge, EBI researchers investigated different biological means to break the chemical bonds that will release the sugars. Such reactions occur widely in nature, for example by bacteria and fungi in the digestive system of animals. Therefore, by replicating this phenomenon in industrial processes and designing microbes that will synthesize desirable fuel molecules, the EBI hoped to improve biofuel production.

"That was the main beauty of having the EBI. Under its umbrella we collaborated with no barrier even between labs or the campuses. We did not have to worry about conflict of interest, we just collaborated for one clear mission—to create a microorganism for better biofuel production," said Yong-Su Jin (BSD/CABBI/MME), an assistant professor in bioengineering.

Assessing the impacts of an emerging biofuels industry

Although transitioning to biofuels will greatly reduce our dependance on fossil fuels, a myriad of potential impacts on economies, societies, and environments have been anticipated once the fuel hits the market for use. Potential issues involve land use, food production, carbon emissions at the local and regional locations, concerns about food and fuel markets, consumer and producer welfare, and the environment.

To address these concerns, the EBI also included researchers who analyzed how land is used and how bioenergy crops could be grown on land not used for food production. They also studied how different feedstock crops affected the ecosystem, including the levels of carbon and nitrogen in the soil, water quality, and the production of greenhouse gases like methane and nitrous oxide. Additionally, many in the world are concerned that the demand for energy is so large that unrestrained conversion of land to biofuel production could have negative environmental effects and could further disadvantage poor people by increasing prices for food, fuel, and fiber. Therefore, the EBI researchers also modeled how the biofuel industry can influence different members of the global society.

"We collaborated with no barrier even between labs or the campuses. We did not have to worry about conflict of interest, we just collaborated for one clear mission—to create a microorganism for better biofuel production."

Increasing fossil fuel yield with the help of microbes

Although it is important to gradually move away from fossil fuels, the change will not be immediate. In the meantime, the EBI sought to make the development and use of fossil fuels a more efficient process by using microbes. Typically, only 33% of oil available from any well is recoverable. The rest is lost due to the challenges associated with harnessing oil from porous rock, and the presence of hydrogen sulfide, a major contaminant in oil and gas reservoirs.

The EBI recognized the value in investigating various microbial processes that could ultimately be used to reduce the environmental footprint of oil recovery. They discovered that microbe-induced iron precipitation facilitated the recovery of oil from porous rock, since the iron coated and homogenized the rock's pores, allowing companies to push water through the rock matrix and extract petroleum. The researchers also addressed problems caused by hydrogen sulfide in a number of ways including using bacteria that were capable of oxidizing hydrogen sulfide to sulfur which is nontoxic.

The EBI paved the way for several important collaborations that enabled scientists to take a holistic approach to developing alternative fuels. After the funding for the EBI ended in 2014, the University of California, Berkeley, Lawrence Berkeley National Laboratory, and the University of Illinois are all still actively pursuing the research questions that the EBI proposed. ■

✦iBioFAB houses liquid handling devices that serve as workhorses for most tasks.

15 Years of IGB: Accelerating biological engineering through automation and artificial intelligence

ONE OF THE BIGGEST CHALLENGES IN traditional laboratory settings is performing countless hours of error-prone lab work: handling reagents, incubating reactions or living cells, synthesizing products, applying treatments, and monitoring outcomes. The Illinois Biological Foundry for Advanced Biomanufacturing was established in 2014 to bypass these cumbersome procedures and support a broad array of research goals.

"iBioFAB highlights the potential of team-based research to achieve goals that would be unreachable for the individual," said Gene Robinson (GNDP), the IGB Director and Swanlund Chair, Entomology. "Only in an interdisciplinary environment such as the IGB could such a system be not only conceived, but successfully constructed, implemented, and used to the realization of its full potential."

Developed under the leadership of Huimin Zhao (BSD/GSE leader/CABBI/CGD/MMG), Steven L. Miller Chair in Chemical Engineering and the Director of the Molecule Maker Lab Institute, iBioFAB is a precisely engineered set of robotic components combined with a highly adaptable software platform. Based in the concourse research lab of the IGB, iBioFAB integrates artificial intelligence/machine learning with automation, and features a robotic arm that travels along a 5-meter-long track to transfer microplates among more than 40 instruments installed on the platform.

The system houses three liquid handling devices that serve as workhorses for most tasks. Additionally, to enable unattended automated operation, iBioFAB also contains instruments for automating standard laboratory tasks: a centrifuge, a barcode labeler, four reagent dispensers, four thermal cyclers, an automated microplate heat sealer, a plate seal remover, and multiple plate shakers and block arrays. At its maximum capacity, iBioFAB can generate thousands of output samples each day using custom-designed workflows.

Although many fields have already turned to automation, several factors make synthetic biology's transition using iBioFAB unique. First, an automated system that produces synthetic biological systems has to take the unpredictability of biology into account. Second, it must be versatile enough to deal with multiple research efforts. In the pharmaceutical industry, for example, automated systems are used for only one task. But in synthetic biology, researchers could be using the system to work on one project one day, and another project the next day. Third, workflows in synthetic biology are complex and therefore the system needs to be adaptable and programmable. And fourth, it needs to deal with data-rich projects; while a researcher might struggle to remember a genome with thousands of genes, an algorithm can keep track.

From 2013-2019, seven papers have been published that highlight iBioFAB's usefulness. Plasmids—small, circular DNA molecules—are used by scientists to introduce new genes into a target organism. Known for their applications in the production of therapeutic proteins like insulin, plasmids are broadly used in the large-scale production of many bioproducts. However, designing and constructing them remains one of the most time-consuming and labor-intensive steps in biology research. To address this issue, researchers at the Center for Advanced Bioenergy and Bioproducts Innovation developed a versatile and automated platform for plasmid design and construction called PlasmidMaker. Once the plasmid was designed, it was built with iBioFAB. With all the improvements it brings to the table, the team members at CABBI hope that PlasmidMaker and iBioFAB will accelerate the development of synthetic biology for biotechnological applications.

In addition to synthesizing DNA, iBioFAB can also edit it. Genome editing tools that can target specific DNA sequences are becoming increasingly important in health, industrial, and food biotechnology applications. However, designing and implementing such tools on a large scale has always been a challenge. Due to iBioFAB, IGB researchers have been able to develop recombinant transcription activator-like effectors and transcription activator-like effector nucleases that can be tailored to specifically target any user-defined DNA sequence. Both TALEs and TALENs can be synthesized efficiently and a low cost, making it easy for researchers to use this tool.

The automated platform of iBioFAB can also create multiple DNA edits, including overexpressing some genes while deleting others, in a single step. Developed in 2017, the genome-scale engineering was carried out in *Saccharomyces cerevisiae*, an important eukaryotic model organism and widely used microbial cell factory. Such manipulations have since helped researchers to quickly identify and improve diverse cellular pathways, including those involved in the production of enzymes and chemicals.

"iBioFAB highlights the potential of team-based research to achieve goals that would be unreachable for the individual."

In 2019, researchers at Illinois combined iBioFAB with artificial intelligence/machine learning to form a closed-loop fully automated system, called BioAutomata, that designed, built, tested, and learned complex biochemical pathways to produce lycopene, a red pigment found in tomatoes and commonly used as a food coloring. "BioAutomata was able to reduce the number of possible lycopene-production pathways constructed from over 10,000 down to about 100 and create an optimized quantity of lycopene-overproducing cells within a week—greatly reducing time and cost," Zhao said.

Former students and postdoctoral researchers from the Zhao group have set up similar integrated robotic systems in three institutions in China, including the Chinese Academy of Sciences Shenzhen Institute of Advanced Technology, Zhejiang University, and the Chinese Academy of Sciences Tianjin Institute of Industrial Biotechnology. Additionally, Illinois is the founding member of the global biofoundry alliance that currently consists of over 30 institutions around the world.

"We are very proud that we built the first integrated robotic system more than eight years ago," Zhao said. "By integrating the recent advances in synthetic biology and artificial intelligence/machine learning with iBioFAB, I envision that iBioFAB can be turned into a self-driving biofoundry that can autonomously design and execute experimental plans and analyze experimental results. We are particularly interested in applying this self-driving biofoundry for enzyme engineering and metabolic engineering for synthesis of chemicals, fuels, and materials from renewable plant biomass, which is one of the main goals of CABBI." ■

✦ *The greenhouses help researchers to precisely control the experimental conditions of their plants.*

RIPE researchers prove bioengineering better photosynthesis increases yields in food crops for first time ever

FOR THE FIRST TIME, RESEARCHERS OF the Realizing Increased Photosynthetic Efficiency project have proven that multigene bioengineering of photosynthesis increases the yield of a major food crop in field trials. After more than a decade of working toward this goal, a collaborative team led by the University of Illinois Urbana-Champaign has transgenically altered soybean plants to increase the efficiency of photosynthesis, resulting in greater yields without loss of quality.

Results of this magnitude couldn't come at a more crucial time. The most recent UN report, The State of Food Security and Nutrition in the World 2022, found that in 2021 nearly 10% of the world population was hungry, a situation that has been steadily worsening over the last few years and eclipsing all other threats to global health in scale. According to UNICEF, by 2030, more than 660 million people are expected to face food scarcity and malnutrition. Two of the major causes of this are inefficient food supply chains and harsher growing conditions for crops due to climate change. Improving access to food and improving the sustainability of food crops in impoverished areas are the key goals of this study and the RIPE project.

RIPE is an international research project that aims to increase global food production by improving photosynthetic efficiency in food crops for smallholder farmers in Sub-Saharan Africa with support from the Bill & Melinda Gates Foundation, Foundation for Food & Agriculture Research, and U.K. Foreign, Commonwealth & Development Office.

"The number of people affected by food insufficiency continues to grow, and projections clearly show that there needs to be a change at the food supply level to change the trajectory," said Amanda De Souza, RIPE project research scientist, and lead author. "Our research shows an effective way to contribute to food security for the people who need it most while avoiding more land being put into production. Improving photosynthesis is a major opportunity to gain the needed jump in yield potential."

Photosynthesis, the natural process all plants use to convert sunlight into energy and yield, is a surprisingly inefficient 100+ step process that RIPE researchers have been working to improve for more than a decade. In this first-of-its-kind work, recently published in *Science*, the group improved the VPZ construct within the soybean plant to improve photosynthesis and then conducted field trials to see if yield would be improved as a result.

The VPZ construct contains three genes that code for proteins of the xanthophyll cycle, which is a pigment cycle that helps in the photoprotection of the plants. Once in full sunlight, this cycle is activated in the leaves to protect them from damage, allowing leaves to dissipate the excess energy. However, when the leaves are shaded—by other leaves, clouds, or the sun moving in the sky—this photoprotection needs to switch off so the leaves can continue the photosynthesis process with a reserve of sunlight. It takes several minutes for the plant to switch off the protective mechanism, costing plants valuable time that could have been used for photosynthesis.

The overexpression of the three genes from the VPZ construct accelerates the process, so every time a leaf transitions from light to shade the photoprotection switches off faster. Leaves gain extra minutes of photosynthesis which, when added up throughout the entire growing season, increases the total photosynthetic rate. This research has shown that despite achieving a more than 20% increase in yield, seed quality was not impacted.

"Despite higher yield, seed protein content was unchanged. This suggests some of the extra energy gained from improved photosynthesis was likely diverted to the nitrogen-fixing bacteria in the plant's nodules," said RIPE Director Stephen Long (BSD/CABBI/GEGC), Ikenberry Endowed University Chair of Crop Sciences and Plant Biology.

The researchers first tested their idea in tobacco plants because of the ease of transforming the crop's genetics and the amount of seeds that can be produced from a single plant. These factors allow researchers to go from genetic transformation to a field trial within months. Once the concept was proven in tobacco, they moved into the more complicated task of putting the genetics into a food crop soybeans.

"Improving photosynthesis is a major opportunity to gain the needed jump in yield potential."

"Having now shown very substantial yield increases in both tobacco and soybean, two very different crops, suggests this has universal applicability," said Long. "Our study shows that realizing yield improvements is strongly affected by the environment. It is critical to determine the repeatability of this result across environments and further improvements to ensure the environmental stability of the gain."

Additional field tests of these transgenic soybean plants are being conducted this year, with results expected in early 2023.

"The major impact of this work is to open the roads for showing that we can bioengineer photosynthesis and improve yields to increase food production in major crops," said De Souza. "It is the beginning of the confirmation that the ideas ingrained by the RIPE project are a successful means to improve yield in major food crops."

The RIPE project and its sponsors are committed to ensuring Global Access and making the project's technologies available to the farmers who need them the most.

"This has been a road of more than a quarter century for me personally," said Long. "Starting first with a theoretical analysis of theoretical efficiency of crop photosynthesis, simulation of the complete process by high-performance computation, followed by application of optimization routines that indicated several bottlenecks in the process in our crops. Funding support over the past ten years has now allowed us to engineer alleviation of some of these indicated bottlenecks and test the products at field scale. After years of trial and tribulation, it is wonderfully rewarding to see such a spectacular result for the team." ■

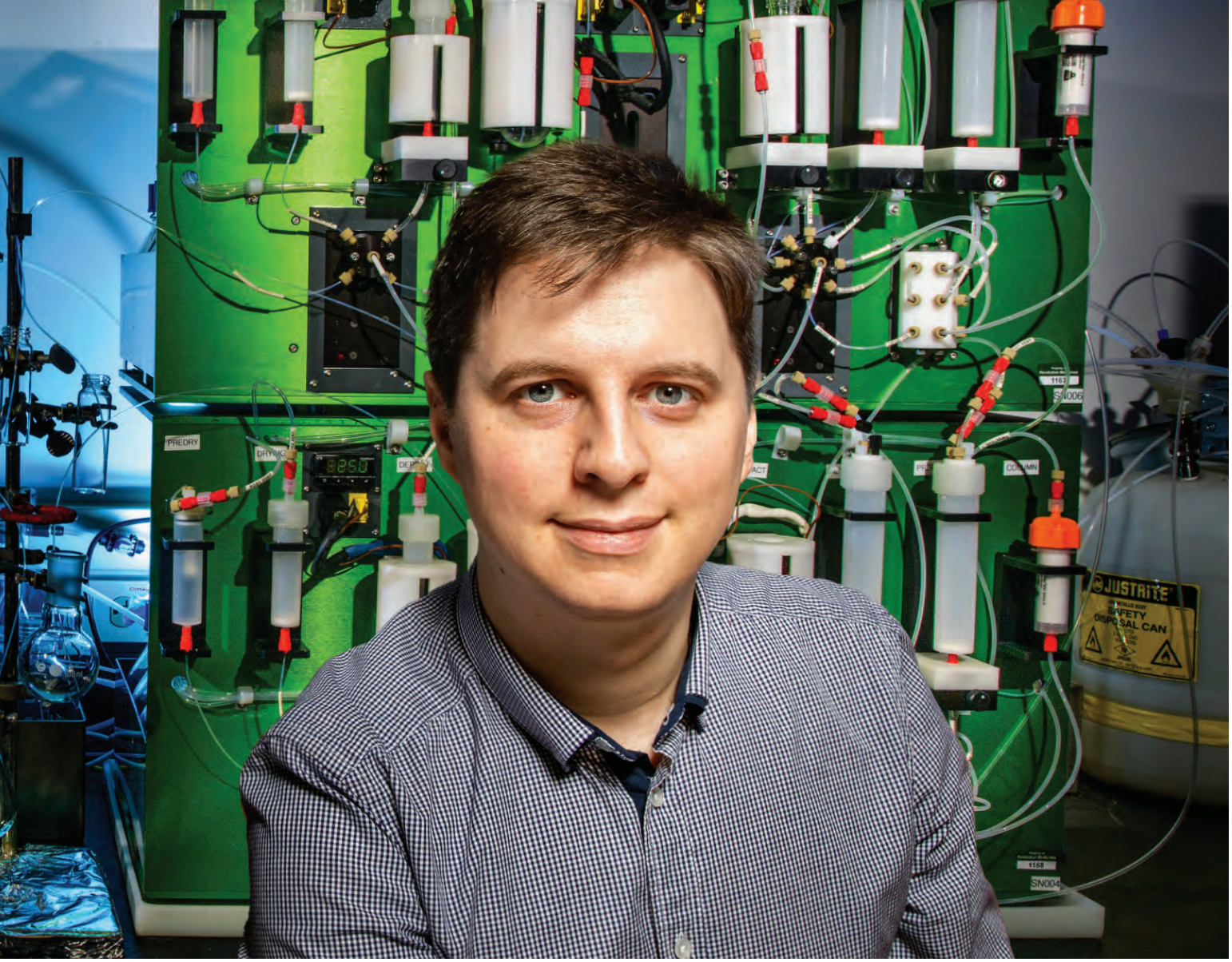
New set of chemical building blocks makes complex 3D molecules in a snap

RESEARCHERS AT THE UNIVERSITY OF Illinois Urbana-Champaign and collaborators at Revolution Medicines Inc. developed a new class of chemical building blocks that simply snap together to form 3D molecules with complex twists and turns, and an automated machine to assemble the blocks like a 3D printer for molecules.

This automation could allow chemists and non-chemists alike to develop new pharmaceuticals, materials, diagnostic probes, catalysts, perfumes, sweeteners and more, said study leader Martin Burke (MMG), a professor of chemistry at Illinois. The researchers reported their findings in *Nature*.

"It makes very complex 3D molecules in a very simple way," Burke said. "This has been the secret chamber that only card-carrying chemists with decades of experience can enter. This new advance blows that door wide open. Now everyone can come in and play in the sandbox, because these very complex molecules become very accessible."

For more than 15 years, Burke's group has pioneered the development of simple chemical building blocks called MIDA boronates, which snap together sequentially using one simple reaction to build small molecules. His lab and collaborators developed a molecule-making machine that automates chemical synthesis



✦ *University of Illinois chemistry professor Martin D. Burke, left, and postdoctoral researcher Daniel J. Blair developed a new class of chemical building blocks and a next-generation molecule-making machine to assemble them into complex small molecules with 3D twists and turns.*

using these building blocks. However, the MIDA blocks are largely limited to making flat, 2D molecules. The new set of building blocks, called TIDA boronates, unlock the missing third dimension, incorporating specific twists and 3D structures directly into the blocks.

"Nature is very good at making three dimensional things a very precise way," said postdoctoral researcher Daniel Blair, the first and co-corresponding author of the paper. "A lot of the molecules we use as inspiration for making many of our medicines are natural products, and those with these 3D structures tend to perform better in clinical applications. Yet until this point it has been very difficult to capture these structures within modular building blocks. The whole goal is to help more people make more molecules as simply as possible."

In addition to incorporating more function, TIDA boronate building blocks are up to 1,000 times more stable than MIDA boronate blocks in important reaction settings. They are also very stable in water, enabling simple synthesis of even more classes of chemicals under a wider array of conditions. The researchers are working to expand the library of TIDA boronate building blocks and plan to make them as widely commercially available as possible, using the success of MIDA boronates as a road map.

"One of the things we're so excited about now is we can make molecular building kits for really complex molecules. Like a plastic block kit has all the specialized pieces and you snap them together, now we can imagine kits for complex, important molecules, and make then accessible to non-chemists. I think it's a chance for us to shatter some of those barriers that have traditionally limited who gets to innovate at the molecular scale," Burke said.

NIH, NSF, the Damon-Runyon Cancer Research Foundation, the Henry Luce Foundation, the American Chemical Society Division of Organic Chemistry, and the Austrian Science Fund supported this work. ■

"This new advance blows that door wide open. Now everyone can come in and play in the sandbox, because these very complex molecules become very accessible."

Acceleration of cancer biomarker detection for point of care diagnostics

THE DETECTION AND QUANTIFICATION OF CANCER-ASSOCIATED molecular biomarkers in body fluids, or liquid biopsies, prove minimally invasive in early cancer diagnostics. Researchers at the University of Illinois Urbana-Champaign have developed an approach that accelerates the detection of cancer biomarkers in samples taken at the time and place of patient care.

> **"Our approach has a one-minute response time, which means that the patient or doctor only waits for one minute before finding out the test result."**

The study, published in *ACS Nano*, focused on the detection of a group of molecular biomarkers called microRNAs, small, single-stranded and noncoding RNAs that play important roles in gene expression and regulation. More importantly, miRNAs have been linked to certain cancer types and stages and as such, have garnered increased attention.

"Since tumor-specific mutations in miRNAs can be linked to tumor progression and metastasis, we can use miRNAs for early cancer diagnostics and therapy selection in the future," said Congnyu Che, bioengineering graduate student in the Cunningham lab and first author of the paper. "Conventional detection methods take up to several hours for the person to get the result so our motivation was to accelerate the response time and make it shorter."

Previously, the Cunningham group developed a technique to capture miRNA biomarkers, called Photonic Resonator Absorption Microscopy, that is capable of visualizing gold nanoparticles bound to target miRNAs. Using gold-only nanoparticles, it would take between 1-2 hours before the nanoparticles found their way to the biosensor. To accelerate the process, Che synthesized magnetic-plasmonic nanoparticles that incorporated iron materials that could then be attracted by a stationary magnet placed under the biosensor. The detection time was reduced to just one minute.

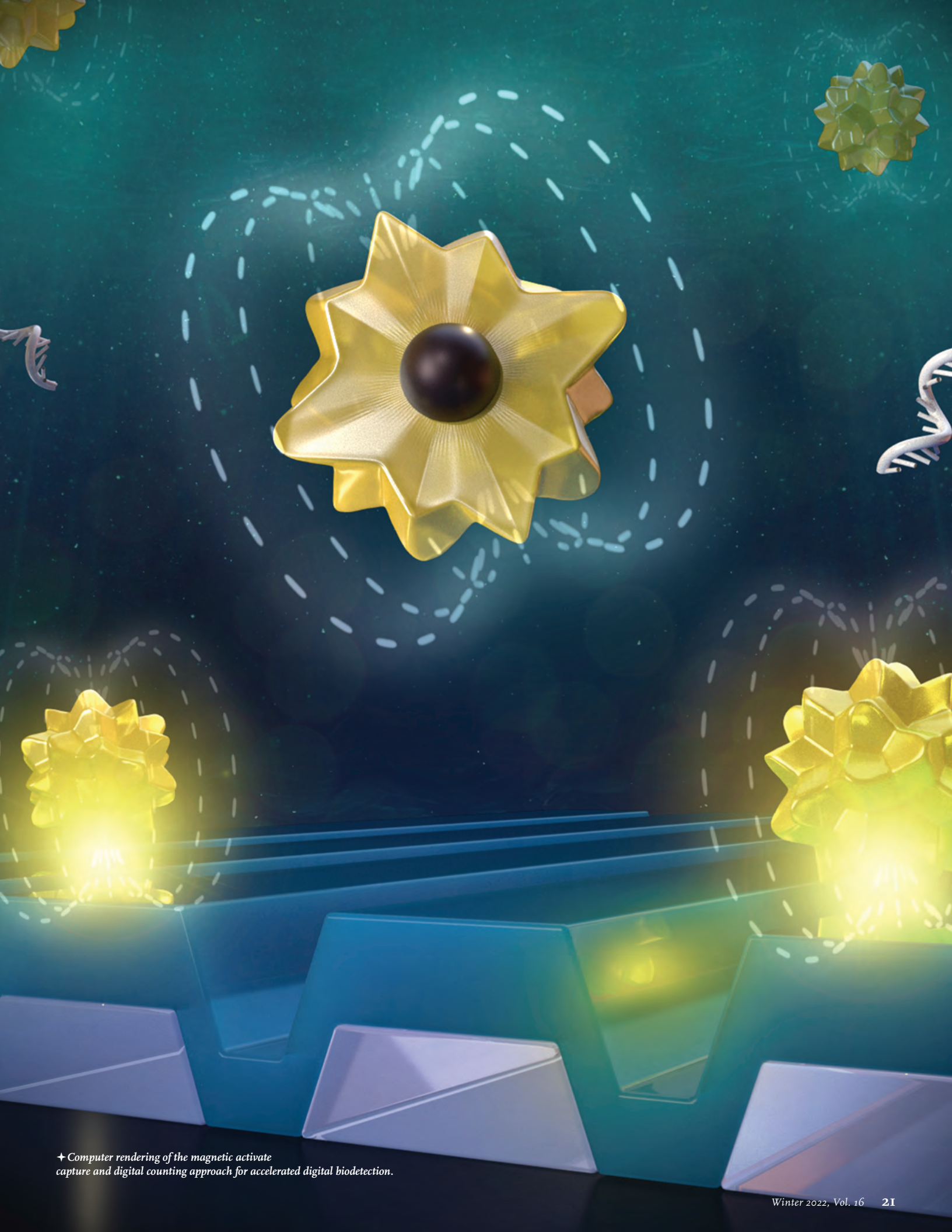
"Our approach has a one-minute response time, which means that the patient or doctor only waits for one minute before finding out the test result," said Che.

"If you have a simple, fast and sensitive test like that, it can be used for detecting cancer, monitoring cancer treatment effectiveness, and following up with treatment," said study leader Brian Cunningham (CGD Director/MMG), the Intel Alumni Endowed Chair of Electrical and Computer Engineering. "We envision this method being used in a health clinic so you wouldn't have to take a sample, send it to a lab, and wait several days."

In the study, the researchers focused on miRNAs associated with advanced prostate cancer since they have a collaboration with prostate cancer experts at the Huntsman Cancer Institute in Utah. They demonstrated a faster detection time and high selectivity when using magnetic-plasmonic nanoparticles to detect the miRNAs in human serum.

"This approach provides much more rapid sample-to-answer analysis of miRNA biomarkers that are used in cancer, nutrition, cardiac health, and maternal health diagnostics in point-of-care scenarios," said Cunningham.

This work was supported by the IGB, NIH, NSF, and the Zhejiang University ZJU-UIUC Joint Research Center. ■



✦ *Computer rendering of the magnetic activate capture and digital counting approach for accelerated digital biodetection.*

Study ties present-day Native American tribe to ancestors in San Francisco Bay Area

A GENOMIC STUDY OF NATIVE PEOPLES IN THE SAN FRANCISCO Bay Area finds that eight present-day members of the Muwekma Ohlone Tribe share ancestry with 12 individuals who lived in the region several hundred to 2,000 years ago.

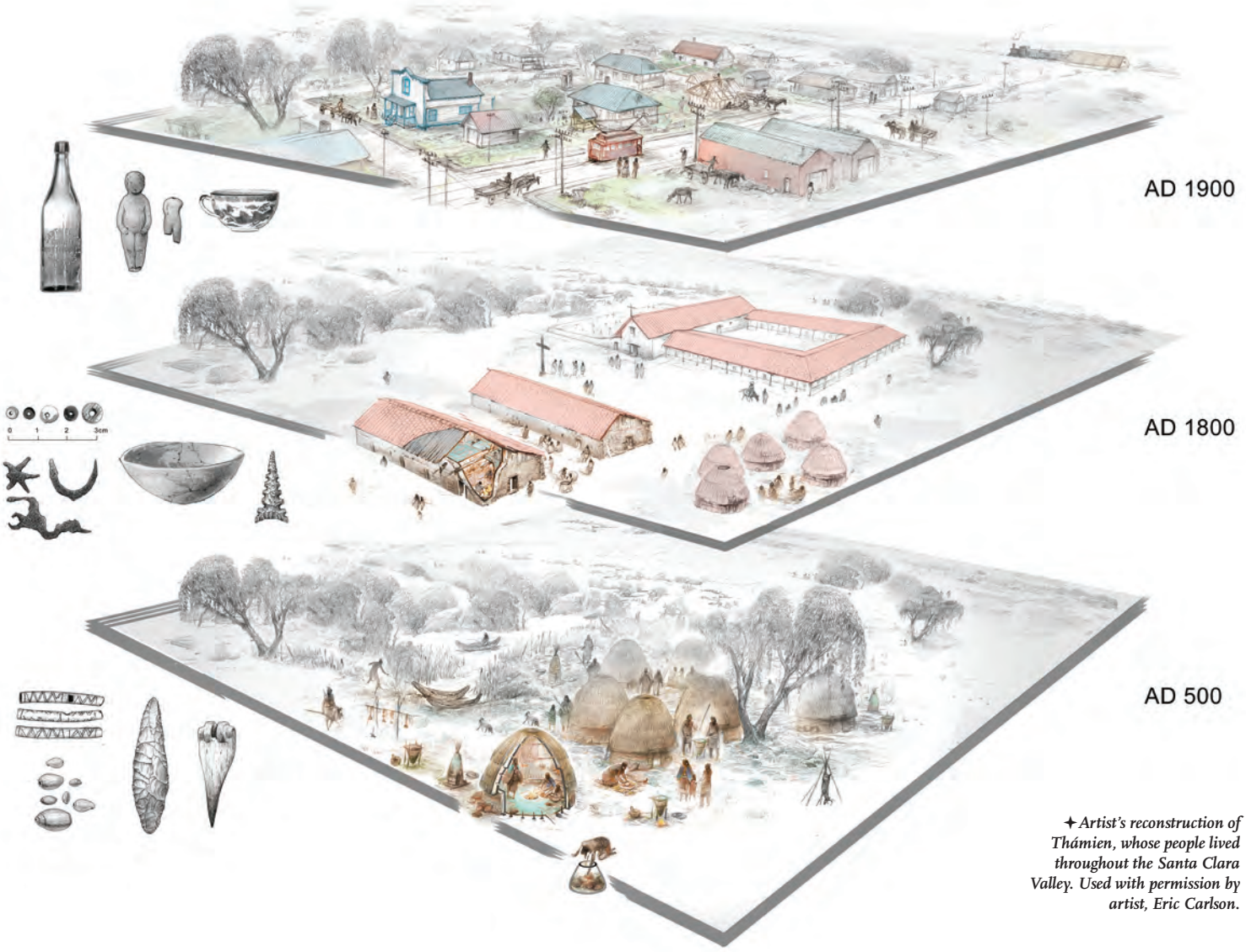
"Part of what we wanted to do is not just rely on the genomics but to have a more holistic approach of having community knowledge or traditional knowledge and genealogical information to tell the story."

Reported in the *Proceedings of the National Academy of Sciences*, the study challenges the notion that the Ohlone migrated to the area between A.D. 500-1,000, said Ripan Malhi (GNDP/GSP/IGOH), a professor of anthropology at the University of Illinois Urbana-Champaign, who led the research with Stanford University population genetics and society professor Noah Rosenberg in collaboration with a team of other scientists and members of the Muwekma Ohlone Tribe. The Muwekma Ohlone Tribal Council requested, contributed to, and oversaw the study.

Previous studies of artifacts and language patterns suggested that the Ohlone were relative newcomers to the region. But the genomic research found a deep signal of continuity between the ancient population and the new one, the team reported.

"We analyzed a large number of ancestral remains for DNA preservation and focused on those with the best DNA preservation for this study," Malhi said. "We also worked with the Ohlone to sample saliva from present-day community members so we could compare the DNA from both groups."

The ancestral individuals belonged to two villages near San Francisco Bay, one that persisted from about 490 B.C. to A.D. 1775, and the other that dated to A.D. 1345-1839. At the request of the Muwekma Ohlone Tribal Council, the Far Western Anthropological Research Group excavated both sites prior to large-scale infrastructure construction. Muwekma tribal members partici-



✦ *Artist's reconstruction of Thámien, whose people lived throughout the Santa Clara Valley. Used with permission by artist, Eric Carlson.*

pated in all aspects of the fieldwork and were the primary excavators of all burials.

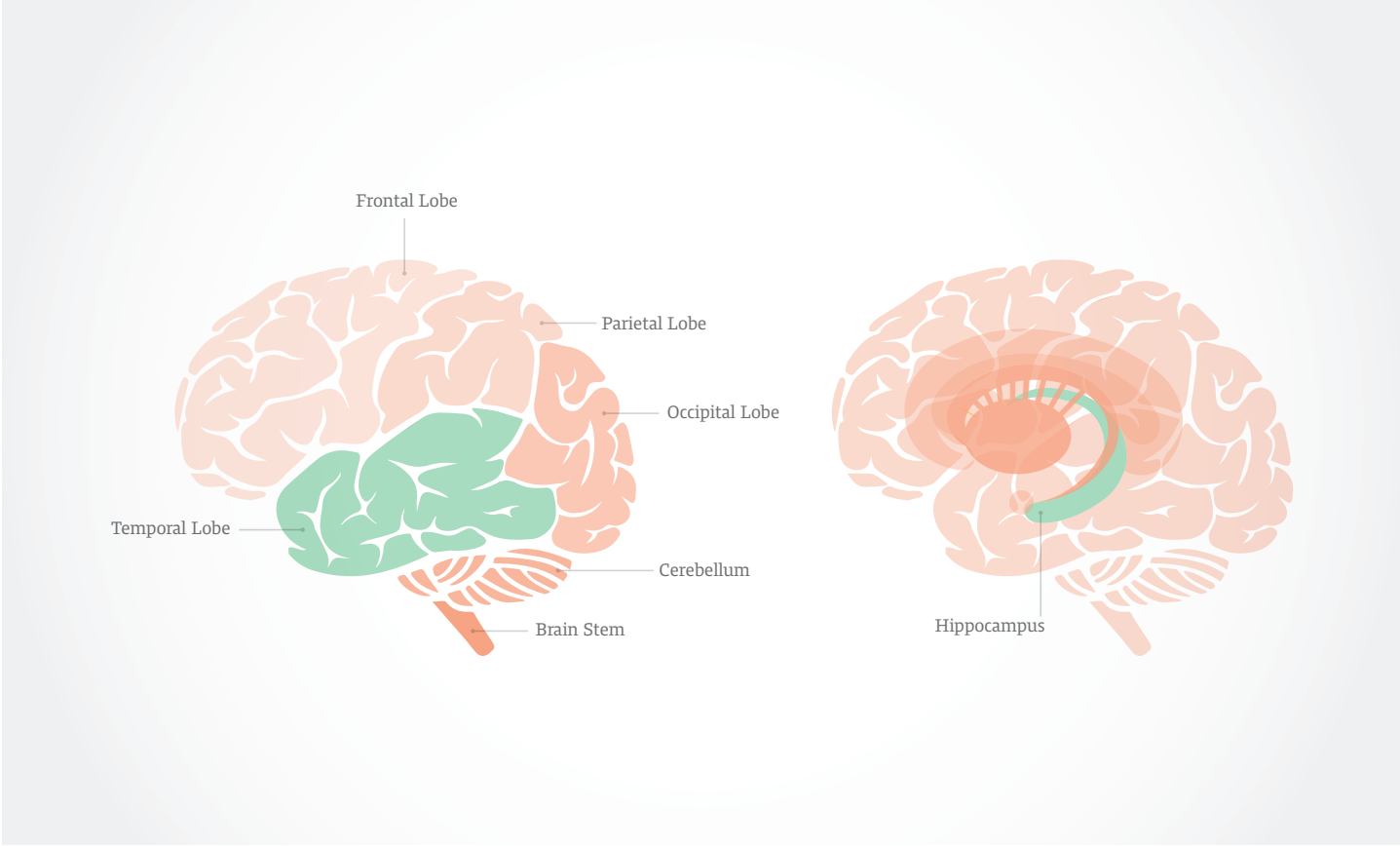
"Part of what we wanted to do is not just rely on the genomics but to have a more holistic approach of having community knowledge or traditional knowledge and genealogical information—along with all the archaeological documentation—to tell the story," Malhi said.

Present-day enrolled members of the Muwekma Ohlone Tribe are directly descended from Native Americans who in the late 18th century through the mid-19th century were incorporated into the three Bay Area missions: San Francisco, Santa Clara and San Jose, the researchers reported. However, European contact disrupted the existing communities. These upheavals led to population losses among the Muwekma Ohlone and other Native tribes, and admixture with Europeans. But a signature of the tribe's ancient history remains embedded in the DNA of contemporary Ohlone community members, the researchers found.

"We were able to find one ancestral component from their genomic analysis that was shared with ancient people from the Bay Area," Rosenberg said. "The Ohlone living today who participated in the study may not be direct descendants of the ancient people whose genomes we sequenced, but the analysis suggests they descended from the broader population to which those ancient people belonged."

The NSF, San Francisco Public Utilities Commission, and Far Western Anthropological Research Group supported this research. ■

✦ *Anthropology professor Ripan Malhi*



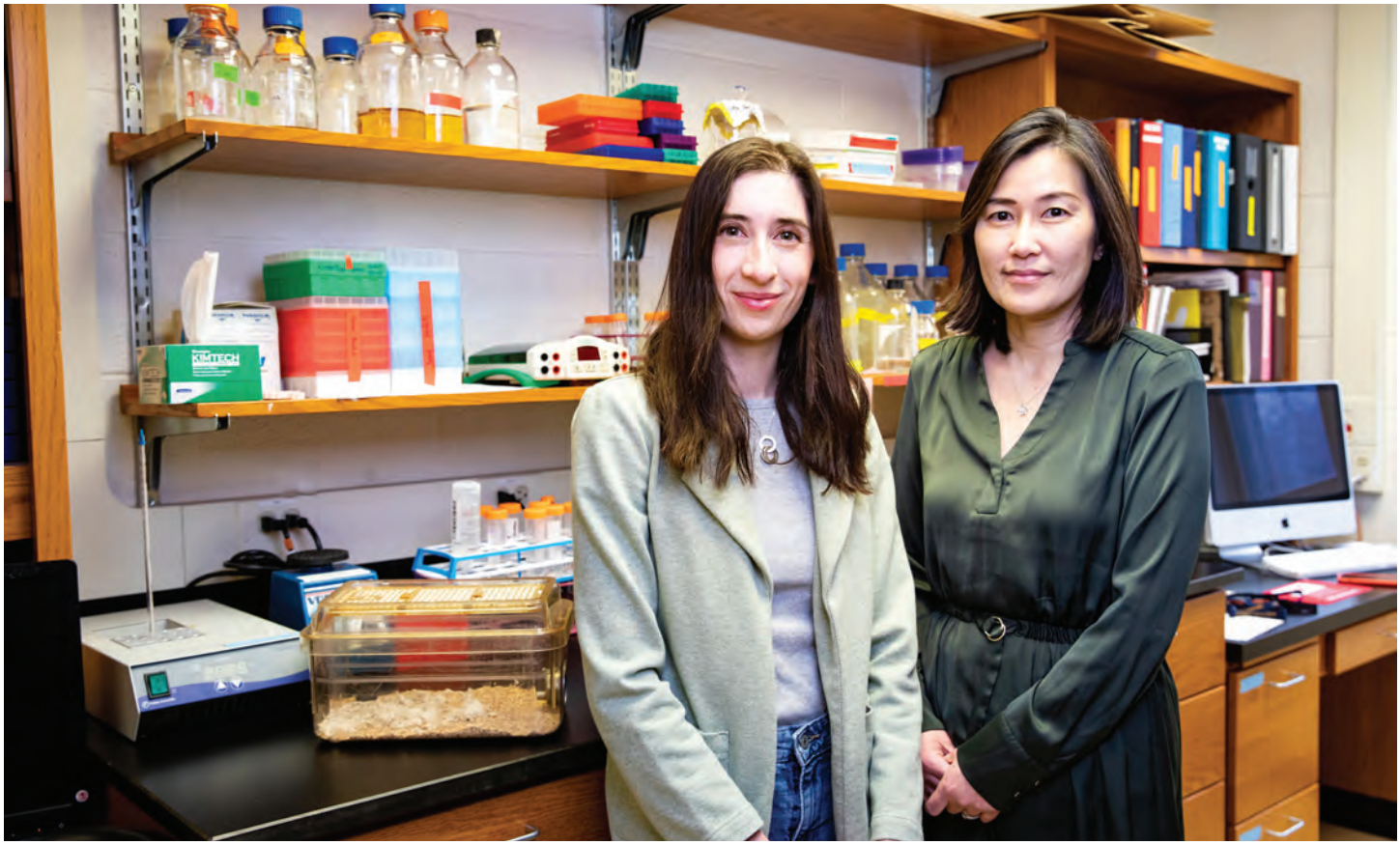
Team identifies compound with potent antiseizure effects

RESEARCHERS STUDYING EPILEPTIC seizures of the temporal lobe—the most common type of epilepsy—discovered a compound that reduces seizures in the hippocampus, a brain region where many such seizures originate. The compound, known as TC-2153, lessened the severity of seizures in mice. The scientists report their findings in the journal *Epilepsia*.

"We found that TC-2153 ultimately reduces seizure severity in mice by decreasing the activity of hippocampal neurons," said Jennifer Walters, a graduate student who led the research with molecular and integrative physiology professor Hee Jung Chung (M-CELS).

"In most temporal lobe epilepsy, the seizures start in the medial temporal lobe, which includes the hippocampus," Chung said. "And 60% or more of patients who have medial temporal lobe epilepsy develop drug-resistant seizures, which correlate with the extent of neuronal death and inflammation in the hippocampus."

The hippocampus plays a central role in learning and memory, so anything that damages it can have devastating consequences for the individual, Chung said.



✦ *Doctoral candidate Jennifer Walters, left, and molecular and integrative physiology professor Hee Jung Chung discovered that TC-2153, an inhibitor of a brain-specific protein known as STEP, reduces seizures that originate in the hippocampus in mice.*

"And 60% or more of patients who have medial temporal lobe epilepsy develop drug-resistant seizures, which correlate with the extent of neuronal death and inflammation in the hippocampus."

The strength of synaptic communication between neurons and the excitability of individual neurons can affect the likelihood that seizures occur.

The finding that TC-2153 lessened the occurrence of seizures was a surprise, according to the researchers, because it is known primarily as an inhibitor of a brain-specific protein called STEP that reduces the strength of synaptic communication between neurons.

"We hypothesized that seizure activity would increase when we used TC-2153 because STEP inhibition would increase synaptic communication," Walters said. "But we found that it actually reduced seizure severity in both male and female mice."

The female mice responded more to treatment with the compound than the males did. To determine whether TC-2153 interacted with sex hormones, the team repeated the experiment in female mice that had their ovaries removed.

"That completely abolished the effect from the TC-2153," Walters said. "Therefore, female sex hormones play a role in its efficacy." This finding may be relevant to sex differences seen in temporal lobe epilepsy, she said.

Follow-up experiments in mouse brains and in neuronal culture revealed a possible mechanism by which TC-2153 decreases seizure severity. The team found that the compound reduced the excitability of individual neurons, suggesting a novel function of STEP, Chung said. Further studies will explore how TC-2153 works and will test its effects in human neurons, the researchers said.

The NIH, University of Illinois Urbana-Champaign Campus Research Board, and Carle Illinois Collaborative supported this research. ■

An NSF Expedition in Computing: Mind *in vitro*—Computing with Living Neurons

NSF AWARDED A 7-YEAR, $15 MILLION PROJECT to a multi-university team led by the University of Illinois Urbana-Champaign. The resulting ground-breaking and path-finding research, entitled "Mind *in vitro*—Computing with Living Neurons," will imagine computers and robots that are human designed, but living.

> **"In this expedition we imagine computers and robots that are human designed, but living. That can be programmed, but whose behaviors are not specified—and instead, emerge. These systems will grow, heal, learn and explore. They will open a new space of possibilities yet to be imagined."**

The project is supported by the NSF Expeditions in Computing program, which was created more than a decade ago by the Foundation's Directorate for Computer and Information Science and Engineering to build off past successes and afford its research community new, ambitious opportunities to pursue.

This Expedition—just one of two to be awarded this year—will seek answers to a host of new and fundamental questions: Can computing systems be built out of living neurons? Can they achieve basic hallmarks of cognition such as learning, attention, curiosity or creativity, so pervasive in biology yet elusive in modern computing? How do we design and fabricate the envisioned 'wetware'? How do we understand its language? How do we think of software in terms of emergence rather than prescribed logic?

The resulting technology will have profound, lasting impact in virtually every field related to information processing, robotics, health and medicine, with deep ramification, across human knowledge. It also has the potential to revolutionize neuroscience, with radically new behavioral models.

"In this expedition we imagine computers and robots that are human designed, but living. That can be programmed, but whose behaviors are not specified—and instead, emerge. These systems will grow, heal, learn and explore. They will open a new space of possibilities yet to be imagined," said Mattia Gazzola (M-CELS), Mind *in vitro* co-director and a professor of mechanical science and engineering.

In addition to Gazzola, the project features co-directors Nancy M. Amato, the Department Head of Computer Science; and Taher Saif (M-CELS/RBTE), a professor of mechanical science and engineering.

Their work will unfold across four thrusts, structured around what makes a system compute and act: wetware will integrate neural cultures on an engineered platform that provides input/output interfaces, architecture will create a programmable substrate to support useful computations, programming will develop a software stack and a programming model to configure and run the substrate, and robotic embodiment will demonstrate multi-sensory processing and probe the emergence of rudimentary cognitive traits in motile biological robots.

Excitement around this project will be leveraged to initiate and grow a Mind *in vitro* community, through internships, workshops, seminars, and a dedicated mini-curriculum. Art-of-Science exhibitions in massive public spaces will allow them to connect with a broad and diverse audience. Finally, full commitment to open science is core, and protocols, software, hardware, and educational material will all be made freely available.

"Both of the 2022 awards support efforts that envision future materials for computing systems in a post- Moore's law era and that map out comprehensive research from the materials themselves to the higher- level application opportunities and societal benefits that can emerge from them," said NSF Assistant Director for Computer and Information Science and Engineering Margaret Martonosi. ■

✦*The expedition aims to design programmable substrates.*

Researchers Develop Powerful Strategy for Creating New-to-Nature Enzymes

A TEAM OF RESEARCHERS HAS DEVELOPED A SIMPLE YET POWERFUL strategy for creating new enzymes with novel reactivity that can produce valuable chemical compounds, building on their previous work using light to repurpose naturally occurring enzymes.

> **"The findings offer practical applications to develop biofuels and biochemicals from crops like miscanthus, sorghum, and energycane instead of petroleum."**

The study, published in *Nature Catalysis*, was led by Xiaoqiang Huang, a former postdoctoral researcher, who carried out this work in the laboratory of Huimin Zhao (BSD/GSE leader/CABBI/CGD/MMG), a professor of chemical and biomolecular engineering.

In the study, visible light was used to excite an engineered ketoreductase enzyme, enabling a new-to-nature biocatalytic reaction known as an asymmetric radical conjugate addition, which is extremely difficult to achieve by chemical catalysis.

Catalysts are substances used to speed up chemical reactions. In living organisms, protein molecules called enzymes catalyze reactions in a process called biocatalysis. Scientists have begun using biocatalysis to synthesize valuable compounds, as its high selectivity allows them to deploy enzymes to act on specific substrates and create target products. Another advantage is that enzymatic reactions are highly sustainable. They are relatively inexpensive, consume low levels of energy, and do minimal damage to the environment—as opposed to chemical catalysts, which typically require organic solvents, heat, and high pressure to function.

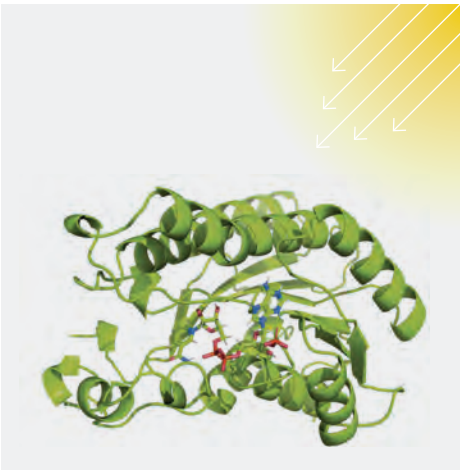
Still, enzymes are complicated to work with. They are normally limited to catalyzing reactions found in nature, meaning scientists often struggle to track down the perfect biocatalyst to meet their needs. Zhao's lab has focused on steering biocatalysis with visible light, a process known as "photobiocatalysis," to produce new enzyme reactivity. In a previous study, Zhao

and Huang developed a visible light-induced reaction using an enzyme named ene-reductase as a biocatalyst to produce high yields of valuable chiral carbonyl compounds, which have potential applications for production of high value chemicals.

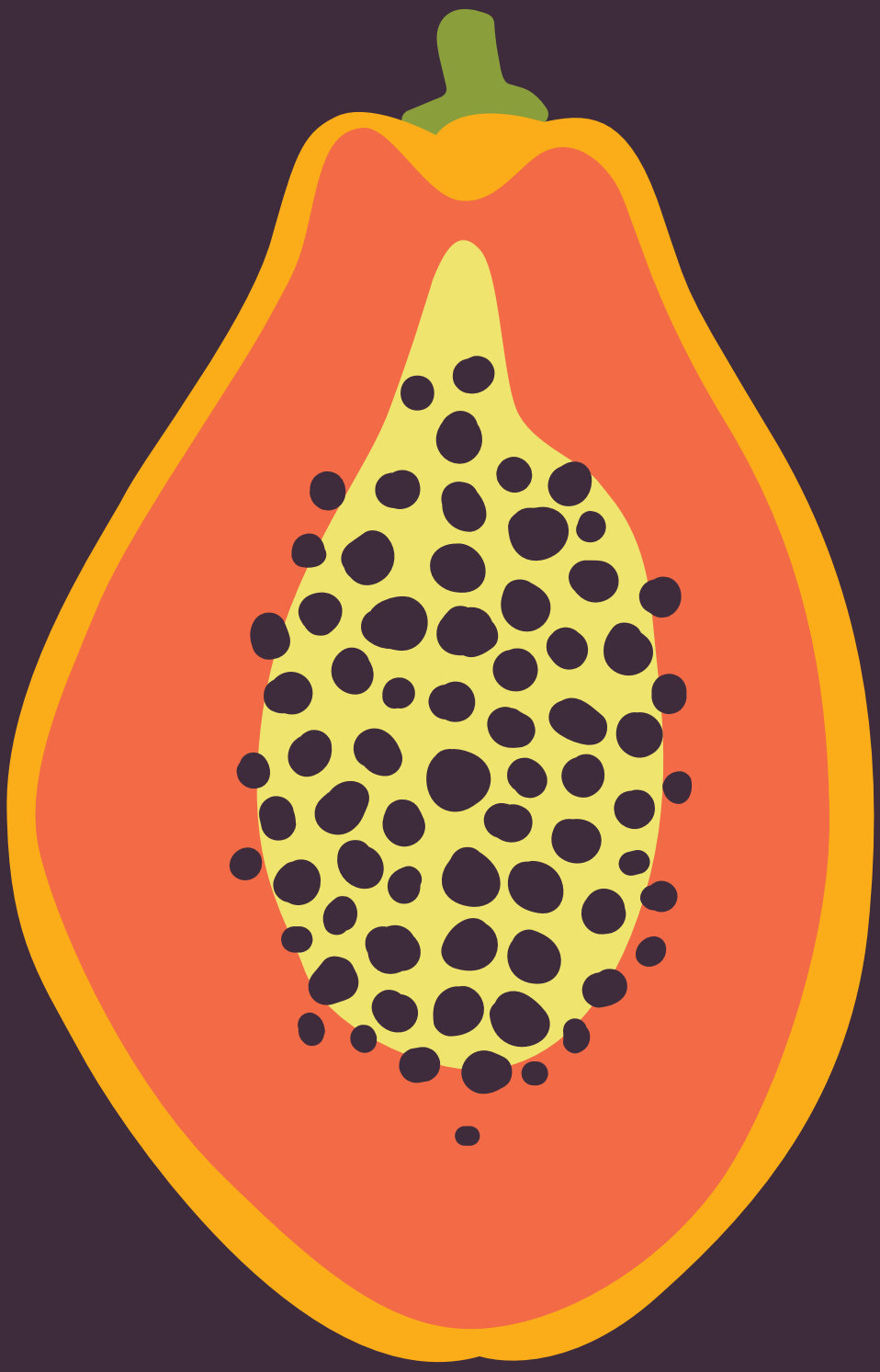
The new study builds on that work, using photobiocatalysis on a different enzyme family—nicotamide-dependent ketoreductases produced by bacteria—and a different chemical mechanism to produce another type of chiral carbonyl compounds known as α-chiral esters. Through the illumination and evolution of ketoreductase, the team achieved an enantioselective biocatalytic Giese-type radical conjugate addition to transform fatty acids to α-chiral esters, Zhao said.

The findings offer practical applications to develop biofuels and biochemicals from crops like miscanthus, sorghum, and energycane instead of petroleum. The new biocatalytic transformation could use the fatty acids from those plants as starting materials to synthesize value-added bioproducts—such as ingredients for soaps or skin-care products—in an environmentally friendly way.

"Although we did not target a specific product for further application, this work provides a practical new method that could be potentially applied to upgrading fatty acids," Zhao said. "Enzymes are the workhorses for biological synthesis of fuels and chemicals from renewable biomass. ■



✦ *Engineered photobiocatalytic enzymes*



Understanding the genomic modifications in transgenic papaya

THE TRANSGENIC PAPAYA "SUNUP" was developed in the 1990s and was widely publicized because of its ability to resist the papaya ringspot virus. Although researchers from the Ming group had identified the genomic sequence of SunUp by 2008, it was unclear where the transgenic insertions were and what effect they had. A new study, published in *Nature Genetics*, has now identified these changes and how they influence the transgenic plants.

Papaya originated and was domesticated in southern Mexico and Central America, and is now cultivated in tropical and subtropical regions worldwide. Wild papaya has small seedy fruits with very little edible flesh, while the domesticated version can weigh more than five pounds. However, there was one major problem: Papaya was susceptible to the papaya ringspot virus, resulting in stunted plants that do not produce mature fruit, and there is no resistance in the papaya genetic code.

To counter this problem, researchers developed the transgenic papaya SunUp, by using a technique called particle bombardment-mediated transformation. Gold particles were covered with the coat protein gene of the virus and shot into the cells of the non-transgenic papaya "Sunset" using a gene gun. SunUp therefore contained gene sequences of the virus, and was protected from infection via RNA-mediated gene silencing.

"It took us 8 years to read each DNA nucleotide in the insertions and rearrangements, and we repeated the sequencing using different technologies to understand the nature of these transgenic insertions," said Ray Ming (GEGC), a professor of plant biology. "The insertion was so complex that although we sequenced the genome in 2008, we didn't know where the transgenic sequences were located."

In earlier studies, the researchers used Sanger DNA sequencing technology that read short stretches of DNA, 500 to 600 bases, making it difficult to accurately place the transgenic sequences in the draft genome. In the current study, they used sequencing technologies from Pacific Biosciences and Oxford Nanopore technologies to read very long stretches of DNA.

The group discovered that SunUp had an insertion of 1.6 million base pairs, which consisted of DNA fragments not only from the gene gun, but also nuclear DNA sequences originating from chloroplasts and mitochondria. Surprisingly, even though there is such a large insertion, the transgenic manipulation did not cause any change in gene expression.

"Since transgenic papaya has such a strong resistance to papaya ringspot virus and thus saved the Hawaiian papaya industry, it was the poster child for transgenic crops. Transgenic papaya was approved by several countries that rejected other such crops," Ming said. "This work will strengthen the message that even after three decades, we can still consume transgenic papaya safely and there is no negative effect on the papaya genome or the consumers."

The work was supported by the US NSF Plant Genome Research Program Award, National Natural Science Foundation of China, Natural Science Foundation of Fujian Province, and the Science and Technology Innovation Fund of Fujian Agriculture and Forestry University. ■

> **"It took us 8 years to read each DNA nucleotide in the insertions and rearrangements, and we repeated the sequencing using different technologies to understand the nature of these transgenic insertions."**

✦From left to right: Dessireé Zerpa-Catanho, Xiaodan Zhang, and Ray Ming studied the genomes of papayas to better understand their domestication history.

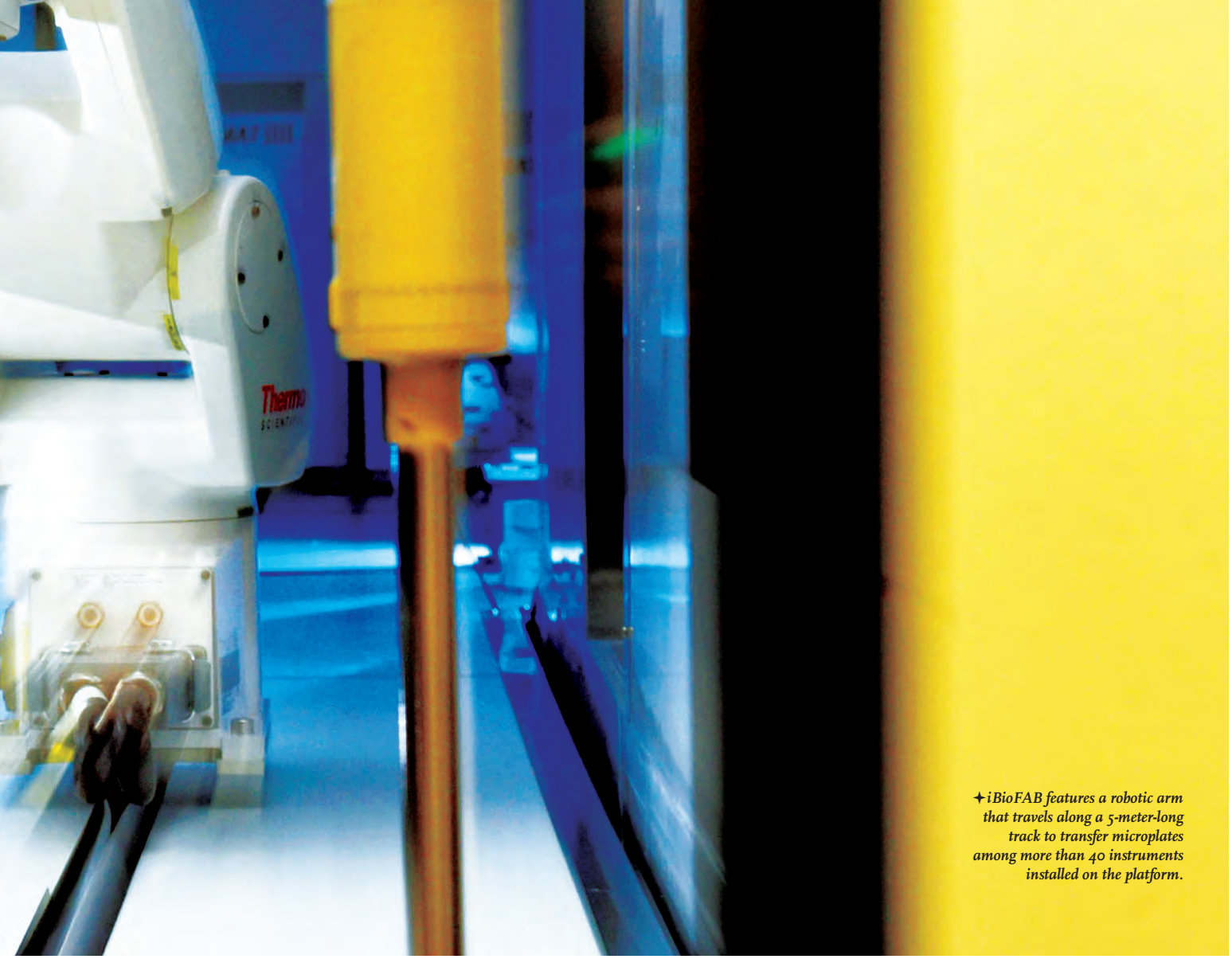
CABBI Team Develops Automated Platform for Plasmid Production

PLASMIDS ARE SMALL, CIRCULAR DNA molecules used by scientists to introduce new genes into a target organism. Well known for their applications in the production of therapeutic proteins like insulin, plasmids are broadly used in the large-scale production of many bioproducts. However, designing and constructing plasmids remains one of the most time-consuming and labor-intensive steps in biology research.

To address this, Behnam Enghiad, Pu Xue, and other University of Illinois Urbana-Champaign researchers at the Center for Advanced Bioenergy and Bioproducts Innovation have developed an automated platform for plasmid design and construction called PlasmidMaker. Their work was recently published in *Nature Communications*.

Creating a plasmid starts with design. To aid in this process, PlasmidMaker has a user-friendly web interface with which researchers can intuitively visualize and assemble the perfect plasmid for their needs.

Once the plasmid has been designed, it is submitted to the PlasmidMaker team, and an order for the plasmid is placed at the Illinois Biological Foundry for Advanced Biomanufacturing, where the plasmid will be built. iBioFAB, located at the IGB, is a fully integrated computational and physical infrastructure that supports



✦ *iBioFAB features a robotic arm that travels along a 5-meter-long track to transfer microplates among more than 40 instruments installed on the platform.*

rapid fabrication, quality control, and analysis of genetic constructs. It features a central robotic arm that transfers labware between instruments that perform distinct operations like pipetting, incubation, or thermocycling.

The plasmid build process is automated: samples are prepared through polymerase chain reaction and purified, the DNA sequence is assembled and transformed, and the plasmids are confirmed and frozen, all with little human involvement.

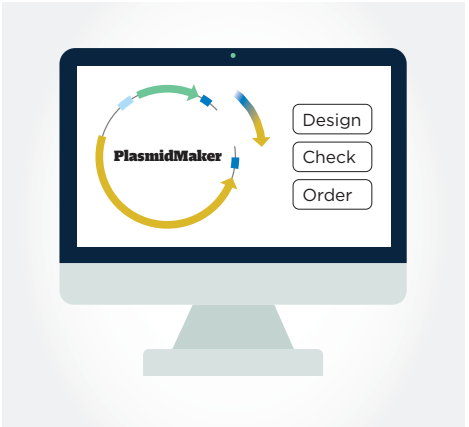
In addition to the automation and precision afforded by iBioFAB, the PlasmidMaker platform also pioneers a highly flexible method for assembling multiple DNA fragments into a plasmid using *Pyrococcus furiosus* Argonaute (PfAgo)-based artificial restriction enzymes.

Restriction enzymes have long been used in plasmid construction, as they can cleave DNA molecules at specific sequences of bases, called recognition sequences. However, these recognition sequences are usually short, making them hard to work with. A short sequence is likely to occur multiple times in a DNA molecule, in which case the restriction enzyme would make too many cuts.

"In previous DNA assembly methods, it would often be hard to find the right restriction enzymes that can cut the plasmid and replace the DNA fragments," said Huimin Zhao (BSD/GSE leader/CABBI/CGD/MMG), co-author and the Steven L. Miller Chair of Chemical and Biomolecular Engineering at Illinois. "The PfAgo-based AREs offer greater flexibility and precision, as they can be programmed to seek out longer recognition sequences at virtually any site."

The team members at CABBI, one of four U.S. Department of Energy-funded Bioenergy Research Centers across the US, hope that PlasmidMaker will accelerate the development of synthetic biology for biotechnological applications.

"This tool will be available to CABBI researchers, and we want to eventually make it available to all researchers at the other three Bioenergy Research Centers," Zhao said. "If things go well, we hope to make it available to all researchers everywhere." ■



Students selected for the 2022 Woese Research Scholar Program

ZUBIN HAVEWALA AND GARRETT MCPHERON WERE selected for the Carl R. Woese Undergraduate Research Scholar Program. They carried out research projects over a 10-week period over the summer, supported by a stipend from the IGB, with the goal of inspiring them to pursue important scientific questions.

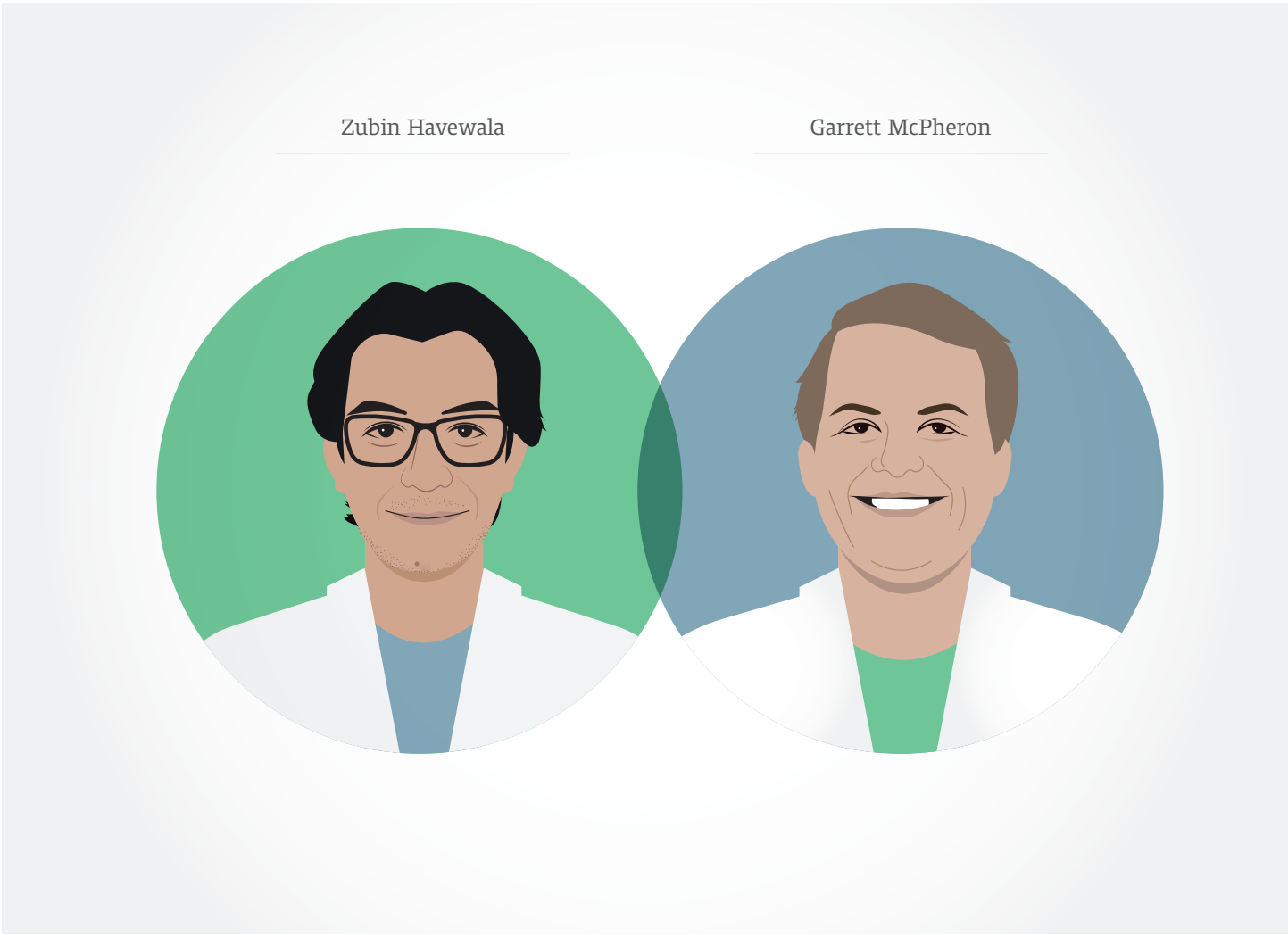
> **"I like it because it has the power to improve countless lives."**

Havewala is pursuing a degree in chemical and biomolecular engineering. In Spring 2021 he joined the Sirk lab (MME), which focuses on engineering microbes that can be used as therapeutics. These bacteria become lodged in specific regions of the body and produce antibodies. Over the past few semesters, Havewala has been working on single-chain variable fragment proteins, which are fragments that link the heavy and light chains in antibodies.

"I have always been drawn to research and I love being able to discover new things," Havewala said. "When I learned about biotechnology in high school, I immediately thought "that's what I want to do." I like it because it has the power to improve countless lives."

Over the summer, Havewala engineered two bacteria—*Lactobacillus casei* and *Corynebacterium glutamicum*—to secrete therapeutic antibody fragments. *L. casei* lives in the gut and in the human respiratory tract whereas *C. glutamicum* is not associated with either, but is commonly used in industries as a model organism. The challenge with engineering these bacteria is ensuring that they secrete the fragments at high levels, which Havewala measured.

Havewala is interested in going to graduate school, although he is unsure whether he



would like to eventually join an academic position or one in the industry. "I know that I like doing research in biotechnology and hopefully that will be my career path," he said.

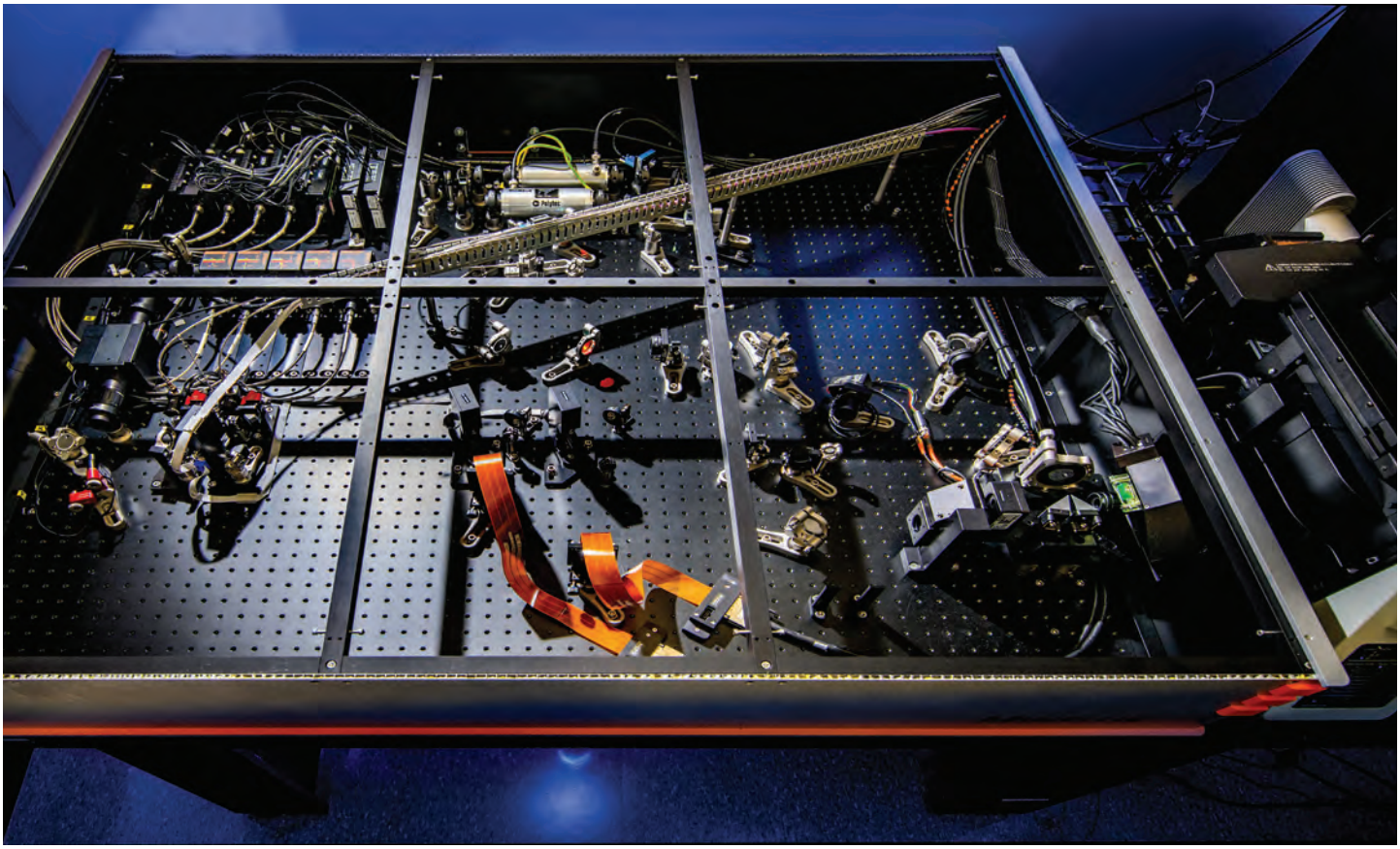
McPheron is pursuing a bioengineering degree with a specialty in cell and tissue engineering. He joined the Gaj lab (BSD) in January 2021 where he helped his graduate mentor use CRISPR to modify proteins associated with Huntington's disease, which causes a breakdown of nerve cells in the brain.

Over the summer, McPheron focused on amyotrophic lateral sclerosis, a debilitating disorder that is characterized by the loss of motor neurons in the brain and spinal cord, leading to muscle atrophy, paralysis, and death. Unfortunately, there is no cure and standard therapies do not help.

McPheron used CRISPR-Cas9 nucleases to modify the expression of SOD1, which is present in a mutated form in 20% of ALS cases. The mutant gene can cause disruptions by triggering protein misfolding, oxidative stress, inflammation, and several other cellular dysfunctions. "We are looking at how to optimize these base editors to prevent off-target effects during gene editing," McPheron said.

"I like the collaborative aspect of science. Everyone I work with loves science and I love talking to them about it and learning new ideas and skills," he added. "I can definitely see myself continuing to do research. I plan on applying in Fall 2023 and I am interested in labs that work on genetic engineering, gene therapy, tissue engineering, and regenerative medicine." ■

"I like the collaborative aspect of science. Everyone I work with loves science and I love talking to them about it and learning new ideas and skills."



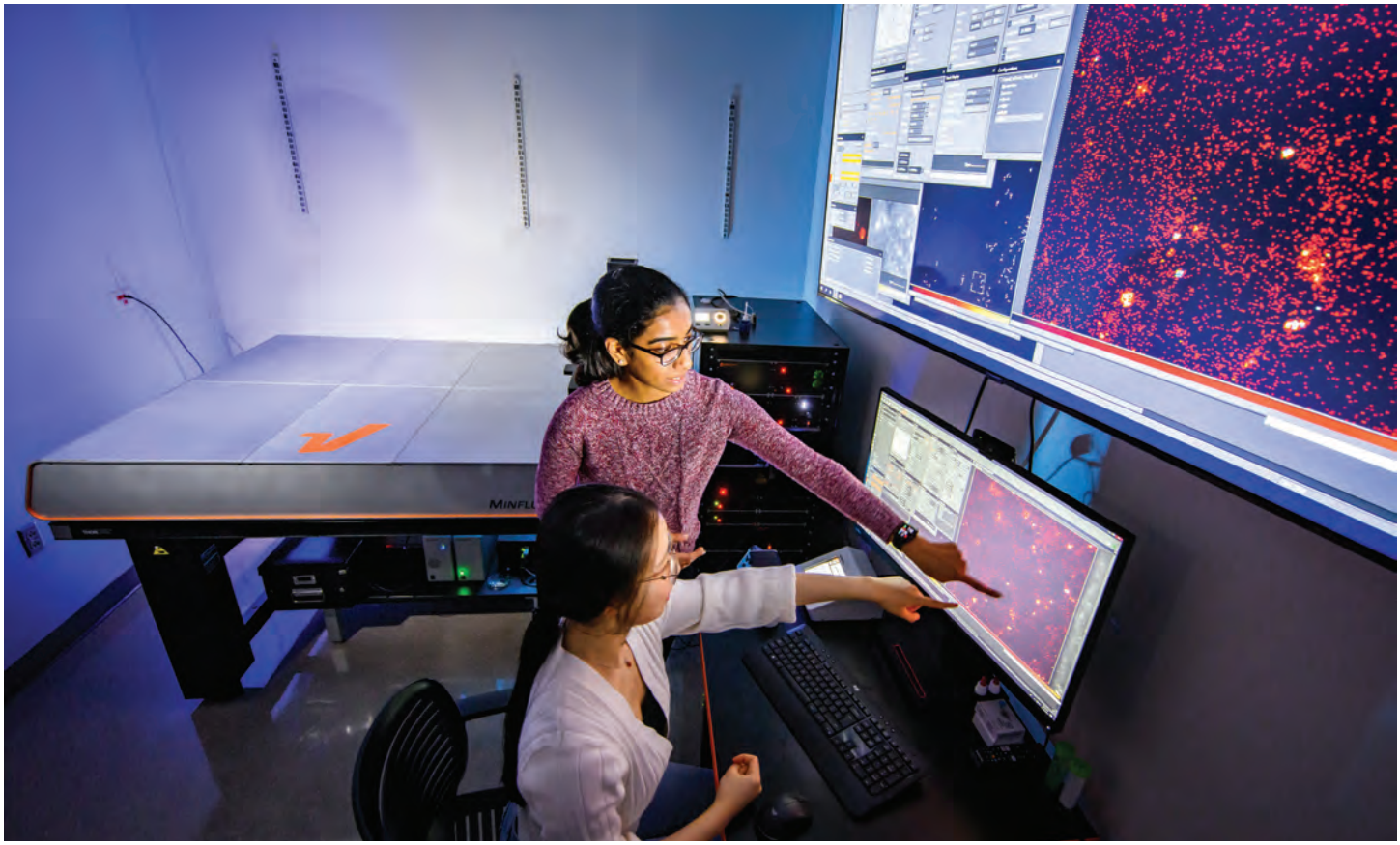
✦ *Minflux with dust covers removed to display the optical path.*

New Minflux microscope improves molecule tracking in live cells

OVER THE PAST CENTURY, OUR understanding of cells—the basic building blocks of living organisms—has progressed largely due to microscopes. The invention of fluorescence microscopy has been a primary tool in this scientific endeavor because it allows researchers to color-label specific cellular components and observe them in live cells. The new two-color 3-D Minflux microscope is a vast improvement on traditional fluorescence microscopy because, for the first time, researchers can track how two molecules can interact with each other on the size scale of the molecules themselves.

"The Minflux microscope will provide 100 times better resolution than typical confocal microscopes and ten times better resolution than many single molecule localization images," said Glenn Fried, the Director of Core Facilities at the IGB.

Developed by the Nobel Laureate Stefan Hell, the microscope can quickly detect how molecules interact with each other in a three-dimensional cellular environment. For



✦ *Hepatitis B virus being tracked by Gopika Gopan and Yuhan Wang in HepG2 human liver cells.*

> **"The Minflux microscope will provide 100 times better resolution than typical confocal microscopes and ten times better resolution than many single molecule localization images."**

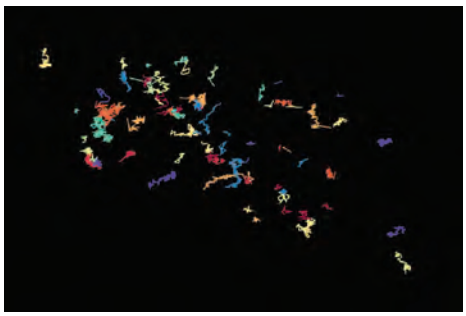
example, RNA-protein interactions can now be easily monitored by first labeling them with two different fluorescent dyes and then imaging the two structures at the same time.

The importance of this break-through technology inspired ten campus units at the University of Illinois Urbana-Champaign to band together and provide $740,000 in funds for a base 2-D Minflux microscope in 2021. The subsequent upgrade to the complete two-color 3-D Minflux system was made possible with a $604,000 fund from the Roy J. Carver Charitable Trust. The microscope will be the third of its kind in the United States, the other two being at the NIH, Maryland and Scripps Research Institute, California.

Housed in the IGB, the complete Minflux instrument will act as a regional research hub as well as a demonstration site for other users, finally moving the bar of 'single molecule' tracking to be able to look at biomolecular interactions.

"We are ideally located to become the go-to place for single particle tracking in the Midwest, while putting our biophysics and cell biology groups at the forefront of in-cell dynamics research," said Martin Gruebele, a James R. Eiszner Endowed Chair in Chemistry, who worked on the Roy J. Carver Charitable Trust grant along with Fried and Zaida Luthey-Schulten, a Murchison-Mallory Endowed Chair in Chemistry. ■

✦ *Laura Troyer from the Kim lab tracked moving RNase E in* E.coli.



Immunotherapy trials show promise for treating canine melanoma

TIMOTHY FAN (ACPP), VETERINARY ONCOLOGIST AND professor at the University of Illinois College of Veterinary Medicine and a Program Leader for the Cancer Center at Illinois, is leading two clinical trials using similar immunotherapies to treat dogs with malignant melanoma. The novel approaches, developed in partnership with cancer researchers in Boston, have yielded encouraging results in canine patients, and human trials using the same therapeutic platforms are expected to begin in 2023.

According to the American Veterinary Medical Association, almost half of dogs over the age of 10 will develop cancer. Melanoma is one of the most aggressive forms of canine cancer given its potential to spread to other parts of the body. The traditional treatment regimen consists of often-extensive surgery and multiple radiation sessions. Still, most dogs with advanced metastatic disease live only a few months after treatment.

The new immunotherapy involves a course of injections of cytokines—protein molecules that help control the immune response—that bind with collagen, a protein that surrounds and promotes the growth of cancer cells. In this way, the cytokines remain within the tumor microenvironment. K. Dane Wittrup, a biopharmaceutical engineer from the Massachusetts Institute of Technology, and his team, developed the injection formula, while Fan and his team enrolled and oversaw eligible canine patients at the University of Illinois Veterinary Teaching Hospital.

In contrast to the low survival for dogs undergoing traditional treatment for melanoma, the 13 dogs enrolled in the first trial all demonstrated measurable tumor shrinkage following treatment. Some patients achieved 100% cancer reduction, with no local recurrence or spreading of the cancer more than a year after treatment.

A second canine clinical trial is sponsored by Ankyra Therapeutics, a Boston-based biotech company co-founded by Wittrup. The new approach uses what the company calls "a novel anchored immunotherapy platform," which includes an injection of the cytokine drug attached to an inert "anchor" that results in retaining the cancer drug within the cancer cell microenvironment, triggers an immune response to attack the cancer, and avoids side effects since the drug stays in the tumor locality, preventing a full-body immune flareup.

The Ankyra clinical trial differs from the earlier trial in that it eliminates the use of radiation and uses a different cytokine, a new way to retain the cytokines within the cancer microenvironment, and a new dosage escalation scheme. To trigger the immune response, the new trial uses a new drug, named cANK-101, that Ankyra created from canine interleukin-12.

The two trials will yield a lot of information about how effective this novel treatment is and help determine the best approach for drug delivery and dosage. Findings will be evaluated to improve patient care, inform human trials, and advance knowledge of cancer biology.

"If the new treatment is effective, it could open the door for new therapies that could be widely available and transformative for veterinarians to add to the toolbox for dogs with melanoma," Fan said. "And the results of this trial can inform and guide a similar trial for people." ■

"The results of this trial can inform and guide a similar trial for people."

Researchers show potential for improved water-use efficiency in field-grown plants

WATER DEFICIT IS CURRENTLY ONE of the most significant limiting factors for global agricultural productivity, further exacerbated by global climate change according to a 2019 report from the Food and Agriculture Organization of the United Nations. As a result, researchers worldwide have been working to improve water-use efficiency in crops to better cope with water-scarce conditions.

> **"For farmers, this could decrease soil water depletion throughout the growing season and reduce reliance on irrigation."**

In a recent study published in the *Journal of Experimental Botany*, a team from the University of Illinois Urbana-Champaign, the Volcani Center , and the University of Cambridge found that by overexpressing a sugar-sensing enzyme, called hexokinase, in field-grown tobacco plants, they could improve intrinsic water-use efficiency without decreasing photosynthetic rates or biomass production.

This study demonstrates the potential to generate plants with more conservative water use throughout the growing season under field conditions and moderate water limitation, without significant yield penalty. For farmers, this could decrease soil water depletion throughout the growing season and reduce reliance on irrigation.

This work is part of Realizing Increased Photosynthetic Efficiency (RIPE), an international research project that aims to increase global food production by developing food crops that turn the sun's energy into food more efficiently with support from the Bill & Melinda Gates Foundation, Foundation for Food & Agriculture Research, and U.K. Foreign, Commonwealth & Development Office.

During photosynthesis, plants open tiny pores in their leaves, called stomata, to take in CO_2. However, when the pores are open, water is also allowed to escape through transpiration. This

✦ *Hoya plant stomata, picture taken by Grace Darby Tan (GEGC).*

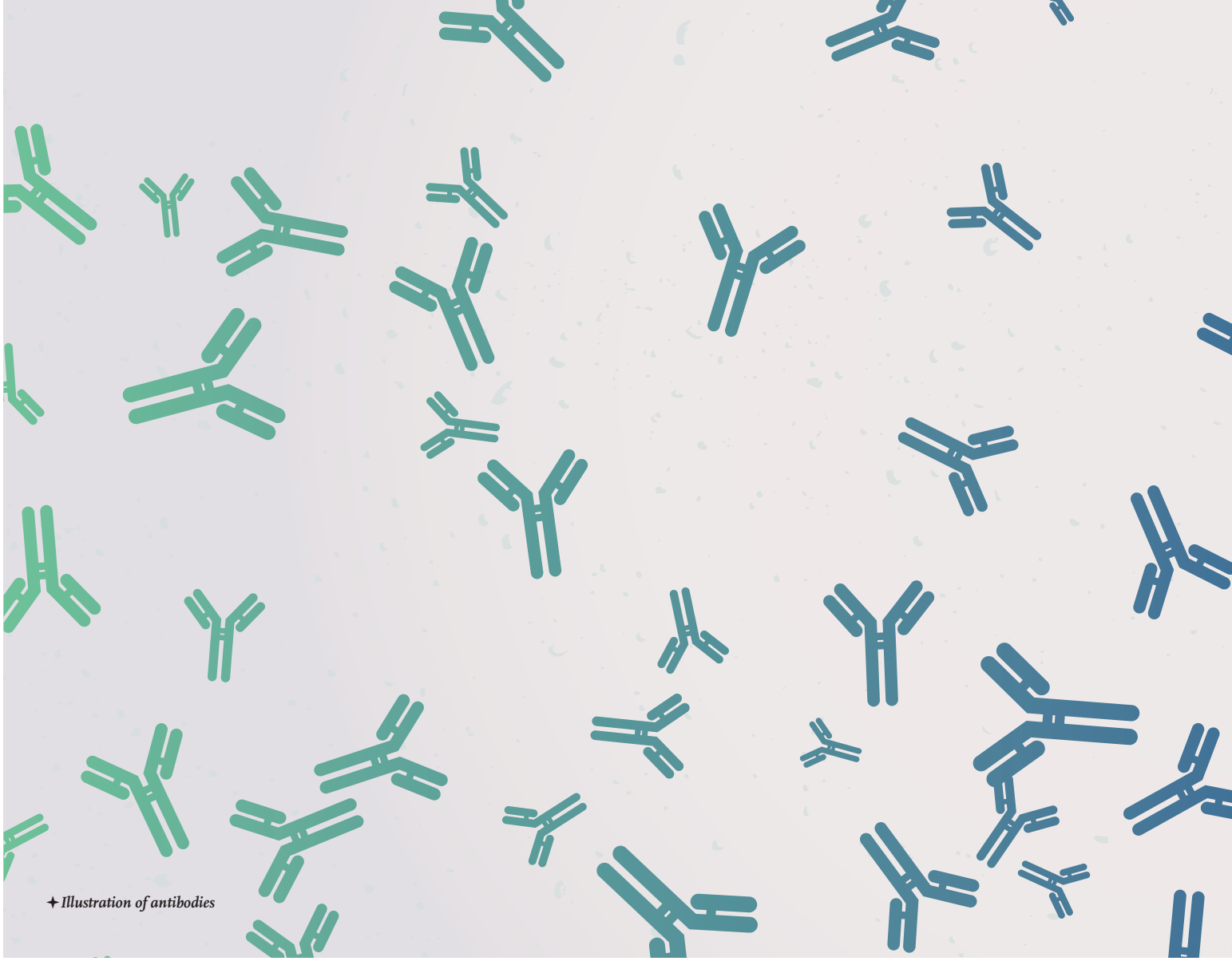
leaves plants with a trade-off between losing too much water for the sake of taking in CO_2.

"Stomatal pores consist of a pair of guard cells that control the opening and closure of the pores," said Liana Acevedo-Siaca, who led this study at Illinois during her time as a postdoctoral researcher. "Previous studies have shown that genetic manipulation of signal elements that trigger stomatal movement, such as overexpressing Arabidopsis Hexokinase 1 (AtHXK1) in the guard cells, can stimulate stomatal closure and adjust that trade-off for plants."

It was previously shown that guard-cell-targeted expression of AtHXK1 can improve WUE in crops, as well as their tolerance to drought conditions and salinity stress because hexokinase signals to the pores that there is enough sugar, eliminating the need to fix more CO_2. However, these previous studies were only evaluated in crops grown in controlled environments, such as greenhouses.

Using two homozygous transgenic lines expressing AtHXK1 and a line that had guard-cell-targeted overexpression of AtHXK1, Johannes Kromdijk, assistant professor at the University of Cambridge, compared traits in these lines to wild-type tobacco to test WUE. "Our results confirmed that constitutive overexpression AtHXK1 decreases productivity. We also showed that guard-cell-targeted overexpression of AtHXK1 could improve WUE relative to wild-type without negatively impacting CO_2 assimilation." ■

✦ *From left to right: Liana Acevedo-Siaca (Illinois), Coralie Salesse-Smith (Illinois), Emily Gibson (Cornell).*



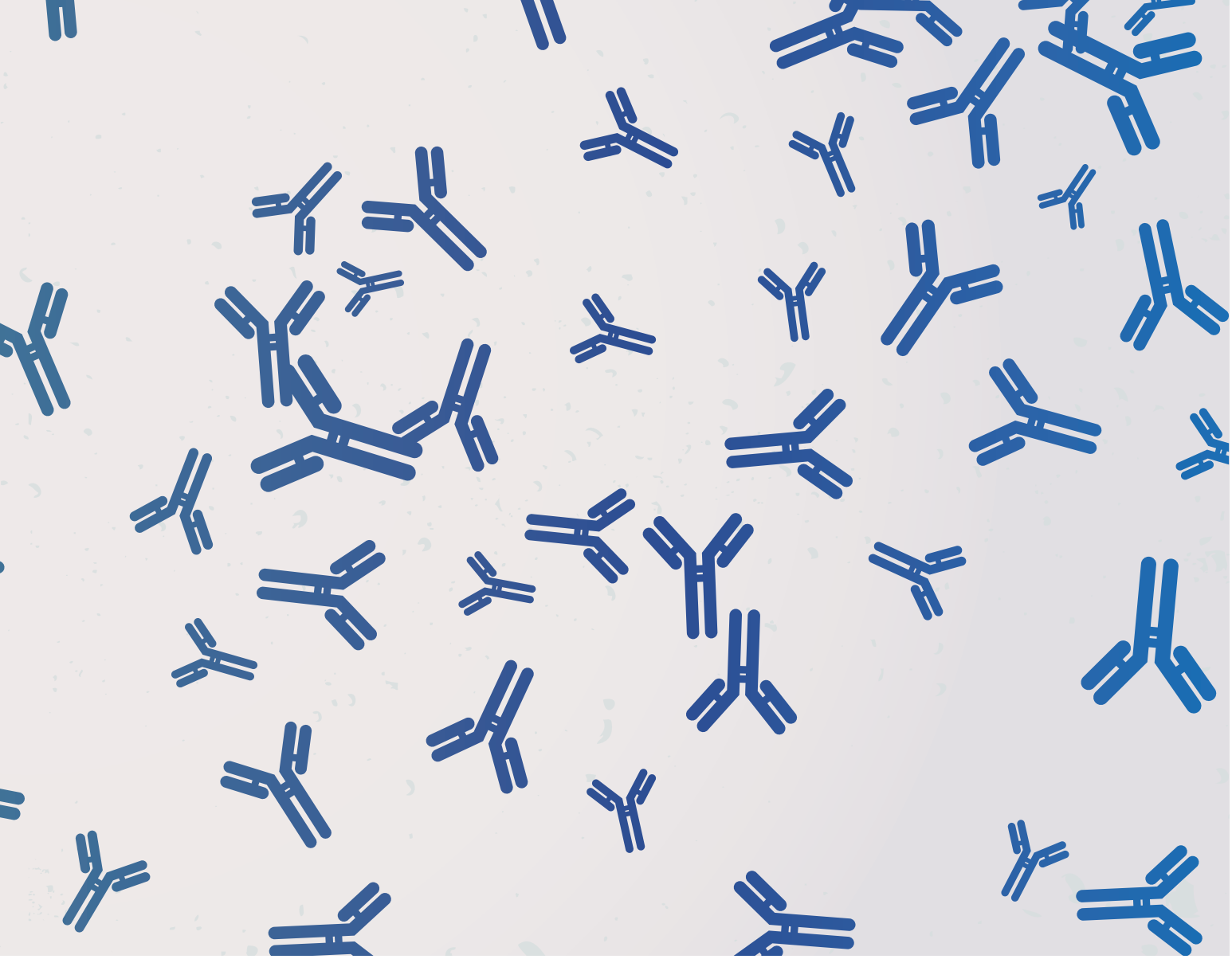
✦ *Illustration of antibodies*

Valuable antibody patents vulnerable to overly broad doctrinal shift in patent law

A NEW PAPER, CO-WRITTEN BY A University of Illinois Urbana-Champaign legal scholar who studies intellectual property protection for advanced biotechnologies, advocates for a middle ground in patent claims involving antibodies.

Antibodies constitute a $145 billion annual market—an amount projected to almost double by 2026, which renders the patents covering them among the most valuable intellectual property in the patent system. But those patents are being struck down due to a recent shift by the U.S. Court of Appeals for the Federal Circuit aimed at strengthening two areas of patent law—enablement and written description—that are ill-equipped to deal with the molecular complexity of antibodies, said Jacob S. Sherkow (GSP), a professor of law. Sherkow's co-author is Mark A. Lemley of Stanford Law School.

"Given the improvement of antibody science as well as the advancement of our understanding of just how genetically diverse antibodies are, the federal circuit's dramatic shift in the



> **"Describing a complex molecule like an antibody atom by atom would be akin to describing an F-15 fighter jet by its every nut and bolt."**

law of antibody patenting just seems like a poor fit," Sherkow said.

Describing a complex molecule like an antibody atom by atom, which is tantamount to what the federal circuit's doctrinal shift would compel those seeking patent protection to do, would be akin to "describing an F-15 fighter jet by its every nut and bolt," Sherkow said.

"Immune receptor production, for example, is a semi-random and a galactically expansive process. It produces antibodies that are startlingly different in both structure and function," he said. "All of this means there's no good way to make claims over antibodies that would satisfy the court's current tests. The science doesn't readily allow what the court is asking for."

Sherkow and Lemley said an old form of patent protection—means-plus-function claims and infringement by the equivalents—would better grant inventors effective control over true substitutes without giving them the power to block improvements by competitors.

"Means-plus-function claiming is a way of defining a new invention by the way it works, but with limits," Sherkow said. "You can make a fairly broad claim, but you only get the exact thing that you describe in your patent. So, you get to employ broad, expansive language, but you also need to describe, essentially, every way that it works, and you're only limited to that description."

The federal circuit's change in jurisprudence is a legitimate reaction to the long-standing practice of claiming antibodies in functional terms, which can lead to overbroad patents that stifle future innovation, similar to what happened in the software industry in the 1980s and 1990s. But applying the federal circuit's current reinvigorated written description and enablement requirements to antibodies and their chemical structure is a poor match with the underlying science, Sherkow said.

With hundreds of billions of dollars at stake, the implications of intellectual property protections for antibodies are likely to be revisited in the next U.S. Supreme Court term in the case Amgen Inc. v. Sanofi, Sherkow said.

Sherkow and Lemley's paper was published by the *Yale Law Journal*. ■

Helping crime laboratories become more efficient

> **"With forensic sciences being such an integral part of the work that our State Police do to provide justice for crime victims, we must do everything we can to ensure these services are being delivered timely and as professionally as they possibly can."**

SINCE MARCH, SOME OF THE MOST pressing issues of forensic science and crime in the state of Illinois have been discussed and debated at the IGB at the University of Illinois Urbana-Champaign.

That's where the Illinois Forensic Science Commission works to analyze the various issues facing state-funded forensic crime laboratories. Created by state law in August 2021 to deal, in part, with a backlog of forensic evidence processing, the IFSC is charged with overseeing the processing of evidence in laboratories such as Northeastern Illinois Regional Crime Laboratory, DuPage County Forensic Science Center, and the Illinois State Police forensic laboratory system.

"Forensic sciences are used daily in the justice system to help solve crimes including robberies, murders and other criminal activity," said State Rep. Lakesia Collins (D-Chicago). "With forensic sciences being such an integral part of the work that our State Police do to provide justice for crime victims, we must do everything we can to ensure these services are being delivered timely and as professionally as they possibly can."

The IFSC is the successor to the now former Forensics Science Task Force which consisted of many of the same members. The former task force successfully assisted the state in decreasing the backlog of DNA evidence processing in cases of sexual assault. Still, with wait times reduced to a six-month maximum, the task force voted for the creation of a permanent commission, which the General Assembly created in August 2021.

Discussions arose at IFSC about use and limitations of genetic genealogy—currently not conducted in state-funded forensic labs—to help solve some crimes. Genetic genealogy is a forensics technique that made waves in 2018 when California police used it to analyze DNA from a decades-old rape kit and arrest Joseph James DeAngelo Jr., also known as "The Golden State Killer."

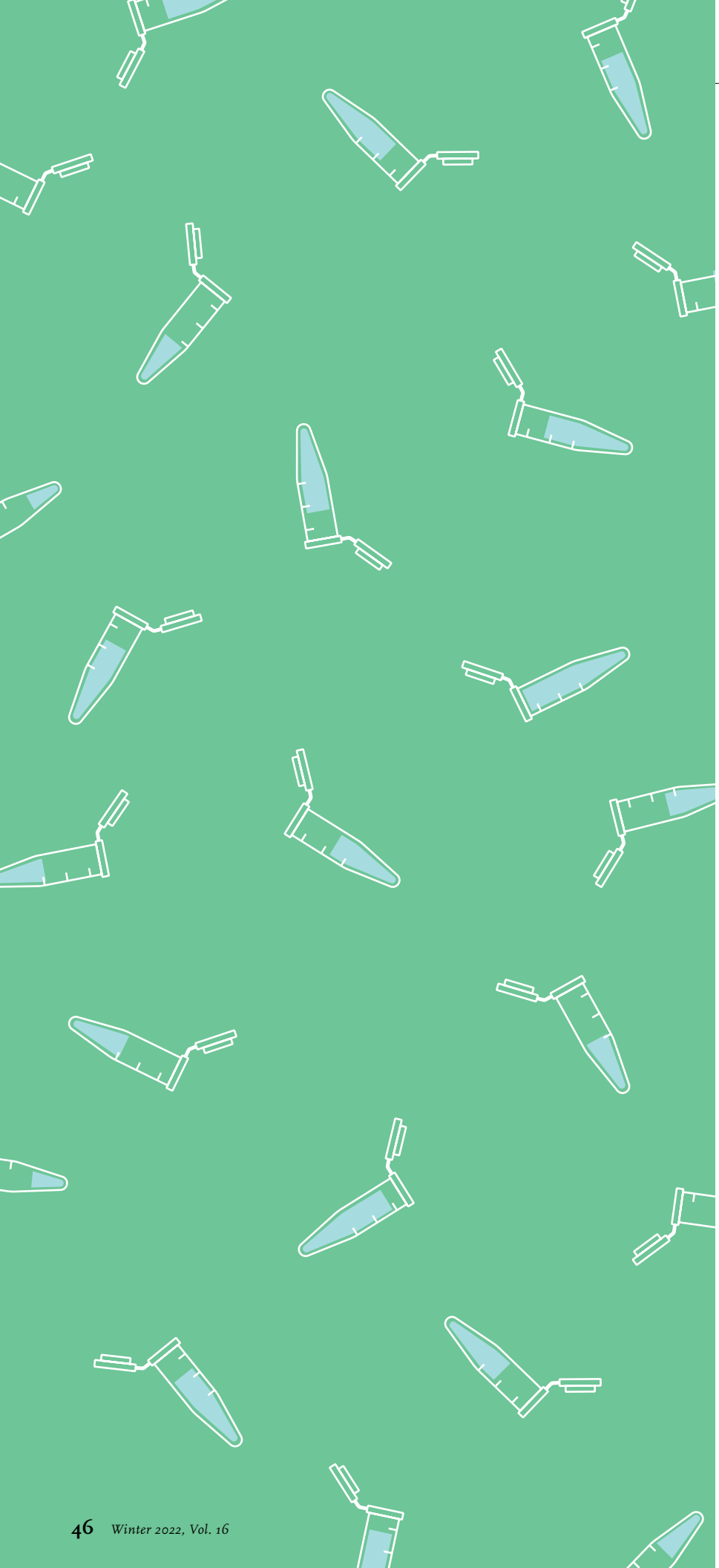
Prior to this case, genetic genealogy hadn't been employed by law enforcement. Genetic genealogy is part of a dynamic shift happening in forensic science genetics, which requires considerations beyond the DNA science into social science, including issues of privacy and data protection. For the last two decades authorities have used the Combined DNA Index System to solve crimes. CODIS uses a panel of DNA markers to individuate identity, but a matching set of DNA must be in the system, from a previous crime, to get a hit.

State labs are facing a major backlog of DNA in CODIS from sexual assault cases. Meanwhile, private labs such as Ancestry.com and FamilyTreeDNA, however, have had widespread success helping people trace their roots through a simple saliva sample.

Carrie Ward, CEO of the Illinois Coalition Against Sexual Assault, serves on the commission as a victim advocate. The state achieved its goal of reducing the forensic case backlog to six months, but Ward says the progress shouldn't end there.

"180 days is a very long time for survivors to wait for their kit to be processed," Ward said. "So, I think our goal would be to reduce that even further." ■

✦The Illinois Forensic Science Commission includes the director of Illinois State Police, law practitioners, forensic scientists, victim and other community advocates, and an academic researcher.



Reducing the carbon footprint through single-use plastics reuse

A staggering 5.5 million tons of single-use plastics are generated each year by science labs, negating 83% of the world's recycled plastics. A team at Illinois was recently awarded a $81,865 grant to reduce dependency on single-use plastics by developing protocols for plastics reuse.

The project, Single-Use Plastics Elimination and Reuse Protocols for Labs, is being funded by the Student Sustainability Committee on campus and is being led by assistant professor of anthropology Jessica Brinkworth (GNDP/IGOH).

"For many years, our lab was concerned with reducing our overall carbon footprint. The amount of waste generated in our lab was pretty profound," said Brinkworth.

The waste elimination protocols will focus on polypropylene and polystyrene reuse and replacement, which includes culture dishes, pipette tips, and conical tubes. Additionally, protocols will largely make use of products and equipment that can be found at hardware and grocery stores.

The goal is to share the verified protocols with research labs who may be interested in reusing or bringing plastics for reuse, especially from larger facilities on campus. Brinkworth foresees an estimated 50-90% plastic waste reduction per lab that decides to adopt the protocols.

"It's exciting to be able to engage students in thinking about their research responsibly," said Brinkworth. "We model how a robust research program incorporates rigorous plastics reuse and reduction protocols in its daily work; that part of being a 'serious' scientist is cleaning up after yourself."

News

In survey, COVID-19 vaccine recipients report changes in menstrual bleeding

A new analysis of reports from more than 35,000 people offers the most comprehensive assessment so far of menstrual changes experienced by pre- and post-menopausal individuals in the first two weeks after receiving the COVID-19 vaccine. Published in the journal *Science Advances*, the study adds to the evidence that significant numbers of people experience this unexpected side effect.

Led by Kathryn Clancy (EIRH), a professor of anthropology, the researchers used a survey to query people about their experiences after vaccination. Launched in April 2021, the survey asked for demographic and other information but focused on respondents' reproductive history and experiences regarding menstrual bleeding. The team downloaded the data from the surveys in June 2021.

A statistical analysis revealed that 42.1 percent of menstruating survey respondents reported a heavier menstrual flow after receiving the COVID-19 vaccine. Roughly the same proportion, 43.6 percent, reported no alteration of their menstrual flow after the vaccine, and a smaller percentage, 14.3 percent, saw a mix of no change or lighter flow.

Because the study relied on self-reported experiences, it cannot establish causality or be seen as predictive of people in the general population. But it can point to potential associations between a person's reproductive history, hormonal status, demographics, and changes in menstruation following COVID-19 vaccination.

The Beckman Institute, the Center for Social and Behavioral Science, and the Interdisciplinary Health Sciences Institute at Illinois supported this research, as did NIH, the Foundation for Barnes-Jewish Hospital in St. Louis, and the Siteman Cancer Center in St. Louis.

Students selected for the 2022 Tracy Undergraduate Research Fellowship

Two undergraduate students were selected for a 10-week summer research program to carry out research at the IGB. Karan Samat and Katy Wolhaupter are working in the labs of Joseph Irudayaraj (CGD/EIRH/MME), a Founder Professor in Bioengineering, and Xing Wang (CGD), Research Associate Professor of Chemistry.

Irudayaraj's group works on treating retinal artery occlusion, a condition where the retinal arteries are blocked resulting in blindness. To treat this disorder, the lab uses oxygen nanobubbles to revive cells from hypoxia and save retinal tissues. One aspect of their work includes developing mathematical models to understand oxygen diffusion characteristics and its availability across the retinal cross-section. Samat is further developing this model, especially to estimate oxygen gradients during the initial periods of depletion and to assess the critical time periods of deficit for different oxygen release conditions.

The Wang group develops affordable and novel diagnostic tools. Current diagnostic methods are mainly complex and lengthy processes that require technical laboratory training. To deal with this challenge, the Wang lab uses DNA nanostructures, which can directly bind to viruses present in a patient's saliva or blood sample. Their overall strategy offers affordable and sensitive tools for rapid disease diagnostics in point-of-care settings. Wolhaupter, a junior in bioengineering, is currently working on optimizing different aspects of the diagnostic tools, including the assembly of DNA nanostructures on gold nanoparticles, improving the DNA-virus binding, and image processing of signals for the measurement of virus particles.

Young Innovator program successfully concludes its second year

The Young Innovator program is designed to help trainees become innovative leaders in their fields. The students attended classes for ten weeks over the summer and, at the end of the program, participated in an idea competition, showcasing the projects. The top three participants were awarded tiered funds ranging from $5,000-$20,000. The winners will use the funds to advance their novel innovations.

Skye Shepherd won first place and is a graduate student in the Cunningham (CGD Director/MMG) Nanosensors Group. She is studying how to better detect proteins that can be used as biomarkers in the blood to detect cancer, cardiovascular disorders, traumatic brain injury, and many other diseases. The second-place winner was Alejandra Zeballos, a graduate student in the Gaj (BSD) lab who is creating new therapies for neurological disorders. Jason Wang, a graduate student from the Kong (GNDP/M-CELS) lab, won third place for his proposal to develop BioNoise, a high-throughput biological noise analysis platform.

The other participants included Amanda Bacon, a graduate student in the Cunningham lab, who is developing an instrument that can detect allergens in food; Devyani Swami, a postdoctoral fellow in the Perez-Pinera (ACPP) lab, who is working on treating various lung disorders using CRISPR tools; and Ruben Sanchez Nieves, a graduate student in the Whitaker (IGOH) lab, who is genetically modifying the archaeon *Sulfolobus islandicus* so that it can be used in industrial processes.

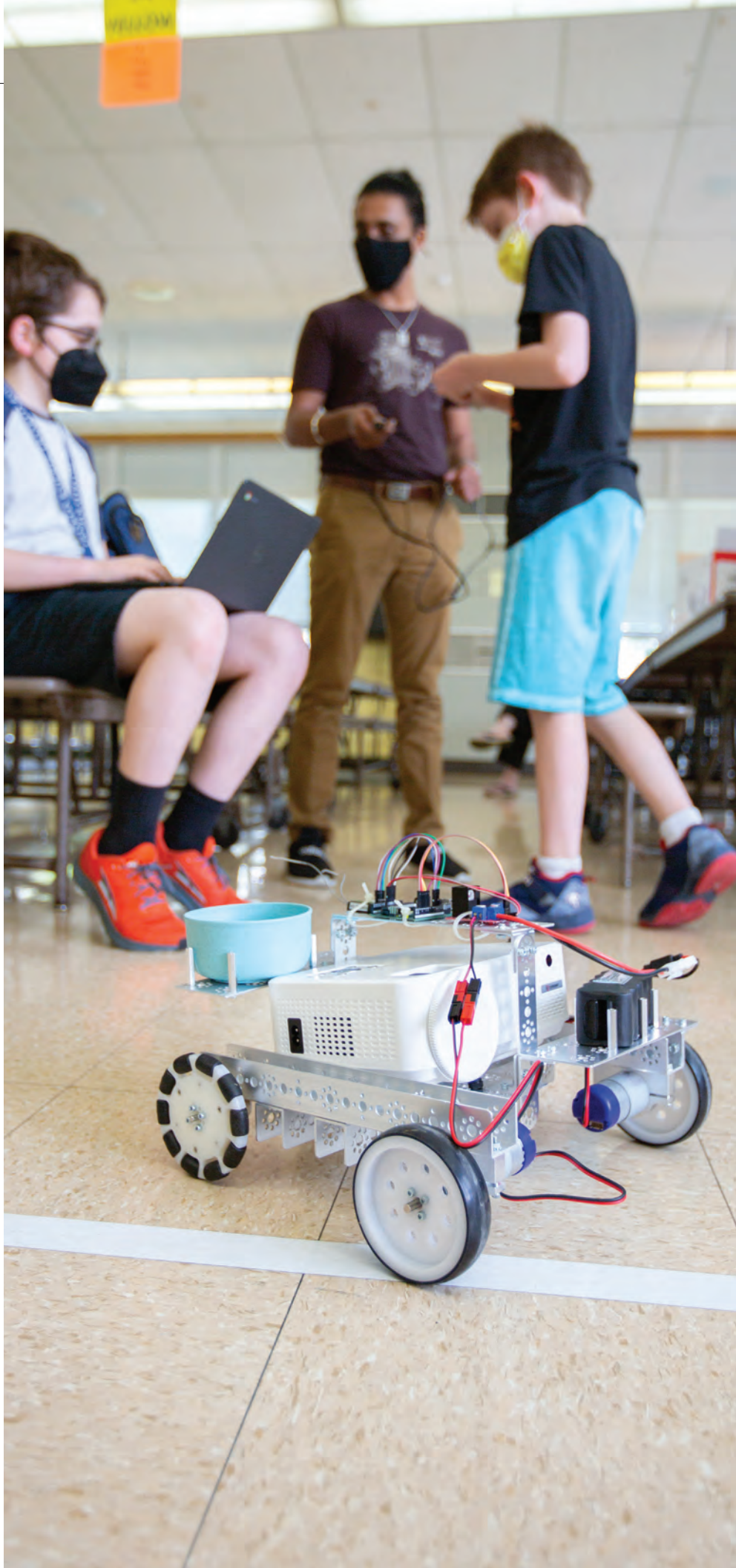
Outreach

STEAM TRAIN 2022 adventure completed

Organized by the IGB's Outreach Senior Activities Coordinator Daniel Urban, Franklin's Magnet Site Coordinator Zanne Newman, and University Laboratory High School's chemistry teacher Melinda Tidrick, STEAM TRAIN aims to inspire independent, curiosity-driven student research through interactions with near-peer mentors. Franklin students discover their love for science by exploring difficult issues that they're passionate about while the Uni High students serve as mentors. The idea is to create a chain of people who are closer in age to improve communication.

The results of these projects ranged from astonishing to delightful. In the realm of artificial intelligence, the students were able to build a home entertainment robot; design an anti-drone weapons device that used animal-inspired characteristics; and compare a ground-based robot with wheels to a drone to test which one can plant seeds better. The other three projects were inspired by biology. One group made 3D printed coral structures. Another discovered that frogs may know how toxic they are; the most toxic ones are often the most adventurous. And the final group made the surprising discovery that Minecraft characters are actually slower than humans on a 100-meter test track. However, when they're allowed to consume potions and are forced to run at their maximum speeds, they outrun the current world record.

"These students created some phenomenal projects, a few of them literally being of graduate school caliber. It's awe inspiring to realize what such young kids are capable of when they are provided with the resources and mentorship to bring their ideas to life," Urban said.



Research

'Molecular Velcro' enables tissues to sense, react to mechanical force

A new study observed that when tugged upon in a controlled manner, the Velcro-like cellular proteins that hold cells and tissues together—called cadherins—communicate with growth factors to influence in vitro tumor growth in human carcinoma cells.

The study was led by chemical and biomolecular engineering professor Deborah Leckband (RBTE) and the findings are published in the *Proceedings of the National Academy of Sciences*.

When bound to cadherin molecules in normal tissue, growth factor receptors cannot communicate with growth factor proteins—the substance they need to promote tissue growth. However, the study shows that changes in tensional stress on cadherin bonds disrupt the cadherin-growth factor interaction to switch on growth signals in tissues.

To demonstrate how tension influences tissue growth, the researchers set up an experiment to observe how in vitro human carcinoma cells convert mechanical information into biochemical signals, Leckband said.

The team used a self-built "cell stretcher" in which the carcinoma cells are grown in a thin layer on the surface of a flexible medium. When the cells are stretched, the researchers observed changes that could increase tissue growth and tumorigenesis.

"This study confirms that cadherins use force to switch on biochemical growth signaling," Leckband said. "By confirming these force-induced disruptions, we may be able to find a way to mutate cadherin molecules in order to prevent certain types of tissue growth, such as metastatic transformation and tumorigenesis."

NIH supported this study.

Circadian rhythm and the blood-brain barrier

An interdisciplinary team received a grant to study the circadian dynamics of the blood-brain barrier, including the extent to which time of day affects its permeability to hormones and drugs. The team includes researchers from Illinois and Purdue University.

Usng a scaffold derived from human stem cell lines, the team will fabricate a biomimetic blood-brain interface. The proposed model will mimic the biological functions of the blood-brain interface, providing insight into its response to blood leakage, as in stroke, and day-night cycles.

The grant, titled "Dynamic circadian regulations of the blood-brain interface in a human brain-mimicking microfluid chip," is funded by the National Heart, Lung, and Blood Institute, an institute of the NIH, and the Department of Defense. The award funds a five-year project and is intended to support high-risk, high-reward work on the blood-brain interface.

Although organ-on-a-chip devices—microdevices that mimic organ function by culturing cells in microfluidic channels—are becoming increasingly popular tools to assess disease physiology in vitro, the proposed model will be more complex than its predecessors; it requires five cell types, including neurons, glia, microglial cells providing central nervous system inflammatory response, and vascular endothelial cells comprising the blood-brain barrier.

"The unique approach we are taking is to incorporate circadian genes into the cells so we can put them in sleep or wake modes and look at barrier permeability dynamics across these cycles," said Hyunjoon Kong (M-CELS leader/EIRH/RBTE), a professor of chemical and biomolecular engineering.

New tests and treatments developed in mice for pulmonary fibrosis

Scientists at the University of Illinois and Mie University in Japan have developed monoclonal antibodies that prevent lung cell death in mouse models for idiopathic pulmonary fibrosis and acute respiratory disease syndrome. The advance, along with new, non-invasive diagnostic tools presented in the same study, could be a critical step in treating the deadly diseases. The work was published in *Nature Communications*.

Developing monoclonal antibodies requires a detailed understanding of the toxin or disease agent causing harm in the body. The researchers previously found that a toxic peptide, corisin, is secreted by *Staphylococcus* bacteria in the lungs and causes significant lung cell death in pulmonary fibrosis in an animal model.

Once they determined the sequence of corisin, the researchers administered a simple synthesized version of the peptide to mice and studied the natural antibody response. This yielded multiple candidate monoclonal antibodies, which the researchers screened for effectiveness in mice exhibiting clinical signs of IPF and ARDS.

The new study also offers novel, non-invasive diagnostic tools to mark the presence and progression of the disease. The researchers found corisin circulates in the blood at higher levels in IPF patients than healthy subjects. In addition, they discovered corisin kills lung cells by damaging mitochondria in the cells.

"These are very exciting and promising findings that open the door for testing this monoclonal antibody as a therapeutic strategy to help stave off progression of pulmonary fibrosis and ARDS in patients," said Isaac Cann (MME leader), a professor of animal sciences.

Research

Study reveals new insights into bat echolocation

Bats are famous for using echolocation and they have a unique inner ear structure that helps them. In a new study, published in *Nature,* researchers have discovered that this structure varies greatly among bats, providing new insights into the evolution of echolocation.

The researchers used computed tomography and histological studies to examine the skulls of 38 bat species that belonged to either Yinpterochiroptera or Yangochiroptera. The researchers found that Yang bats did not have a typical canal for their neurons. Instead, the canal is open on one side and has a larger space.

The study also provides evidence for resolving the long-standing controversy surrounding the evolutionary classification of bats. Traditionally, bats were divided into two groups: Megachiroptera, which use sight and smell, and Microchiroptera, which use echolocation. However, genetic evidence uncovered in the 2000s suggested that some of the Microchiroptera were more closely related to Megachiroptera than to other echolocating bats. As a result, two new groups of bats, Yin and Yang, were proposed.

"There was no actual anatomical characteristic that supported this DNA hypothesis, until now. This study shows the differences in the ganglion canal are consistent with the split between Yin and Yang bats," said Daniel Urban, a senior outreach activities coordinator at the IGB and an author on the paper.

The work was funded by the University of Chicago, NSF, the Field Museum, the JRS Biodiversity Foundation, and the University of Illinois.

Treatment of liver metastases in breast cancer patients improved by low-carb diets

A new study led by Zeynep Madak-Erdogan (CGD/EIRH/GSP), an associate professor of food science and human nutrition has found a new mechanism of endocrine resistance in breast cancers metastasized to the liver.

The study, published in *Molecular Cancer Research*, found that liver metastases rely on increased amounts of glucose, revealing the possibility of a dietary intervention to reduce tumor burden and increase treatment efficacy.

The study began by observing differences in the breast cancer patient population and found that patients with liver metastases typically did not respond to the standard of care endocrine therapy, Fulvestrant, very well.

"We found that the tumors had an increased reliance on glucose, so we provided the animals with diets of varying carbohydrate levels," Madak-Erdogan said.

The researchers discovered that liver metastases decreased with carbohydrate levels and low-level carbohydrate diets restored the efficacy of Fulvestrant in reducing metastatic tumor burden in mice.

The study also found indicators of special survival mechanisms that become activated during these times of stress. Madak-Erdogan intends to pursue these findings in future research to determine the role of these regulatory pathways.

"We are so excited about the possibilities, especially in terms of dietary intervention, where there are not as many regulatory steps. Low-carb diets can easily be tested in the clinic, and one of our near-future goals is to get this to clinical trials," Madak-Erdogan said.

This research was supported by grants from the University of Illinois, Cancer Center at Illinois, and National Institute of Food and Agriculture.

Research

New engineering approach enhances antibody fragments for cancer therapy

Bioengineering professor Shannon Sirk (MME) and her lab are engineering human commensal microbes into living therapeutics, delivering proteins directly in the body, to make cancer treatment more accessible.

The research team specifically studied trastuzumab, a well characterized and widely used therapeutic antibody used to treat HER2-positive breast cancer. HER2 is a growth factor protein that triggers cellular division; when HER2 is overexpressed, it can lead to out-of-control replication or cancer. Trastuzumab binds to HER2 which limits tumor growth.

Since full-length antibodies are too complex to be produced in bacteria, the team engineered microbes to express a smaller antibody fragment that recognizes the HER2 cancer antigen. This fragment is a sixth of the size of trastuzumab. However, the part of the antibody that they removed has important functions, including the ability to be transported from the gut into the blood by binding to a cell-surface protein called FcRn and to keep the antibody circulating in the blood for longer periods of time.

The team's goal is to re-enable these critical functions in the truncated antibody fragment by adding short FcRn-binding peptides. These peptides mimic the Fc domain, without the added bulk, thus maintaining the benefits of the fragment's small size while regaining the functionality of the lost Fc domain. Future goals include expanding their functional peptide platform to recapture other lost Fc-mediated activity, including the recruitment of tumor-killing immune cells to enhance therapeutic impact.

They published their findings in *ACS Chemical Biology*. The work was supported by the University of Illinois.

Study investigates the effects of DiNP on the colon

Di-isononyl phthalate is commonly used used as a replacement for di(2-ethylhexyl) phthalate to make products, such as vinyl clothing and construction materials, more flexible or stable. However, scientists do not completely understand if or how it harms the human body.

"The problem is that although we know DEHP is associated with female reproductive problems, we don't know if DiNP harms us," said Karen Chiu, a graduate student in the Flaws group.

To understand whether DiNP is harmful, the team tested how it affects the colon walls, the immune system, and colonic microorganisms of female mice that were dosed with different concentrations of DiNP. Although it did not affect the length or weight of the colon, DiNP changed the tissue structure by causing inflammation. Normal colon sections have intestinal folds and thick muscle layers. However, the colon of mice that were exposed to 20 µg/kg or 200 µg/kg DiNP had no folds and abnormal muscle layer thickness.

The researchers used 16S rRNA gene sequencing to identify the bacteria in the colon contents. Two genera—*Lachnoclostrium* and *Blautia*—differed in the DiNP-treated mice compared to the control. The researchers also identified three microbes that were capable of growing on DiNP. "The next step is to find the enzymes that break down DiNP and see whether they can alter the hormone levels in mice. The results would give us further insights into how DiNP affects the colon," Chiu said.

The study was published in *Toxics* and was supported by NIH and the University of Illinois.

Research

CRISPR-Cas13 targets proteins causing ALS, Huntington's disease in mouse nervous system

A new study by University of Illinois researchers used a targeted CRISPR technique in the central nervous systems of mice to turn off production of mutant proteins that can cause ALS and Huntington's disease. The new approach uses CRISPR-Cas13, which can target mRNA—the messenger molecule that carries protein blueprints transcribed from DNA. The team published its results in *Science Advances*.

"Targeting RNA rather than DNA has some unique advantages, including the fact that, in theory, its effects within a cell can be reversed since RNAs are transient molecules," said Colin Lim, a graduate student in the Gaj lab who helped lead the study.

The researchers found that CRISPR-Cas13 effectively reduced the amount of mutant protein present in the nervous system for both diseases—specifically, the protein SOD1 within the spinal cords of mice with ALS, and the protein "huntingtin" within the brains of mice with Huntington's disease. The reduction in mutant SOD1 protein also correlated with better therapeutic outcomes: Mice with ALS that received the CRISPR-Cas13 injection had slower disease progression, improved survival and a slower rate of decline in grip strength and motor skills compared with mice that did not receive the treatment.

The researchers said this study provides crucial evidence that CRISPR-Cas13 can knock down target genes in the nervous system, a key step toward eventually developing targeted therapeutics based on the technology.

NIH, the Muscular Dystrophy Association, and the Judith & Jean Pape Adams Foundation supported this work.

New study investigates the microbiomes of dogs across the world

Although the microbiomein the fecal matter of dogs has been investigated extensively, those studies have mostly been limited to domesticated dogs.

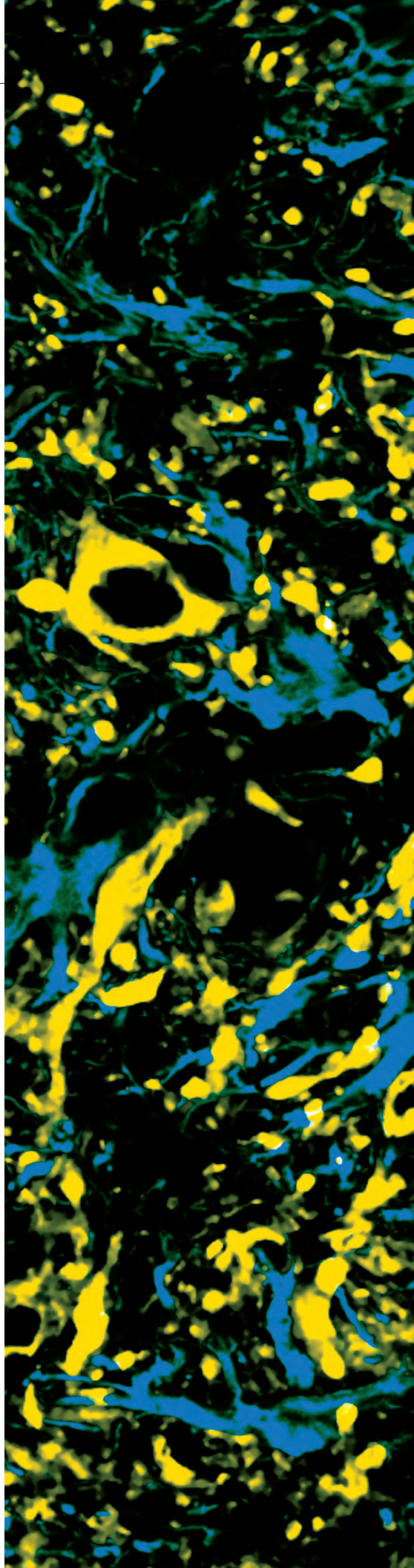
"The studies work with dogs in veterinary centers, which lead a very different life from dogs that don't live as pets," said Karthik Yarlagadda, a former graduate student in the Malhi group.

In a new study, published in *Proceedings of the Royal Society B: Biological Sciences,* researchers sampled the fecal microbiomes across three geographical locations: pets from South Africa, stray dogs and shelter dogs in India, and dogs from a rural village in Laos. The samples were collected on FTA cards, which contain chemicals that preserve the DNA so it can be sequenced and analyzed later.

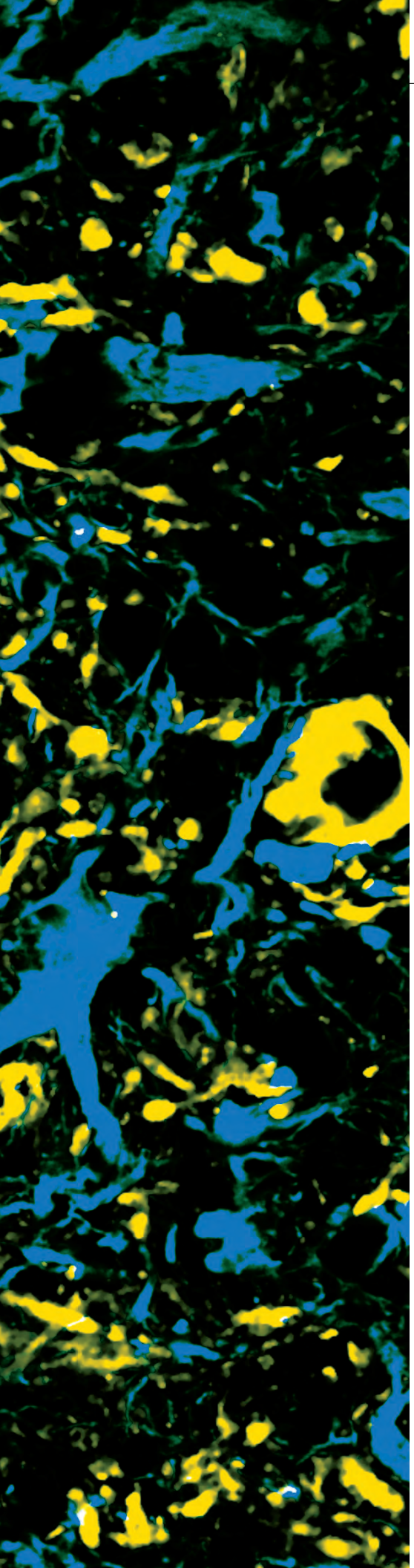
The dogs had different diets across locations, ranging from local agricultural products, human leftovers, meat, and commercial dog food. Interestingly, although the microbiomes among the populations differed, functionally they were the same. "It was cool to see that you can have different microbiomes, but they all fulfil the same metabolic function," Yarlagadda said.

The researchers also wanted to contrast these samples with ancient microbiomes, obtained from fossilized dog feces. They observed that dogs in non-US populations that live outdoors with a mixed diet have similar microbiomes to that of ancient dogs, potentially due to overlapping diets and more environmental exposures. Further work will elucidate whether the human microbiome diversity in non-industrialized settings will also follow similar trends.

The study was funded by the USDA and the University of Illinois.



Research



Small molecule transports iron in mice, human cells to treat anemia

A new study stemming from a collaboration between researchers at the University of Illinois Urbana- Champaign, the University of Michigan, Ann Arbor and the University of Modena in Italy, demonstrated that the small molecule hinokitiol, derived from cypress trees, potentially could function as a "molecular prosthetic" when the iron-transporting protein ferroportin is missing or defective. The new study, conducted in mice and published in *Proceedings of the National Academy of Sciences*, builds upon previous work detailing hinokitiol's ability in zebrafish.

"This is a really striking demonstration that an imperfect mimic of a missing protein can reestablish physiology, acting as a prosthesis on a molecular scale," said study co-leader Martin D. Burke (MMG), a professor of chemistry at Illinois and a member of the Carle Illinois College of Medicine.

Ferroportin is a protein that forms a channel for transporting iron in and out of cells. Patients without the protein have an excess buildup of iron in the liver, spleen and bone marrow, particularly in cells macrophage. Macrophages in the liver chew up old red blood cells and transport the iron in them for recycling into new red blood cells. However, without ferroportin, the iron builds up inside the cells and can't be recycled.

The researchers verified that hinokitiol functioned the same way in human cells by studying its action in liver macrophages from human patients with ferroportin disease. The researchers are working with the company Kinesid Therapeutics, founded by Burke, to facilitate further work toward clinical application for hinokitiol or its derivatives.

NIH supported this work.

New Tool to Identify Genes Associated with Coronavirus

Much has changed about the COVID-19 pandemic, and researchers like Illinois Computer Science professor Mohammed El-Kebir (IGOH) continue to investigate the virus to ensure the medical and scientific community are better prepared to respond to potential pandemics in the future.

In a new paper, published in *Molecular Biology and Evolution*, transcription regulatory sequences are found to have an important role in discontinuous transcription in coronaviruses.

"The work allows scientists to quickly identify these TRS sites as well as the genes of future, yet undiscovered, coronaviruses," El-Kebir said. "This information essentially allows us to classify the virus and accurately place it into the phylogeny of coronaviruses."

The workgroup included one of El-Kebir's graduate students, Palash Sashittal and Chuanyi Zhang—a graduate student in the Department of Electrical & Computer Engineering. Two computer science undergraduate students, Ayesha Kazi and Michael Xiang, and one ECE undergraduate student, Yichi Zhang, contributed to the effort by creating a web interface to make the findings accessible.

The group created an algorithm called CORSID-A to solve the TRS idenitification problem. The group states this solution "outperforms existing motif-based methods in identifying TRS sites in coronaviruses." The paper also demonstrates "for the first time how TRS sites can be leveraged to identify gene locations in the coronavirus genome."

"I think it's impressive to see how quickly we came to understand the problem and to see how quickly we responded. There has been a tremendous exchange of ideas in all forums that has been inspiring." El-Kebir said.

The study was funded by NSF.

Research

Tree fern genome provides insights into its evolution

For the first time, researchers have characterized the genome arrangement of tree ferns, shedding new insight into how ferns evolved. The study was published in *Nature Plants*.

A major event in the evolution of land plants was the invention of their vascular systems, which help conduct water, nutrients, and food throughout their bodies. These systems consist of two tissues: xylem and phloem, and only xylem cells are lined with lignin

Researchers including Ray Ming (GEGC), a professor of plant biology sequenced the genome of flying spider-monkey tree fern *Alsophila spinulosa* and found that two Vascular-related Mac-Domain genes were highly expressed in xylem compared to other tissues, indicating that these might be key regulators in the formation of xylem-specific cells.

Using microscopy and biochemical methods, they also found that lignin made up 40% of the stem cell wall. In comparison, wood generally contains 25%. They also discovered a new secondary metabolite primarily made in the xylem, which they named "alsophilin".

To understand how ferns evolved, the researchers compared the genomic sequence of *A. spinulosa* to other members of the same species in China. The researchers then reconstructed the history of the fern population and saw that the species underwent a drastic decrease in population numbers 35.6 – 34.5 million years ago as well as 2.5 – 0.7 million years ago.

The study was funded by the Chinese Academy of Forestry; the National Natural Science Foundation of China; the Beijing Forestry University; CAMS Innovation Fund for Medical Sciences; PUMC Disciplinary Development of Synthetic Biology; and the DOE.

New smartphone clip-on can detect Zika virus in blood samples

In a new study, published in *Analyst,* researchers including Brian Cunningham (CGD Director/MMG) have developed an instrument that can be clipped on to a smartphone to rapidly test for Zika virus in a single droplet of blood.

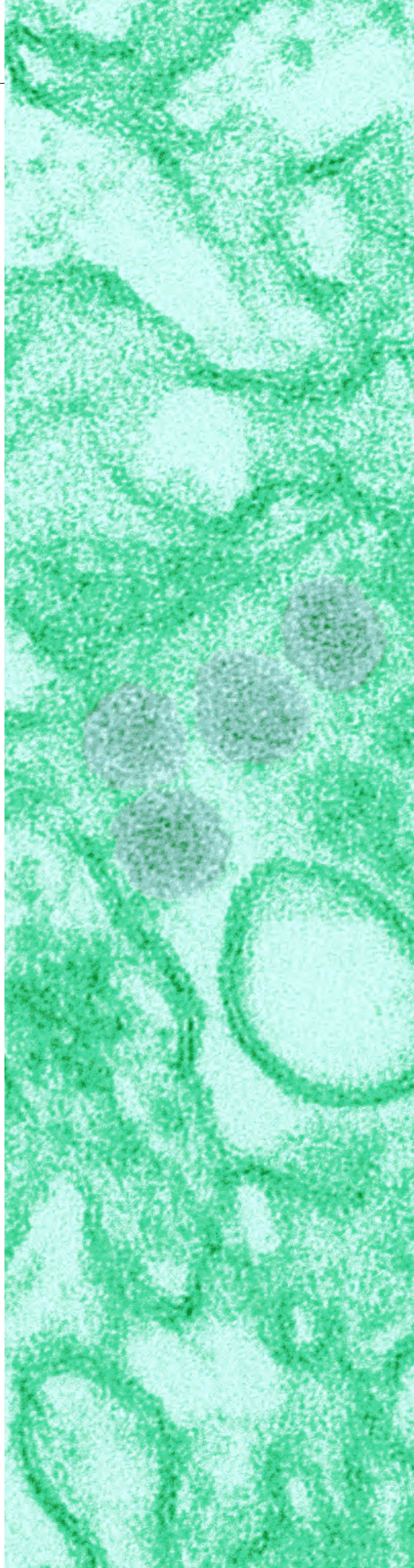
Zika virus is primarily transmitted through *Aedes aegypti* mosquitoes. Although the disease is largely asymptomatic or results in mild symptoms in adults, it causes developmental disorders in newborn babies if their mothers are infected during early pregnancy.

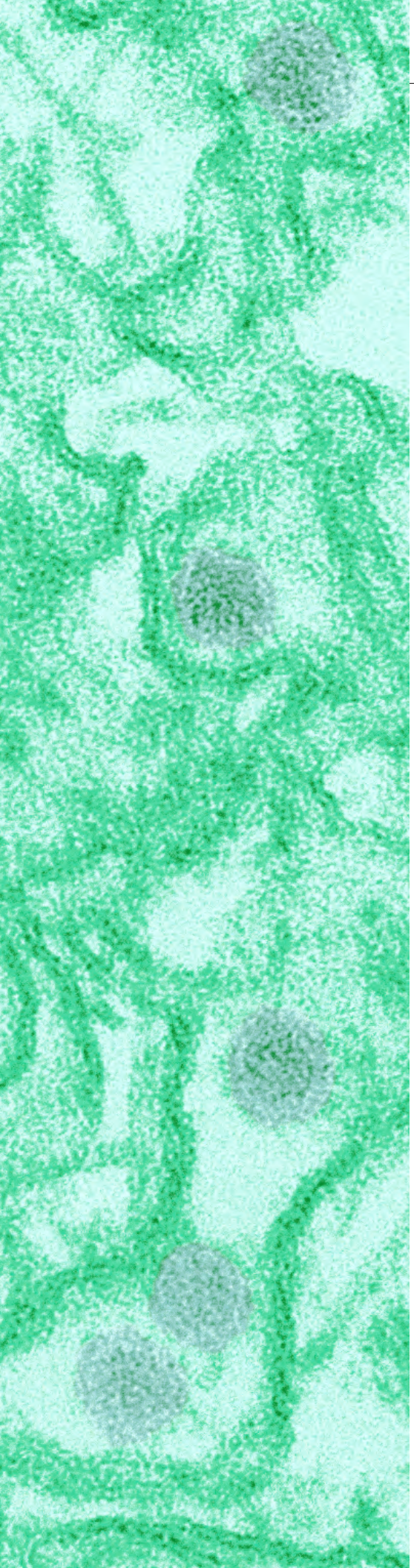
Zika virus infections are currently detected through polymerase chain reaction tests performed in a laboratory, which can amplify the genetic material of the virus. In this study, researchers used Loop-Mediated Isothermal Amplification to detect the virus in the blood samples using an approach suitable for point-of-care clinics. While PCR requires 20-40 repeated temperature shifts to amplify the genetic material, LAMP only requires one temperature—65 °C—making it easier to control.

A cartridge that contains reagents required to detect the virus is inserted into the instrument and clipped onto a smartphone. Once the patient adds a drop of blood, chemicals break open the viruses and the blood cells within five minutes. A heater heats it up to 65 °C, and then another set of chemicals amplifies the viral genetic material. The cartridge fluoresces bright green if the blood sample contains the Zika virus, with the entire process taking only 25 minutes.

The researchers are now developing similar devices to simultaneously detect other mosquito-borne viruses and are working on making the devices even smaller.

The work was funded by NIH and NSF.





Research

Scientists improve BRAF inhibitor for better blood-brain barrier penetration

Cancers that begin in the brain are notoriously difficult to treat, in part due to the blood-brain barrier, which keeps foreign compounds out of the brain via a process called efflux. Drugs might be able to enter the brain initially, but are pumped out rapidly via efflux transporters such as P-glycoprotein. One such drug includes dabrafenib, a drug that is used to treat cancers including metastatic melanoma.

A recent paper published by Paul Hergenrother (ACPP leader/MMG), a Kenneth L. Rinehart Jr. Endowed Chair in Natural Products Chemistry, and Timothy Fan (ACPP/CGD), a professor of veterinary clinical medicine, studied the features that enable efflux evasion, and attempted to embed those features into dabrafenib. Aya M. Kelly, a student in Hergenrother's lab, led these efforts and developed a new compound, everafenib. Matthew Berry, a student from Fan's lab, also contributed to the study.

Everafenib evades BBB efflux and it is much more successful in treating stereotactically-implanted melanomas in mouse brains, compared to dabrafenib. The drug was created after the group found that two chemical features are correlated with the evasion of efflux: the addition of a carboxylic acid group and a lower molecular weight. Everafenib also achieves a higher absolute concentration in the brain, meaning higher concentrations of the drug are retained in the brain, increasing the chances of successfully treating a cancer.

The study was published in the *Journal of American Chemical Society*. The work was funded by the University of Illinois, NIH, and the Damon Runyon Cancer Research Foundation.

Understanding cooperation and conflict in plant symbionts

The traditional idea of symbiosis is that the participants mutually benefit each other. However, researchers have debated whether the interests of the symbionts always line up with the hosts they inhabit.

A new study, published in *Proceedings of the Royal Society B: Biological Sciences*, investigates this question. The researchers examined 191 naturally occurring strains of the microbial symbiont *Sinorhizobium meliloti*, paired with its host *Medicago truncatula*, a clover-like Mediterranean plant. The microbe resides in the root nodules of the plant and supplies it with nitrogen. The group paired each microbial strain with an individual plant and also used a mix of different strains and infected the same plant, a competitive situation that often occurs in nature.

The researchers sequenced the genomes of the microbial strains and, using genome-wide association, they compared which bacterial genes are associated with plant growth.

When they compared how many symbiont genes align with the host's interest, they found that ~80% of the genes that they identified seemed to be associated with alignment. "This is a striking result because it shows that even though the symbionts are not evolving in order to benefit their hosts, it often pays for them to be beneficial." said Rebecca Batstone, a former postdoctoral fellow at the IGB .

The group says in the future they would like to look at more hosts to see whether this trend still holds true with different plant types or environmental conditions.

The work was funded by NSF and IGB.

Research

Ultra-sensitive biosensing technique can spot individual molecules that reveal cancer

A new paper in *Nature Communications* has reported a highly sensitive new method for performing a liquid biopsy that can identify tiny numbers of individual cancer molecules, requiring only a drop or two of blood from a fingertip.

Brian Cunningham (CGD Director/MMG), a professor of electrical and computer engineering and one of the paper's authors, says for several years there's been a focus on a "liquid biopsy" concept whereby one can monitor cancer by detecting tumor DNA circulating in the bloodstream. The new method measures microRNA in the blood, a nucleic acid like DNA that, for tumors, contains a genomic sequence that originates as part of the genetic alterations that caused cancer.

"We're using light-generating nanoparticles that are called 'quantum dots': very small particles made out of semiconductors," Cunningham says. "We can prepare the dots with nucleic acid molecules that will match and bind with the microRNA molecule that we want to detect, and we can do that in such a way that one quantum dot equals one microRNA molecule."

They then use a photonic crystal biosensor that amplifies the light from the quantum dots thousands of times over, making it possible to see individual quantum dot + microRNA pairs.

One ultimate goal will be to leverage the test to understand changes in a patient's cancer over time, so that treatment can be adjusted accordingly. While something like a CT scan can only provide crude information, a microRNA test could give clinicians more precise information about the tumor, and inform appropriate treatment options.

The work was supported by NIH.

New therapeutic target identified for triple-negative breast cancer

There are, unfortunately, limited options for triple negative-breast cancer patients. In a new study, published in *BBA Molecular Basis of Disease*, researchers have discovered that the nuclear receptor TLX can potentially be used for therapeutic intervention.

Erik Nelson (ACPP), an associate professor of molecular and integrative physiology, and his lab, specialize in studying nuclear receptors—a class of proteins that regulate a host of biological processes —like TLX.

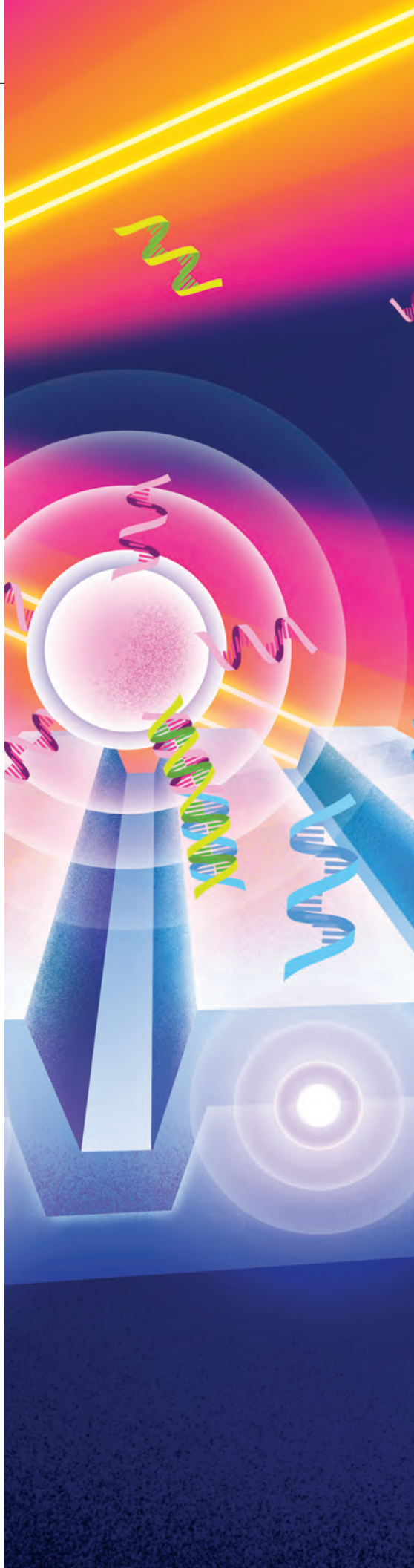
"TLX has previously been characterized in brain and prostate cancer as being a driver of those. However, when we looked at clinical data, we saw that triple-negative breast cancer patients who higher expression of TLX have better survival rates," said Adam Nelczyk, a graduate student in the Nelson lab.

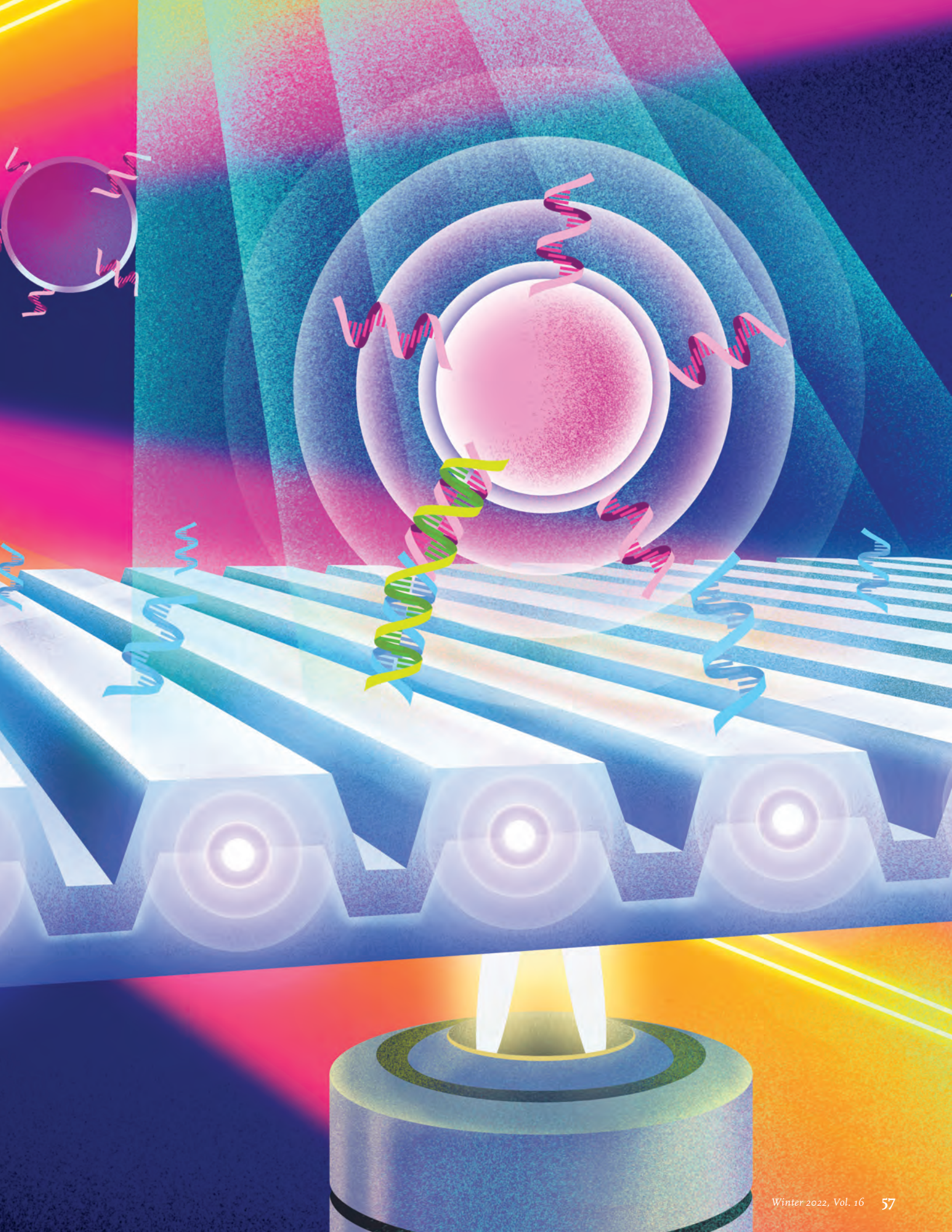
The researchers then carried out experiments in triple-negative breast cancer cell lines to determine whether increased TLX expression could lower the classic hallmarks of cancer: tumor growth, migration, invasion, and metastasis.

Using cell lines, researchers found that cells that expressed TLX showed lower growth and migration, and were invaded less by nearby cancerous cells.

The same hallmarks were also measured in mouse models, coupled with RNA sequencing, to measure the changes in TLX expression, and histology studies. Although the results are promising, the mouse models do not completely capture what happens in humans. "However, together with the patient data, they indicate that TLX is a good drug target." Nelson said.

The work was funded by NIH, the Department of Defense, the American Institute for Cancer Research, and the University of Illinois.





AWARDS

Martin Burke

May and Ving Lee Professor for Chemical Innovation, and Professor of Chemistry (MMG)

Fellow, American Association for the Advancement of Science

Rohit Bhargava

Founder Professor in Bioengineering (CGD)

Gold Medal Award, New York/New Jersey Society for Applied Spectroscopy

May Berenbaum

Professor and Head of Entomology (GEGC/IGOH)

President's Committee on the National Medal of Science

Alison Bell

Professor of Evolution, Ecology, and Behavior (GNDP leader)

Quest Award, Animal Behavior Society

Sara Pedron Haba

Research Assistant Professor of Chemical and Biomolecular Engineering (RBTE)

2022 Awardee, American Association for Cancer Research

Peter Fox

Founder and Principal of Fox Ventures, LLC and IGB Leadership Council member

Distinguished Service Award, University of Illinois Alumni Association

Kathryn Clancy

Associate Professor of Anthropology (EIRH)

Dean's Distinguished Professorial Scholar, College of Liberal Arts and Sciences

Carla Cáceres

Professor of Evolution, Ecology and Behavior (IGOH)

G. William Arends Professor

Joseph Irudayaraj

Founder Professor in Bioengineering (CGD/EIRH)

Fellow, American Association for the Advancement of Science

Katy Heath

Associate Professor of Plant Biology (IGOH)

Dean's Distinguished Professorial Scholars, College of Liberal Arts and Sciences; Fellow, American Association for the Advancement of Science

Mark Hauber

Harley Jones Van Cleave Professor of Host-Parasite Interactions, Evolution, Ecology, and Behavior (GNDP)

Alexander von Humboldt Research Award, Alexander von Humboldt Foundation; Fellow, American Association for the Advancement of Science

Hee-Sun Han

Mark A. Pytosh Scholar and Assistant Professor of Chemistry (GNDP/IGOH)

Amy L. Devine Award, Illinois chapter of Alpha Omega Epsilon

Ripan Malhi

Professor of Anthropology (GNDP/GSP/IGOH)

Fellow, American Association for the Advancement of Science

Cecilia Leal

Associate Professor and Racheff Faculty Scholar in Materials Science and Engineering (M-CELS)

2022 College Award for Sustained Excellence in Diversity, Equity and Inclusion, Grainger College of Engineering

Madhu Khanna

Professor of Agricultural and Consumer Economics (CABBI)

Alvin H. Baum Family Chair; Director, Institute for Sustainability, Energy, and Environment

Yong-Su Jin

Professor of Food Microbiology (BSD/CABBI/MME)

University Scholar

Gene Robinson

IGB Director, Swanlund Chair, Professor of Entomology (GNDP)

National Academy of Sciences Councilor

Jason Ridlon

Associate Professor of Animal Sciences (MME)

2022-23 Center for Advanced Study Associate

Donald Ort

Robert Emerson Professor in Plant Biology and Crop Sciences (GEGC Leader/BSD/CABBI)

Jalal Aliyev Lecture Scholarship, International Society of Photosynthesis Research

Elizabeth Murphy

Managing Director, Institute for Sustainability, Energy, and Environment (CABBI)

2022 SPaRC Outstanding Service Award, Sponsored Programs Administration

Tandy Warnow

Associate Head for Research and Faculty Development, Department of Computer Science (IGOH)

Fellow, American Association for the Advancement of Science

Amy Wagoner Johnson

Professor and Andersen Faculty Scholar, Mechanical Science and Engineering (EIRH/RBTE)

Fellow, American Institute for Medical and Biological Engineering

Andrew Smith

Professor of Bioengineering (CGD)

Fellow, American Institute for Medical and Biological Engineering

GRANTS

Indrani Bagchi
Milan Bagchi

"Extracellular vesicles as mediators of cell-cell communication during implantation"

NIH

John Gerlt
Doug Mitchell

"Web-Based Resource for Genomic Enzymology Tools"

NIH

Carl Gunter
Aleksander Ksiazkiewicz
Jacob Sherkow
Stephen Schneider

"A Sociotechnical Approach to Improving Security and Privacy in the Genomic Data Ecosystem"

NIH

Paul Hergenrother
Erik Nelson
David Shapiro
Timothy Fan

"A Novel Therapeutic Strategy for Ovarian Cancer"

NIH

Hyun Joon Kong
Stephan Boppart

"Self-Locomotive Antimicrobial Micro-Robot (SLAM) Enhancing Biofilm-Infected Wound Healing"

NIH

Jason Ridlon
Isaac Cann
Rex Gaskins

"Gut bacterial metabolism of the side-chain of corticosteroids"

NIH

Andrew Smith
Rashid Bashir

"Digital Multiplexed Analysis of Circulating Nucleic Acids in Small-Volume Blood Specimens"

NIH

Mattia Gazzola
Nancy Amato
Karin Dahmen
Hyun Joon Kong
M. Taher Saif

"Expeditions: Mind *in Vitro*—Computing with Living Neurons"

NSF

Ripan Malhi
Julian Catchen

"Collaborative Research: Salmon Stewardship: Mapping a Cultural Keystone and Building Genomics Capacity for Alaska Native Peoples"

NSF

Amy Wagoner Johnson
Rosa Espinosa-Marzal
Gabriel Juarez

"Collaborative Research: ECO-CBET: From Molecules to Sustainable Reef Platforms: Engineering Ecosystems for Coral Recruitment and Survival"

NSF

Gene Robinson

"AmE-711 Cell Line as a Platform for Reporter Gene Assays"

USDA

Gene Robinson

"Genomics for Faith Leaders"

The Wayfarer Foundation

Gene Robinson

"When the Going Gets Tough the Tough (Flies?) Get Social"

Canadian Institute for Advanced Research

Daniel Urban

"IGB Gene Drive: A Mobile STEM Lab Broadening Science Accessibility Interest and Proficiency"

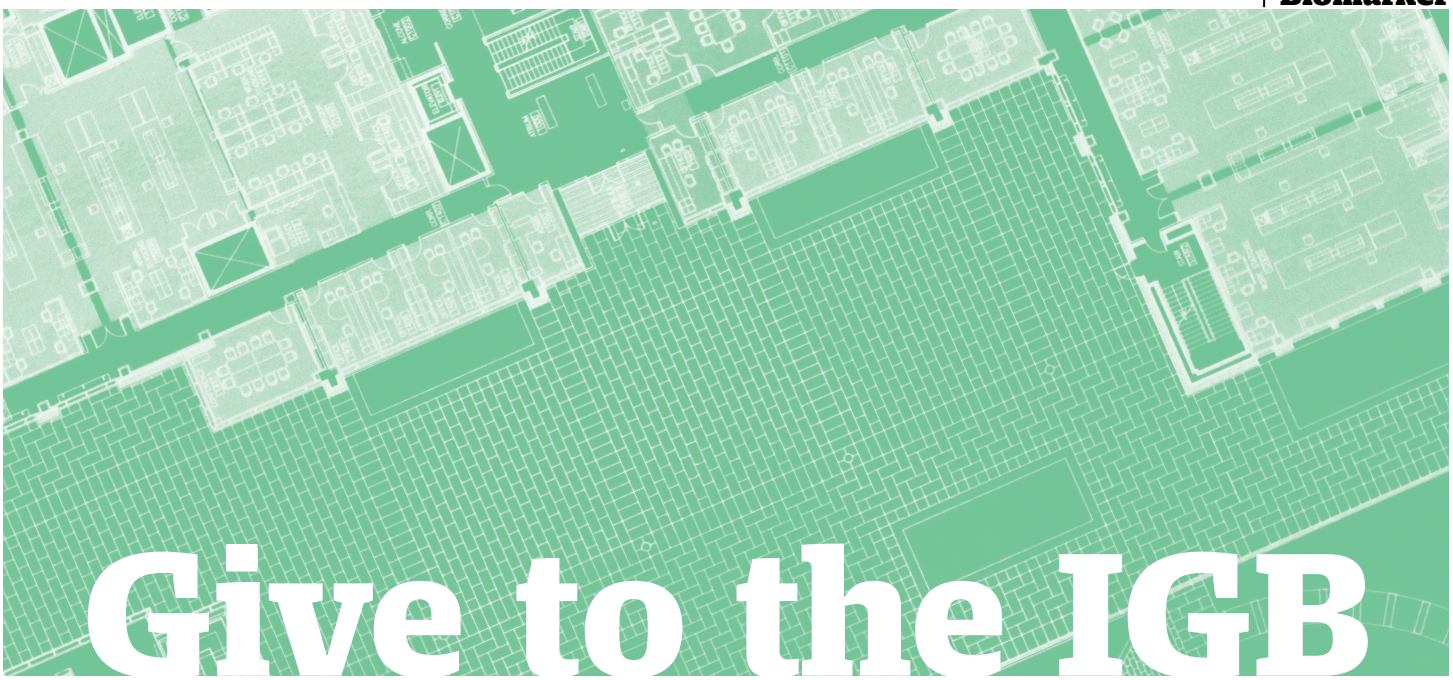
Illumina Corporate Foundation

Huimin Zhao
Vijay Singh
Christopher Rao
Jeremy Guest
Xiao Su

"New Technologies for Industrial Production of Succinic Acid"

BioMADE


MA-PJ '02



Give to the IGB

The vision of scientific research is limited by the pace of innovation. New technologies let us see the physical world more clearly, in greater detail, in finer scales of space and time. Genomic research, around which the IGB is focused, is particularly tied to advancing technologies.

To continue our record of high-quality research, we need to maintain our position at the forefront of the field. We move past traditional divisions between disciplines of study by constructing a network of collaborations. With your help, we will continue to forge a path toward our vision of a better world.

Carl R. Woese Research Fund

Donations may be made to the Carl R. Woese Research Fund to support research on evolution, systems biology, and ecosystem dynamics at the IGB. Professor Woese approved this fund in his name to help the next generation of scientists and to recognize his discoveries and work that spanned nearly half a century at the University of Illinois Urbana-Champaign.

Stay Connected with the IGB

Stay connected to news, events, and program information at the Carl R. Woese Institute for Genomic Biology. By joining our mailing list, you'll receive our e-newsletter, publications, and details about seminars, workshops, and symposia at the IGB.

Visit *www.igb.illinois.edu/subscribe*

For more information

Tracy Parish
Director of External Relations and Strategic Partnerships

217-265-0880
tparish@illinois.edu

IGB Annual Fund

Gifts to the IGB help us to foster the collaborative environment that we believe is vital for progress in genomic research. Philanthropy helps us create opportunities for building strong working relationships with intelligent, talented researchers from our own campus, and from across the world. It allows us to provide grants for promising, but risky, research projects that more traditional funding agencies might be hesitant to support. Research needs evolve quickly and unrestricted gifts to the IGB Annual Fund permit us to optimize funds by allocating them for the projects that need them most.

iGEM Undergraduate Team

The IGB hosts a team of undergraduates from multiple departments to participate in the International Genetically Engineered Machine (iGEM) competition. This opportunity provides students the development of open community and collaboration for the advancement of synthetic biology. Funds for the iGEM team will give undergraduates the chance to present their research to an international audience in Boston.