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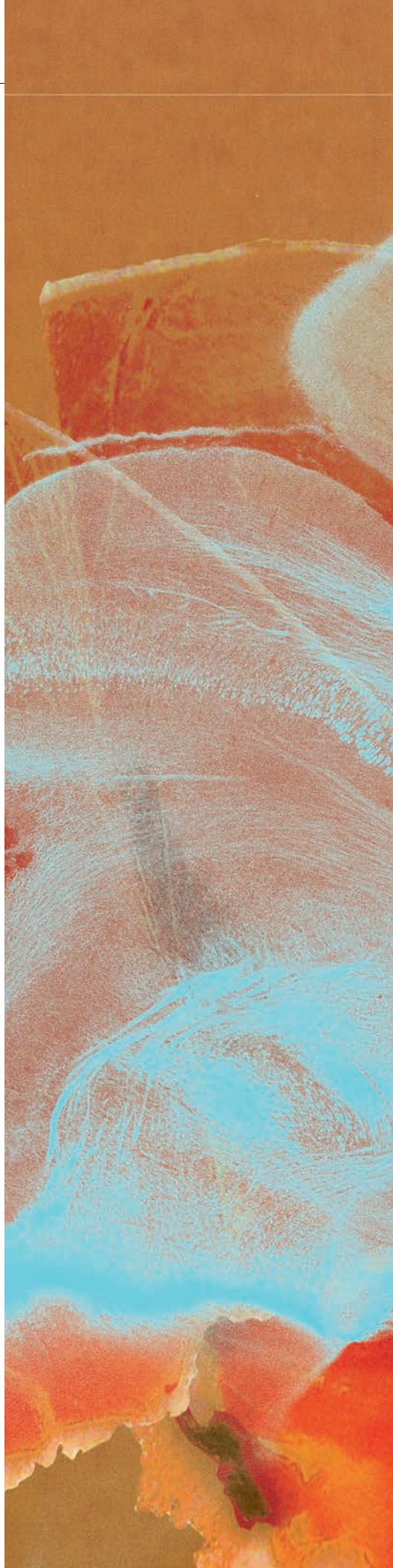


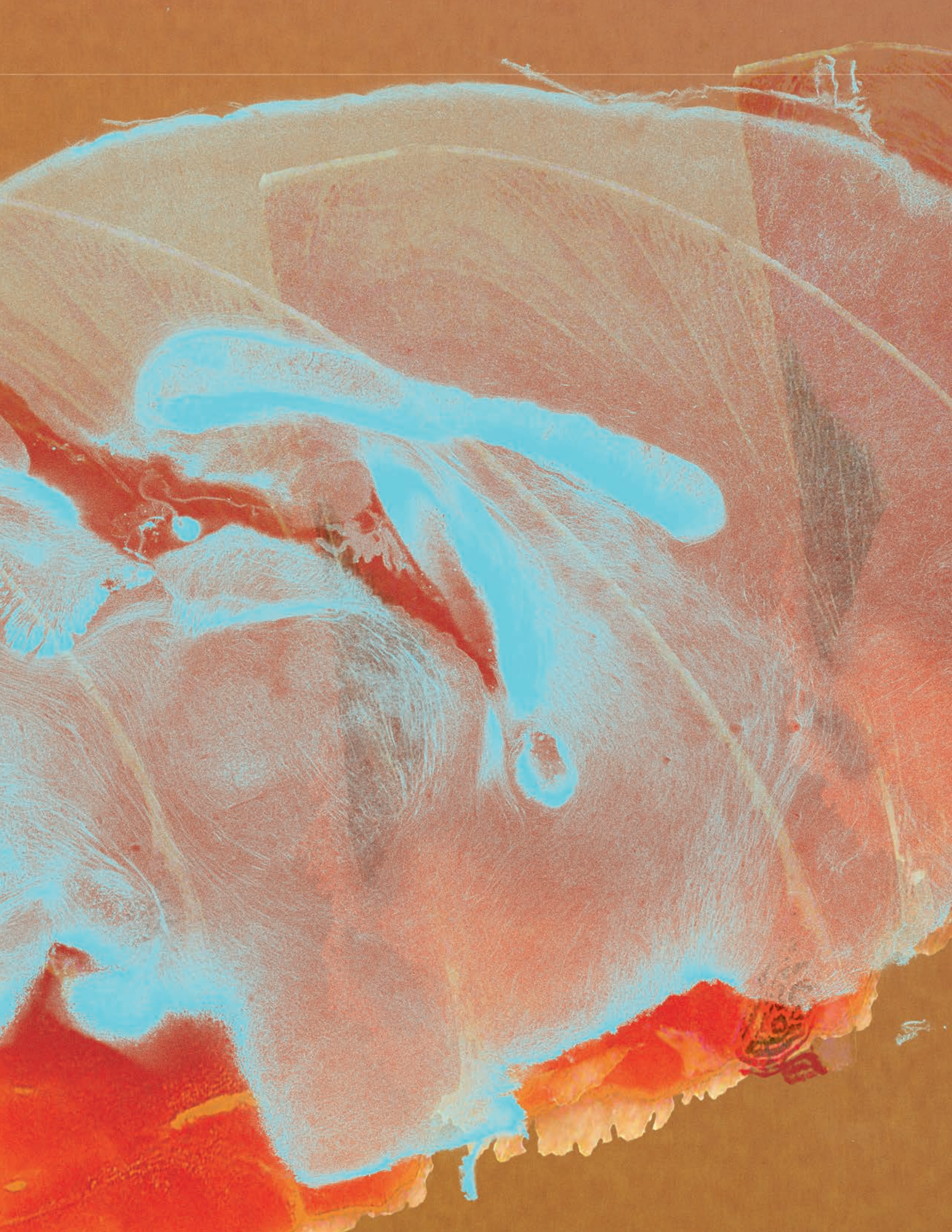
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN

Where Science Meets Society

Now is the time to understand more, so that we may fear less.

—Marie Curie





IGB Themes

ACPP	Anticancer Discovery from Pets to People
BCXT	Biocomplexity
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
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
CNLM	Center for Nutrition, Learning, and Memory
HPCBio	High-performance Biological Computing

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



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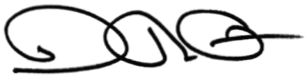
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Director's Message

"In the face of adversity, we are witnessing a period of growth and renewed sense of purpose within the IGB community."





Don Ort

ACTING DIRECTOR,
CARL R. WOESE
INSTITUTE FOR GENOMIC BIOLOGY

IN A YEAR OF CHALLENGES, WE FIND OPPORTUNITY

Genomics is key to unlocking nature's hidden secrets, informing us about the natural world and leading us to better solutions in therapeutics, health, agriculture and technology. This year's annual report reminded us about the interconnectivity between genomics and our everyday lives and the choices we make. The complex yet unifying feature of the genome is fascinating, revealing previously unidentified connections between us and the world we live in. As a society, we are experiencing a year full of challenges and unexpected events but also opportunities. When faced with the unknowns of the pandemic, we were able to turn to the power of genomics to better understand and mitigate this emerging infectious disease.

In this year's edition of *Biomarker*, we highlight the accomplishments, discoveries, and initiatives that have transpired this year at the IGB. Amidst the pandemic, our researchers, staff, students, and faculty were at the forefront, leading cutting-edge research and answering the call from the State of Illinois in the fight against COVID-19. We are proud to share previous and ongoing campus wide efforts in this edition and are especially proud of members of the IGB who were involved. Within these pages, you will learn about new research themes and centers focusing their research efforts on areas that are both timely and exciting. You will hear about a new enzymatic reaction, learn about photosynthetic efficiency in rice cultivars, and identify new approaches to induce antibiotic production in bacteria. In addition to highlighting genomic research that continues to accelerate diagnostics and personalized medicine, we are shedding light on our budding diversity, equity and inclusion efforts. Recent events have left the scientific community shaken, spurring discussions on unconscious biases and institutional racism in science. As a science institution, we have a responsibility to our community at large to remain transparent, honest, and intentional. We can, and will do better, to make the IGB a more inclusive and diverse environment.

Our dedication to connecting genomics with society has never changed. Despite suspension of in-person activities, we were able to adapt our outreach events, seminars, and other interactions to virtual formats. In the face of adversity, we are witnessing a period of growth and renewed sense of purpose within the IGB community. What comes next is just as important: there is still more work to be done, but we are ready. ■



Illustration by Richard A. Chance

Diversity, equity and inclusion efforts at the IGB

IN LIGHT OF RECENT EVENTS, especially the killing of George Floyd, Ahmaud Arbery, Breonna Taylor and all too many others, more people across the nation are calling for change. Black Lives Matter protests against racism and police brutality continue and are gaining strength every day. However, institutional racism not only exists in law enforcement but also in science. As a scientific community, the IGB values equality and respect for every member. 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. We are proud of our ongoing efforts to create programs to diversify science and increase participation from members of minority groups in genomics, including Pollen Power, SING and our partnership with Fisk University. Still, at this moment, the IGB can and should do more to diminish racism and other intersectional inequities.

Diversity, equity and inclusion efforts will be bolstered to create a more welcoming and inclusive environment for all members and visitors of the IGB. To do so, we are intensifying efforts to develop programs centering on diversity, equity and inclusion in science, funding new initiatives to help eliminate institutional racism at the IGB, and strengthening intercultural relationships across campus.

Committe on Diversity Task Force

With the guidance and support of the IGB Committee on Diversity (COD), we have organized a COD Task Force that will amplify diversity, equity, and inclusivity efforts of the COD through programs, partnerships, dialogues, and other actionable events.

We are seeking volunteers who are willing to make a significant commitment to developing, organizing, and realizing these efforts. At a time when these issues are highly visible, we must continue to advocate to keep ourselves and our community motivated and involved. Members of the IGB community that are interested in joining the task force can email codtf@igb.illinois.edu.

Ongoing collaboration approved for additional funding

A collaboration with Fisk University was approved for an additional five years of continued financial support from the Office of Executive Associate Chancellor for Administration and University Relations and the Office of the Vice Chancellor for Research (OVCRI). Founder Professor of Physics Jun Song (ACPP) will oversee hands-on bioinformatics, data analysis, and biophysics training for under-represented minority undergraduate students from Fisk University, a minority-serving institution (MSI) in Nashville, Tennessee.

The IGB and the Department of Physics will provide administrative and technological support to hosting students and also manage faculty-faculty collaborations between Fisk University and the University of Illinois. The Grainger College of Engineering will also contribute funds, and its new "Institute for Inclusion, Diversity, Equity, and Access" (IDEA) Institute will help establish research collaborations between Illinois and Fisk faculty members. The Carver Biotechnology Center's High-Performance Biological Computing group (HPCBio) will also provide personalized training resources and consulting.

Formed in 2014, the Fisk collaboration emerged as Illinois was granted one of the Big Data to Knowledge (BD2K) grants from the National Institutes of Health. In that same year, an R25 program/partnership between the Knowledge Engine for Genomics (KnowEnG) Center, which included Mayo Clinic and Fisk University, was forged.

Students take part in two consecutive summer training programs, where they become acclimated to the campus and research environment in the first year by externing with HPCBio before choosing a faculty member to conduct research with at either the University of Illinois' SROP (Summer Research Opportunities Program) or Mayo Clinic's SURF (Summer Undergraduate Research Fellowship) in their second year.

"We provided hands-on training for utilizing a high-performance computing cluster and performing statistical analyses of genomic data," said Song. "In the end, they got to analyze real sequencing data that were produced by Illinois faculty."

In partnership with Mayo Clinic, a computational biology summer course is also offered to Fisk University faculty members and students, organized by IGB Director of Computational Genomics Saurabh Sinha (BSD/CABBI/GNDP/GSP) who co-directed the BD2K center with Professor of Computer Science Jiawei Han (GNDP) and taught by IGB and HPCBio faculty and staff. In addition, a bioinformatics seminar, taught by Professor of Animal Sciences Sandra Rodriguez-Zas (GNDP), is broadcasted from the IGB to Fisk University in the spring, which has been ongoing for four years.

Since 2016, eight students have participated in the Fisk program, including one student who conducted research at Mayo Clinic, and two students who conducted research at Illinois' SROP. The majority of those students are now pursuing a degree in higher education or applying to medical schools.

Previously, two Fisk University students, Jaia Holleman and Skye Faucher, spent five weeks learning programming languages, executing a bioinformatics pipeline, gaining professional development skills, and touring facilities and labs within the IGB.

"It was so great being able to meet new people, broaden my horizons, and explore a field that I didn't know I would have necessarily been interested in," said Holleman.

"I enjoyed being surrounded by a group of aspiring young scientists, much like myself, and experiencing the true interdisciplinary nature of science through discussions about our educational and career goals," said Faucher.

Fisk University students who successfully complete the full two stages of training in the biophysics track will be automatically eligible to enroll in the physics PhD program at Illinois.

Song views the collaboration with Fisk University as a springboard for future partnerships with other MSI, with the goal of increasing overall diversity on campus.

"The IGB, HPCBio, SROP, the Department of Physics, and the Center for the Physics of Living Cells are the core components of the future direction that we will take. I think this initiative is a major accomplishment that would not have been possible without the dedicated effort of many people involved and the support from the Chancellor's Office." ■



A testing volunteer bags test samples in a COVID-19 testing facility on the Illinois campus

University of Illinois at the forefront in the battle against Covid-19

THE EMERGENCE OF THE SARS-COV-2 virus has devastated countries around the world, with the COVID-19 pandemic taking a heavy toll on the United States. Leading groundbreaking research in the fight against COVID-19 is the University of Illinois, which at one point was churning out more than 15,000 tests per day across its 17 testing sites during the fall 2020 semester.

Answering the call

Launched in April, a collaborative effort spearheaded by microbiology professor Chris Brooke (IGOH) at the University of Illinois produced enough viral transfer media (VTM) to support some 200,000 coronavirus tests across the state.

"This was a clear example where U of I students, postdocs, faculty, and staff stepped up and volunteered a ton of time and hard work to help save lives in the community," said Brooke. "What we're doing is small compared to the health workers who are actually serving patients on the front lines."

"It has been deeply gratifying to see how faculty, staff, and students have stepped up to make it possible for the institute to contribute to this critical effort," said Gene Robinson (GNDP), Swanlund Chair of Entomology and director of the Carl R. Woese Institute for Genomic Biology. "This has been an inspirational team effort fueled by altruism."

Another call was answered by Illinois researchers when leaders from the Illinois RapidVent team explained they had built a prototype of an emergency ventilator to address a nationwide shortage amid the COVID-19 pandemic. Professor of animal sciences Matt Wheeler (RBTE) got the call in March to launch an experiment to test device function in animals. A few tweaks and a few days later, final testing in pigs was complete and the RapidVent worked. The device was designed for short-term, emergency respiratory support in hospitals when regular ventilators are not available.

"I signed up in ag more than 40 years ago to feed people, to take care of people, and help people who needed help," Wheeler said. "That's what we do in agriculture, and what we do in the College of ACES."

Donating testing equipment, supplies, and personnel

Another campus wide effort was launched earlier in the year to help with equipment, personnel, and supply shortages. The effort has not only allowed healthcare workers at Carle to begin testing for COVID-19, but has allowed expanded partnership to the Illinois Department of Public Health (IDPH) and Illinois Emergency Management Agency to ramp up testing operations.

"It's been a tremendous team effort, involving lots of people and lots of different partnerships," said Marty Burke (MMG), May and Ving Lee Professor for Chemical Innovation in the Department of Chemistry and associate dean for research at the Carle Illinois College of Medicine. "It's so amazing to see everybody team up and try to get something done that's impactful."

Equipment, supplies, and personnel to support the work were loaned by three campus units: the IGB, the Roy J. Carver Biotechnology Center (CBC), and the College of Veterinary Medicine.

Another team, which included Alumni Research Scholar Professor of Chemistry Doug Mitchell (MMG), Stanley O. Ikenberry Chair and Professor of Chemistry and Materials Science and Engineering and director of the Beckman Institute for Advanced Science & Technology Jeffery Moore (BSD), Swanlund Chair and head of the Department of Materials Science and Engineering Nancy Sottos, and James R. Eiszner Endowed Chair in Chemistry Martin Gruebele, launched the mass production of nasopharyngeal swabs. In collaboration with Carle diagnostic labs, the team reverse-engineered a commercial swab to design and test their own.

Developing rapid, saliva-based COVID-19 testing

Under the umbrella of an approved FDA Emergency Use Authorization, the University of Illinois is now performing its new rapid, saliva-based COVID-19 test. The CLIA-certified lab at Illinois performed a bridging study to a recently approved FDA EUA, granted to Yale School of Public Health, showing that the Illinois test performs at least as well as the recently approved saliva-testing protocol.

"Today's news puts the University of Illinois and the entire state of Illinois on the cutting edge of testing innovation on a national level," said Illinois Gov. J.B. Pritzker. "I'm so proud—but not at all surprised—to see this type of groundbreaking work come out of our own University of Illinois and I want to applaud President Killeen and the entire research and development team at University of Illinois for this achievement."

> **"This has been an inspirational team effort fueled by altruism."**

Unlike most coronavirus tests, the Illinois-developed saliva test asks those tested to drool a small amount into a sterile test tube. The test yields results in hours, even at high testing volumes: By the end of October Illinois had performed more than 670,000 testssince making walk-up testing available to faculty members, staff and students in July.

The Illinois protocol has one key element that makes it uniquely suited for large-scale adoption, said Professor of Chemistry Paul Hergenrother (ACPP leader/MMG), who helped to develop the test. "We inactivate the virus without opening any tubes by immediately heat-inactivating samples at 95 C for 30 minutes," said Hergenrother. "That makes it very safe for the workers in the diagnostic lab."

The university has developed SHIELD, a three-pronged "target, test, tell" system that incorporates testing with data reporting, modeling and a smartphone app, working closely with the Champaign-Urbana Public Health District for contact tracing and isolation for individuals who test positive.

"The bridge to FDA Emergency Use Authorization is extremely exciting and important news for all of us in this pandemic," said Robert J. Jones, the chancellor of the Urbana campus. "We're proud to be the university that is home to a huge team of amazingly dedicated and talented researchers who came together so quickly to move this test from concept to use approval in just a matter of months." ■



Illustration by Macrovector

Teams awarded NSF grants for artificial intelligence & biology integration institutes

IN A YEAR OF UNPRECEDENTED EVENTS, research at the University of Illinois Urbana-Champaign continues to push boundaries and establish new research institutes. This year alone, the NSF has invested a combined total of $52 million across a five-year period into three institutes at the University of Illinois: the AI Institute for Molecular Discovery, Synthetic Strategy and Manufacturing (Molecule Maker Lab Institute or MMLI), the AI Institute for Future Agricultural Resilience, Management and Sustainability (AIFARMS), and the Genomics and Eco-evolution of Multi-scale Symbioses (GEMS) institute.

University of Illinois to lead two new artificial intelligence institutes

The NSF, along with the U.S. Department of Agriculture's National Institute of Food and Agriculture, is establishing seven new AI institutes, with two of the seven led by teams at the University of Illinois Urbana-Champaign, to accelerate research, expand America's workforce, and transform society in the decades to come. Enabled by sustained federal investment and channeled toward issues of national importance, continued advancement in AI research holds the potential for further economic impact and improvements in quality of life. With an investment of over $100 million over the next five years, NSF's AI Institutes represent the nation's most significant federal investment in AI research and workforce development to date.

The USDA-NIFA will fund AIFARMS, which will be led by Professor of Computer Science Vikram Adve. AIFARMS will advance AI research in computer vision, machine learning, soft-object manipulation and intuitive human-robot interaction to solve major agricultural challenges. Such challenges include sustainable intensification with limited labor, efficiency and welfare in animal agriculture, the environmental resilience of crops and the preservation of soil health. The institute will feature "a novel autonomous farm of the future, new education and outreach pathways for diversifying the workforce in agriculture and technology, and a global clearinghouse to foster collaboration in AI-driven agricultural research," Adve said.

A team led by Steven L. Miller Chair Professor of Chemical and Biomolecular engineering Huimin Zhao (BSD leader/CABBI/MMG) will spearhead research at the MMLI. The multi-institutional team consists of researchers and collaborators from the Grainger College of Engineering, the College of Liberal Arts and Sciences, the Beckman Institute for Advanced Science and Technology, and the National Center for Supercomputing Applications at the University of Illinois Urbana-Champaign, and from University Laboratory High School, Northwestern University, Penn State University, and Rochester Institute of Technology.

The MMLI focuses on development of new AI-enabled tools to accelerate automated chemical synthesis and advance the discovery and manufacture of novel materials and bioactive compounds. Researchers use the data generated from the analysis of these molecules to guide further development of synthesis planning and catalyst design tools using AI and machine learning. The institute also serves as a training ground for the next generation of scientists with combined expertise in AI, chemistry, and bioengineering.

"Over the past decade there have been major advances in both AI and automated chemical and biochemical synthesis, making the timing for the launch of the MMLI both judicious and urgent," said Zhao. "Synergistically integrating these powerful disciplines now has the potential to dramatically accelerate and advance the manufacturing and discovery of molecules with important functions that address major unsolved problems in society. Not doing so would result in a major missed opportunity for the U.S. research community."

"The NSF and USDA-NIFA recognize the breadth and depth of Illinois expertise in artificial intelligence, agricultural systems and molecular innovation," U. of I. Chancellor Robert Jones said. "It is no surprise to me that two of seven new national AI institutes will be led by our campus. I look forward to seeing the results of these new investments in improving agricultural outcomes and innovations in basic and applied research."

"The NSF & USDA-NIFA recognize the breadth & depth of Illinois expertise in artificial intelligence, agricultural systems & molecular innovation."

Collaborative team awarded NSF grant for biology integration institute

In addition to the seven new AI institutes, the NSF recently established the GEMS institute for integration of biology. The interdisciplinary team of 27 professors from microbiology, plant biology, entomology, ecology, evolution, computational biology, and education will be led by Professor of Microbiology Rachel Whitaker (IGOH leader/BCXT), Professor of Evolution, Ecology and Behavior Carla Cáceres (IGOH), Professor of Plant Biology Katy Heath (IGOH), Professor of Ecology and Evolution Mercedes Pascual (University of Chicago), and Professor of Biology Irene Newton (Indiana University). GEMS researchers will integrate recent discoveries in the field of microbial symbiosis with evolution and ecology using molecular, organismal, computational and theoretical approaches.

"The inspiration behind GEMS is to integrate biology since all too often, fields of biology are siloed by funding, approach, language and culture," said Whitaker. "Surprisingly, some of the most significant divides on many campuses are between molecular and organismal approaches to biology. Because microbes lie at the interface between these spheres, our focus is on bringing the natural microbial world into view to integrate biology.

"What we don't truly understand is how genetic and molecular mechanisms used by microbes to interact with their hosts translates to large scale ecological and evolutionary processes," said Newton. "With this institute, we will study biology at multiple scales (from genetic and microbial to organismal, ecological, and evolutionary) and involve multiple disciplines within and outside of biology to fill these gaps in knowledge." ■



Illustration by Jillian Nickell

Three new research themes and one center take shape at the IGB

ENGINEERED LIVING SYSTEMS, PERSON-alized medicine, genomic data protection, and reproductive health: these research areas are represented by the three newly established research themes and one research center at the IGB.

Personalizing medicine and revolutionizing diagnostics

The research theme Omics Nanotechnology for Cancer Precision Medicine (ONC-PM), established in 2016, was converted to the Center for Genomics Diagnostics (CGD) in early 2020 and is helmed by Donald Biggar Willett Professor in Engineering Brian Cunningham (MMG). The CGD is broadening their focus on cancer to include a wide variety of diseases and conditions in an effort to revolutionize diagnostics and personalized medicine. The center's vision begins with molecules called biomarkers that are naturally produced as part of a healthy biological state or disease process.

The center will also be supported by the Grainger College of Engineering and will take advantage of specialized laboratory space and equipment in Illinois' Holonyak Micro and Nanotechnology Lab. With its expanded scope, the CGD will work closely with the Cancer Center at Illinois, Illinois' Health Care Engineering Systems Center, Mayo Clinic, and Illinois Alliance.

"Our goal for the center is first to use genomics and bioinformatics to identify novel biomarkers," said Cunningham. "As we seek to validate how biomarker presence and concentration changes with a specific health condition, we're also interested in developing novel biochemistry methods for selectively detecting those molecules with methods that are simple, yet extremely sensitive."

Protecting genomic data

Established in late 2019, the Genomic Security and Privacy (GSP) research theme addresses issues of genomic data used in healthcare, privacy protection, and making ethical choices that respect the rights of communities and populations. The GSP theme is led by Professor of Computer Science Carl Gunter while Professor of Political Science Aleksander Ksiazkiewicz leads policy-based work within the theme.

"As the methods get cheaper to produce sequencing data . . . people are going to be a lot more concerned," said Gunter. "Going back ten years ago when it cost hundreds of millions of dollars to sequence something, it wasn't really that much of a concern, whether the data might be captured . . . but now, it seems like every time you turn around, there's some new security- or privacy-related concern."

Gunter and Ksiazkiewicz represent the two-pronged approach that the theme takes, simultaneously pursuing the identification of privacy concerns and development of strategies in the arenas of technology and policy.

The theme's work is strengthened by the interdisciplinarity of its research team, which includes Professor of Electrical and Computer Engineering Zbigniew Kalbarczyk, Professor of Food Science and Human Nutrition Zeynep Madak-Erdogan (CGD), Professor of Anthropology Ripan Malhi (GNDP/IGOH), Hoeft Endowed Chair in Information Systems at Gies College of Business Michael Shaw, Professor of Computer Science and IGB Director of Computational Genomics Saurabh Sinha (BSD/CABBI/GNDP), and Mildred Van Voorhis Jones Chair in Law Robin Wilson.

Gunter and members have contributed to related events around campus, including a recent NIH workshop on issues of equity and diversity in genomics and a TEDxUIUC talk by Gunter highlighting the urgency and everyday relevance of genomic privacy and security issues.

Engineering living systems

Another new theme, Multi-Cellular Engineered Living Systems (M-CELS), will develop systems composed of living cells and extracellular matrices organized to perform novel functions absent in natural systems. Two research programs—bio-hybrid robots and biological processors—form the foundation of the M-CELS theme, which is led by Robert W. Schafer Professor of Chemical and Biomolecular Engineering Hyunjoon Kong (EIRH/RBTE).

"We can utilize M-CELS to assemble various transformative engineering systems, such as a biohybrid robot, an organic computer, and an energy generation device, as well as other new and unforeseen possibilities," said Kong.

Theme members include Professor of Bioengineering Rashid Bashir (CGD), Professor of Cell and Developmental Biology Martha Gillette (GNDP), Professor of Mechanical Science and Engineering Mattia Gazzola and Professor of Mechanical Science and Engineering Taher Saif (RBTE).

Improving reproductive health

Most recently formed, the Environmental Impact on Reproductive Health (EIRH) theme will focus on improving reproductive health by gaining fundamental knowledge in both normal variation in reproductive function and fertility disorders/diseases and developing therapeutic tools. The EIRH theme represents the first co-led theme, with Professors of Comparative Biosciences Indrani Bagchi and Jodi Flaws (MME) serving as co-theme leaders.

Researchers will examine the effects of exposure to endocrine disrupting chemicals (EDCs) on fertility, placental function, and endometriosis and investigate the impact of stress and high fat diets on fertility and pregnancy outcomes.

EIRH theme members include Professor of Molecular and Integrative Physiology Milan Bagchi, Professor of Anthropology Katrhyn Clancy, Professor of Chemical and Biomolecular Engineering Brendan Harley (RBTE leader), Professor of Chemical and Biomolecular Engineering Amy Wagoner Johnson (RBTE), Professor of Comparative Biosciences CheMyong Ko (MME), Professor of Chemical and Biomolecular Engineering Hyunjoon Kong (M-CELS leader/RBTE), Professor of Animal Science David Miller, Professor of Animal Science Romana Nowak, Professor of Molecular and Integrative Physiology Lori Raetzman (GNDP), and Professor of Comparative Biosciences Jing Yang. Along with research endeavors, theme members will participate in the Summer Undergraduate Research Experience in Toxicology (SURE Tox) and Grainger College of Engineering Illinois Scholars Undergraduate Research (ISUR) programs at Illinois.

"We thought it would be great to bring basic scientists and bioengineers together to work on important research questions in the field," said Bagchi and Flaws. "If we can better understand how the environment impacts reproductive health, we can develop methods to prevent or treat reproductive diseases that are caused by environmental exposures." ■



Paving the way for genomic research at the IGB

AS A RESULT OF SEED FUNDS FROM alumnus Scott Fisher, Professor of Cell and Developmental Biology Lisa Stubbs and Robert W. Schaefer Professor of Chemical and Biomolecular Engineering Brendan Harley (RBTE leader/EIRH) were further funded by the National Cancer Institute within the NIH to use three-dimensional hydrogel systems to study neurodegenerative disease models, particularly Alzheimer's disease.

"The funding from Scott Fisher was essential for us," said Harley. "It allowed us to gather the preliminary data we needed to show that we could adapt the biomaterials we are developing to study brain cancer in order to investigate processes related to neurodegeneration."

In a proof-of-principle study led by Research Assistant Professor Sara Pedron-Haba, PhD student Samantha Zambuto, and postdoc Julio Serrano, hydrogels, which are polymers used for soft tissue regeneration, were demonstrated as viable cell culture platforms for investigating neurodegenerative processes. More importantly, the hydrogel system could be used to investigate the effects of hypoxia-mediated stress on neural cell populations. Their findings were reported in the journal *MRS Communications*.

"This supplement is letting us expand the work Scott helped initiate," said Harley. "Each is

The IGB's Walk of Life

a stepping stone to larger scientific questions, but honestly without the initial seed from Scott this never would have gotten off the ground."

Established earlier this year, the Drs. Martha Oehmke Loustaunau and Joaquin O. Loustaunau Graduate Travel Fellowship for Computational Genomics will provide professional development support to graduate students in the areas of computational genomics, systems biology, genome technology, and metabolic engineering.

Growing up in the small rural town of Monticello, Illinois, Martha Loustaunau began her studies at the University of Illinois, receiving her BA in Latin American Studies and later a MS in Journalism. Loustaunau had attended summer school in Guadalajara, Mexico the previous summer and was therefore interested in connecting with Latin American students at the U of I. It was there that she met Joaquin, who was pursuing a PhD in mathematics.

Later on, the Loustaunau's interests in genomic biology stemmed from a passion for horses.

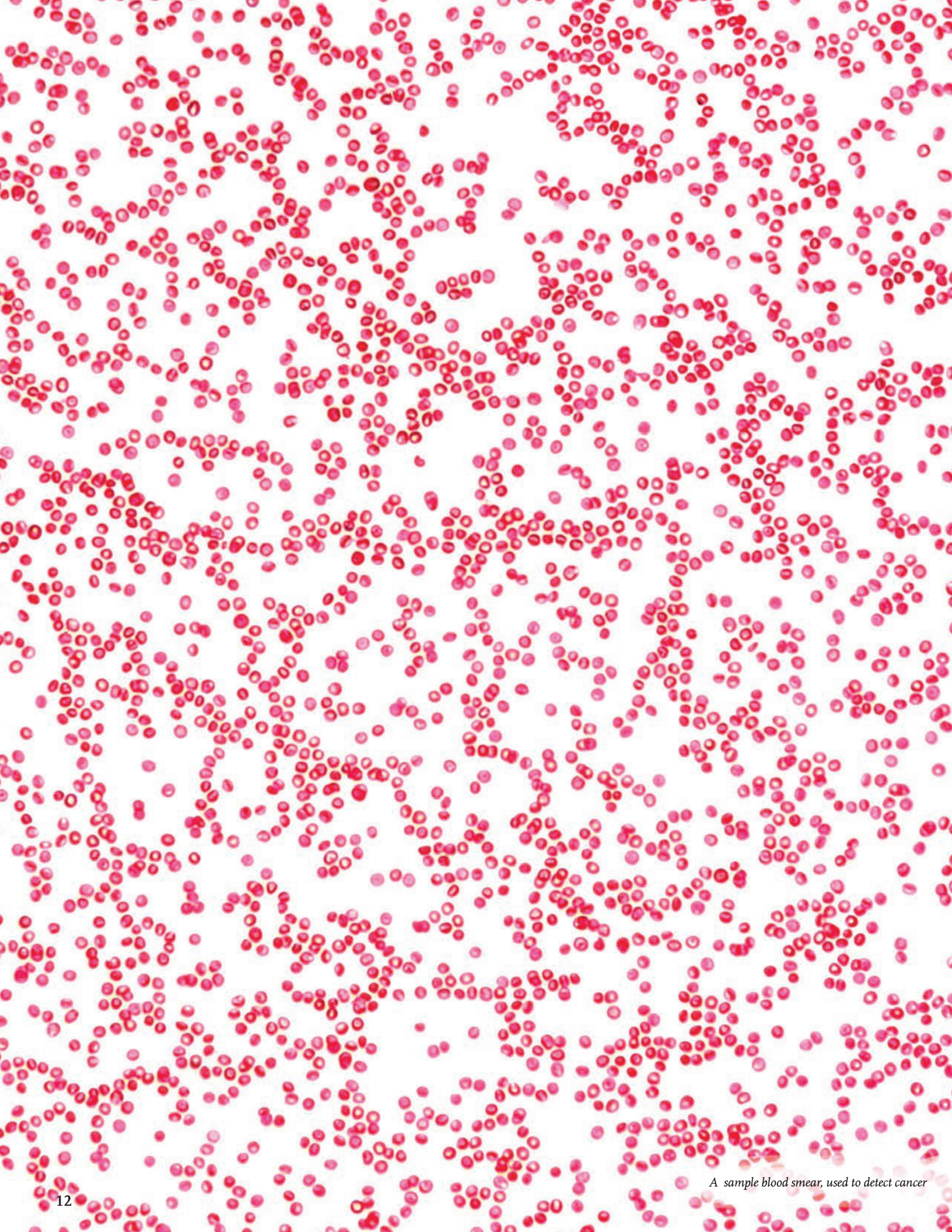
"His interest in genetics grew and expanded to animal and human genetics, and he told me that if he had to do it all over again, he would become a geneticist," said Loustaunau.

After Joaquin's passing in 2002, Loustaunau started an academic graduate scholarship in Joaquin's name at NMSU geared towards underrepresented minority students from the departments of mathematics, biology, and sociology, with a focus on genetics. Thereafter, Loustaunau established a similar scholarship at the U of I.

Alongside other pavers that comprise the IGB Walk of Life, one can find the words "In gratitude that our walk of life brought us together, Drs. Joaquin and Martha Loustaunau" inscribed on her paver. This paver represented the Loustaunau's lasting connection to the U of I, both sharing a strong desire to contribute what they could for the benefit of others and ultimately, to making the world a better place. ■



Lisa Stubbs (left), with Brendan Harley and Sara Pedron-Haba



A sample blood smear, used to detect cancer

Personalizing cancer diagnostics

WHEN ASSESSING WHETHER OR NOT a tumor is benign or cancerous, a needle biopsy is the usual method of diagnosis. The tissue can then be analyzed to determine what mutations are present that are specific to the patient. Because this method is invasive, it's generally only used once. During and after chemotherapy, imaging tests are used to monitor the size of the tumor; however, imaging only shows the physical characteristics of the tumor—it fails to monitor what is actually happening to the cells.

Research funded by NIH and conducted through the Holonyak Micro & Nanotechnology Lab is working to develop a device that can detect cancer biomarkers with just a few drops of blood. The method would provide rapid results, enabling the clinician to quantitatively observe the effects of treatment on the tumor by measuring increases or decreases in strategically selected molecules.

"The future of cancer diagnosis is moving towards the idea of "liquid biopsy" in which cancer-specific molecules can be found and measured from easily obtained bodily fluids," says Brian Cunningham (CGD Director/MMG), the Intel Alumni Endowed Chair with appointments in electrical and computer engineering and bioengineering. "Since each person is genetically unique, each cancer can also be unique, and medicine is driving towards something becoming known as 'personalized medicine' in which a highly effective treatment can be selected based on measured characteristics from the patient."

The team will develop a new approach for detecting a novel class of cancer biomarkers from just a few droplets of blood, such as those collected with a finger prick. Cunningham's team will use molecules called "microRNA" that have specific nucleic acid sequences present in a cancerous mutation.

Cunningham's team invented a new type of biosensor microscope and a new detection approach so this test can be performed very simply and easily. While this microscope has many applications, the challenging demands of detecting microRNA from blood was a motivating factor in its invention. This technology makes repetition of this test simple so it can be performed as often as necessary to evaluate how exosomes change during and after cancer treatment.

"We think that our approach could be used to enable the physician to pivot from a non-working treatment to a better one based on measured changes in the microRNA molecules," says Cunningham, who is also affiliated with the Cancer Center at Illinois (CCIL). "They can measure how the tumor is responding on a much more detailed and frequent basis than measuring the tumor size by imaging."

The Illinois research team also includes Manish Kohli at the Huntsman Cancer Institute and Utkan Demirci at Stanford University, as well as chemistry professor Yi Lu (BSD/CABBI/CGD) and Professor of Epidemiology Rebecca Smith (IGOH).

"My parents both passed away from cancer at too young of an age," says Cunningham. "Since that time, I have been working towards using engineering tools to develop better drugs and diagnostic methods for cancer. My hope is that someday cancer will become a disease that is effectively managed, but to do so will require detailed knowledge about the genetics of each patient's tumor." ■



Brian Cunningham, Intel Alumni Endowed Chair

Cowpea research boosts canopy CO2 assimilation, water-use efficiency

CROPS GROW DENSE CANOPIES THAT CONSIST OF SEVERAL layers of leaves – the upper layers with younger sun leaves and the lower layers with older shaded leaves that may have difficulty intercepting sunlight trickling down from the top layers.

In a recent study published in *Food and Energy Security*, scientists from Realizing Increased Photosynthetic Efficiency (RIPE) aimed to understand how much variation exists within diverse cowpea lines in light absorption and carbon dioxide (CO2) assimilation throughout the canopy. This information can ultimately be used to design more efficient canopies—with greater CO2 assimilation and water-use efficiency—to increase yields.

> **"This work has established that variation exists that can be used to improve productivity and efficiency of an important food security crop."**

RIPE, which is led by the University of Illinois, is engineering crops to be more productive by improving photosynthesis, the natural process all plants use to convert light energy to produce biomass and yields. RIPE is supported by the Bill & Melinda Gates Foundation, the U.S. Foundation for Food and Agriculture Research (FFAR), and the U.K. Government's Department for International Development (DFID).

Cowpeas, commonly known as black-eyed peas in the U.S., are one of the oldest domesticated crops in the world, responsible for feeding more than 200 million people per day. Cowpeas, commonly known as black-eyed peas in the U.S., are one of the oldest domesticated crops in the world, responsible for feeding more than 200 million people per day.

"They are a staple crop in Africa, providing a source of protein for humans and livestock, and restoration of soil nutrition through nitrogen fixation," said Lisa Ainsworth, a research plant physiologist with the U.S. Department of Agriculture, Agricultural Research Service (USDA-ARS).

The RIPE team screened 50 cowpea genotypes from a multi-parent advanced generation inter-cross (MAGIC) population for canopy architecture traits, canopy photosynthesis, and water-use efficiency by using a canopy gas exchange chamber.

"Since sub-Saharan Africa is the region where important yield gaps persist, it is crucial that we develop a high yielding crop that can be easily grown there," said first author Anthony Digrado, a USDA-ARS postdoctoral researcher in Ainsworth's lab based at Illinois.

The team used Principal Component Analysis (PCA) models to first group the 50 MAGIC genotypes into five general canopy architectural types to study plant traits, including leaf area index, leaf greenness, and canopy height and width. This analysis gave researchers the ability to gather an overview of the traits, or combinations of traits, that could be modified to have the strongest impact on canopy photosynthesis to maximize growth.

Overall, canopy architecture significantly affected canopy photosynthetic efficiency and water-use efficiency, suggesting that optimizing canopy structures can contribute to yield enhancement in crops.

"There is still a lot to do to improve cowpea yields and much more research is needed," Digrado said. "But this work has established that variation exists that can be used to improve productivity and efficiency of an important food security crop."

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. ■



Cowpeas growing in the RIPE research fields

SynFoNI: Strengthening synthetic biology in food, nutraceutical production

OVER THE YEARS, THE DEMOCRATIZATION OF SYNTHETIC biology for the production of food has led to products like the Impossible burger, a burger impostor that uses plant tissues instead of meat. Despite this, food companies remain hesitant to utilize synthetic biology due to concerns with genetically modified foods.

"SynFoNI will be a good testbed for interactions with the industry and a great way to close the gap between IGB and commercializaiton."

With the emergence of genome editing techniques, such as CRISPR-Cas, Professor of Food Science and Human Nutrition (FSHN) Yong-Su Jin (BSD/CABBI/MME) believes both the consumer and manufacturer can benefit from synthetic biology with minimal risks. This idea was used to propose the Synthetic Biology for Food and Nutrition Innovation (SynFoNI) program for which Jin currently serves as Director along with Deputy Director and Professor of FSHN Mike Miller (IGOH/MME).

"The clear goal of SynFoNI is to make ACES and Illinois a world leader in applying synthetic biology to food and nutritional problems," said Jin. "We are going to leverage excellent research facilities and programs here, which will provide the infrastructure to facilitate collaborations between the industry and the scientists on campus. Instead of changing many things which are mostly undesirable in the cell, we can use molecular surgery to change desirable base pairs with CRISPR-Cas. If we can do that, we can reduce the risks and create consumer products in a highly safe manner."

SynFoNI plans to build a network that integrates the IGB, the Integrated Bioprocessing Research Laboratory, the FSHN program, Agricultural, Consumer and



Illustration by Kelsey King

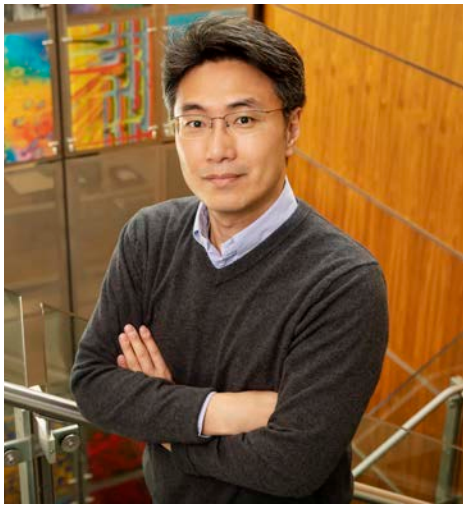
Environmental Sciences (ACES) farms, and numerous food companies in the Chicago area, with plans to create a Food Innovation Center at the Discovery Partners Institute in Chicago.

The initiative will also provide a new professional science master's (PSM) program in synthetic biology for food and nutrition, in addition to a new minor in fermentation science at ACES. Students in the PSM program will also get a unique training opportunity by learning about and using the Illinois Biological Foundry for Advanced Biomanufacturing (iBioFAB) machine for their research projects.

"We view the workforce as a critical limiting factor in synthetic biology," said Jin. "In this program, we will teach students the technology and skillset required for applying synthetic biology towards food and nutritional problems."

Jin believes that now is the time of a new revolution where genome editing technology replaces genetically modified foods. With SynFoNI in place, the strengthening of the Illinois Food and Agricultural industry research and training will take synthetic biology in food production to the next level.

"I am really grateful for the support from the IGB and opportunities to collaborate with top notch scientists," said Jin. "I would like to evolve this relationship by bringing more external industry people to the IGB. SynFoNI will be a good testbed for interactions with the industry and a great way to close the gap between the IGB and commercialization." ■



Professor of Food Science & Human Nutrition Yong-Su Jin



Illustration by Jillian Nickell

IGB Outreach receives first grant for STEAM TRAIN project

THIS YEAR, THE STEAM TRAIN (TRANS-disciplinary Research Across Institutional Near-Peers) project conceived by the IGB outreach staff was one of five projects awarded seed funding and up to two years of subsequent support from the Community + Research Partnership Program (CO+RE). The CO+RE grant represents the first awarded grant for outreach endeavors at the IGB.

Launched earlier this year, the Community + Research Partnership Program (CO+RE) —supported by the Office of the Vice Chancellor for Research and Innovation—is dedicated to fostering relationships between the community and researchers. Proposals are selected by a selection committee comprised of community and campus members based on potential impact in creative, scientific, and humanistic fields.

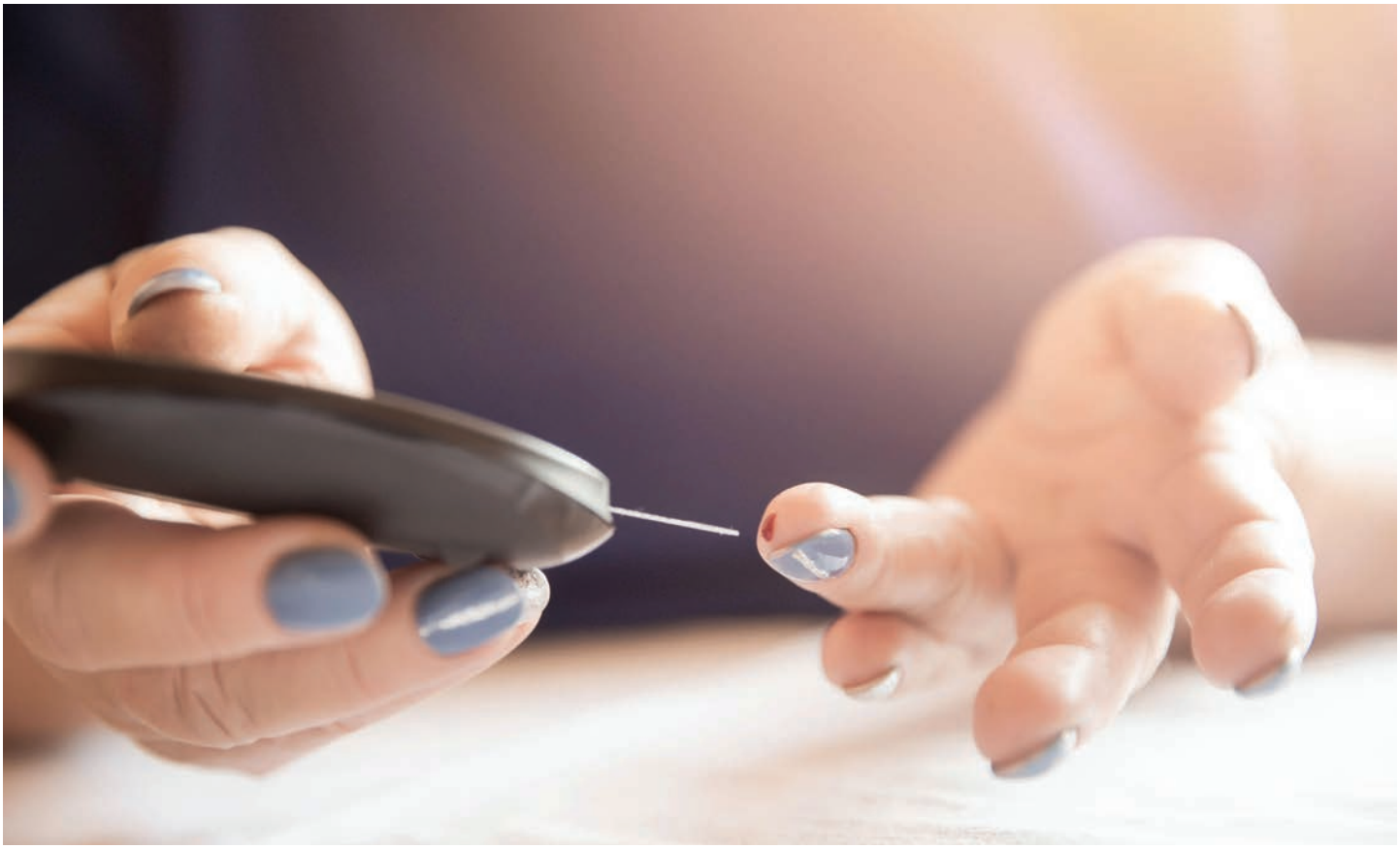
The STEAM TRAIN project is a student-led effort consisting of a partnership between Franklin STEAM Academy (Franklin) students, University of Illinois Laboratory High School (Uni) students, Illinois graduate and undergraduate students, and the IGB outreach staff. Through collaborations and multi-generational mentorship teams, students explore their own ideas for tackling grand life science challenges.

"For the past year we have been fostering a new relationship with the Franklin STEAM Academy, with coordination through Zanne Newman and Christopher Brunson," said Outreach Activities Coordinator Daniel Urban, who submitted the CO+RE grant. "This spring we taught an Agora Days class focused on bacteria and antibiotic resistance at Uni High School, which started a conversation with Uni chemistry professor David Bergandine who was interested in creating new opportunities for Uni students. When we heard about the CO+RE grant, we thought this would be a great way to combine our IGB outreach efforts with both Uni and Franklin students."

Students in the program partake in projects dependent on their science interests and research technologies that could lead to scientific advancement in their respective field. To help students complete their projects, the mentorship chain consisting of Franklin, Uni, and Illinois students, together with the IGB outreach staff, provide guidance and resources for modeling and testing project ideas.

> **"Ultimately, STEAM TRAIN seeks to promote increased science literacy and prolonged involvement, especially geared toward groups underrepresented in STEAM fields."**

"The primary goal of STEAM TRAIN is to create a mentorship chain between Illinois students, Uni students, and Franklin students where each group works with and provides guidance to their near-peers at the next level," said Urban. "Ultimately, STEAM TRAIN seeks to promote increased science literacy and prolonged involvement, especially geared toward groups underrepresented in STEAM fields. To this end, we will empower younger students to explore their own ideas for the future of science." ■



Pregnant women who develop gestational diabetes are at greater risk of developing Type II diabetes.

BRIDGE-ing the gap between diagnostics and gestational diabetes

AS A RESULT OF INTERSECTING research interests in women's health, a new collaboration was forged between Zeynep Madak-Erdogan (CGD/GSP), Assistant Professor in Food Science and Human Nutrition, and Justina Zurauskiene (CGD), Birmingham-Illinois Partnership for Discovery, Engagement and Education (BRIDGE) fellow and fellow at the Institute of Cancer and Genomic Sciences in Birmingham, England. Founded in 2014, the BRIDGE program is an ongoing partnership between the University of Birmingham and the University of Illinois Urbana-Champaign. The goal of the program is to provide a platform for exchange of creative knowledge through research and academic excellence, with the goal of addressing major global challenges.

Zurauskiene will be working with Madak-Erdogan for one year, where she plans to harness her computational biology expertise for generating and analyzing diverse datasets. Emphasis will be placed on health disparities in pregnant women and environmental factors that impact birth.

"We are focusing on gestational diabetes, a type of diabetes that appear in pregnant



Justina Zurauskiene (left) and Zeynep Madak-Erdogan

> **"We are trying to catch these things as early as possible so that the future generations are healthier."**

women who didn't have the condition before," said Madak-Erdogan.

"This disease is multifaceted. Once pregnant women develop the disease, the ball starts rolling and these women are at greater risk of developing Type II diabetes and so require more frequent monitoring of their health. They are also at risk of developing cardiovascular diseases later in life–so lots of long-term risks," explained Zurauskiene.

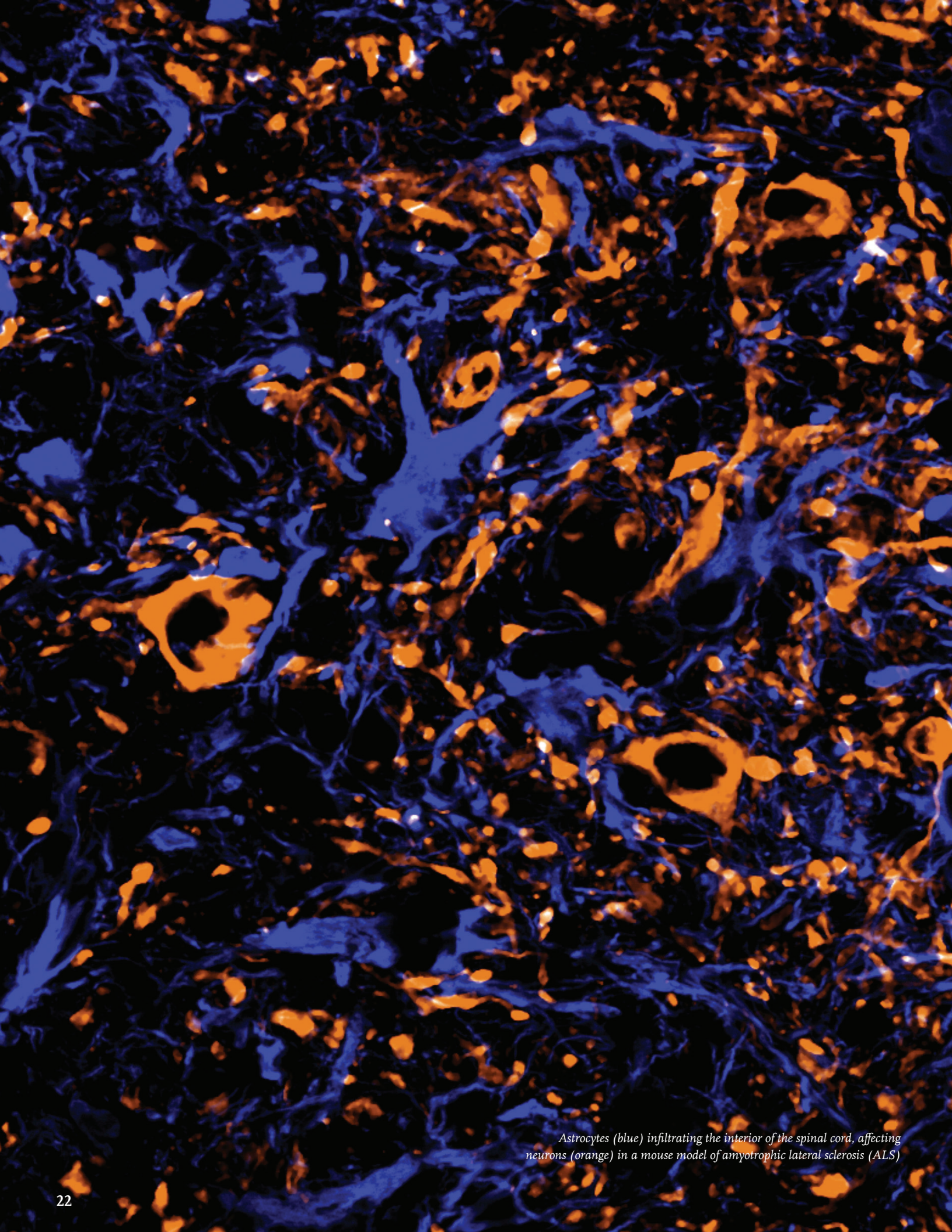
The researchers pointed out that the baseline for levels of the detected predictors of the disease might be variable across different races. Given that the majority of the tests are developed in Caucasian populations, the diagnostic tests represent one of the gaps or health disparities associated with this condition.

"We are partnering with a local public health department in Champaign-Urbana and they have a clinic within the department called Women Infants Children (WIC) Clinic. Their clientele are women who come from less advantaged backgrounds or don't have such a good medical care plan," said Zurauskiene. "We will be recruiting those women and hope to target a diverse population."

"In the long run, we would love to look into any changes in DNA that might be associated with the condition and any changes that come from the message of DNA or mRNA for example that might have differences," said Madak-Erdogan.

Given that sugars taken in during pregnancy are redirected to the developing baby, perspective mothers are less efficient at using glucose. Due to exposure to higher levels of glucose in the uterus, the baby is also at higher risk of developing obesity, Type II diabetes, and cardiovascular disease. More than ever, robust diagnostic tests are crucial to take necessary precautions early in development.

"The impact will be great given that obesity is rising and we are now learning more and more that exposures in the uterus are actually changing the outcomes for the baby," said Madak-Erdogan. "We are trying to catch these things as early as possible so that the future generations are healthier and you know, they are born with a biology that is less prone to these problems later in life." ■



Astrocytes (blue) infiltrating the interior of the spinal cord, affecting neurons (orange) in a mouse model of amyotrophic lateral sclerosis (ALS)

New CRISPR base-editing technology slows ALS progression in mice

WITH A NEW CRISPR GENE-EDITING methodology, Illinois scientists inactivated one of the genes responsible for an inherited form of amyotrophic lateral sclerosis—a debilitating and fatal neurological disease for which there is no cure. The novel treatment slowed disease progression, improved muscle function and extended lifespan in mice with an aggressive form of ALS.

"ALS unfortunately has few treatment options. This is an important first step in showing that this new form of gene editing could be used to potentially treat the disease," said bioengineering professor Thomas Gaj (BSD), who co-led the study with bioengineering professor Pablo Perez-Pinera (ACPP).

The method relied on an emerging gene-editing technology known as CRISPR base editors.

Traditional CRISPR gene-editing technologies cut both strands of a DNA molecule, which can introduce a variety of errors in the DNA sequence, limiting its efficiency and potentially leading to a number of unintended mutations in the genome. The Illinois group instead used base editing "to change one letter of the DNA sequence to another without cutting through both DNA strands," Perez-Pinera said.

"Base editors are too large to be delivered into cells with one of the most promising and successful gene therapy vectors, known as adeno-associated virus," Gaj said. However, in 2019, Perez-Pinera's group developed a method of splitting the base editor proteins into halves that can be delivered by two separate adeno-associated virus (AAV) particles. Once inside the cell, the halves reassemble into the full-length base editor protein.

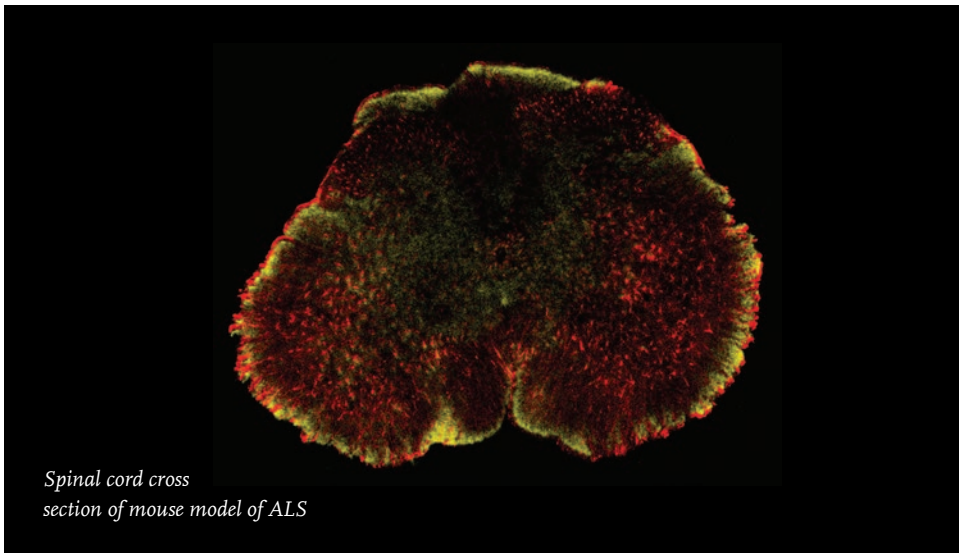
By combining the power of AAV gene delivery and split-base editors, Gaj and Perez-Pinera targeted and permanently disabled a mutant SOD1 gene, which is responsible for roughly 20% of inherited forms of ALS. They published their results in the journal *Molecular Therapy*.

"Many ALS studies are focused on preventing or delaying the onset of the disease. However, in the real world, most patients are not diagnosed until symptoms are advanced," said graduate student Colin Lim. "Slowing progression, rather than preventing it, may have a greater impact on patients." Lim is the co-first author of the study along with graduate students Michael Gapinske and Alexandra Brooks.

"Moving forward, we are thinking about how we can bring this and other gene-editing technologies to the clinic so that we can someday treat ALS in patients," Gaj said. "For that, we have to develop new strategies capable of targeting all of the cells involved in the disease. We also have to further evaluate the efficiency and safety of this approach in other clinically relevant models."

The split-base editor approach has potential for treating other diseases with a genetic basis as well, Perez-Pinera said. Though ALS was the first demonstration of the tool, his group has studies underway applying it to Duchenne muscular dystrophy and spinal muscular atrophy.

The Muscular Dystrophy Association, the Judith and Jean Pape Adams Foundation, the American Heart Association and the NIH supported this work. Perez-Pinera is affiliated with the Carle Illinois College of Medicine and the Cancer Center at Illinois. ■



Spinal cord cross section of mouse model of ALS

Nanostimulators boost stem cells for muscle repair

IN REGENERATIVE MEDICINE, AN IDEAL treatment for patients whose muscles are damaged from lack of oxygen would be to invigorate them with an injection of their own stem cells.

In a new study published in the journal *ACS Nano*, Illinois researchers demonstrated that "nanostimulators"—nanoparticles seeded with a molecule the body naturally produces to prompt stem cells to heal wounds—can amp up stem cells' regenerative powers in a targeted limb in mice.

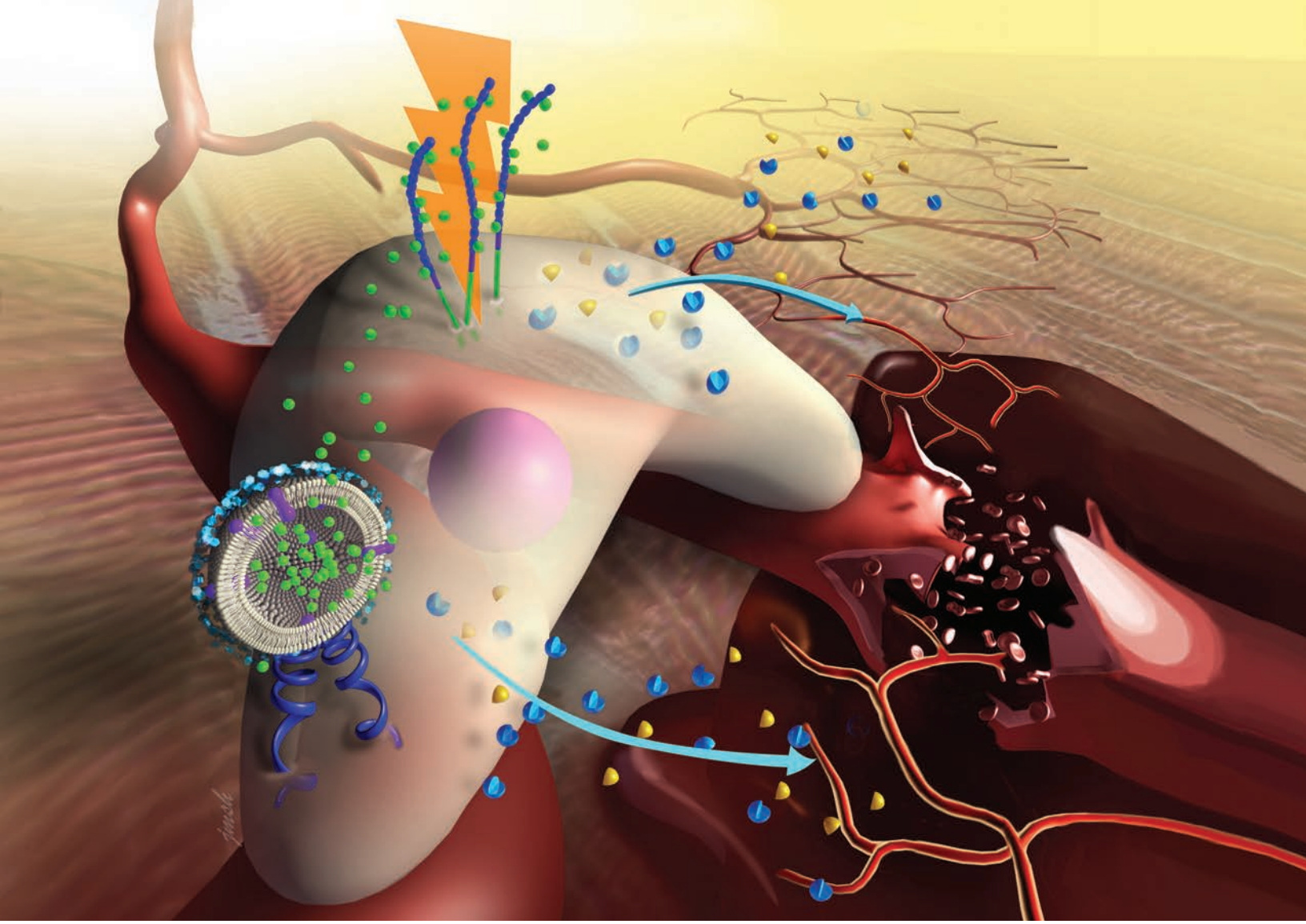
"We wanted to utilize the natural functions of the stem cells and the stimulating factors to address muscle ischemia locally," said study leader Hyunjoon Kong (M-CELS leader/EIRH/RBTE), a Robert W. Schafer Professor of Chemical and Biomolecular Engineering.

Muscle ischemia, or damage to muscle from limited oxygen or blood supply, can result from multiple causes, such as injury to a limb or peripheral artery disease. Stem cells derived from a patient's own fat tissue are known to produce factors that prompt new blood vessels to grow into the damaged muscle, restoring oxygen and nutrients, and to modulate inflammation in the damaged tissues. However, *in vivo* experiments have shown limited benefits, as the stem cells' activity seems to decline after injection into the muscle.

A molecule naturally produced in the body called tumor necrosis factor alpha can spur the stem cells to secrete more of the desired factors. Other studies have tried incubating the cells with TNF-alpha before injection, but the effects fade quickly, Kong said.

"We propose that this method is better than methods that require chemical preconditioning, which can ... have limited-time effects."

The Illinois team decided to try tethering the TNF-alpha directly to the stem cells, creating nanostimulators—nanoparticles laced with TNF-alpha. The nanoparticles bind to



Nanostimulators bind to the surface of stem cells, delivering agents that spur the cells to release factors that promote blood vessel growth and modulate inflammation in damaged muscle.

a receptor on the surface of the stem cells, providing localized, targeted and extended delivery of TNF-alpha.

"The primary benefit of stem cells toward tissue regeneration is not necessarily the ability for the cells to replace lost tissue, but to release beneficial growth factors and cytokines that assist in the process," said study co-author Marni Boppart (RBTE), a professor of kinesiology and community health.

The researchers tested their approach on mice with surgically induced ischemia in one of their hind legs. They isolated the stem cells from fat tissue, mixed them with the nanostimulators and injected them locally to the mice's affected legs.

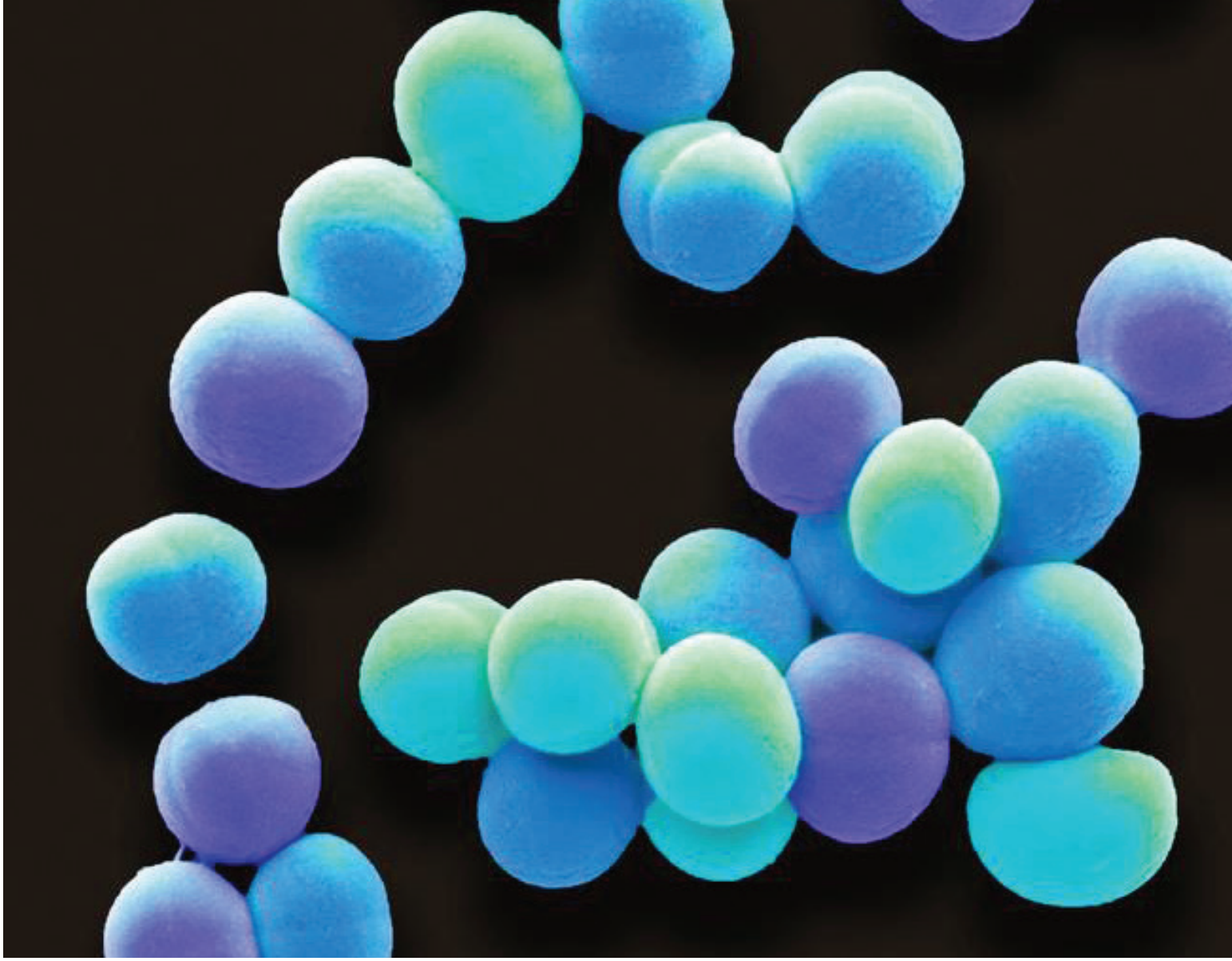
The researchers saw increased blood flow and oxygen levels in the ischemic legs. They also witnessed improvements in mobility—the treated mice could walk longer distances and their legs were stronger.

"We propose that this method is better than methods that require chemical preconditioning, which can affect the viability of the stem cells, take 24 hours or more of culturing and have limited-time effects," Kong said. "Our idea is to collect adipose tissue in the operating room, separate the stem cells, mix in the nanostimuators and reinject them to the patient—all in one procedure."

NIH,the Korea Institute of Science and Technology and A*STAR in Singapore supported this work. Boppart and Kong also are affiliated with the Beckman Institute for Advanced Science and Technology and the Carle Illinois College of Medicine. ■



Hyunjoon Kong, Professor of Chemical & Biomolecular Engineering



Bacterial protein fragment kills lung cells in pulmonary fibrosis

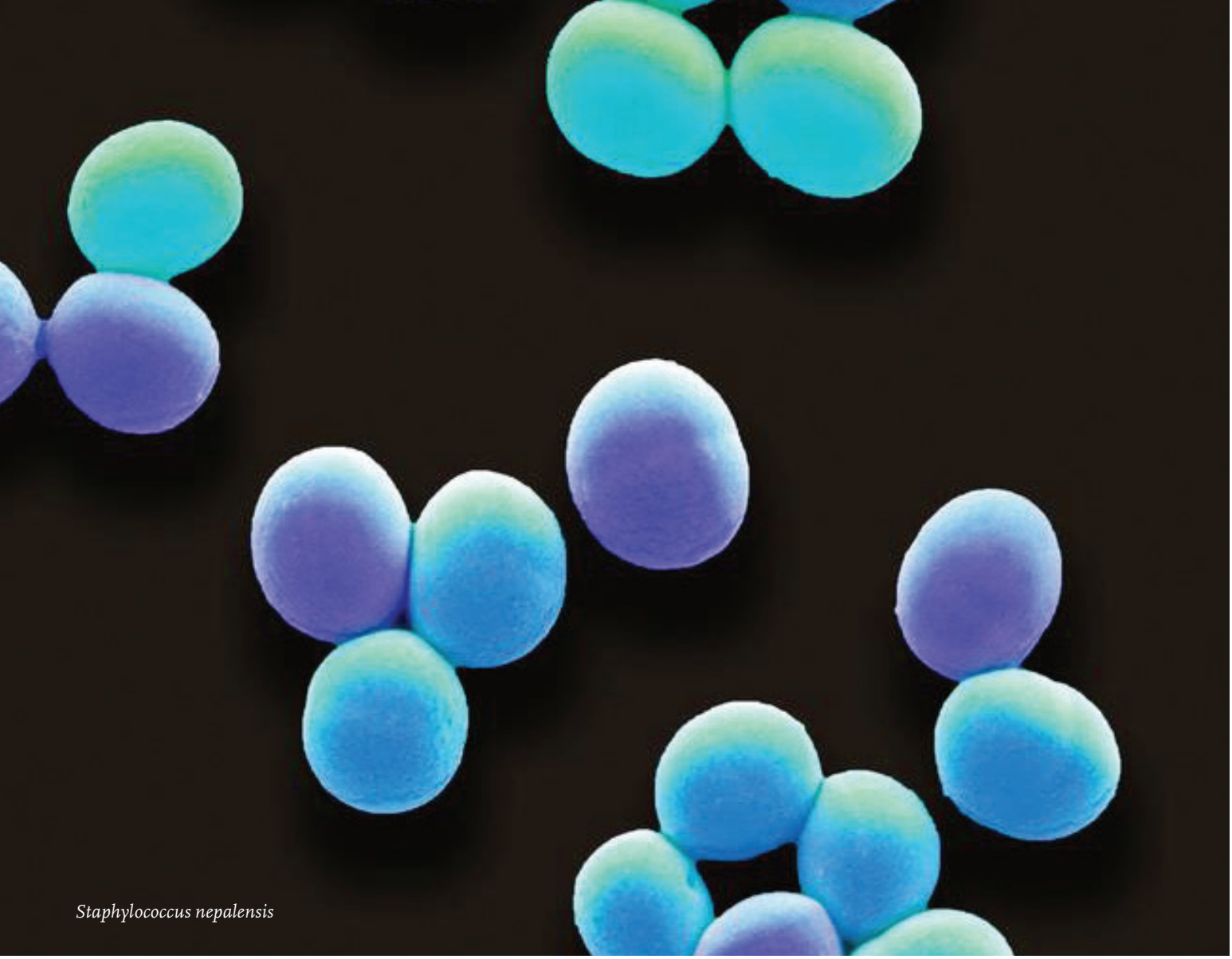
A BACTERIAL PROTEIN FRAGMENT instigates lung tissue death in pulmonary fibrosis, a mysterious disease affecting millions of people worldwide, according to a new study from researchers at Illinois and Mie University in Japan.

Led by Illinois microbiology and animal sciences professor Isaac Cann (MME leader/BCXT) and Mie University immunology professor Dr. Esteban Gabazza (MME), the researchers published their findings in the journal *Nature Communications*.

"We discovered salt-loving bacteria in the lungs of patients with pulmonary fibrosis, and these bacteria secrete a peptide that marks the lung cells it touches for death," Cann said.

In people with pulmonary fibrosis, lung tissue becomes progressively more scarred and stiffened, with a prognosis of only three to five years of life after diagnosis. Certain environmental factors, infections or medications are linked to disease onset; however, the majority of cases are of unknown origin. These mysterious cases are called idiopathic pulmonary fibrosis (IPF), causing the death of roughly 50,000 U.S. patients each year.

The disease progresses slowly until a point when a patient experiences a rapid worsening of breathing and loss of lung function, a phase called acute exacerbation. Yet doctors



Staphylococcus nepalensis

> **"Anybody trying to characterize the large protein to find what it does would never know it has this destructive element hidden inside it.**

do not know what triggers acute exacerbation in a stable patient.

"More than half of the patients with IPF die because of acute exacerbation of the disease," Gabazza said. Of those who survive an acute exacerbation event, only 50% live more than four months, he said.

Previous studies found that certain bacteria, such as strains of *Halomonas*, *Staphylococcus* and *Streptococcus*, proliferate in the lungs of IPF patients, likely as a result of high amounts of salt in the lining of patients' lungs. The researchers wondered if the bacteria played a role in acute exacerbation, so they cultured bacteria associated with fibrotic lung tissue in a salty environment and studied what the bacteria secreted.

They found a small peptide, secreted by *Staphylococcus nepalensis*, that rapidly kills lung cells. They named the peptide corisin.

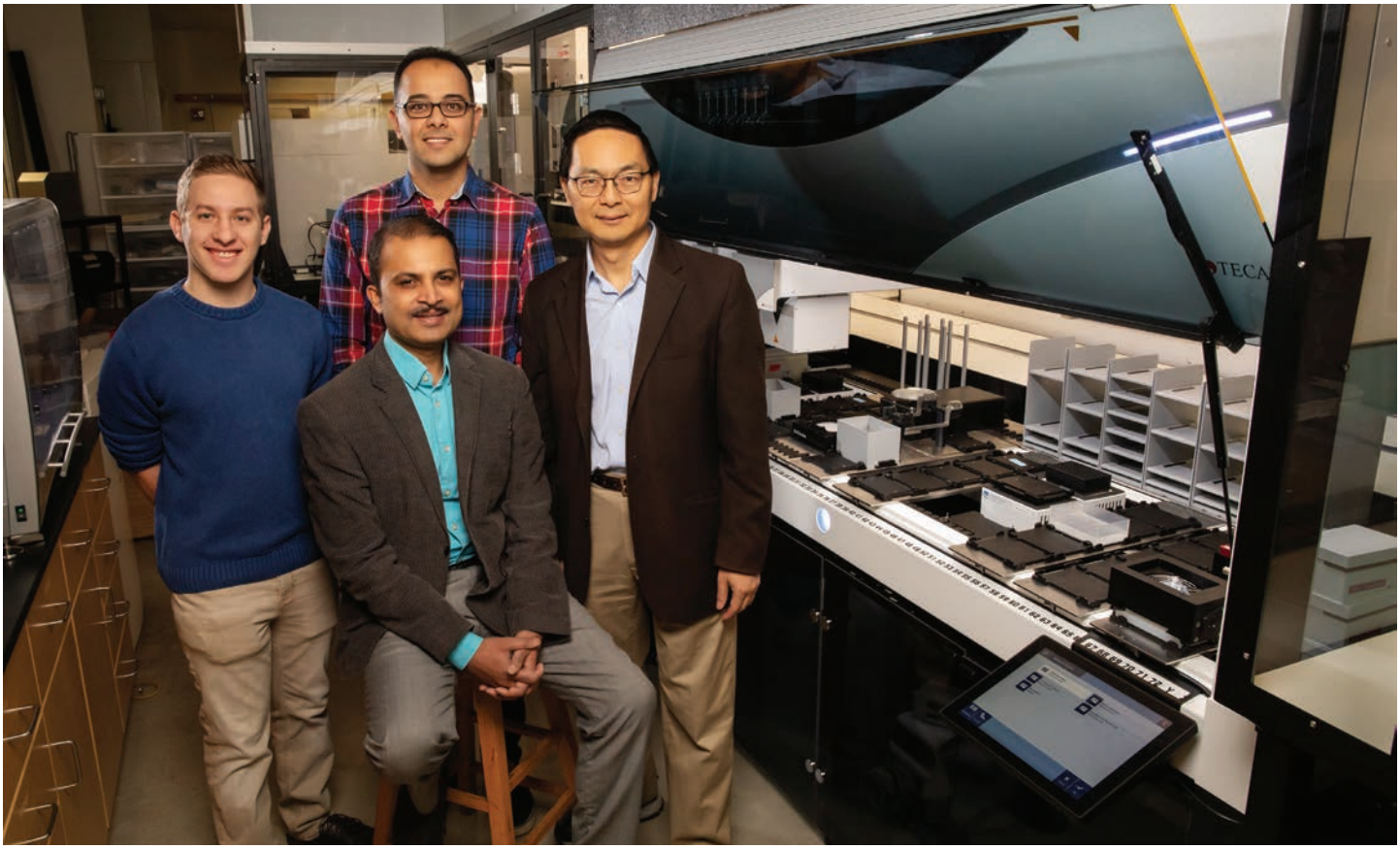
To confirm that corisin was the exacerbating culprit, Gabazza's group ran an experiment on mice with IPF. They compared mice given corisin itself, those infected with corisin-secreting *Staphylococcus nepalensis*, those infected with a Staph strain that did not secrete corisin, and an untreated control group. They found that the mice given corisin or the bacterium that secretes it showed much greater signs of acute exacerbation.

They also looked at lung tissue samples from human patients and found that those who had undergone acute exacerbation had higher levels of corisin in their lungs.

Cann's group then searched the genome of *Staphylococcus nepalensis* to figure out where corisin comes from. They found that it is a fragment cut from a larger protein. They tested the larger protein on lung tissue and found it did not have the destructive properties of the fragment.

"It's like a Trojan horse," Cann said. "Anybody trying to characterize the large protein to find what it does would never know it has this destructive element hidden inside it. The microbe makes the polypeptide and then it cuts out that small piece of it, the corisin, and that is very deadly."

The findings also may have important implications for the current coronavirus pandemic, as some patients may develop pulmonary fibrosis after recovering from COVID-19, similar to the fibrosis seen in some patients after the outbreak of the SARS coronavirus, Cann and Gabazza said. ■



From left: Scott Weisberg, former undergraduate researcher; Saurabh Sinha, Professor of Computer Science; Mohammad (Sam) Hamedi Rad, former graduate student; and Huimin Zhao, Professor of Chemical and Biomolecular Engineering

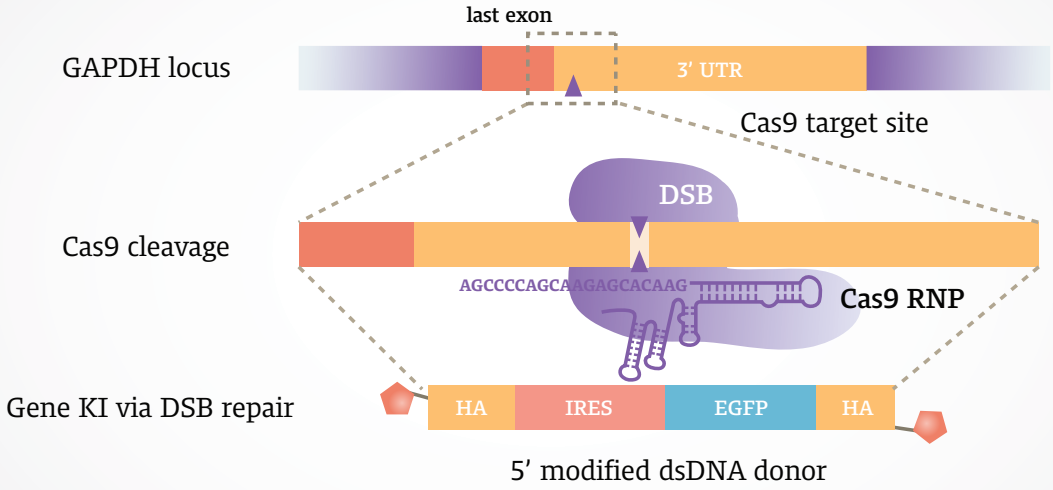
For CRISPR, tweaking DNA fragments yields highest efficiency rates yet

UNIVERSITY OF ILLINOIS RESEARCHERS achieved the highest reported rates of inserting genes into human cells with the CRISPR-Cas9 gene-editing system, a necessary step for harnessing CRISPR for clinical gene-therapy applications.

By chemically tweaking the ends of the DNA to be inserted, the new technique is up to five times more efficient than current approaches. The researchers saw improvements at various genetic locations tested in a human kidney cell line, even seeing 65% insertion at one site where the previous high had been 15%.

Led by chemical and biomolecular engineering professor Huimin Zhao (BSD leader/CABBI/MMG), the researchers published their work in the journal *Nature Chemical Biology*.

Researchers have found CRISPR to be an efficient tool to turn off, or "knock out," a gene. However, in human cells, it has not been a very efficient way to insert or "knock in" a gene.



CRISPR inserting new DNA

"We speculate that the efficiency improved so much because the chemical modification to the end stabilizes the DNA we are inserting."

"A good knock-in method is important for both gene therapy applications and for basic biological research to study gene function," said Zhao. "With a knock-in method, we can add a label to any gene, study its function and see how gene expression is affected by cancer or changes in chromosome structure. Or for gene therapy applications, if someone has a disease caused by a missing gene, we want to be able to insert it."

Searching for a way to increase efficiency, Zhao's group looked at 13 different ways to modify the inserted DNA. They found that small changes to the very end of the DNA increased both the speed and efficiency of insertion.

Then, the researchers inserted end-modified DNA fragments of varying sizes at multiple points in the genome, using CRISPR-Cas9 to precisely target specific sites for insertion. They found efficiency improved two to five times, even when inserting larger DNA fragments—the most difficult insertion to make.

"We speculate that the efficiency improved so much because the chemical modification to the end stabilizes the DNA we are inserting," Zhao said. "Normally, when you try to transfer DNA into the cell, it gets degraded by enzymes that eat away at it from the ends. We think our chemical addition protects the ends. More DNA is getting into the nucleus, and that DNA is more stable, so that's why I think it has a higher chance to be integrated into the chromosome."

Zhao's group already is using the method to tag essential genes in gene function studies. They purposely used off-the-shelf chemicals to modify the DNA fragments so that other research teams could use the same method for their own genetic studies.

"We've developed quite a few knock-in methods in the past, but we never thought about just using chemicals to increase the stability of the DNA we want to insert," Zhao said. "It's a simple strategy, but it works."

NIH supported this work. Zhao also is affiliated with the Carle Illinois College of Medicine. ■



Hyperspectral cameras are used to screen entire research plots for high-yielding photosynthesis traits

Technology to screen for higher-yielding crop traits now more accessible

LIKE MANY INDUSTRIES, BIG DATA IS driving innovations in agriculture. Scientists seek to analyze thousands of plants to pinpoint genetic tweaks that can boost crop production—historically, a Herculean task. To drive progress toward higher-yielding crops, a team from Illinois is revolutionizing the ability to screen plants for key traits across an entire field.

"For plant scientists, this is a major step forward," said Katherine Meacham-Hensold, postdoctoral researcher at Illinois and co-first author who led the physiological work on two recent studies published in the *Journal of Experimental Botany (JExBot)* and *Plant, Cell & Environment (PC&E)*. "Now we can quickly screen thousands of plants to identify the most promising plants to investigate further using another method that provides more in-depth information but requires more time. Sometimes knowing where to look is the biggest challenge, and this research helps address that."

This work is supported by Realizing Increased Photosynthetic Efficiency (RIPE), an international research project that is creating more productive food crops by improving photosynthesis. RIPE is sponsored by the Bill & Melinda Gates Foundation, the U.S. Foundation for Food and Agriculture Research (FFAR), and the U.K. Government's Department for International Development (DFID). The team analyzed data collected with specialized hyperspectral cameras that capture part of the light spectrum (much of which is invisible to the human eye) that is reflected off the surface of plants. Using hyperspectral analysis, scientists can tease out meaningful information from these bands of reflected light to estimate traits related to photosynthesis.

"Hyperspectral cameras are expensive and their data is not accessible to scientists who lack a deep understanding of computational analysis," said Carl Bernacchi (CABBI/GEGC), a research plant physiologist with the USDA Agricultural Research Service at the IGB. "Through these studies, our team has taken a technology that was out of reach and made it more available to our research community so that we can unearth traits needed to provide farmers all over the world with higher-yielding crops."

The RIPE project analyzes hundreds of plants each field season. The traditional method used to measure photosynthesis requires as much as 30 minutes per leaf. While newer technologies have increased efficiency to as little as 15 seconds per plant, the study published in *JExBot* has increased efficiency by an order of magnitude, allowing researchers to capture the photosynthetic capacity of hundreds to thousands of plants in a research plot.

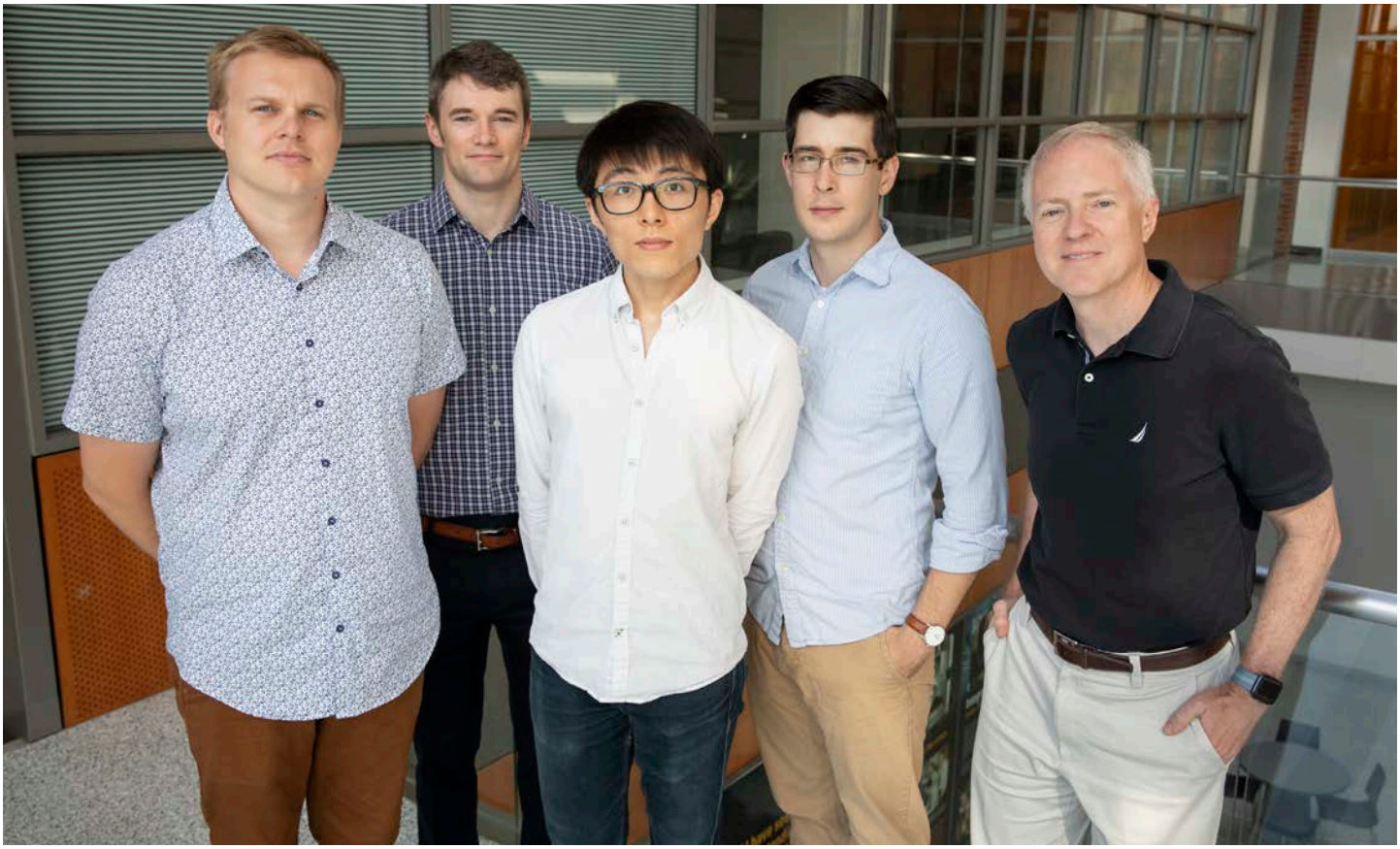
In the *JExBot* study, the team reviewed data from two hyperspectral cameras; one that captures spectra from 400-900 nanometers and another that captures 900-1800 nanometers. In the *PC&E* study, the team resolved to make hyperspectral information even more meaningful and accessible to plant scientists. Using just 240 bands of reflectance spectra and a radiative transfer model, the team teased out how to identify seven important leaf traits from the hyperspectral data that are related to photosynthesis.

"Our results suggest we do not always need 'high-resolution' reflectance data to estimate photosynthetic capacity," said co-first author Peng Fu, a RIPE postdoctoral researcher who led the computational work on both studies. "We only need around 10 hyperspectral bands—as opposed to several hundred or even a thousand hyperspectral bands—if the data are carefully selected. This conclusion can help pave the way to make meaningful measurements with less expensive cameras."

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. ■



Illinois Research Technician Evan Dracup (left) and Postdoctoral Researcher Katherine Meacham-Hensold



From left: Taylor Canady, postdoctoral scholar; Andrew Smith, Professsor of Bioengineering; Nantao Li, graduate student; Lucas Smith, postdoctoral scholar; Brian Cunningham, Professor of Electrical and Computer Engineering.

Single-molecule detection of cancer markers brings liquid biopsy closer to clinic

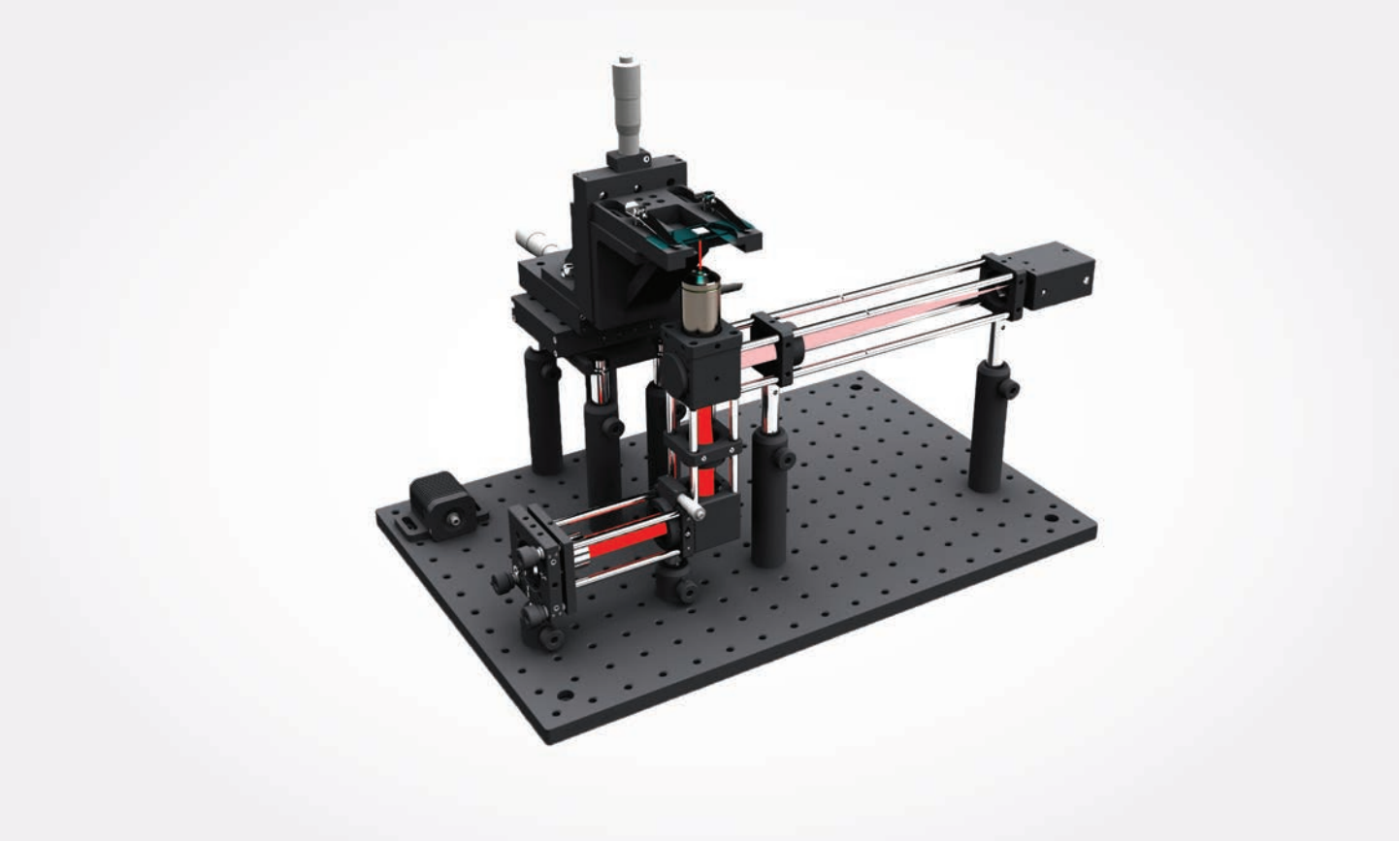
A FAST, INEXPENSIVE YET SENSITIVE technique to detect cancer markers is bringing researchers closer to a "liquid biopsy"—a test using a small sample of blood or serum to detect cancer, rather than the invasive tissue sampling routinely used for diagnosis.

Researchers at Illinois developed a method to capture and count cancer-associated microRNAs, or tiny bits of messenger molecules that are exuded from cells and can be detected in blood or serum, with single-molecule resolution. The team published its results in the *Proceedings of the National Academy of Science*.

"Cancer cells contain gene mutations that enable them to proliferate out of control and to evade the immune system, and some of those mutations turn up in microRNAs," said study leader Brian Cunningham (CGD Director/MMG), an Illinois professor of electrical and computer engineering. Cunningham also directs the Holonyak Micro and Nanotechnology Lab at Illinois.

"There are specific microRNA molecules whose presence and concentration is known to be related to the presence and aggressiveness of specific types of cancer, so they are known as biomarkers that can be the target molecule for a diagnostic test," he said.

Cunningham's group developed a technique named Photonic Resonator Absorption Microscopy (PRAM) to capture and count microRNA biomarkers. In collaboration with professor Manish Kohli at the Moffitt Cancer Center in



Photonic Resonator Absorption Microscopy (PRAM)

> **"This approach makes the idea of performing a 'liquid biopsy' for low-concentration cancer-related molecules a step closer to reality."**

Florida, they tested PRAM on two microRNAs that are known markers for prostate cancer.

They found it was sensitive enough to detect small amounts that would be present in a patient's serum, yet also selective enough to detect the marker among a cocktail of molecules that also would be present in serum.

"One of the main challenges of biosensing is to maintain sensitivity and selectivity at the same time," said Nantao Li, a graduate student and co-first author. "You want it to be sensitive enough to detect very small amounts, but you don't want it to pick up every RNA in the blood."

PRAM achieves both qualities by combining a molecular probe and a photonic crystal sensor. Each individual probe that binds sends a separate signal that the researchers can count.

"With PRAM, we squirt a sample into a solution and get a readout within two hours," said IGB Fellow Taylor Canady, a co-first author of the study. "Other technologies that produce single-molecule readouts require extra processing and additional steps, and they require a day or more of waiting. PRAM seems like something that could be much more feasible clinically. In addition, by using an optical signal instead of fluorescence, we could one day build a miniaturized device that doesn't need a trained laboratory technician."

The PRAM approach could be adapted to different microRNAs or other biomarkers, the researchers say, and is compatible with existing microscope platforms.

"This approach makes the idea of performing a 'liquid biopsy' for low-concentration cancer-related molecules a step closer to reality," Cunningham said. "This advance demonstrates that it is possible to have an inexpensive and routine method that is sensitive enough to require only a droplet of blood. The results of the test might tell a physician whether a regimen of chemotherapy is working, whether a person's cancer is developing a new mutation that would make it resistant to a drug, or whether a person who had been previously treated for cancer might be having a remission."

The IGB and NIH supported this work. Illinois chemistry professor Yi Lu (BSD/CABBI/CGD) and bioengineering professor Andrew Smith (GCD) were coauthors of the work. ■

Outreach

At-home activities for families and friends

In accordance with health guidelines and wellness practices, the suspension of in-person activities this year found many at home much more than before. During the summer, the IGB provided a suite of fun and educational activities that could be done from the comfort of one's home. These activities provided opportunities to engage with others while learning about something new and exciting. From an ongoing COVID-19-themed escape room series to a flower dissection activity, the activities allowed families and friends to stay engaged and connected while stuck at home. All of the activities are archived and available on the website, with some activities currently ongoing: go.igb.illinois.edu/couchreach.

Pollen Power offers an online adventure experience

In lieu of an in-person event, Pollen Power, a summer camp offered by the IGB, is currently offering an online adventure of exploration and discovery. Geared towards middle school girls, the camp introduces girls to plant biology research while empowering women in STEM fields. To take part in this year's online adventure, campers are encouraged to visit go.igb.illinois.edu/pollen to start exploring with Persephone, the Pollen Power virtual camper. Afterwards, campers can fill out a quick survey on past Pollen Power experiences. The camp facilitators and IGB staff, led by IGB Outreach and Communication Specialist Adrienne Gulley, are currently evaluating the safest and most engaging options for summer 2021 with the health and welfare of the campers and counselors at the forefront.

Art of Science 10.0 goes hybrid

The IGB's Art of Science program, now in its 10th year, is a celebration of common ground between science and art that illuminates the beauty and fascination encountered in daily scientific endeavors. Every year, current IGB Artist and Creative Program Manager Julia Pollack works with IGB scientists and their research images to create pieces that highlight the power and aesthetics of science imagery. In response to the COVID-19 pandemic, the Art of Science 10.0 installation was converted to a hybrid format this year, offering both in-person and online experiences. This year's theme was "Dynamism."

"I love the fact that we have imagery in science because I think it paints a better picture," said Kadeem A. Richardson, one of the scientists featured in AoS 10.0. "When people see an actual image, it captures their attention and they can see first hand what's going on and what we are looking at."

The installation was open for in-person, socially-distant viewing for four days outside the IGB building. Pieces from Art of Science 10.0 are available in an online gallery along with brief video discussions with scientists about their featured work here: go.igb.illinois.edu/AOS10.



Art of Science piece "Life in the Dunes" by scientist collaborator Kadeem A. Richardson of the Romana Nowak Laboratory.



Stephen Long (left) and Donald Ort

Awards

Lisa Ainsworth of USDA-ARS elected to National Academy of Sciences

Lisa Ainsworth (CABBI/GEGC), a research plant physiologist with the USDA Agricultural Research Service and Adjunct Professor of Plant Biology and Crop Sciences at the University of Illinois, has been elected to the National Academy of Sciences—largely considered one of the highest honors that a scientist can receive.

Ainsworth leads the USDA-ARS Global Change and Photosynthesis Research Unit and Soybean Free Air Concentration Enrichment (SoyFACE), a cutting-edge research facility where scientists can explore the current and future impact of the climate crisis on crops that are grown outdoors in real-world field conditions.

In 2019, Ainsworth received the NAS Prize in Food and Agriculture Sciences, a recognition that honors both her contributions to agriculture and "tireless advocacy for science" by working to increase the representation of women through several initiatives, including a summer camp for middle school girls called Pollen Power. She is also a Fellow of the American Association for the Advancement of Science and a recipient of the Crop Science Society of America Presidential Award, among many other awards and recognitions.

Ainsworth is also a research leader of Realizing Increased Photosynthetic Efficiency (RIPE), an international research effort to ensure food security by improving photosynthesis, the natural process all plants use to convert sunlight into yield. RIPE is supported by the Bill & Melinda Gates Foundation, the U.S. Foundation for Food and Agriculture Research, and the U.K. Government's Department for International Development.

Stephen Long invested as Ikenberry Chair Professor, Plant Biology & Crop Sciences

Stephen Long (BSD/CABBI/GEGC) was invested as the Stanley O. Ikenberry Chair Professor of Plant Biology and Crop Sciences. The endowment—named for the 14th president of the University of Illinois—is made possible by a gift from Geraldine B. Cooke and other sources.

Long joined the University of Illinois in 1999, where he established an internationally acclaimed laboratory dedicated to using computational and experimental approaches to understand all 170 steps of photosynthesis. Since then, Long has worked tirelessly to build connections worldwide and across generations of graduate students, postdoctoral researchers, and faculty to transform our knowledge of photosynthesis into higher-yielding crops and address the effects of climate change on crop productivity. Among many contributions to the university and his field, Long helped establish the Energy Farm and the SoyFACE research facility.

Long leads the international research project Realizing Increased Photosynthetic Efficiency (RIPE) that has demonstrated technologies that promise to substantially increase the productivity of staple food crops under his leadership. The RIPE project is supported by the Bill & Melinda Gates Foundation, the U.S. Foundation for Food and Agriculture Research, and the U.K. Government's Department for International Development.

"It gives me special pleasure to know that a person of your stature who has committed their career to science, focused on understanding the responses of plants to global atmospheric and climate change, will occupy the Ikenberry Chair," said Professor Emeritus Stanley Ikenberry in remarks read by IGB Director Gene Robinson (GNDP). "No mission could be more relevant to the time in which we live and the challenges facing humankind going forward."

Three IGB researchers rank among world's most influential

Three faculty members from the IGB have been named to the 2019 Highly Cited Researchers list, a global listing of scientists who produced the past decade's most influential papers. Compiled by the Web of Science group, the list recognizes researchers "who produced multiple papers ranking in the top 1% by citations for their field and year of publication, demonstrating significant research influence among their peers."

The IGB faculty include USDA Agricultural Research Service and Adjunct Professor of Plant Biology and Crop Sciences Lisa Ainsworth (CABBI/GEGC, highly cited for cross-field impact), crop sciences and plant biology professor Stephen P. Long (BSD/CABBI/GEGC, cross-field), and plant biology professor Donald Ort (GEGC leader/BSD/CABBI, plant and animal science).

Ainsworth conducts research aimed at increasing crop production under changing climates. Her research uses physiological, biochemical, and genetic approaches to understand the mechanisms of plant responses to air pollution and climate change.

Long uses computational and experimental approaches to improve photosynthetic efficiency, and works to address the effects of climate change on crop yield. He directs Realizing Increased Photosynthetic Efficiency, a multinational project supported by the Bill & Melinda Gates Foundation, the Foundation for Food and Agricultural Research, and the U.K. Department for International Development.

Ort is the Robert Emerson Professor of Plant Biology and Crop Sciences, and the Acting Director of the IGB. His research focuses on improving photosynthesis and addresses crop responses to global change factors including increases in atmospheric carbon dioxide and temperature.

Research

New approach drives bacteria to produce potential antibiotic, antiparisitic compounds

Research led by Professor of Biochemistry Satish Nair (MME/MMG) developed a method to spur the production of new antibiotic or antiparasitic compounds hiding in the genomes of actinobacteria, which are the source of drugs such as actinomycin and streptomycin and are known to harbor other untapped chemical riches, as reported in the journal *eLife*.

Nair and colleagues wanted to determine how hormones influence the production of antibiotics in actinobacteria. By exposing their bacteria to the right hormone or combination of hormones, the researchers hope to spur the microbes to produce new compounds that are medically useful.

For the new study, chemistry graduate student Iti Kapoor developed a more streamlined process for synthesizing the hormone avenolide in the lab than was previously available. This allowed the team to study the hormone's interactions with its receptor both inside and outside bacterial cells.

"Using a method called X-ray crystallography, Iti and biochemistry graduate student Philip Olivares were able to determine how the hormone binds to its receptor and how the receptor binds to the DNA in the absence of hormones," Nair said. "Typically, these receptors sit on the genome and they basically act as brakes."

The researchers discovered that when the hormone binds to it, the receptor loses its ability to cling to DNA. This turns off the brakes, allowing the organism to churn out defensive compounds like antibiotics.

Integration of gene regulatory networks in understanding animal behavior

Scientists have long attributed animal behavior to the coordinated activities of neuronal cells and its circuits of neurons, known as the neuronal network (NN). However, researchers are pushing the boundaries in understanding animal behavior through the integration of gene regulation.

IGB Director and entomology professor Gene Robinson (GNDP) and IGB Director of Computational Genomics and computer science professor Saurabh Sinha (BSD/CABBI/GNDP/GSP) hosted a workshop that resulted in a perspective article published in the *Proceedings of the National Academy of Science*.

"The starting point for this perspective is that the NN is the de facto standard for understanding what goes on in the brain as pertinent to behavior," said Sinha. "Our goal was to highlight another level of dynamics that accompany behavior and not just the dynamics of the NN."

The authors of the perspective synthesized current evidence on the role of the gene regulatory networks (GRNs)—a collection of regulatory interactions between genes—in the context of animal behavior along with the NN. Behavior-associated GRNs (bGRNs) impact gene expression changes associated with a certain animal behavior while developmental GRNs (dGRNs) influence development of new cells and connections in the brain. The integration of NNs, bGRNs and dGRNs across multiple scales holds potential in understanding how these networks work in concert to regulate animal behavior.

"The fact that we have single-cell technology really taking off means that we can have a proper resolution of GRNs in the brain, and therefore, examine how cell type-specific GRNs interact with signal transmission through the NN," said Sinha. Through experimental mapping of these networks, the changes in gene expression can be corresponded with behaviors in different cell types.



Research



Photosynthesis varies greatly across rice cultivars, diversity could boost yields

A team from Illinois and the International Rice Research Institute (IRRI) examined how diverse varieties of rice photosynthesize, finding small differences in photosynthetic efficiency under constant conditions but a 117 percent difference in fluctuating light, suggesting a new trait for breeder selection.

"Photosynthesis has traditionally been assessed under 'constant conditions' where plants are exposed to constant, high levels of light, but field conditions are never constant, especially considering the light that drives photosynthesis," said Stephen Long (CABBI/BSD/GEGC), Ikenberry Endowed University Chair of Plant Biology and Crop Sciences at Illinois. "We looked at 14 cultivars of rice that represent much of the crop's diversity and asked the question: could there be variability in photosynthesis in fluctuating light that we might be able to capitalize on?" Long is also the director of the Realizing Increased Photosynthetic Efficiency (RIPE) project.

The researchers compared results from constant and fluctuating light conditions and found no correlation, which supports findings from a 2019 study on cassava. In other words, varieties that do well in fluctuating light might not do well in constant light and vice-versa, suggesting that selection for these traits should be conducted independently.

"At the end of the day, the goal would be to have plants that can respond more quickly to light fluctuations to enable them to be more productive," said Liana Acevedo-Siaca, graduate student in the College of Agriculture, Consumer, and Environmental Sciences (ACES). "I am interested in ways that we can improve this process while preserving some of the germplasm we have out there. There's so much diversity with which we could work. I think it would be a shame if we didn't examine all of our options more deeply."

Engineered immune cells recognize, attack solid-tumor cancer cells

A method known as CAR-T therapy has been used successfully in patients with blood cancers such as lymphoma and leukemia. It modifies a patient's own T-cells by adding a piece of an antibody that recognizes unique features on the surface of cancer cells. In a new *Proceedings of the National Academy of Sciences* study, researchers report that they have dramatically broadened the potential targets of this approach—their engineered T-cells attack a variety of solid-tumor cancer cells from humans and mice.

"Cancer cells express on their surface certain proteins that arise because of different kinds of mutations," said Preeti Sharma, a postdoctoral researcher at the University of Illinois Urbana-Champaign who led the research with biochemistry professor David Kranz (ACPP), a member of the Cancer Center at Illinois. "In this work, we were looking at protein targets that have short sugar chains attached to them."

Study co-author Qi Cai, a postdoctoral researcher in the Kranz lab, tested whether changes in the sequence of amino acids in the vicinity of the abnormal sugar affected the receptor's binding to the site. This allowed the team to determine if the antibody could be slightly changed to accommodate other sugar-linked cancer targets.

"Our engineered T-cells are showing activity against both human and mouse cancer cell lines," Sharma said. "And the T-cells can now recognize several different proteins that have short sugars attached to them. This is really important because in cancer therapy, most of the time you are going after a single target on a cancer cell. Having multiple targets makes it very difficult for the cancer to evade the treatment."



Cowbirds change their eggs' sex ratio based on breeding time

Brown-headed cowbirds show a bias in the sex ratio of their offspring depending on the time of the breeding season, with more female than male offspring hatching early in the breeding season in May, and more male hatchlings emerge in July.

The researchers studied the interactions between cowbirds and warblers for seven years to determine whether there was a difference in the relative number of males and females among cowbird offspring. They collected DNA samples from cowbird eggs or newly hatched chicks.

"Other scientists have not seen any difference in the sex ratios of brood-parasitic birds," said study co-author Mark Hauber (GNDP), a professor of evolution, ecology, and behavior at Illinois. "This is the first time anyone has detected a seasonal bias and we believe that it is due to our large sample svizes."

The researchers think their results may reflect the different developmental trajectories of male and female cowbirds. Although the eggs and newly hatched chicks both show the seasonal sex bias, it is unclear whether the differing sex ratios persist in birds that grow up and leave the nest.

"We have not looked at what happens to the chicks after they fledge," Hauber said. "We know that adult cowbird flocks are heavily male-biased, so perhaps increased mortality or dispersal by early-hatched female cowbirds impacts the eventual adult sex ratios."

The researchers hope to understand the molecular mechanisms that female cowbirds use to influence the sex of their offspring.

Virus-infected honey bees more likely to gain entrance to healthy hives

Honey bees that guard hive entrances are twice as likely to allow in trespassers from other hives if the intruders are infected with the Israeli acute paralysis virus (IAPV), a deadly pathogen of bees, researchers report in a new study in the *Proceedings of the National Academy of Sciences*. IAPV infection alters honey bees' behavior and physiology in ways that boost the virus's ability to spread.

"The most important finding of our study is that IAPV infection increases the likelihood that infected bees are accepted by foreign colonies," said Adam Dolezal (IGOH), a professor of entomology who led the research. "Somehow, the infected bees are able to circumvent the guards of foreign colonies, which they shouldn't be able to do."

To capture the behavior of individual bees, researchers tagged each one with the equivalent of a QR code and continuously monitored their interactions. The scientists were able to simultaneously track the behaviors of as many as 900 bees.

While infected bees were just as mobile as the other bees, their lower rates of trophallaxis (a process by which honey bees exchange regurgitated food and other liquids) were not the result of being sick. The researchers believe this change in behavior is a general response to a health threat and not specific to IAPV infection, which is in line with previous research.

When the scientists placed honey bee workers at the entrance of a foreign hive, however, the infected bees engaged in more trophallaxis with the guards. The guards were more likely to admit them than to let in healthy bees or bees whose immune systems had been stimulated, a response specific to IAPV infection.



Research

Pattern analysis of phylogenetic trees could reveal connections between evolution, ecology

In biology, phylogenetic trees represent the evolutionary history and diversification of species—the "family tree" of Life. Illinois researchers have presented a new analysis of the patterns generated by phylogenetic trees, suggesting that they reflect previously hypothesized connections between evolution and ecology, led by Swanlund Professor of Physics Nigel Goldenfeld (BCXT leader/GNDP), with graduate student Chi Xue and former undergraduate student Zhiru Liu, now at Stanford University, published in the *Proceedings of the National Academy of Science*.

The study revolved around a concept in evolutionary ecology known as niche construction, where organisms modify their environment, thereby creating new ecological niches in the ecosystem and changing the environment. In turn, these new niches affect the overall evolutionary trajectory of the organisms that share the environment. The end result is that evolution and the environment are coupled closely together. The idea that evolution is not occurring on a purely static environmental background is controversial. Their findings add to the existing body of work by identifying the long term effects of niche construction in a way that can be detected by modern genomics and phylogenetic tree construction.

"Our model has a small number of components and assumes simple mathematical form and yet, it generates the power-law scaling with the right exponent that is observed in actual biological data," Xue explained. "It's simply amazing to see how much a minimal model can do."

"We were able to reproduce not only the power-law behavior but also a non-trivial exponent that's very close to reality," Liu said. "In other words, the simulated trees are not only scale-invariant but also realistic in a way."

Researchers shed light on new enzymatic reaction

Researchers have identified key ingredients for producing high-value chemical compounds in an environmentally friendly fashion: repurposed enzymes, curiosity, and a little bit of light. A *Nature* paper describes a study led by IGB postdoctoral researcher Xiaoqiang Huang in the Department of Chemical and Biomolecular Engineering (ChBE). Huang works in the lab of ChBE Professor Huimin Zhao (BSD leader/CABBI/MMG).

Biocatalysis is rapidly emerging as a nuanced, agile way to synthesize valuable compounds. Scientists are investigating the ability of enzymes to catalyze diverse reactions, and for good reason: biocatalytic reactions are highly selective, meaning that scientists can use enzymes to act on specific substrates and create target products.

The research team developed a visible-light-induced reaction that uses the enzyme family ene-reductase (ER) as a biocatalyst and can produce high yields of valuable chiral carbonyl compounds.

"Our solution might be considered 'repurposing.' We take known enzymes that occur in nature, and repurpose them for a novel reaction," Zhao said.

These "repurposed" enzymatic reactions are not only economically and environmentally efficient, but highly desirable: chiral carbonyl compounds have potential applications in the pharmaceutical industry to be used for drug production.

The team's solution is particularly unique in that it merges biocatalysis with photocatalysis—wherein light is used as a renewable source of activation energy—in a novel, photoenzymatic reaction.

Environmental contaminants alter gut microbiome, health

In a new paper in *Toxicological Sciences* scientists from Illinois review the research linking dozens of environmental chemicals to changes in the gut microbiome and associated health challenges, including compounds used in manufacturing consumer goods, bisphenols found in plastic food packaging, and phthalates which are used in everything from vinyl flooring to plastic films.

"More than 300 environmental contaminants or the metabolic byproducts of those contaminants have been measured in human urine, blood or other biological samples," said Jodi Flaws (EIRH co-leader/MME), a professor of comparative biosciences who led the analysis with PhD student Karen Chiu. "Chemicals such as bisphenols, phthalates and some pesticides, persistent organic pollutants and heavy metals can alter hormone metabolism and are associated with adverse health outcomes."

Studies have found that exposure to glyphosate herbicides alters the bacterial makeup of the gut microbiome in cattle, rodents and honey bees. It increased anxious and depressive symptoms in the mice and was associated with an increase in pathogenic bacteria in cattle. The pesticide chlorpyrifos affects microbial populations in male rodents and fish exposed during development and adulthood, and also causes inflammation and oxidative stress in the gut.

"All of these data together suggest that exposure to many of these environmental chemicals during various stages of life can alter the gut microbiome in ways that influence health," Chiu said. "The pathologies associated with altered microbiomes after exposure to environmental chemicals include immune dysfunction, altered carbohydrate and lipid metabolism, and neurological and behavioral impairments. We are also seeing that these effects highly depend on an individual's sex and age."

Spinal cord gives bio-bots walking rhythm

Illinois researchers developed tiny walking "spinobots," powered by rat muscle and spinal cord tissue on a soft, 3D-printed hydrogel skeleton. While previous generations of biological robots could move forward by simple muscle contraction, the integration of the spinal cord gives them a more natural walking rhythm, said study leader Martha Gillette (GNDP/M-CELS), a professor of cell and developmental biology.

"These are the beginnings of a direction toward interactive biological devices that could have applications for neurocomputing and for restorative medicine," Gillette said.

To make the spinobots, the researchers printed a skeleton consisting of two posts for legs and a flexible "backbone" only a few millimeters across. Muscle cells were seeded which grew into muscle tissue, followed by the integration of a segment of lumbar spinal cord from a rat.

The researchers had to devise a method to extract the intact spinal cord, culture it, integrate it onto the bio-bot and culture the muscle and nerve tissue together in a way that the neurons form junctions with the muscle.

"The development of an *in vitro* peripheral nervous system—spinal cord, outgrowths and innervated muscle—could allow researchers to study neurodegenerative diseases such as ALS in real time with greater ease of access to all the impacted components," graduate student Collin Kaufman said. "There are also a variety of ways that this technology could be used as a surgical training tool. These applications are, for now, in the fairly distant future, but the inclusion of an intact spinal cord circuit is an important step forward."

Adapting photosynthesis to fleeting shadows boosts soybean yields

In a special issue of *Plant Journal*, a team from Illinois reports a new mathematical computer model that is used to understand how much yield is lost as soybean crops grapple with minute-by-minute light fluctuations on cloudy and sunny days.

"Soybean is the fourth most important crop in terms of overall production, but it is the top source of vegetable protein globally," said Yu Wang, a postdoctoral researcher at Illinois, who led this work for the Realizing Increased Photosynthetic Efficiency (RIPE) project. "We found that soybean plants may lose as much as 13 percent of their productivity because they cannot adjust quickly enough to the changes in light intensity that are standard in any crop field. It may not sound like much, but in terms of the global yield—this is massive."

Past models have only examined hour-by-hour changes in light intensity. For this study, the team created a dynamic computational ray-tracing model that was able to predict light levels to the millimeter across every leaf for every minute of the day in a flowering soybean crop. The model also takes into account two critical factors: photoprotection and Rubisco activase.

"Models like these are critical to uncovering barriers—and solutions—to attain this crop's full potential," said RIPE Director Stephen Long, Ikenberry Endowed University Chair of Plant Biology and Crop Sciences (BSD/CABBI/GEGC). "We've already begun to address these bottlenecks and seen significant gains, but this study shows us that there is still room for improvement."

Group genomics drive aggression in honey bees

A new study of Africanized honey bees reveals that the genetic inheritance of individual bees has little influence on their propensity for aggression. Instead, the genomic traits of the hive as a whole are strongly associated with how fiercely its soldiers attack, as reported in the *Proceedings of the National Academy of Sciences*.

"We've always thought that the most significant aspects of an organism's behavior are driven, at least in part, by its own genetic endowment and not the genomics of its society," said Matthew Hudson (CABBI/GNDP), a professor of bioinformatics in the department of crop sciences who led the research with IGB Director and entomology professor Gene Robinson (GNDP). The researchers focused on a unique population of gentle Africanized honey bees in Puerto Rico, which have evolved to become more docile than Africanized bees anywhere else in the world.

The researchers compared the genomes of soldier and forager bees from each of nine honey bee colonies in Puerto Rico. They also tested how aggressively the soldier bees responded to an assault on the hive.

"Many behavioral traits in animals and humans are known to be strongly affected by inherited differences in genome sequence, but for many behaviors, how an individual acts also is influenced by how others around it are acting —nature and nurture, respectively," Robinson said. "We now see that in the beehive, nurture can also have a strong genomic signature."

Such behavioral genomic influences may be particularly pronounced in honey bees, which live in an extraordinarily cooperative society where each individual has a defined social and functional role.

News

Donovan director of new Personalized Nutrition Initiative

Sharon Donovan, professor and Melissa M. Noel Endowed Chair in Diet and Health at University of Illinois, has assumed the role of director of the newly established Personalized Nutrition Initiative (PNI), a partnership between the IGB and the College of Agricultural, Consumer and Environmental Sciences (ACES) supported by the Office of the Vice Chancellor for Research and Innovation (OVCRI).

Precision or personalized nutrition, which was identified as a key area for strategic investment in the U of I's The Next 150 2018-2023 Strategic Plan, is also a keystone of the new NIH 10-year Strategic Plan for Nutrition.

"Personalized nutrition offers a way to optimize human health and the quality of life by tailoring recommendations based not only on diet history and phenotype, but also on an individual's genetics, microbiome, and metabolome," Donovan explains. "As it encompasses almost all known aspects of science, ranging from the genomes of humans, plants and microorganisms, to the highest levels of analytical sciences, computing and statistics of large systems, as well as human behavior."

Donovan holds appointments in the Department of Food Science and Human Nutrition and the Division of Nutritional Sciences in the College of ACES, as well as the Carle-Illinois College of Medicine, and the Microbiome Metabolic Engineering theme in the IGB. She has been recognized by campus with the Paul A. Funk Recognition Award and the Spitze Land-Grant Professorial Career Excellence Awards from the College of ACES and as a University Scholar for her distinction in scholarship and service. She was elected to the National Academy of Medicine in 2017.

IGB 2019 Annual Report available online

As we go about our daily lives, we are faced with endless decisions, both large and small. The choices we make are influenced by a multitude of factors. But how often are we aware of the science that lies behind the options we are presented with and the thought processes we use to weigh them? Part of our mission at the Carl R. Woese Institute for Genomic Biology is making sure that every person is able to join the conversation on how genomics enters into their life. Becoming aware of the choices that new technologies present to us and having the information to make them mindfully is empowering.

In this year's Annual Report, you will be transported into everyday scenarios that reveal the interconnectivity between genomics and the world around us. From an ordinary trip to the grocery store to a hike in the park, you will uncover the science behind familiar objects and discover how science permeates our everyday lives. We highlight genomics' relevance to modern life and its ability to uncover new insights in every area of biological research.

We've translated the annual report experience to a digital format for the 2019 edition, with new ways to explore and enjoy the stories of the past year. We welcome you to begin at www.igb.illinois.edu/ar2019.

Our thanks to the support and involvement of our community of partners, stakeholders, donors, legislators, and citizens, without which the work we do would not be possible.

Illinois team tracks covid

Six undergraduates are pooling their talents —remotely—to contribute to the fight against SARS-CoV-2, the coronavirus that causes COVID-19, as members of the Illinois International Genetically Engineered Machine (iGEM) team. They're creating a web tool to build visual models of a key part of the virus as it mutates —specifically the infamous "spike" protein that allows it to attack human cells so easily.

The Illinois iGEM team, sponsored by the IGB and the Center for Advanced Bioenergy and Bioproducts Innovation (CABBI), is advised by Christopher Rao (BSD/CABBI/MME), Professor of Chemical and Biomolecular Engineering (ChBE), with bioengineering junior Mary Cook, molecular and cellular biology senior Sachin Jajoo, bioengineering sophomore Yan Luo, bioengineering junior Suva Narayan, biochemistry sophomore Royal Shrestha, and integrative biology junior Angela Yoon as members. They are mentored by CABBI researchers Matthew Waugh, a chemistry postdoc, and ChBE graduate students William Woodruff and Carl Schultz. CABBI Research Coordinator Anna Fedders and IGB Outreach Activities Coordinator Daniel Ryerson provide administrative support.

The project has been an enormous learning experience on many levels. To write the tool, the students had to learn about viruses, programming, bioinformatics, DNA sequences, protein modeling, viral structures, graphic software, and antibody design. They've also had to manage expenses, divvy up tasks, and help each other sort through problems.

"Any research that I'd participated in before has been with a graduate student or with a mentor who had the project and the goals laid out," Cook said. "Here, we had to start from scratch. That has been probably the most rewarding part of iGEM."

Faculty receive three NSF rapid grants for COVID-19 testing

Three IGB faculty have received NSF Rapid Response Research (RAPID) program grants, all of which aim to shorten the time to process COVID-19 tests.

Rapid electrical detection of COVID-19 at point-of-care: A team led by Rashid Bashir (CGD/M-CELS/RBTE), Dean of the Grainger College of Engineering, has proposed the development of a point-of-care device that uses nasal fluid samples to detect the presence of COVID-19 within 10 minutes.

"Our approach can provide for a rapid electrical detection of the RNA amplification using graphene sensors and result in a miniaturized format for the test," said Bashir, Abel Bliss Professor of Engineering and of Bioengineering.

Rapid Single-Step Reagentless SARS-CoV-2 Viral Load Test by Detection of Intact Virus Particles: A newly-invented type of biosensor imaging could capture intact COVID-19 viruses with custom-designed DNA nanostructures to be immediately counted, with the process producing results in under 15 minutes.

"Our approach would represent a new paradigm for virus diagnostics that does not require the chemical enzymatic amplification of nucleic acids," said Brian Cunningham (CGD Director/MMG), Donald Biggar Willett Professor in Engineering and of Electrical and Computer Engineering.

RAPID: Developing a novel biosensor for rapid, direct, and selective detection of COVID-19 using DNA aptamer-nanopore: Professor of Chemistry and Bioengineering Yi Lu (BSD/CABBI/CGD) is developing a biosensor that could detect and differentiate infectious and noninfectious SARS-CoV-2, granting patients proper timely treatment and releasing non-infected patients from quarantine.

The project aims to develop a modular and scalable sensor for direct detection of the intact coronavirus using DNA aptamers, short, single-stranded DNA molecules that can selectively bind infectious SARS-CoV-2.



AWARDS

Lisa Ainsworth
USDA Agricultural Research Service (CABBI/GEGC); National Academy of Sciences

Brian Allan
Associate Professor of Entomology (IGOH); Positive Impact on Graduating Seniors, Chancellor's Senior Survey

Rashid Bashir
Grainger College of Engineering Dean, Professor of Bioengineering (CGD/M-CELS); 2020-21 President's Executive Leadership Program Fellow, University of Illinois

Christopher Brooke
Assistant Professor of Microbiology (IGOH); 2020 Forty Under 40 Man of the Year, Central Illinois Business Magazine

Martin Burke
Professor of Chemistry (MMG); A Researcher to Know, Illinois Science and Technology Coalition

Carla Cáceres
School of Integrative Biology Director, Professor of Evolution, Ecology, and Behavior (IGOH); 2020-21 President's Executive Leadership Program Fellow, University of Illinois Executive Officer Distinguished Leadership Award, Office of the Provost

Brian Cunningham
Professor of Engineering and of Electrical and Computer Engineering (CGD Director/MMG); Fellow, Royal Society of Chemistry

Roy Dar
Assistant Professor of Bioengineering (BCXT/GNDP/M-CELS); NSF CAREER Award

Sharon Donovan
Professor of Food Science & Human Nutrition (MME); Center for Advanced Study Professor

Paul Hergenrother
Professor of Chemistry (ACPP leader/MMG); Cancer Center at Illinois Deputy Director

Matthew Hudson
Professor of Crop Sciences (CABBI/GNDP); Runge Faculty Distinguished Achievement Award, College of Agricultural, Consumer and Environmental Sciences, University of Illinois

Madhu Khanna
ACES Distinguished Professor (CABBI); president-elect, Agricultural and Applied Economics Association

Stephen Long
Professor of Crop Sciences and Plant Biology (BSD/CABBI/GEGC); Stanley O. Ikenberry Chair Professor of Plant Biology and Crop Sciences

Ting Lu
Associate Professor of Bioengineering (BCXT/BSD/CABBI/MME); Donald Biggar Willett Faculty Scholar, University of Illinois

Jeffrey Moore
Professor of Chemistry and Materials Science & Engineering (BSD); Center for Advanced Study Professor

Thanh (Helen) Nguyen
Professor of Civil and Environmental Engineering (IGOH); Ivan Racheff Endowed Professor in Civil and Environmental Engineering

Donald Ort
IGB Acting Director, Professor of Plant Biology & Crop Sciences (GEGC leader/BSD/CABBI); Center for Advanced Study Professor
Charles Reid Barnes Life Membership Award, American Society of Plant Biologists

Jian Peng
Assistant Professor of Computer Science (CABBI); Overton Prize, International Society for Computational Biology

Vijay Singh
Professor in Agricultural and Biological Engineering (CABBI/GEGC); International Food Engineering Award, American Society of Agricultural and Biological Engineers

Andrew Smith
Associate Professor of Bioengineering (CGD); Donald Biggar Willett Faculty Scholar, University of Illinois

Andrew Suarez
Evolution, Ecology, and Behavior Head, Professor of Entomology (GNDP); Jeffrey S. Elowe Professor in Integrative Biology

Wilfred Van der Donk
Professor of Chemistry (MMG); Royal Society of Chemistry's Pedler Award

Amy Wagoner Johnson
Professor of Mechanical Science and Engineering (EIRH/RBTE); Distinguished Engineering Educator Award, Society of Women Engineers
2020 Andersen Faculty Scholar Outstanding Advisor Award, Engineering Council, Grainger College of Engineering

Tandy Warnow
Professor of Computer Science (BCXT/IGOH); Chief Scientist, Executive Committee Member, C3.ai Digital Transformation Institute

Robin Fretwell Wilson
Professor and Associate Dean, College of Law (GSP); Director, Institute of Government and Public Affairs

GRANTS

Brendan Harley
National Institutes of Health
"Amniotic Membrane Derived Matrix for Large Bone Defect Repair (Admin Supp R21)"

Ripan Malhi
National Institutes of Health
"Expanding the Impact of the Summer Internship for Indigenous Peoples in Genomics (SING) Short Course (R25)"

John Gerlt
Nils Oberg
National University of Singapore
"Enzyme Function Initiative at the National University of Singapore (EFI@NUS)"

Bruce Fouke
Mayandi Sivaguru
Dornier MedTech America
"Morphometric and Geobiological Characterization of Kidney Stone Fragments Produced by ESWL and Laser Ablation"

Rachel Whitaker
Hee Sun Han
Moore Foundation
"Dynamic Virus-Microbe Symbiosis in Geothermal Hot Spring Metapopulations"

Nathan Schroeder
National Science Foundation
"Collaborative Research: REU Site: Phenotypic Plasticity Research Experience for Community College Students (Renewal)"

Brian Cunningham
Yi Lu
Rebecca Smith
National Institutes of Health
"Exosome Separation and Digital Resolution Detection of Blood-Based Nucleic Acid Biomarkers for Noninvasive Therapeutic Diagnostics in Cancer (R01)"

Jason Ridlon
Yong-Su Jin
Andrew Steelman
Sharon Donovan
National Institutes of Health
"Role of Gut Bacterial Side-Chain Cleavage of Cortisol in Host 11Beta-Hydroxyandrostenedione Formation (R01)"

Brian Cunningham
Taylor Canady
Xing Wang
National Science Foundation
"RAPID: A Rapid and Ultrasensitive Technology for Sensing Intact SARS-CoV-2 Using Designer DNA Nanostructure Capture Probes and Photonic Resonator Interference Scattering Microscopy"

Sivaguru Mayandi
Bristol Myers Squibb/Forbius
"Imaging Second Harmonic Generation in Clinical Tissue Samples"

Rachel Whitaker
Carla Caceres
Katy Heath
National Science Foundation
"BII-Implementation: GEMS: Genomics and Eco-evolution of Multi-scale Symbioses"

Hannah Holscher
Nicholas Burd
Jason Ridlon
U.S. Department of Agriculture
"Walnuts, The Human Gastrointestinal Microbiome, and Metabolic Health"

Gene Robinson
U.S. Department of Agriculture
"Automated Honey Bee Rearing Platform to Promote Pollinator Health"

Huimin Zhao
Saurabh Sinha
Martin Burke
Jian Peng
Scott Denmark
National Science Foundation
"AI Institute: Molecule Maker Lab Institute (MMLI), an Artificial Intelligence Driven Ecosystem for NextGen Molecule Discovery and Manufacturing"



Postdoctoral researcher Yajie Wang at work in 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.

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.

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.

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.

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*.

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Laboratory Technical Specialist Emily Gaither at work in the concourse lab of IGB

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