
MAGAZINE
Biomarker
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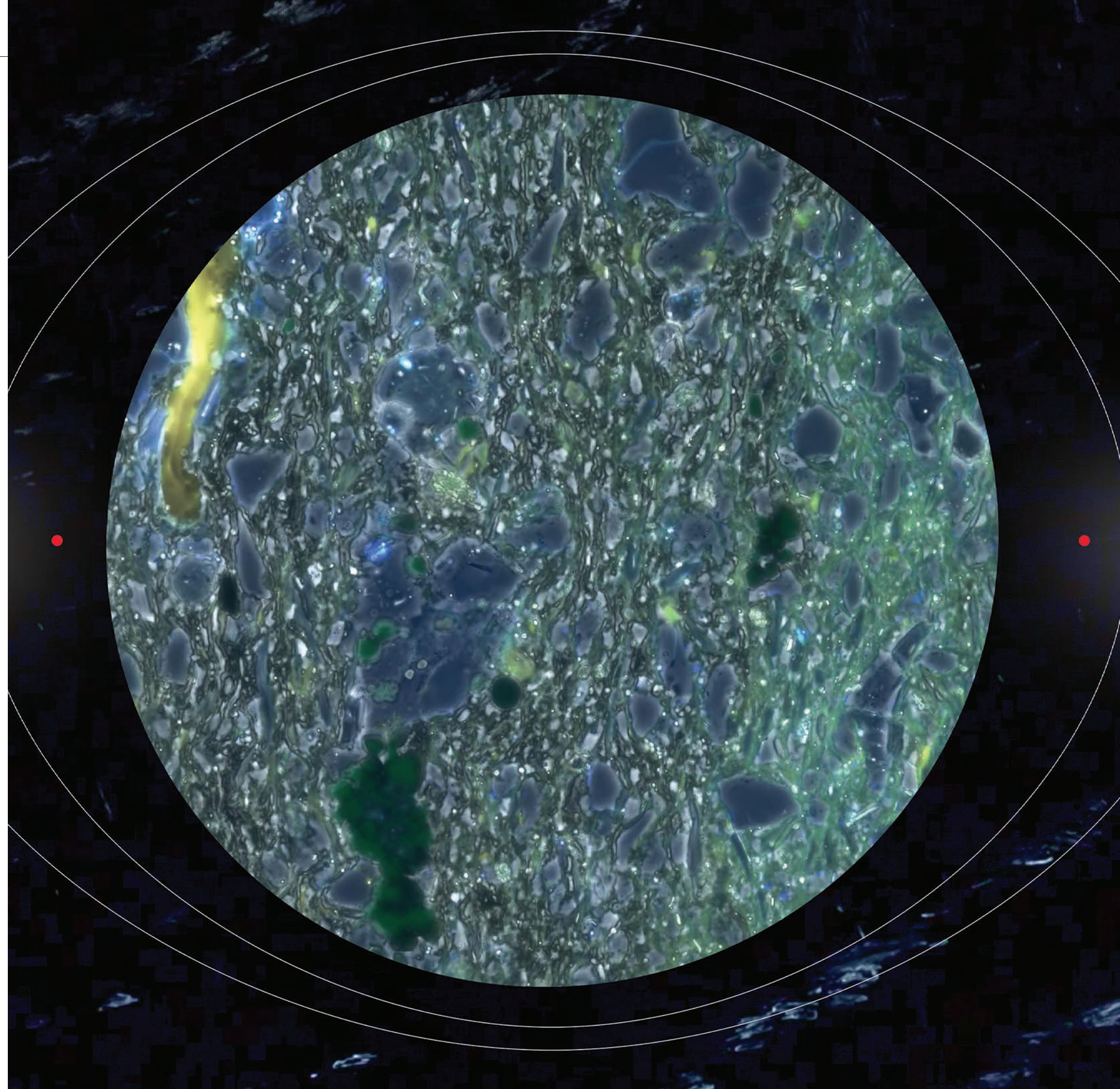
Carl R. Woese Institute for Genomic Biology
UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN
Where Science Meets Society

We can only see a short distance ahead, but we can see plenty there that needs to be done.

—Alan Turing



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
GSE	Genomic Scale Engineering Center
GSP	Genomic Security and Privacy
IGOH	Infection Genomics for One Health
M-CELS	Multi-Cellular Engineered Living Systems
MME	Microbiome Metabolic Engineering
MMG	Mining Microbial Genomes
RBTE	Regenerative Biology & Tissue Engineering

IGB Strategic Partnerships

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

IGB Funding Agencies

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

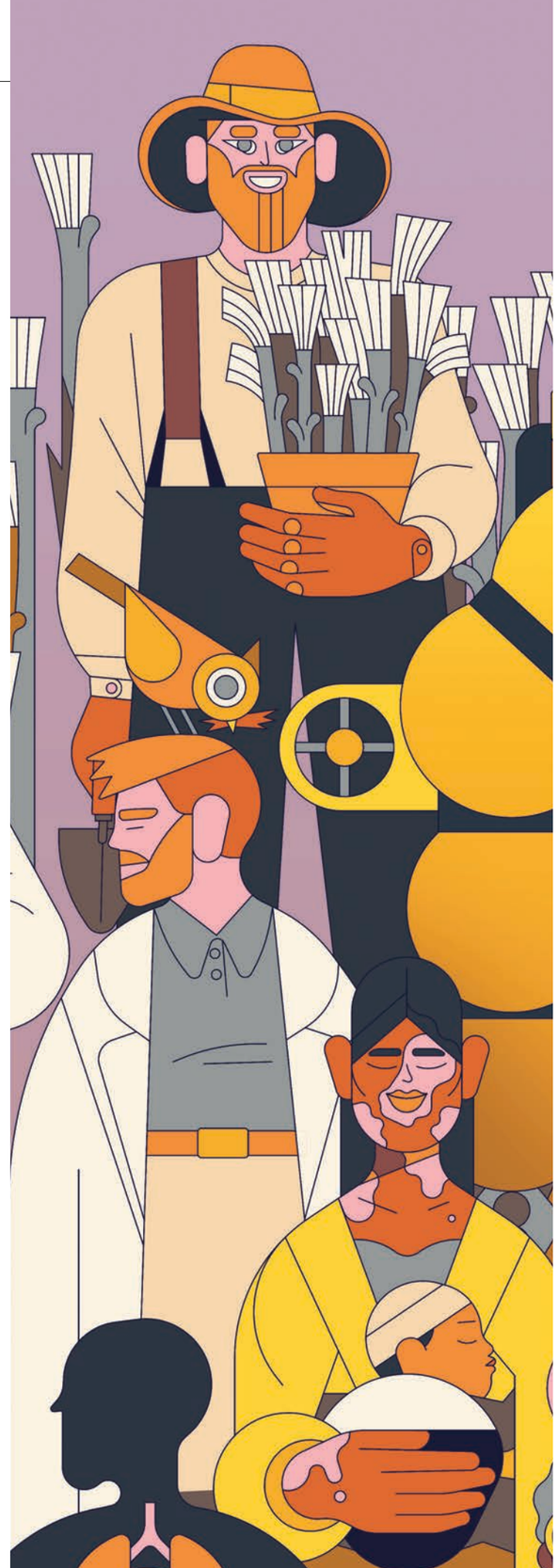


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Illustration by Jillian Nickell

Director's Message

> "Science does not exist in a vacuum: It requires a multitude of scientific minds to answer complex questions."

Gene Robinson

DIRECTOR,
CARL R. WOESE
INSTITUTE FOR GENOMIC BIOLOGY

MANY SCIENTIFIC ENDEAVORS HAVE A COMMON UNDERLYING intent: harnessing the power of nature to improve our lives. Our focus at the IGB has always been to address grand societal challenges using teams of researchers. Although the scientific questions we strive to answer are important, it is equally imperative that we build a community of diverse viewpoints. Such efforts can be a challenge at the best of times, but even in the middle of a global pandemic, we were able to make significant strides in our inclusion efforts.

In this year's edition of *Biomarker*, we are highlighting the diversity, equity, and inclusion efforts at the IGB as well as the numerous discoveries and accomplishments that our community has made. It has become increasingly obvious that crises—born out of poverty, racism, or a pandemic—have disparate effects on society. We have rediscovered the insidious outcomes of such inequalities. For example, gene activity in immune cells differs in women who live in low-income, violent neighborhoods; there are lower vaccination rates in minority communities; and a greater distrust in science. This past year we have made several efforts, including organizing seminars and workshops that discuss strategies for creating inclusive and supportive lab environments, outreach efforts that empower women and minority groups in STEM fields, and providing students from minority-serving institutions with a streamlined path to pursue a doctoral degree at the University of Illinois. We also welcomed nine new faculty members, all hailing from diverse backgrounds, into the Microbial Systems Initiative. We are excited that they have found homes in the different research themes at the IGB and we look forward to seeing the efforts of these scientists. We hope our inclusion initiatives will foster greater innovations in the future.

As always, the discoveries made at the IGB this year have dramatically expanded our views on how our world works. We have discovered new treatments for breast cancer, cavities, and middle ear infections; dissected the underlying mechanisms of obesity and HIV; added more techniques, such as DNAzymes and TALEN, to our arsenal of genetic tools; and have gained insights into a thousand-year-old staple of Japanese cuisine. You will also read about some other notable other inhabitants of our planet: thieving birds, endangered rhinos, symbiotic corals, and new crops that offer much-needed alternatives to fossil fuels.

Science does not exist in a vacuum: It requires a multitude of scientific minds to answer complex questions. The exclusion of any of those voices leaves us poorer, both as a community and as scientists. Although we have made several advances, we can, and need to, do better in striving for inclusive excellence so that we can progress together towards a better future. ■

Illustration by Jillian Nickell

Diversity, equity and inclusion efforts underway at the IGB

THE IGB VALUES EQUALITY AND RESPECT for every member of its community. Investigators, students and staff from diverse backgrounds bring their lived experiences and unique perspectives together. This diversity improves the IGB's ability to solve problems and be responsive to societal needs. Since its inception in 2018, the IGB Committee on Diversity (COD) has been dedicated to creating a more inclusive, diverse and welcoming environment within the IGB community. The COD is comprised of IGB community members spanning the breadth of IGB, including theme leaders, faculty, staff and postdoctoral researchers. Current IGB COD members are Professor of Anthropology Ripan Malhi (GNDP/GSP/IGOH), Associate Professor of Sociology Ruby Mendenhall (GNDP), Professor of Integrative Biology Carla Cáceres (IGOH), Associate Professor of Plant Biology Katy Heath (IGOH), Associate Professor of Food Science & Human Nutrition Zeynep Madak-Erdogan (CGD/EIRH/GSP), Assistant Professor of Plant Biology Steven Burgess (GEGC), Professor of Microbiology Gary Olsen (BCXT), science writer Alisa King-Klemperer and Professor of Chemical and Biomolecular Engineering Hyunjoon Kong (M-CELS leader/EIRH/RBTE).

Spurred by recent events, the COD Task Force was formed to gather more individuals to take action on the COD's ideas and bring new initiatives to light. Under the guidance of the COD, the COD Task Force has accelerated initiatives meant to increase dialogue and create change internally in working towards a more inclusive environment. Although many efforts are underway, the IGB realizes more work needs to be done to diminish racism, other inequities and where they intersect.

The COD Task Force helped to organize talks aimed at increasing awareness and dialogue centered around DEI in science. Some topics included the importance of DEI and accessibility in strengthening STEM communities, the importance of preserving the Hawaiian Mauna Kea mountain, strategies for advancing health equity through community engagement and anti-racism, and service dog handlers in science laboratories.

In collaboration with the Office of the Vice Chancellor for Diversity, Equity & Inclusion (OVCDEI), the COD Task Force organized a training workshop that focused on strategies for creating an inclusive and supportive workplace. At the conclusion of the workshop, participants learned skills they can use for promoting fairness in the workplace. Moving forward, the IGB and OVCDEI plan to work closely together on other projects to increase equity in science.

The IGB is proud of ongoing efforts to create programs to diversify science and increase participation from members of minority groups in genomics. Current ongoing programs are the Pollen Power camp, the Summer Internship for INdigenous People in Genomics (SING) program, and the collaboration with Fisk University.

The COD and COD Task Force members thank the IGB community members for helping to bolster DEI efforts at the IGB and look forward to future accomplishments.

Program increases underrepresented groups in biomedical data science, quantitative biology

When Founder Professor of Physics Jun Song (ACPP) speaks of the need for greater investment in the training of underrepresented groups in the computational sciences, he often points out that education isn't a great equalizer without equal opportunity.

"The historic disparity of access to scientific education means that we need to provide more than equal opportunity to underrepresented groups," asserts Song. "The more mathematical and computational skills a discipline requires, the lower the enrollment of students from underrepresented groups. Our FUTURE-MINDS-QB program will help by equalizing access to high-level, rigorous training for participants and by streamlining the PhD application process here at UIUC through our partnership with Fisk University."

Song is the program director of the newly founded bridge program Fisk-UIUC Training of Under-Represented Minds in Data Science and Quantitative Biology, or FUTURE-MINDS-QB. The program has been awarded a $1.3M 5-year T-32 training grant by the National Institute of General Medical Sciences (NIGMS), a member organization of the NIH.

The program offers two tracks from a master's degree program at Fisk University, a historically Black university in Nashville, to a doctoral degree program at UIUC in a field relevant to quantitative biology. One track includes a traditional two-year master's program. The program additionally establishes a new 4+1 master's track at Fisk—students enrolled in this track will complete relevant master's courses during their senior year to enable finishing a master's program in just one year. The 4+1 track will require applicants to have participated in a formal summer program of preparatory research and workshops at UIUC as undergraduates enrolled at Fisk.

Built on a longstanding Fisk-Illinois partnership

Fisk University and the University of Illinois Urbana-Champaign have been collaborating since 2014 with the help of the Big Data to Knowledge (BD2K) grant from the NIH. In the same year, an R25 partnership between the Knowledge Engine for Genomics (KnowEnG), housed at the IGB, Mayo Clinic, and Fisk University was established. The overall goal was to encourage collaborations between institutions where the BD2K centers are located and institutions that serve students from backgrounds that are underrepresented in research. The partnerships have helped build summer training programs, helping Fisk students to become acclimated to the campus and experience a research environment.

Faculty opportunities

Song is putting out a call to colleagues to volunteer their time and expertise to the new bridge program, which aims to make data science more accessible to underrepresented groups. Faculty will receive special training in mentoring students from diverse ethnic, racial, and gender groups.

"As scientists and leaders in our respective fields, it's important that we ask ourselves what we can do to correct the longstanding inequality of access to computational sciences," says Song. "Our new program will produce a talented, insightful, and diverse pool of graduate students. Our job will be to make sure their experiences not only train them well on the fundamentals and applications of big-data science, but also to ensure their experiences are positive and that they are prepared and willing to enter the field and make their own contributions to biomedical and computational biology." ■

Illinois professors pictured, from left: Sandra Rodriguez-Zas, animal sciences; Andrew Greenlee, urban and regional planning; Gene Robinson, entomology and IGB Director; and Ruby Mendenhall, sociology and African American studies

Hunker down stress genes boosted in women in violent neighborhoods

STRESS AND TRAUMA ARE RISK FACTORS associated with negative health outcomes in humans and can be observed from as early as childhood into adulthood. Particularly, studies have shown that negative health outcomes are amplified when stressful conditions are combined with factors that arise from systemic or social inequality. In some predominantly Black and low-income communities, individuals are subjected to a higher rate of neighborhood violence, which can heighten stress and predispose individuals to various diseases. Specifically, these stressful environments can influence genome function in individuals.

According to a new study of low-income single Black mothers on the South Side of Chicago, the chronic stress of living in neighborhoods with high rates of violence and poverty alters gene activity in immune cells. The changes in stress-related gene expression reflect the body's "hunker down" response to long-term threat, a physiological strategy for lying low and considering new actions rather than launching an immediate "fight-or-flight" response. This has implications for health outcomes in communities of color and other marginalized populations, said researchers at the University of Illinois Urbana-Champaign and collaborators at the University of Kentucky and the University of California, Los Angeles (UCLA). The researchers published the study in the journal *Psychoneuroendocrinology*.

"The question we asked is, how does stress get under the skin to affect health and wellness? We wanted to hear the stories of low-income single Black mothers on the South Side of Chicago and really try to understand what it's like to live in neighborhoods with high levels of violence and how it affects these women," said study leader Ruby Mendenhall (GNDP), an Illinois professor of African American studies and of sociology, and the assistant dean for diversity and democratization of health innovation at the Carle Illinois College of Medicine.

Mendenhall's group surveyed 68 women from high-violence neighborhoods. They shared stories, filled out stress assessments and gave blood samples. From the women's accounts and surveys, as well as from police records of violent crime, the researchers measured levels of stress related to racism, poverty and neighborhood violence. Then, the researchers studied how genes related to stress and immunity were expressed in white blood cells, called leukocytes, found in the participants' blood samples.

"Leukocytes are part of the immune system. They become activated to help fight disease and infection, and also respond to certain stress hormones, and that means their genes are good indicators for the effects of stress on health and well-being," said study co-author Gene Robinson (GNDP), an entomology professor and Director of the IGB.

When looking at genes associated with a flight-or-flight stress pathway, the researchers saw no significant differences between participants who perceived their neighborhoods as dangerous and those who did not. However, they found that women who reported greater neighborhood danger showed significantly greater activity of genes regulated by the glucocorticoid receptor—a stress-response pathway that previously has been documented in animals' hunker-down response to persistent, overwhelming threat, said study co-author Steve Cole, a professor of medicine and psychiatry and biobehavioral sciences at UCLA.

"These hunker-down responses are the body's strategy for conserving resources and persevering in the face of overwhelming adversity," Cole said. "Instead of preparing to fight or flee, the body bides its time and preserves itself for better days in the future. But it's important to get to that better future, or the hunkered-down body may not do the ongoing maintenance work needed for optimal health."

The distinction between the two stress pathways is important for planning health interventions and improving health outcomes, said study co-author Clare Rittschof, a professor of entomology at the University of Kentucky and former postdoctoral researcher in Robinson's group.

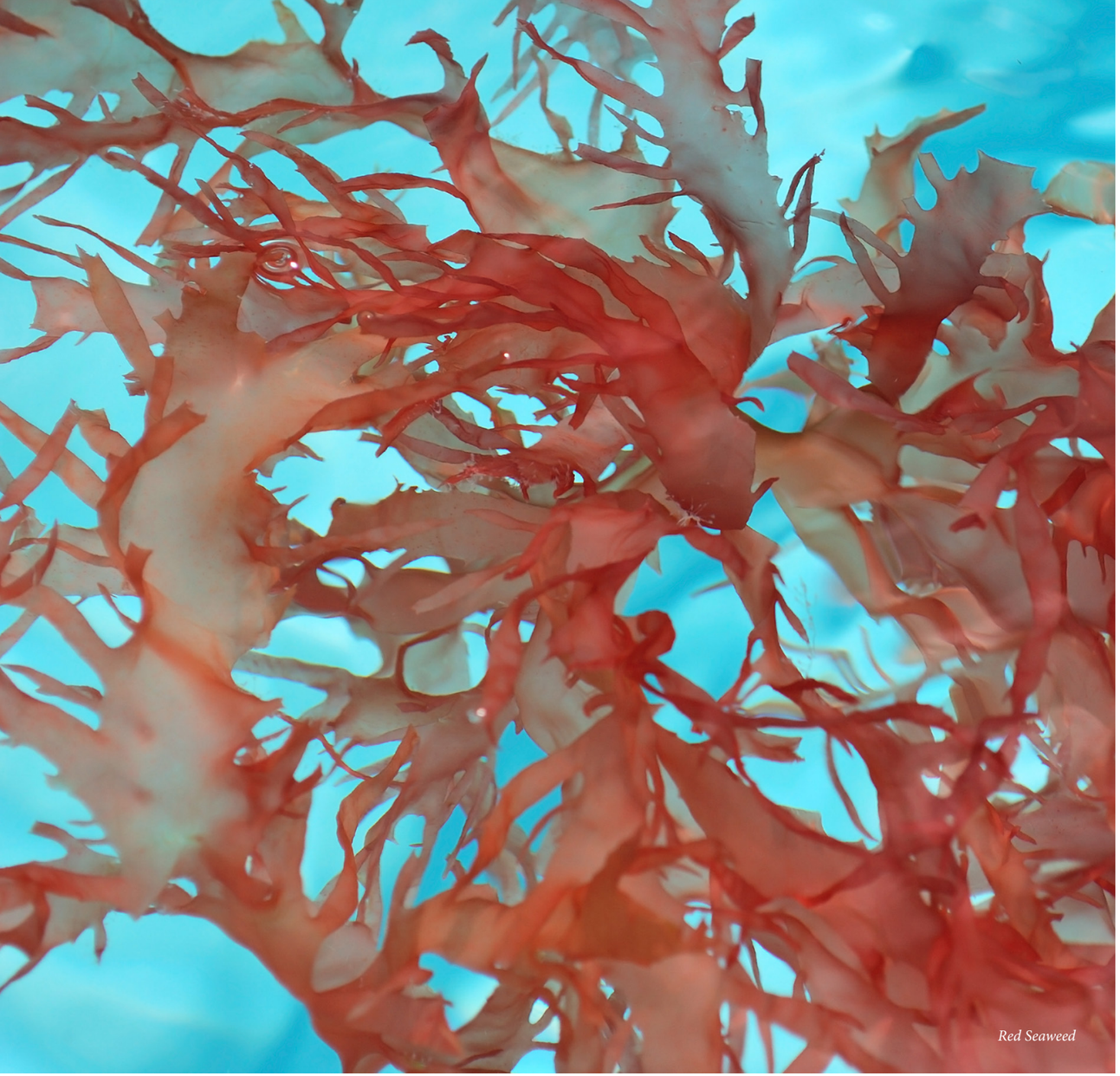
> **"Instead of preparing to fight or flee, the body bides its time and preserves itself for better days in the future. But it's important to get to that better future."**

"Increased glucocorticoid activity is typically associated with aging, so it's as if these women are showing signs of accelerated aging, which is thought to be one reason that stress can lead to worse health outcomes," Rittschof said.

Future studies will examine how post-traumatic stress disorder affects the lives and genome activity of study participants. In addition, researchers are exploring the cultural coping mechanisms the Black women in the study community rely on in their daily lives, as well as training health care and social services providers and policymakers on ways to decrease stress, improve health outcomes, decrease disparities and foster health equity.

"These efforts must be coupled with policies broadly aimed to eliminate structural racism in our society, a big source of stress for African Americans," the authors said in a joint statement. "This is consistent with medical schools around the country declaring racism as a health crisis, including the Carle Illinois College of Medicine."

Illinois graduate student Meggan Lee, Illinois professors Andrew Greenlee and Sandra Rodriguez-Zas (GNDP), and Vanderbilt University professor Kedir Turi were co-authors of the paper. The University of Illinois Urbana-Champaign, the Richard and Margaret Romano Professorial Scholarship and the USC/UCLA Center on Biodemography and Population Health supported this work. ■



Red Seaweed

New health benefits of red seaweed unveiled

RED SEAWEED HAS BEEN PREVALENT in the diets of Asian communities for thousands of years. They are a rich source of minerals, carbohydrates, dietary fibre, and protein. Compared to soybean, they can produce as much as five times more protein per acre. Additionally, the global supply chain of red seaweed is over 18 million tons per year. They are used in food products and cosmetics as thickening agents and the polysaccharides are often incorporated into toothpaste and ice cream. Nori, a type of red seaweed, is ubiquitous in Japanese cuisine in soups, salads, and as a wrap for sushi rolls. In a new study, published in *Marine Drugs*, researchers have shown how these red algae confer health benefits.

Researchers have long known that the modern lifestyles have caused health disorders on a global level. Additionally, diet and the human gut microbiome—a community of microorganisms—is known to play crucial roles in various human diseases. It is therefore likely that the diet, such as dietary fibres, can modulate the microbiome and confer health benefits.

"In the past, people have wondered why the number of colon cancer patients in Japan is the lowest in the world," said Yong-Su Jin (BSD/CABBI/MME), a professor of food microbiology. "Many assumed that it was due to some aspect of the Japanese diet or lifestyle. We wanted to ask whether their seaweed diet was connected to the lower frequency of colon cancer."

Although several studies have shown that Asians who eat seaweed regularly have lower risk of colon, colorectal, and breast cancer, it was unclear which component was responsible for the anti-cancer effects. Red seaweeds are abundant in carbohydrates. For example, agarose, which is a major component of their cell walls, consists of alternating units of d-galactose and 3,6-anhydro-l-galactose (AHG), which are linked. Agarose is also unique because it can reach the large intestine, where it is degraded by the gut microbiota.

In the study, the researchers broke down the structure of different types of red seaweed using a cocktail of enzymes and tested the sugars that were produced to see which one of them caused health benefits. Among the six different sugars produced, agarotriose and AHG showed the most promise.

"After we produced these sugars, we tested their prebiotic activity using the bacteria *Bifidobacterium longum ssp. infantis*," said Eun Ju Yun, a former postdoctoral researcher in the Jin lab. *B. infantis* is a probiotic bacterium; it colonizes the gut of infants and provides health benefits. The researchers added the six different seaweed-derived sugars to the bacteria and followed their growth for approximately 40 hours. Among the different sugars, *B. infantis* could only consume agarotriose, indicating that it works as a prebiotic i.e., it improves the growth of probiotic bacteria.

The researchers also wanted to test if other species of *Bifidobacterium* would exhibit similar growth behaviour or whether *B. infantis* is unique. Only one other species stood out. "We tested *B. kashiwanohense*, and found that it also consumed agarotriose," Jin said. The researchers believe that agarotriose is brought into the cells and is broken down to release galactose and neoagarotetrose. The latter cannot be broken down further and is exported from the cells.

"These results show us that when we eat red seaweed, it gets broken down in the gut and releases these sugars which serve as food for the probiotic bacteria. It could help explain why Japanese populations are healthier compared to others," Jin said.

"Our work explains why red seaweeds are beneficial by providing the molecular mechanism."

The researchers also tested the seaweed-derived sugars AHG, galactose, and neoagarotetrose to see if they had any anti-cancer activity. "We found that AHG specifically inhibits the growth of human colon cancer cells and does not affect the growth of normal cells," Yun said. The anti-cancer activity of AHG is due to its ability to trigger apoptosis or cell death. Together, the results suggest that AHG can be used to develop anti-colon cancer agents.

"There is a lot of information on how red seaweeds are degraded by microorganisms in the ocean and in the human body," said Kyoung Heon Kim, a professor of biotechnology and the co-advisor on the paper. "Our work explains why red seaweeds are beneficial by providing the molecular mechanism. We will continue studying their function in animal models and hopefully we will be able to use them as a therapeutic agent in the future."

The paper "*In vitro* prebiotic and anti-colon cancer activities of agar-derived sugars from red seaweeds" was funded by the Mid-career Researcher Program through the National Research Foundation (NRF) of Korea; by the Ministry of Oceans and Fisheries, Korea; by the Korea Institute of Planning and Evaluation for Technology in Food, Agriculture, Forestry, and Fisheries (iPET); and by the Brain Pool Program through the Korean Federation of Science and Technology Societies. ■

Classroom at the University of Illinois Urbana-Champaign following SHIELD protocols

K-12 SHIELD Playbook offers guidance for reopening schools

THE UNIVERSITY OF ILLINOIS SYSTEM, with a $1.4 million grant from The Rockefeller Foundation, announced the expansion of its SHIELD Illinois and SHIELD CU COVID-19 testing initiatives to help safely reopen underserved K-12 schools in communities across the state using the covidSHIELD test, an innovative, saliva-based test developed at the University of Illinois Urbana-Champaign. The new program, SHIELD Illinois: Target, Test, Tell for Underserved K-12 Districts, will be rolled out in schools located in the three cities, targeting vulnerable areas that have been disproportionately impacted by the pandemic.

"We worked with school districts to select a representative sample of the different kinds of schools across Illinois, focusing on schools that work with low-resource populations," said Rebecca Smith, Professor of Pathobiology at University of Illinois Urbana-Champaign and Project Lead of SHIELD Illinois' K-12 testing program.

A new resource is also available to help guide teachers and school administrators as they reopen schools amid the ongoing COVID-19 pandemic, assembled by researchers and experts at the University of Illinois Urbana-Champaign. The K-12 Shield Playbook is based on the SHIELD Illinois program used to mitigate the COVID-19 pandemic at the university.

The "Target, Test, Tell" approach combined extensive disease modeling with a low-cost, rapid saliva-based test and an app to report and track test results and virus exposures. In addition to masking, distancing and facilities maintenance, this approach can be applied in other school settings as well, the researchers said.

"We've seen this program work at Illinois, and now we need to make it as accessible as possible to other universities, K-12 schools and communities throughout the U.S. and the world to help build a bridge to widespread global vaccination," said Martin Burke (MMG), the associate dean for research at the Carle Illinois College of Medicine and a professor of chemistry.

The SHIELD Illinois: Target, Test, Tell for Underserved K-12 Districts program includes collaborations with Johns Hopkins University, Duke University, University of Southern California, and Arizona State University and partnerships with the Illinois Governor's Office, the Mayor of Chicago's Office, the Illinois Department of Public Health, and the City of Chicago Department of Public Health. Rebecca Smith will oversee the project with Catherine Cheung, a researcher at the IGB who is coordinating operations across the University of Illinois System, SHIELD CU, OSF HealthCare and selected K-12 schools. The program is also seeking additional support to sustain efforts on reopening K-12 schools and plans to share protocols and guidelines with other K-12 schools across the country.

The Shield Playbook received support from the Consortia for Improving Medicine with Innovation & Technology through the Point of Care Technology Research Network program. CIMIT and POCTRN are supported by the RADx Tech program and have been funded in part with federal funds from the National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Department of Health and Human Services, under Grant No. U54 EB015408.

To learn more about SHIELD Illinois, please visit www.uillinois.edu/shield. ■

Quantum leaps in understanding how living corals survive

CORAL REEFS HAVE THRIVED FOR MILLIONS OF YEARS in their shallow ocean water environments due to their unique partnerships with the algae that live in their tissues.

Corals provide a safe haven and carbon dioxide while their algal symbionts provide them with food and oxygen produced from photosynthesis. Using the corals *Orbicella annularis* and *Orbicella faveolate* in the southern Caribbean, researchers at the IGB have improved our ability to visualize and track these symbiotic interactions in the face of globally warming sea surface temperatures and deepening seawaters. The study was reported in *Scientific Reports*.

"This study has allowed us to establish a comprehensive understanding of the coral systems, as well as make connections to the formation of layered rock in other systems."

"Corals are one of the most resilient organisms on the planet," said Mayandi Sivaguru, the co-lead author of the study and Assistant Director of Core Facilities at the IGB. "They have survived ice ages, greenhouse conditions with no ice, and everything else in between that the planet has thrown at them."

Although they have a long history of weathering disruptions, coral reefs are also sensitive enough to serve as indicators of climate change and oceanic health. As an example, when the sea surface temperature or the seawater acidity increases, corals eject their algal partners—a phenomenon called coral bleaching—which converts the corals from green to white. To understand why bleaching occurs, it is important to visualize how the corals interact with their algal partners.

Previously, researchers had to peel the skin of corals and place the samples in a blender to study their symbiotic algal partners. The current study uses a non-invasive technique instead. The technique uses light to scan living tissues, allowing the researchers to keep the corals in their original growth structure.

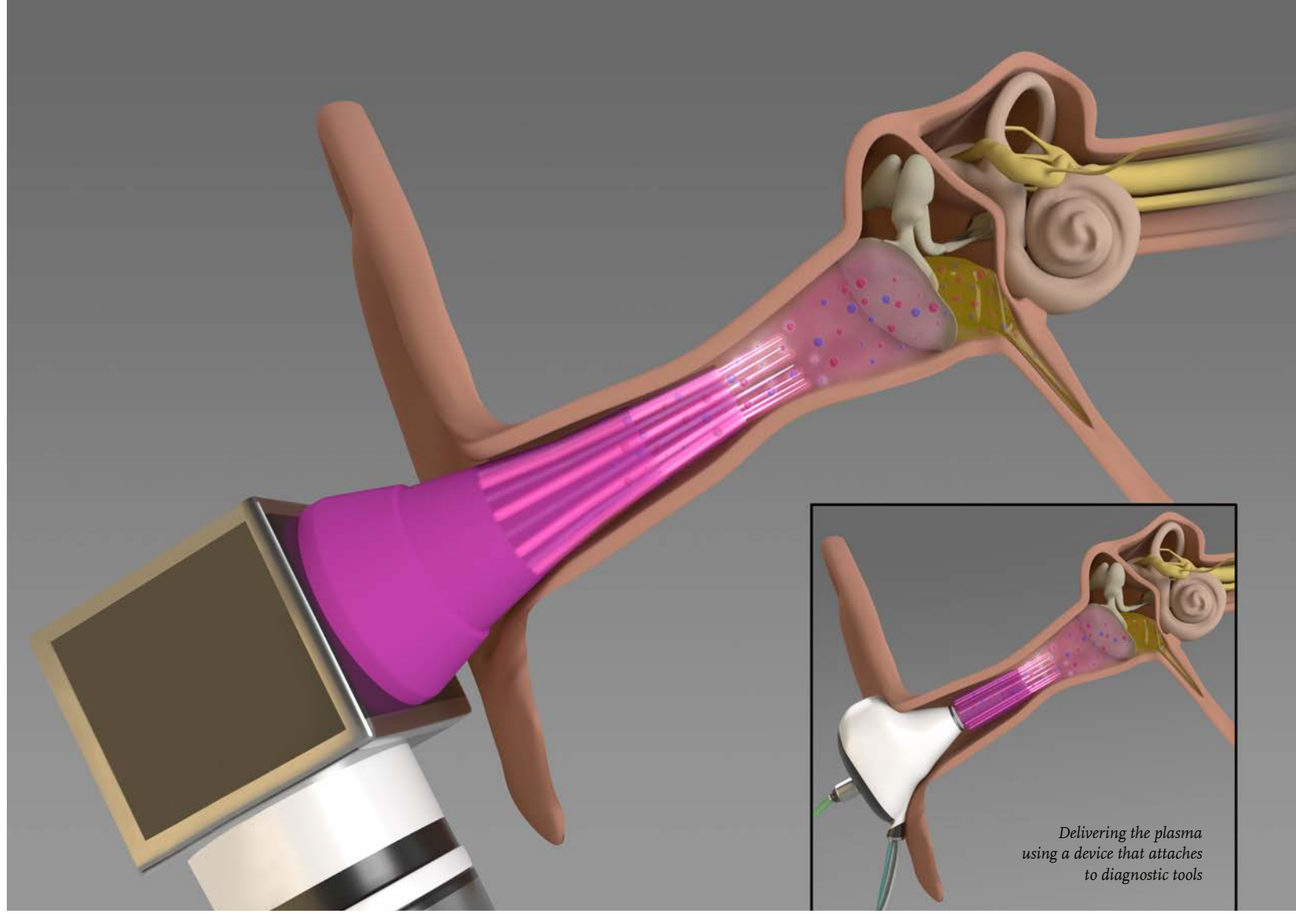
The microscopy studies revealed that shallow water corals have lower algal concentrations and produce higher levels of chromatophores, which are biomolecules that protect algae from sunlight damage. On the other hand, the researchers found the opposite pattern in deeper water corals. These corals receive lesser sunlight and would therefore require more algae to keep up with the photosynthetic demand. During seasonal sea surface temperature changes, the warmer water caused decreased mucus production and algal concentrations, but increased photosynthesis and coral skeleton growth. Conversely, cooler waters caused the opposite effect.

"We have combined the results of this study to identify universal mechanisms of biomineralization found between water, microbes, living organisms, and rock," said Lauren Todorov, the co-lead author, who completed this research as part of her undergraduate B.Sc. thesis at Illinois and is now completing her M.Sc. in Geology. "This study has allowed us to establish a comprehensive understanding of the coral system as well as make connections to the formation of layered rock in other systems such as hot springs, roman aqueducts, and even human kidney stones."

The work was funded by the Office of Naval Research, the IGB Undergraduate Summer Research Fellowship, the IGB Mark Tracy Fellowship for Translational Research, the Department of Molecular and Cellular Biology Jenner Family Summer Research Fellowship, and the Edward and Barbara Weil Research Fund. ■

Orbicella annularis, *one of the corals researched in this study*

Researchers develop a new technique to treat middle ear infections



An illustration of how the microplasma was delivered to the eardrum

MIDDLE EAR INFECTIONS, ALSO KNOWN AS OTITIS media, affect more than 80% of the children in the U.S. In a new study, researchers have designed a miniaturized 3D-printed device to inactivate *Pseudomonas aeruginosa*, a common bacterium that causes the infection.

"Middle ear infections & the over-prescription of antibiotics to treat these are major clinical challenges that are in need of new treatment technolgies & solutions."

The device—a microplasma jet array—generates plasma, which is composed of charged particles and reactive molecules that have been previously shown to inactivate various pathogens. "This is the first time anyone has tried treating middle ear infections using plasma technology," said Jungeun Won, a graduate student in the Boppart lab. "Usually, the treatment involves using antibiotics or surgical intervention."

The problem with using antibiotics is two-fold. First, antibiotics are ineffective in more than 30% of the patients with acute infections. Second, their use can lead to increased antibiotic resistance because the bacteria form biofilms—aggregates that attach to the surface of the ear.

"Biofilms are very dense, making it difficult for the antibiotics to penetrate," said Helen Nguyen (IGOH), an Ivan Racheff Professor in Civil and Environmental Engineering. "Our idea was that if we could disrupt the structure of the biofilm, we could increase the penetration of the antibiotics."

The researchers tested the microplasma jet array by building a model of the middle ear. They used an excised rat eardrum and tested the antimicrobial effects of the microplasma on the bacteria that were located behind the eardrum.

"We used different duration times for the treatment and found that 15 minutes and longer was effective in inactivating the bacteria," Won said. "We also monitored the tissue to see if we had created any holes or ruptures, but we didn't find any obvious physical damage."

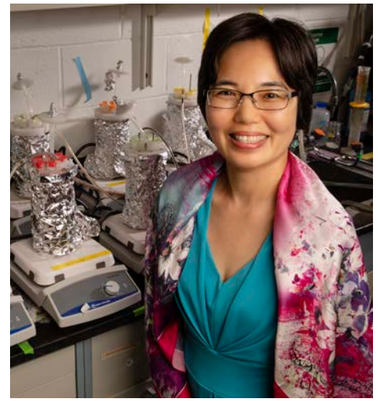
"We think that the microplasma disrupts the biofilm by disturbing the bacterial cell membrane," Nguyen said. "So far, we only have indirect measurements supporting our idea, but we will look into it in the future."

Although the thickness of the rat eardrum is 30% lower than that of a human, which is about the width of a hair strand, the results suggest that the microplasma treatment could be used to treat middle ear infections in humans.

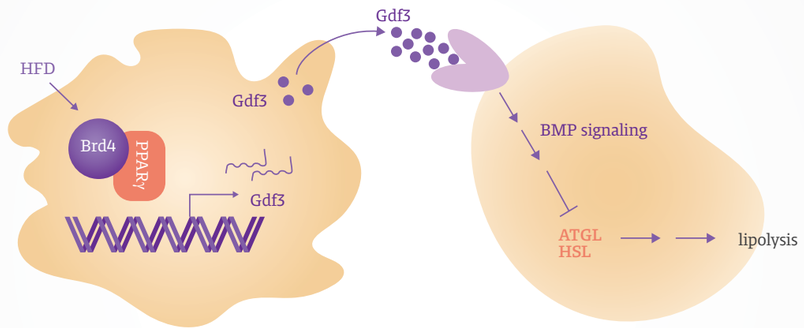
"Middle ear infections and the over-prescription of antibiotics to treat these are major clinical challenges that are in need of new treatment technologies and solutions," said Stephen Boppart, Grainger Distinguished Chair in Engineering, who is also a medical doctor.

The researchers are now designing a smaller, earbud-shaped jet array for treatments that will allow longer exposure times. They will also test the devices on animal models using biofilms of the other bacteria that cause middle ear infections, including, but not limited to, *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*, to test whether the treatment is also effective with these bacteria. Additionally, the researchers will closely monitor the tissues of the middle ear to ensure that there is no structural and functional tissue damage from the plasma technology.

The work was published in *npj Biofilms* and *Microbiomes* and funded by the NSF, the U.S. Air Force Office of Scientific Research, and the NIH. ■



Ivan Racheff Professor in Civil and Environmental Engineering Helen Nguyen



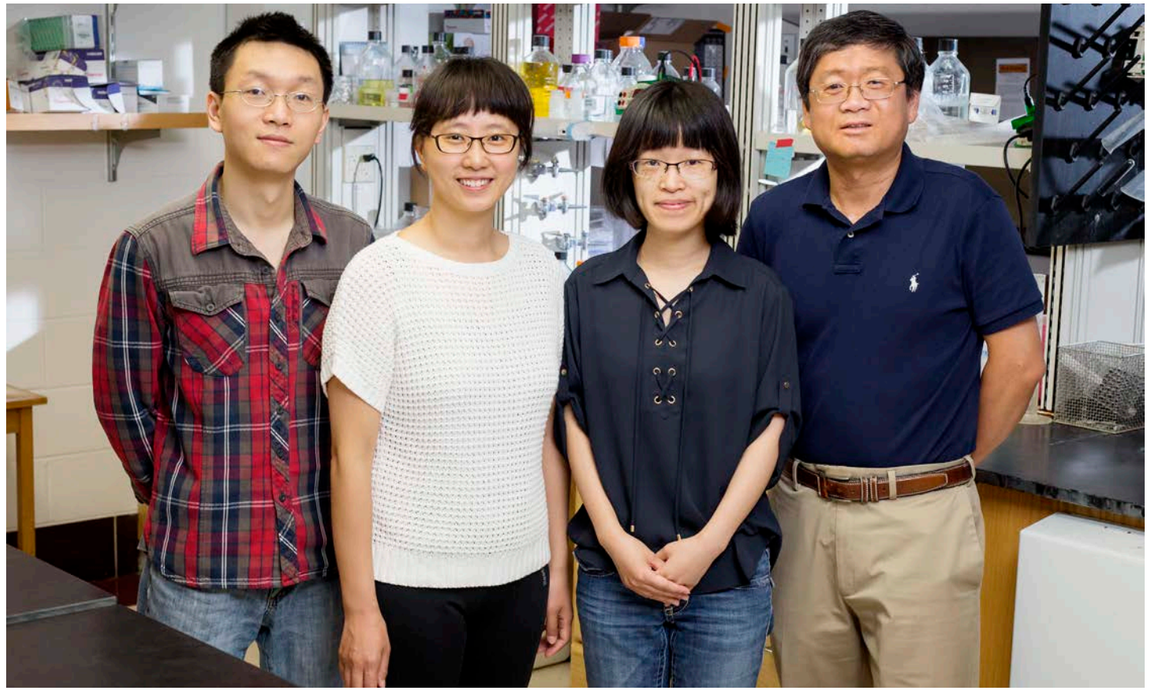
Brd4 cooperates with PPARy in adipose tissue macrophages to regulate the expression of Gdf3, which acts on the apdiocytes to suppress lipolysis, resulting in fat accumulation and the development of obesity

Investigating the role of Brd4 in diet-induced obesity

A NEW STUDY, PUBLISHED IN *JCI Insight*, looks at how Brd4, a regulator of the innate immune response, influences diet-induced obesity. The researchers believe that Brd4 could be used as a target for obesity and insulin resistance.

Approximately one-third of the adults and one in five children in the U.S. have obesity problems. Unfortunately, the condition is also associated with the development of other diseases including diabetes, cardiovascular disorders, and cancer. "One of the biggest challenges we face is trying to understand how people develop obesity. If we can understand that, we can develop solutions for treating or preventing these diseases," said Lin-Feng Chen (MME), a professor of biochemistry.

The researchers investigated the role of the innate immune response, which is the defense system we are born with and the first line of defense against invading microbes. Although the innate immune response is important in fighting against infections, it also causes different kinds of diseases.



From left: Xiangming Hu, postdoc; Yan Bao, postdoc; Jinjing Chen, postdoc; and Lin-Feng Chen, professor of biochemistry and medical biochemistry at the College of Medicine

"If we can understand (how people develop obesity) we can develop solutions for treating or preventing (associated) diseases."

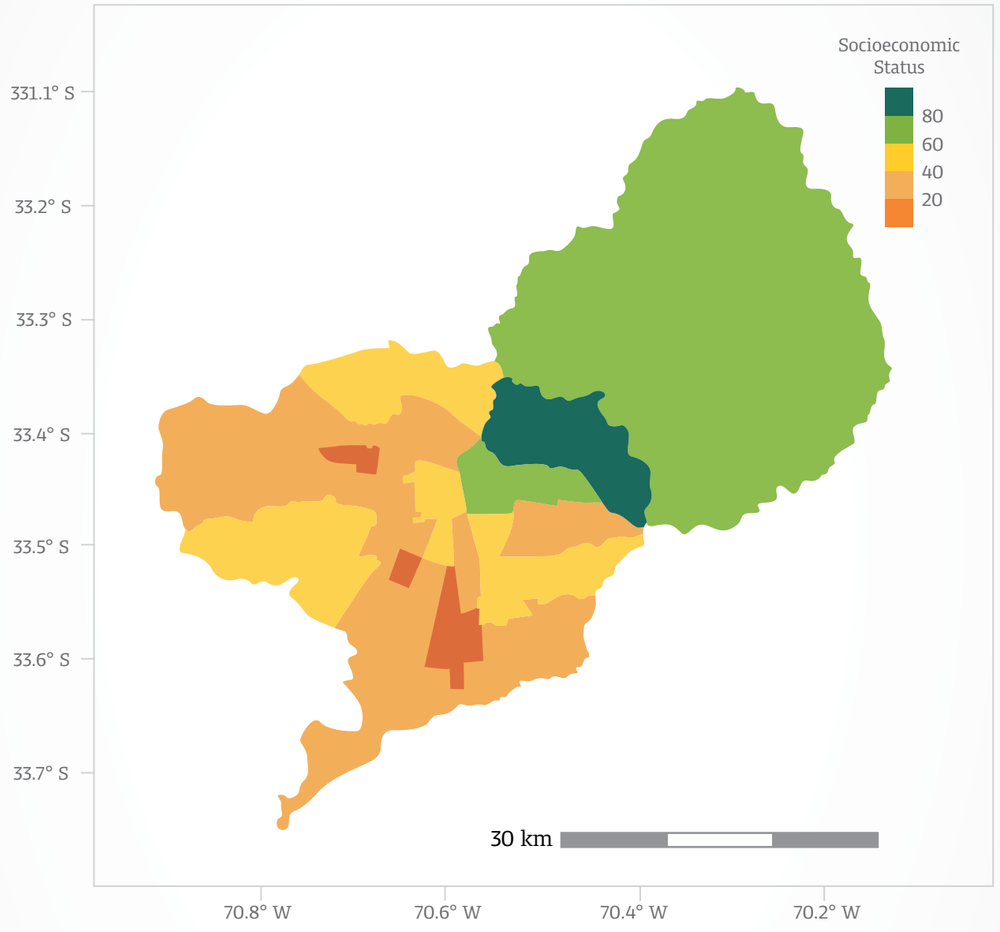
Since obesity is accompanied by low levels of inflammation, the researchers wanted to test whether the inflammation is caused by the innate immune response and whether Brd4 is also involved. "Our previous studies showed that Brd4 plays an important role in the innate immune response, so we were trying to understand how it influences the development of diseases such as obesity," Chen said.

The researchers used mice that lacked the Brd4 gene in their macrophages, which are a part of innate immunity. These cells cause inflammation and have been previously associated with obesity. The mice lacking Brd4 were fed a high-fat diet, which is known to trigger obesity, and were compared to normal mice on the same diet.

"We observed that after several weeks of the high-fat diet, the normal mice became obese while the mice lacking Brd4 did not. They also had reduced inflammation and higher metabolic rates," Chen said. These results suggest that the mice which did not have Brd4 used fat as the energy source, as opposed to sugar, which is usually used as the primary source of energy.

To understand the molecular mechanism by which Brd4 contributes to obesity, the researchers compared the gene expression profiles during high-fat diets in normal mice and mice that lacked the Brd4 gene. They found that Brd4 was essential for the expression of Gdf3, a protein whose release suppressed the breakdown of fats and lipids in adipose tissues. Without Brd4, the mice had reduced levels of Gdf3 and increased breakdown of fat.

The researchers believe that controlling lipid metabolism is only one of the mechanisms through which Brd4 contributes to obesity. Another mechanism they are interested in studying includes the gut microbiome. "We know that bacteria in the gut can sometimes trigger diet-induced obesity. ■



Municipalities that are part of Greater Santiago are colored according to their socioeconomic status (SES), where a lower score is indicative of a lower SES

Study maps COVID-19 health disparities in Greater Santiago

PEOPLE UP TO AGE 40 LIVING IN ECON-omically depressed municipalities in the Greater Santiago, Chile, metropolitan area were three times more likely to die as a result of the infection than their counterparts in wealthier areas, researchers report in the journal *Science*. People ages 41-80 in low socioeconomic-status municipalities also suffered more from the pandemic than their peers in more affluent areas, the team found.

The study used new methods to analyze COVID-19 death counts, reported cases, testing rates and delays in testing results across location, time and age group. The results reveal striking disparities between high and low socioeconomic-status municipalities, and also help explain the factors that contribute to differences in COVID-19-related infections and mortality in these regions, said Pamela Martinez (IGOH), a professor of microbiology and of statistics at Illinois who led the research with Gonzalo Mena, a postdoctoral fellow at the University of Oxford.

Greater Santiago is composed of 34 municipalities and is home to nearly 7 million people. The researchers used anonymized mobile phone data available through the Facebook Data for Good initiative to assess residents' mobility during the pandemic.

"People living in municipalities with low socioeconomic status did not reduce their mobility during lockdowns as much as those in more affluent municipalities," the researchers wrote. "This supports the hypothesis that people in poorer regions cannot afford to stay at home during lockdowns."

In the early weeks of the pandemic, COVID-19 testing was more available to people in the affluent parts of the metropolitan area than in the poorer locations, the researchers found. People in less affluent regions also appear to have waited longer for their test results.

"Because public health authorities plan their response based on the number of reported infections in a given area, this led to a poorer health care response in lower income areas than was needed," Martinez said. "This likely contributed to higher death counts in those areas."

Access to health care also was less abundant in the economically depressed areas, another contributor to worse health outcomes there, the researchers report.

"We found that the south and west zones of the Greater Santiago metropolitan area had four times fewer beds per 10,000 residents and four times fewer people enrolled in the private health system than the east zone, which includes all of the most affluent municipalities," Martinez said. "We also discovered that more than 90% of the deaths attributed to COVID-19 in the south and west zones occurred in places other than health care facilities."

Perhaps most strikingly, the team found that people under the age of 40 in less affluent parts of the region experienced significantly higher COVID-19-related mortality than their peers in wealthier areas.

"The infection-fatality rate for people 0-40 years old was 3.1 times higher in municipalities with the lowest socioeconomic status," Mena said. "Our results show that the socioeconomic inequalities we documented disproportionately affected younger people."

"Our results align with the recent literature on uneven health risks globally, which has highlighted how socially and economically deprived populations are more vulnerable to the burden of epidemics," they wrote. ■

Pamela Martinez, professor of microbiology and statistics at Illinois.

Using a multipronged approach to investigate the diet of ancient dogs

Researchers studying coprolites in the lab

COPROLITES, OR FOSSILIZED DOG FECES, ARE OFTEN used to understand the dietary preferences of ancient civilizations. However, the samples are often contaminated, making the analysis difficult. A new study, published in *Scientific Reports*, uses different techniques to improve the investigation of coprolites.

"Talking to community members about what their ancestors ate and how they interacted with dogs helps us understand our results better."

"We have been interested in analyzing coprolites for many years. We have attempted to extract DNA and look at the microbiome before, but the tools were not as robust," said Ripan Malhi (GNDP/GSP/IGOH), a professor of anthropology. "As far as I know, this is the first time anyone has used multiple approaches to provide a snapshot of the daily diet, health, and the long-term trends in ancient dogs of the Americas, all in one study."

The samples were recovered from Cahokia, near modern St. Louis, Missouri. At its peak, Cahokia was a large urban center with a population greater than London or Paris. Several other investigations have shown that there is an overlap between the diet of dogs and humans, either because the dogs were fed the same food or because they ate human food scraps. Therefore, investigating coprolites also provides an insight into human health and diet.

"Initially, the residents were growing crops such as squash and sunflowers. As the city got bigger, it is believed that the diet shifted to maize. Our analysis suggests the same since we saw that some of the dogs were also eating maize," said Kelsey Witt, a postdoctoral researcher at Brown University and former PhD student in the Malhi lab.

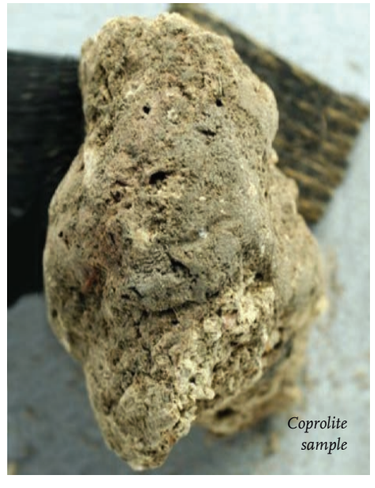
The maize samples were examined using stable isotope analysis, which is used to measure different forms of carbon in a sample. Depending on the carbon concentrations, one can identify what kind of plant was consumed. The researchers also investigated the animal and plant remains in the coprolites to show that walnuts, grapes, a variety of fish, and duck were a part of the dogs' diet.

The researchers also used DNA sequencing to determine the microbiome—the community of microbes—of the coprolites. "The technique we used came out in 2020. It helped us verify whether the samples were from dogs or humans, as well as confirm general aspects of diet which can only be done by comparing the microbiomes," said Karthik Yarlagadda, a PhD student in the Malhi lab.

"One of the biggest challenges we faced was dealing with sample contamination," Yarlagadda said. "These samples were deposited a thousand years ago. After that, the environment changed, certain microbes died off, and new microbes took over. All these factors complicate the analysis."

The researchers are working with the Indigenous communities to further understand what the diets looked like in their ancestors. "Since there are a lot of limitations to our research, talking to community members about what their ancestors ate and how they interacted with dogs helps us understand our results better," Witt said.

The work was sponsored by the Vice Chancellor for Research, University of Illinois, and the Illinois State Archaeological Survey. ■



Coprolite sample

Illustration by Jillian Nickell

Some birds steal hair from living mammals

DOZENS OF ONLINE VIDEOS DOCUMENT an unusual behavior among tufted titmice and their closest bird kin. A bird will land on an unsuspecting mammal and, cautiously and stealthily, pluck out some of its hair.

A new paper in the journal *Ecology* documents this phenomenon, which the authors call "kleptotrichy," from the Greek roots for "theft" and "hair." The authors found only a few descriptions of the behavior in the scientific literature but came up with dozens more examples in online videos posted by birders and other bird enthusiasts. In almost all the recorded cases, the thief is a titmouse plucking hair from a cat, dog, human, raccoon or, in one case, porcupine.

Many species of titmice, chickadees and tits are known to use hair or fur to line their nests, said Mark Hauber (GNDP), a professor of evolution, ecology and behavior who led the write-up with postdoctoral researcher Henry Pollock. The hair's role in the nest is still debated, although it is more commonly used by birds nesting in temperate climates, so maintaining warmth in the nest is thought to be one advantage.

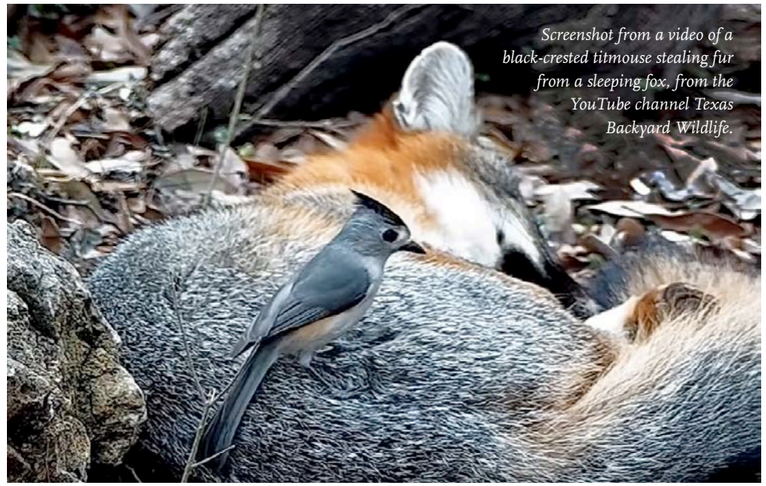
The impetus for the study came from a chance sighting. Jeffrey Brawn, a natural resources and environmental sciences professor and co-author first observed the behavior with Pollock while on a spring bird count in central Illinois. Scientists once assumed that birds with hair in their nests had collected it from the carcasses of dead mammals or found hair that had been shed into the environment, Brawn said. "But the titmouse I saw was plucking hair from a live animal," he said. "This was from a live raccoon with claws and teeth. And the raccoon didn't seem to mind because it didn't even wake up."

"We know, of course, that birds use a variety of materials to line their nests," Hauber said. "But why are these birds risking their lives to approach these mammals?"

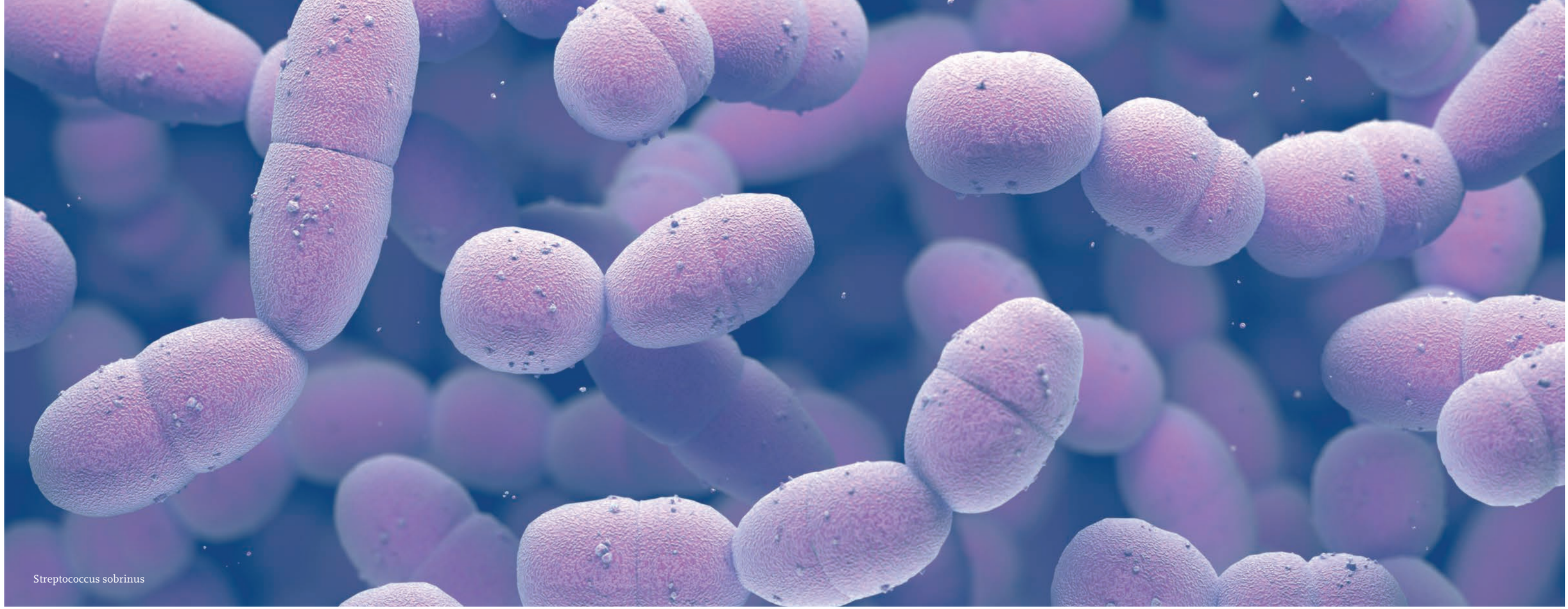
It may be that the birds simply need the hair to insulate their nests, but the presence of mammal hair—and the associated odor of the mammal—could also deter nest predators like snakes or other birds, the researchers said. The hair also may repel nest and nestling parasites, which are a common threat to chick survival, especially in cavity nests like those of titmice.

Regardless of the purpose of the behavior, the new paper is the first to document so many examples of hair-plucking by birds in a single report. In addition to citing nine papers about the phenomenon, it also links to dozens of online videos. Collectively, the videos show titmice—and in one case, a black-capped chickadee—plucking hair from 47 humans, 45 dogs, three cats, three raccoons and a porcupine.

"Unexpected interactions such as these remind us that animals exhibit all types of interesting and often overlooked behaviors and highlight the importance of careful natural history observations to shed light on the intricacies of ecological communities," Pollock said. ■



Screenshot from a video of a black-crested titmouse stealing fur from a sleeping fox, from the YouTube channel Texas Backyard Wildlife.



Streptococcus sobrinus

Novel pathway to support research for targeted treatments of cavities

TOOTH DECAY, ALSO KNOWN AS CAVIties in the U.S., is the most common human disease in the world, caused by a bacterial infection. Oral bacteria ferment sugars in the mouth, proliferate, and secrete excessive acid which leads to a breakdown of enamel and demineralization of the tooth structure.

Two bacteria have been linked to the initiation of dental caries or tooth decay: *Streptococcus mutans* and *Streptococcus sobrinus*. Between these two bacteria, *S. mutans* has been extensively studied while relatively little is known about *S. sobrinus*. A research team led by bioengineering professor Paul Jensen (MMG) has discovered a quorum-sensing pathway in *S. sobrinus*, which controls its natural competence and enables scientists to manipulate the *S. sobrinus* genome. This research was published in the *Journal of Dental Research*.

"The three key properties for caries-linked microbes are the ability to produce acid, the ability to tolerate acid, and the ability to colonize the tooth surface," said Walden Li, a bioengineering Ph.D. candidate and a co-author of this paper. He noted earlier studies indicating that *S. sobrinus* is stronger in such abilities than *S. mutans*.

"Deep down, I never believed that *S. sobrinus* was not genetically competent. It didn't make sense to me."

Regarding this research, Li said, "while we know *S. sobrinus* has strong capacities to cause tooth decay, we don't know the genetic mechanisms that enable it to do so."

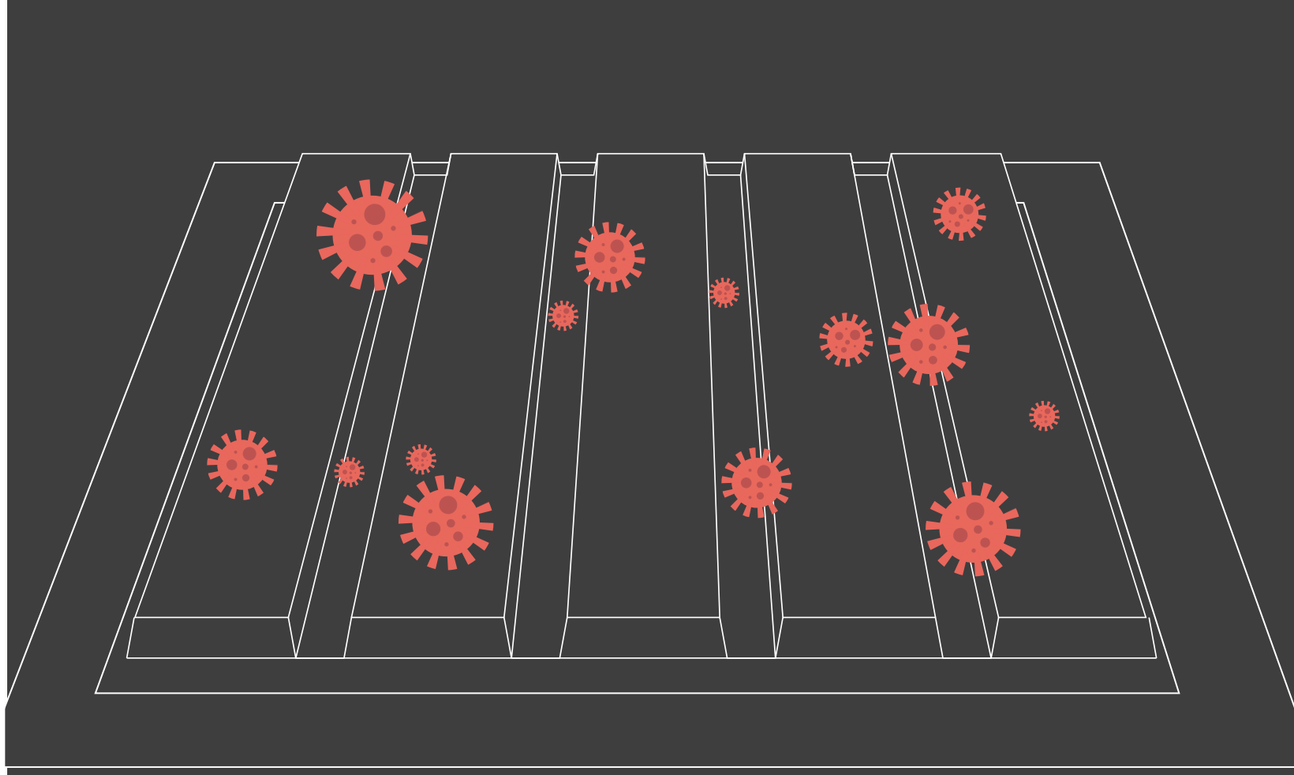
Current microbial control for dental caries uses mostly wide-spectrum treatments that indistinguishably kill good and bad bacteria in the mouth, potentially disrupting a healthy oral microbiome. A more effective way of controlling dental caries would be to understand the genetic mechanisms of *S. sobrinus* and leverage this knowledge to develop targeted treatments.

According to Jensen, *S. sobrinus* has been understudied because most researchers believed that it lacks the competence pathways to regulate growth, virulence, bacteriocin production and quorum sensing, even though most streptococcal bacteria are naturally competent. Competence is the capacity of a bacteria to uptake foreign DNA and undergo genetic transformation. This is a decades long-unsolved challenge for the dental research field. "Deep down, I never believed that *S. sobrinus* was not genetically competent. It didn't make sense to me," said Jensen.

Bioengineering Ph.D. candidate and co-author Ryan Wyllie found a promoter sequence in *S. sobrinus* similar to the salivarius group of streptococcal bacteria. With this clue, the team uncovered the ComRS pathway for *S. sobrinus* based on *S. salivarius* instead of *S. mutans*. Their findings challenged the assumption of the relationship between *S. sobrinus* and *S. mutans*. *S. sobrinus'* ComRS system has two *comR* genes with opposite effects on its competence and this is the first time that researchers have seen two *comR* genes in one bacterium. Furthermore, *S. sobrinus* has ComRS-controlled bacteriocins that kill *S. mutans* and other oral bacteria, an astounding finding to the team since it was presumed that the bacteria work together during infection.

"I guarantee that this is not the last interesting bacterium to be found in the oral microbiome," said Jensen, whose lab centers on systems biology, "And we need to scale up how we can study them all in the future." ■

Microscope that detects individual viruses could power rapid diagnostics



PRISM microscopes detect viruses using photonic crystals that reflect only one wavelength of light

A FAST, LOW-COST TECHNIQUE TO SEE AND COUNT viruses or proteins from a sample in real time, without any chemicals or dyes, could underpin a new class of devices for rapid diagnostics and viral load monitoring, including HIV and the virus that causes COVID-19.

> **"We are also going to use this as a research tool for biology and cancer."**

Researchers at Illinois described the technique, called Photonic Resonator Interferometric Scattering Microscopy, or PRISM, in the journal *Nature Communications*.

"We have developed a new form of microscopy that amplifies the interaction between light and biological materials. We can use it for very rapid and sensitive forms of diagnostic testing, and also as a very powerful tool for understanding biological processes at the scale of individual items, like counting individual proteins or recording individual protein interactions," said study leader Brian Cunningham (CGD director/MMG), the Intel Alumni Endowed Chair of electrical and computer engineering and a member of the Holonyak Micro and Nanotechnology Lab.

In optical microscopes, light bounces off any molecules or viruses it encounters on a slide, creating a signal. Instead of a regular glass slide, the PRISM technique uses photonic crystal: a nanostructured glass surface that brilliantly reflects only one wavelength of light. Cunningham's group designed and fabricated a photonic crystal that reflects red light, so that the light from a red laser would be amplified.

"The molecules we are looking at—in this study, viruses and small proteins—are extremely small. They cannot scatter enough light to create a signal that can be detected by a conventional optical microscope," said graduate student Nantao Li, the first author of the paper. "The benefit of using the photonic crystal is that it amplifies the light's intensity so it's easier to detect those signals and enables us to study these proteins and viruses without any chemical labels or dyes that might modify their natural state or hinder their activity—we can just use the intrinsic scattering signal as the gauge for determining if those molecules are present."

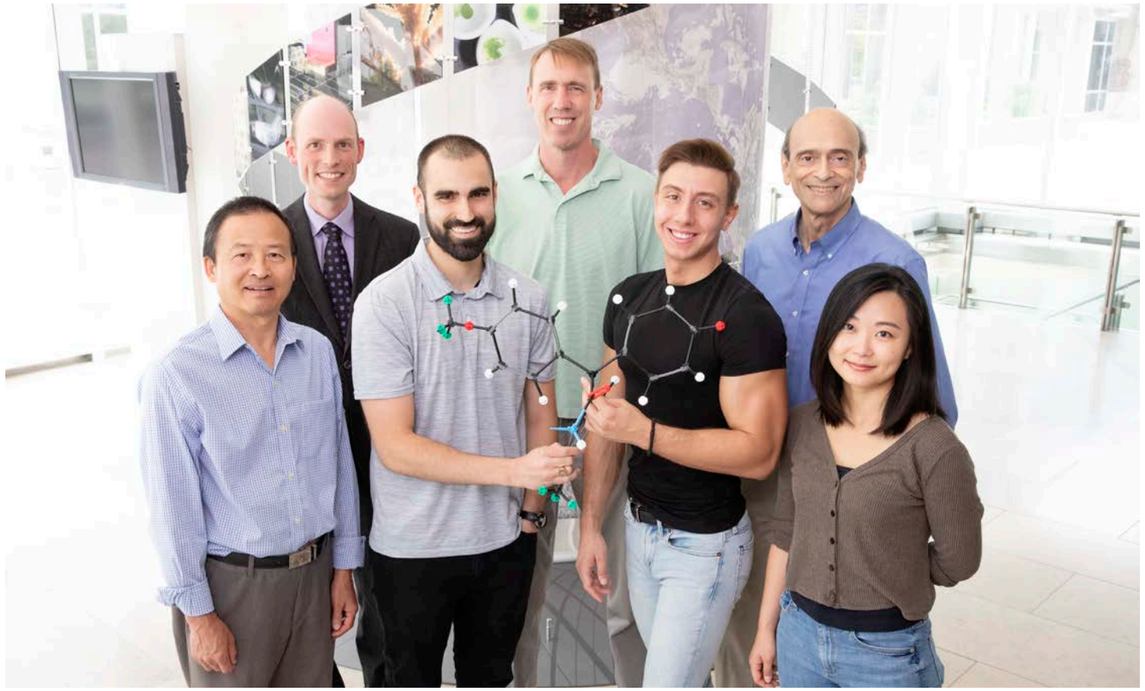
The researchers verified their technique by detecting the virus that causes COVID-19. PRISM detected individual coronaviruses as they traveled across the slide's surface. The technique could allow researchers to study such biological targets in their natural states—watching as proteins interact, for example—or researchers could seed the surface of the photonic crystal slide with antibodies or other molecules to capture the targeted items and hold them in place.

Cunningham's group is working to incorporate PRISM technology into portable, rapid diagnostic devices for COVID-19 and HIV viral load monitoring. The group is exploring prototype devices that incorporate filters for blood samples and even condensation chambers for breath tests.

"We are also going to use this as a research tool for biology and cancer," Cunningham said. "We can use it to understand protein interactions that are parts of disease processes. We are interested in using it to detect these tiny vesicles that cancer cells shed, and to see what tissues they come from, for diagnosis, and also to study what cargo they are transporting from the cancer cells."

The NSF and the NIH supported this work. ■

Professor Brian Cunningham



From front left, research scientist Chengjian Mao and graduate students Matthew Boudreau, Darjan Duraki and Ji Eun Kim. In the back row, from left, are molecular and integrative physiology professor Erik Nelson, chemistry professor Paul Hergenrother and biochemistry professor David Shapiro

New approach eradicates breast cancer in mice

A NEW APPROACH TO TREATING breast cancer kills 95-100% of cancer cells in mouse models of human estrogen-receptor-positive breast cancers and their metastases in bone, brain, liver and lungs. The newly developed drug, called ErSO, quickly shrinks even large tumors to undetectable levels. The research team reported the findings in the journal *Science Translational Medicine*.

"Even when a few breast cancer cells do survive, enabling tumors to regrow over several months, the tumors that regrow remain completely sensitive to retreatment with ErSO," said biochemistry professor David Shapiro, who led the research with chemistry professor Paul Hergenrother (ACPP leader/MMG). "It is striking that ErSO caused the rapid destruction of most lung, bone and liver metastases and dramatic shrinkage of brain metastases, since tumors that have spread to other sites in the body are responsible for most breast cancer deaths," Shapiro said.

The activity of ErSO depends on a protein called the estrogen receptor, which is present in a high percentage of breast tumors. When ErSO binds to the estrogen receptor, it upregulates a cellular pathway that prepares cancer cells for rapid growth and protects them from stress. This pathway, called the anticipatory Unfolded Protein Response, or a-UPR, spurs the production of proteins that protect the cell from harm. "The a-UPR is already on, but running at a low level, in many breast cancer cells," Shapiro said. "It turns out that this pathway shields cancer cells from being killed off by anti-cancer drugs."

ErSO was tolerated well in mice even when higher doses were used

> **"ErSO is fast-acting and its effects on breast cancers in mice are large and dramatic."**

For the new research, Shapiro and Hergenrother worked together on a search for a much more potent small molecule that would target the a-UPR. Their analysis led to the discovery of ErSO, a small molecule that had powerful anticancer properties without detectable side effects in mice, further tests revealed.

"This anticipatory UPR is estrogen-receptor dependent," Hergenrother said. "The unique thing about this compound is that it doesn't touch cells that lack the estrogen receptor, and it doesn't affect healthy cells—whether or not they have an estrogen receptor. But it's super-potent against estrogen-receptor-positive cancer cells."

Further studies in mice showed that exposure to the drug had no effect on their reproductive development. And the compound was well tolerated in mice, rats and dogs given doses much higher than required for therapeutic efficacy, the researchers found.

ErSO also worked quickly, even against advanced, human-derived breast cancer tumors in mice, the researchers report. Often within a week of exposure to ErSO, advanced human-derived breast cancers in mice shrank to undetectable levels."Many of these breast cancers shrink by more than 99% in just three days," Shapiro said. "ErSO is fast-acting and its effects on breast cancers in mice are large and dramatic."

Study co-authors also include veterinary clinical medicine professor Timothy Fan (ACPP), molecular and integrative physiology professor Erik Nelson (ACPP), and professor emeritus of pathology Edward Roy.

Funders of this work include the University of Illinois, the U.S. Department of Defense, the NIH, and Systems Oncology. ■

Development of microsatellite markers for censusing of endangered rhinoceros

TODAY, THE SUMATRAN RHINOCEROS IS CRITICALLY endangered, with fewer than 100 individuals surviving in Indonesia on the islands of Sumatra and Borneo. To ensure survival of the threatened species, accurate censusing is necessary to determine the genetic diversity of remaining populations for conservation and management plans.

A new study reported in *BMC Research Notes* characterized 29 novel polymorphic microsatellite markers—repetitive DNA sequences—that serve as a reliable censusing method for wild Sumatran rhinos.

> **"We hope that we can use these markers on more samples collected in the field to provide island-wide population data... which will help us devise better conservation strategies."**

"It's hard to do population censusing for this species because there's not a ton of them and they're very elusive so it's hard to figure out how many there are," said Jessica Brandt, former PhD student in the Roca lab who led the study. "We were looking for ways to do that without handling the species."

Sumatran rhinos live in dense rainforests that are hard to traverse through, making it difficult to track Sumatran rhinoceros populations. The researchers relied on fecal DNA collected from Sumatran rhino dung samples, requiring little interaction with individuals in the wild. Although dung sampling poses many benefits, fecal DNA can be degraded and the age of the samples hard to determine. In order to overcome these challenges, researchers designed optimized microsatellite markers that were short and easy to amplify from dung samples.

"Microsatellite markers are found in non-coding regions and because of that, they evolve pretty quickly," said Brandt. "They're really useful in populations where you want to identify individuals because you're going to see more variation at those particular markers than if you're using a protein-coding gene."

"During replication of the DNA, these markers can very easily expand or contract like a genomic accordion" said animal sciences professor Alfred Roca (EIRH/GNDP). "By looking at enough of these markers, you can distinguish animals because microsatellites evolve very quickly and are highly variable within species."

Using high quality DNA sequences from captive Sumatran rhinos, researchers identified 29 polymorphic candidate loci for further optimization. To test its utility for censusing, 13 of the 29 markers were randomly tested on fecal samples collected from wild Sumatran rhinos. The researchers were able to amplify nine of the markers from 11 wild fecal samples.

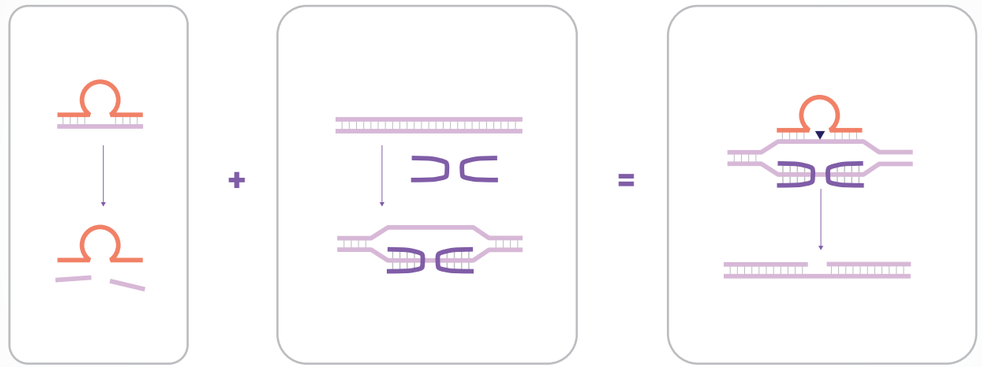
"We hope that we can use these markers on more samples collected in the field to provide island-wide population data for Sumatran rhinoceros species, which will help us devise better conservation strategies for this critically endangered species," said Sinta Saidah, co-author and research assistant at the Eijkman Institute for Molecular Biology in Indonesia.

Other authors of the study include Kai Zhao, Isabella Apriyana, Oliver Ryder, Widodo Ramono, Herawati Sudoyo, Helena Suryadi, and Peter Van Coeverden de Groot.

Funding was provided by the US Fish and Wildlife Service Rhinoceros and Tiger Conservation Fund, the International Rhino Foundation, the Ministry of Research and Technology/National Research and Innovation Agency of the Republic of Indonesia, the World Wildlife Fund, the National Science and Engineering Research Council, and the Illinois ACES Office of International Programs. ■

Sumatran rhinos
Illustration by Jillian Nickell

DNAzymes could outperform protein enzymes for genetic engineering



ssDNA-cleaving DNAzyme | PNA "openers" | dsDNA-nicking "PANDA" system

Sequence-specific nicking activity of PANDA on dsDNA

RESEARCHERS HAVE DEVELOPED A technique that, for the first time, allows DNAzymes—small DNA molecules that can function like protein enzymes—to target and cut double-stranded DNA. When it comes to genetic engineering applications such as gene editing or gene therapy, DNAzymes have faced a challenge: they have only been able to target sites on single-stranded DNA, while the DNA coding for genes in cells is double-stranded. The researchers published their findings in the *Journal of the American Chemical Society*.

"DNAzymes have many advantages, including higher stability, smaller size and lower cost than protein enzymes. These advantages perfectly fit the requirement for genetic engineering tools," said study leader Yi Lu (BSD/CABBI/CGD), a professor of chemistry.

In double-stranded DNA, the two strands are specifically paired together with complementary sequences. To make it possible for DNAzymes to cut the double-stranded DNA, the team developed a technique that pairs DNAzymes with helper molecules called peptide nucleic acids.

"PNA is a very strong DNA binder, strong enough to bind to one strand of the double-stranded DNA even though all of the bases are already paired with the other strand," said Mingkuan Lyu, a graduate student and first author of the paper. "Once this process happens, one strand of the double-stranded DNA will be occupied by PNA, and the other strand will be exposed as single-stranded DNA, available for the DNAzyme to interact."

The team first demonstrated the technique, called PNA-assisted double-stranded DNA nicking by DNAzymes, or PANDA, on a synthetic testing sequence to prove it worked to cut one or both strands of a double-stranded DNA target. They also tested PANDA's ability to distinguish a specific target sequence from similar sequences. This is important as unintended off-target activity is one of the challenges that has limited the clinical applications of protein-based gene editing techniques, such as CRISPR.

> **"The PANDA system can serve as a novel alternative tool for a wide range of genetic engineering and other biochemical and biotechnological applications."**

"In CRISPR-Cas9, the guide RNA is responsible for customized target recognition, but in PANDA, both the DNAzyme and the PNA are. Therefore, there is an inherent 'double-check' mechanism in PANDA, making it more stringent in target specificity," Lyu said.

Another advantage of PANDA is its small size—the PNA and DNAzyme together are about five times smaller than the CRISPR-Cas9 complex, Lu said—allowing it to access crowded sites within a chromosome's tightly-packed DNA.

Next, the researchers plan to investigate the PANDA system's performance targeting genes of interest in living cells. They also plan to expand the catalog of genes that the PANDA system can target.

"The targeting sequences can be readily changed and customized for specific applications," Lu said. "Therefore the PANDA system can serve as a novel alternative tool for a wide range of genetic engineering and other biochemical and biotechnological applications."

CABBI, the NIH and the Chemistry Discovery Fund at the University of Illinois supported this work. ■

Yi Lu, Professor of Chemistry

Illustration of Gram-stained Clostridium paraputrificum

Microbial gene discovery could mean greater gut health

THE MICROSCOPIC ORGANISMS IN YOUR body aren't just hitching a ride; many of them perform essential chemical reactions that regulate everything from our digestion to our immune system to our moods.

One important set of reactions relates to fat absorption via bile acids. Our livers make these acids to help digest fats and fat-soluble vitamins as they travel through the small intestine. Near the end of the small intestine, microbes convert the acids into new forms, which can either be beneficial or harmful.

New research identifies the last in a set of microbial genes involved in these conversions.

"Locating these bacterial genes will allow mechanistic studies to determine the effect of bile acid conversion on host health. If we find this is a beneficial reaction, therapeutic strategies can be developed to encourage production of these bile acids in the gastrointestinal tract," says Jason Ridlon (MME), Associate Professor in the Department of Animal Sciences and corresponding author of a new article in *Gut Microbes*.

"This is helpful for human microbiome researchers because the field is moving towards trying to link function with disease."

Microbes produce enzymes that flip the orientation of three hydroxyl groups on bile acid molecules. Flipping them into different configurations rearranges the acid molecules into forms that can be harmful or beneficial. Ridlon and other scientists had already identified the genes for two of these enzymes, but one was still unknown.

To find the missing gene, Ridlon and his collaborators looked back in time. Previous research links the flipping of a specific hydroxyl group—one attached to a location on the acid molecule known as carbon-12—with a microbe called *Clostridium paraputrificum*.

"Using the genome sequence of *C. paraputrificum*, we identified all the candidate reductases, engineered the genes into *E. coli* and determined which reductase was able to flip the polar group on bile acids," he adds.

The research team then searched for similar sequences in the human microbiome.

"We were able to identify the gene in numerous bacterial species that were previously unknown to have this bile acid metabolizing function. This is helpful for human microbiome researchers because the field is moving towards trying to link function with disease. Now we know the precise DNA sequences that encode an enzyme that flip carbon-12 of bile acids," Ridlon says.

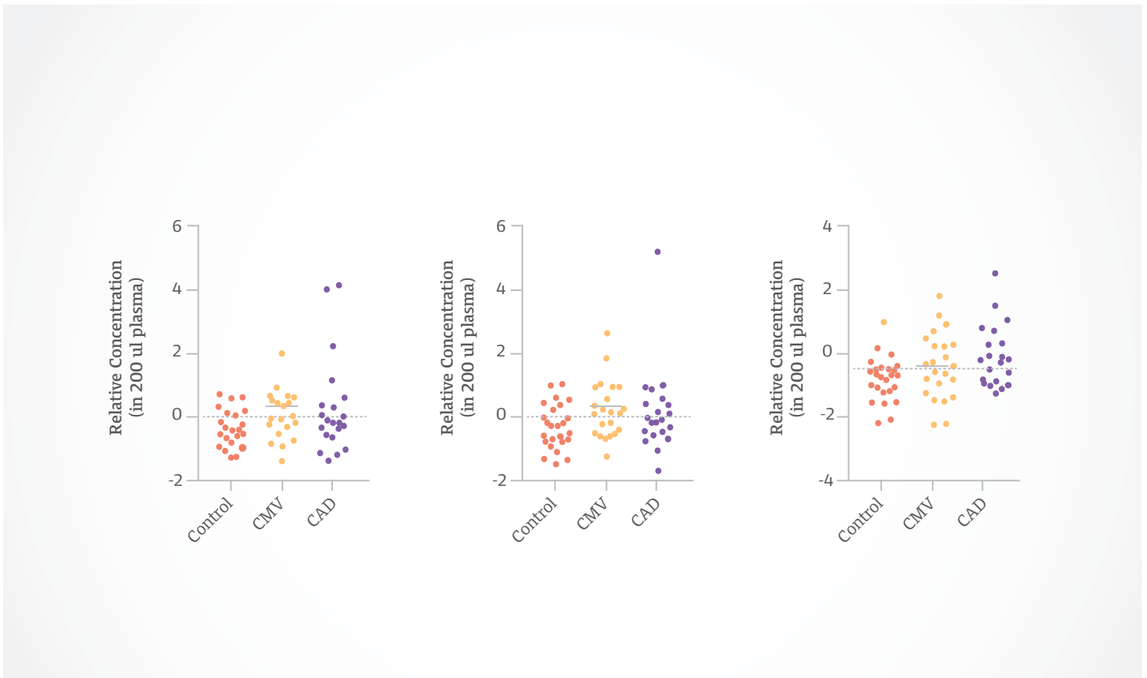
The researchers haven't yet figured out if flipping the hydroxyl group at carbon-12 is a good or a bad thing. In the "good" category, the flip may play a role in detoxifying harmful bile acids such as deoxycholic acid (DCA) and lithocholic acid (LCA), chemicals known to damage DNA and cause cancers of the colon, liver, and esophagus. But Ridlon notes that "good vs. bad" framing oversimplifies reality.

While there is still more to learn, Ridlon says identifying and characterizing these new microbial genes responsible for bile acid conversion is a major step forward for gut health.

Other authors of the study include Heidi Doden, Patricia Wolf, Rex Gaskins (RBTE), Karthik Anantharaman, and João Alves.

Funding for this research came from the NIH and the USDA. ■

Associate Professor Zeynep Madak-Erdogan and Alicia Arredondo Eve



Using an unpaired t-test, researchers identified high stearic acid (left) and ornithine (middle) as an indicator of CMV and valine (right) as statistically different in the CAD group compared to the control group

New markers for coronary microvascular disease identified

ALTHOUGH CARDIOVASCULAR DISEASE is the main cause of illness among women in the U.S., certain conditions such as coronary microvascular disease (CMD) cannot be easily diagnosed. In a new study, published in *Metabolites*, researchers have identified specific biomarkers for CMD, which might reduce future hospitalizations.

CMD damages the inner walls of blood vessels causing spasms and decreased blood flow to the heart muscle. "Clinicians look for plaque formation in the blood vessels, which does not occur in CMD," said Zeynep Madak-Erdogan (CGD/EIRH/GSP), an associate professor of nutrition. "Usually, women leave without having the root causes of the chest pain addressed and they come back with further complications within a year. Since this condition is more common in postmenopausal women, we want to identify the biomarkers that are associated with CMD."

The researchers collected blood samples from three different groups containing 20-25 women each: postmenopausal women who were healthy, those with coronary artery disease, which is characterized by plaque formation, and those with CMD. The blood serum samples were then analyzed to see if there were any molecules that were different in the CMD group.

> **"Our observations imply that the increase in ornithine means that the second branch is not working, which is why we can use this molecule as a biomarker for the disease."**

Out of 175 molecules scanned, the researchers identified stearic acid, which is found in animal and plant fats, and ornithine, an amino acid commonly found in meat, fish, diary, and eggs, as indicators of CMD.

Ornithine is formed from the amino acid arginine which is broken down by two separate pathways. One forms ornithine and the other forms nitric oxide, which helps in maintaining the normal functioning of the blood vessels.

"Our observations imply that the increase in ornithine means that the second branch is not working, which is why we can use this molecule as a biomarker for the disease," Madak-Erdogan said.

Interestingly, other researchers have found that estrogen may have a role in the development of CMD, as evidenced by hormone-replacement therapies which decrease CMD risk up to 30%. "Our observations further indicate that estrogen is involved because we know that it improves the function of nitric oxide," Madak-Erdogan said. "Since postmenopausal women have lower levels of estrogen, it would explain why this condition is more prevalent in these populations."

The researchers are trying to identify more biomarkers, such as proteins, that can be used to detect CMD. Additionally, they are testing more women to validate their findings. "This study was done with patients in Turkey, so we don't know if the same biomarkers will be present in the U.S. We want to look at bigger populations to see if we can combine the data to find efficient signatures for CMD," Madak-Erdogan said.

The work was funded by the University of Illinois, the ACES Future interdisciplinary research explorations grant, the Office of International Programs-Conrad Award, National Institute of Food and Agriculture, USDA, NCSA Faculty Fellows, and TÜBİTAK 2219 Post Doctorate Research Scholarship Program. ■

Outreach

Students complete their first STEAM TRAIN Journey

Starting from September 2020, six groups of 38 students from Franklin STEAM Academy in Champaign met every Tuesday afternoon after school to conduct research on important topics. The project, called "STEAM TRAIN," involved the 6th-8th grade students, researchers from the IGB, and a dozen students from University Laboratory High School, or Uni High. The projects concluded in May 2021.

The project goal was to help the Franklin students discover their love for science by exploring difficult issues that they're passionate about. The Uni High students were recruited to serve as a bridge since students may feel more comfortable forming connections with mentors who are closer to them in age.

Unfortunately, due to COVID-19, the format for STEAM TRAIN had to be adjusted. Instead of meeting at Franklin every other week after school, all the participants met on Zoom. "COVID certainly limited the scope of what we wanted to achieve and made us readjust our plans on the fly. While Zoom would not have been our first choice, the students quickly adjusted to the online format," said IGB Outreach Activities Coordinator Daniel Urban. Nevertheless, the topics that were researched by the students rivaled what is explored by cutting-edge laboratories across the world: rocket fuels, bird navigation in adverse weather, carbon capture, designing disposable packaging, tissue regeneration, and bioluminescence.

"Throughout the year, the persistence and creativity of the students continued to astound us. As much as we hope the program benefited them, these kids served as a source of inspiration for us as well," Urban said.

Pollen Power concludes its first online camp

The Pollen Power camp, which takes place over the summer, targets 6th-8th grade students from underrepresented populations in STEM with the goal of training them to observe their surroundings like scientists. Usually, it takes place in-person and the campers study pollen to see how they germinate, use them as a time capsule to study the climate that existed millions of years ago, and use the facilities to image pollen.

This year, however, the organizers had to conduct the camp virtually from June 7th to July 30th. The campers were assigned weekly activities, including dissecting flowers, following the growth of plants, making clay flowers, and identifying insects. They were guided by the camp counselors and the IGB staff through weekly check-ins.

"It was interesting to see all the different pieces when I took it apart and the different bugs that were in the flower," said Allison, one of the campers. Other campers enjoyed the chlorophyll extraction activity and identifying different fruits in an online game. "I learned that lychee nuts were real and that they look like walnuts but are tinier," said Evie, another camper.

"It was definitely interesting moving to a virtual camp," said Daniel Ryerson, an Outreach Activities Coordinator at the IGB. "It was a challenge to design activities that the campers could do at home, on their own, that were still informative and engaging. Fortunately, it turned out better than I hoped—the campers had a blast sharing what they learned and they taught us counselors some things too."

Undergraduate students selected as 2021 Woese Research Scholars

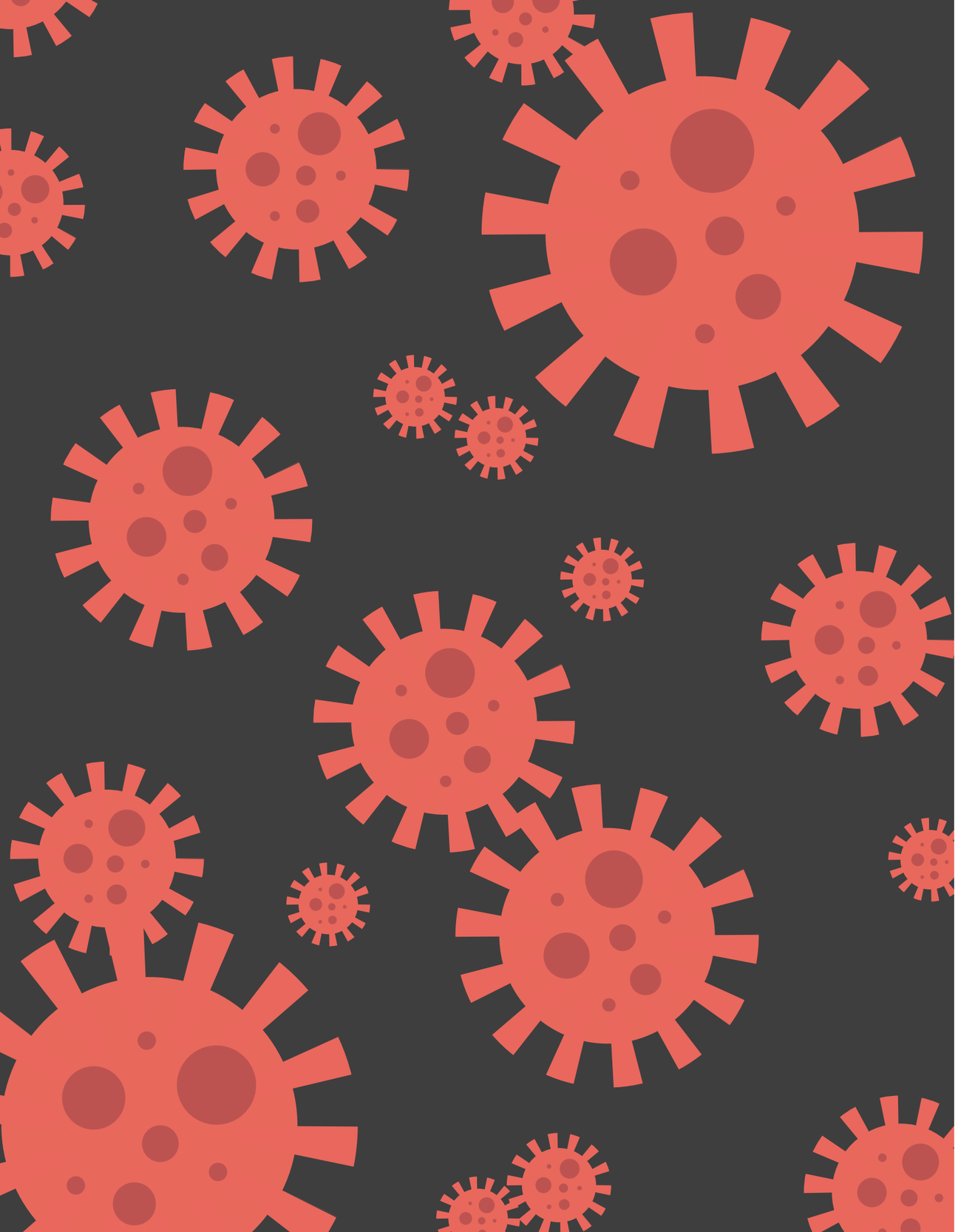
The Carl R. Woese Undergraduate Research Scholar program is designed to inspire students to pursue important scientific questions. This year, Peyton Hopkins and Shreyaa Khanna have been selected to carry out their research for a 10-week period, supported by a stipend from the IGB.

Peyton Hopkins is pursuing a degree in molecular and cellular biology and has been working in the Reddi lab since 2020. Hopkins will continue his research in the same lab where he will study the involvement of the protein TDP-43 in spermatogenesis. Using mice models, Hopkins will investigate the role of this protein.

"I have always loved nature and I came to appreciate biology during my time in high school and community college," Hopkins said. "This will be my first summer research experience and I'm excited."

Shreyaa Khanna is also pursuing a degree in molecular and cellular biology, with a minor in bioinformatics. During the summer she will be working in the Dar lab where she will investigate the cell cycle in embryonic stem cells using a fluorescent indicator called FUCCI.

"I have had summer research opportunities in the past that have helped me understand the fundamental aspects of research. Lab work always came to me very naturally and I feel like I have invested in something that I am passionate about," Khanna said. "I am excited for this summer because I will be able to use the state-of-the-art facilities at the IGB to pursue my research inquiries."



Research

Lab team creates fast, cheap, and accessible COVID-19 antibody test

As the numbers of those infected with COVID-19 continued to climb, the desperate need for a vaccine was apparent. Even now with the invention and administration of several COVID-19 vaccinations, the question remains: How effective are these vaccines? Holonyak Micro & Nanotechnology Lab students Congnyu Che, Weijing Wang, and Nantao Lialong with IGB Fellow Bin Zhao and Professor Brian Cunningham (CGD Director/MMG) have recently been published in the journal *Talanta* for the development of a cost efficient COVID-19 antibody test.

"Compared with other detection methods, our method is a simple, 15-minute sample-to-answer test," says Zhao, a postdoctoral research associate. "It costs less than $2 per test and is used with a desktop detection system that is suitable for point-of-care situations like clinics and physician offices."

This highly sensitive, fast, and low-cost test demonstrates great potential for wide applications in diverse working environments. COVID antibody testing could become routine and simple as a variety of vaccines are deployed whose long-term protection is not yet fully known. The test is simple enough to be performed at schools, health clinics, pharmacies, and parts of the world where diagnostic laboratories are not available.

"We are very glad we did it," says Zhao. "Without any one of us, this group couldn't have finished the work so quickly and efficiently. We all put forward many great ideas and were all very active during the experimental process."

How does the structure of cytolysins influence their activity?

Although *Enterococcus faecalis* is usually an innocuous member of the bacterial community in the human gut, it can also cause several infections. The bacteria produce cytolysins, which are molecules that destroy cells. In a new study, researchers have uncovered how they do so.

Cytolysin is made up of two subunits, CylLL" and CylLS", which have been previously shown to kill both mammalian and bacterial cells. The structure of the subunits is stabilized with the help of rings, called macrocycles, that staple the ends and prevent the structure from unfolding. The researchers replaced each amino acid in both these subunits to determine which amino acids are important.

"After mutating the amino acid residues, we purified and tested the mutants to see whether they had anti-bacterial activity or if they could lyse rabbit blood cells," said Imran Rahman, a graduate student in the van der Donk lab. "We found that the macrocyclizations in both subunits are important for both activities."

The researchers are interested in identifying the targets of cytolysin. "These molecules are unusual because unlike our current antibiotics, which bind to big cellular targets, these bind to small molecules and seem to use them to make holes in the membrane," said Wilfred van der Donk (MMG), a professor of chemistry. "We don't know what their targets are and we're working to find them."

The study was published in *ACS Infectious Diseases* and was funded by the HHMI and the NIGMS-NIH Chemistry-Biology Interface Training Grant.

Chemical reactions break free from energy barriers using flyby trajectories

A new study led by Beckman Institute of Advanced Science and Technology director and chemistry professor Jeffrey Moore (BSD) demonstrates how external mechanical forces alter atomic motions to manipulate reaction outcomes. The study findings are published in the journal *Science*.

"We think of chemical reactions as molecules moving on a surface of potential energy, the way hikers follow the contour map along a trail," said lead author Yun Liu, a post-doctoral researcher in Moore's research group. "The relative height of barriers control which path the molecules will most likely choose."

Liu developed an experimental design using a carbon-13 isotope-labeled ring molecule with two polymer chains attached. Liu placed the polymers into a reaction vessel and applied a mechanical force, which rips the ring into two separate groups.

Liu hypothesized that with the excitation of mechanical force, the atoms heat up along specific reaction directions, rather than following the directions shaped by the potential energy surface. The researchers named this departure from the conventional concept of chemical reactions a "flyby trajectory."

"The hypothesis is equivalent to saying that a hiker just decided not to follow the map," Liu said. "Instead, the hiker was excited enough to hop onto a hang-glider and just fly."

"Our findings will give researchers a more complete understanding of how force can alter the course of chemical reactions to increase production efficiency," Moore said. "It's another tool in our toolbox to make the things we use every day."

The NSF, the Army Research Office, the Dr. Leni Schoninger Foundation and the Deutsche Forschungsgemeinschaft supported this research.

Research

Magnets intensify electrolysis, utilize carbon dioxide more efficiently

For decades, researchers have been working toward mitigating excess atmospheric carbon dioxide emissions. One promising approach captures atmospheric CO_2 and then, through electrolysis, converts it into ethanol, ethylene, and other useful chemicals. In *ACS Energy Letters*, researchers use magnetism to reduce the energy required for CO_2 electrolysis by up to 60% in a flow electrolyzer.

In a typical CO_2 flow electrolyzer, electricity is supplied to drive the reactions at the cathode (where carbon dioxide is reduced into useful byproducts) and the anode (where water is oxidized, producing oxygen).

Most studies have not looked at the oxidation reaction at the anode—which often accounts for more than 80% of the energy required for CO_2 electrolysis, and therefore, offers the most room for improvement.

"The answer was staring us right in the face—the trick is to reduce the energy consumption at the anode," said first-author Saket S. Bhargava, a graduate student in chemical and biomolecular engineering. "If oxygen evolution is the problem, why not use a magnetic field at the oxygen evolving electrode and see what happens to the entire system?"

The researchers achieved energy savings ranging from 7% to 64% by enhancing mass transport to/from the electrode. "Our ultimate goal is to transform carbon dioxide back into carbon-based chemicals," said lead author Paul Kenis (RBTE), a chemical and biomolecular engineering professor. "We have demonstrated how to further reduce the significant energy requirements for CO_2 electrolysis, hopefully making this process more viable."

The Link Foundation, 3M, and Shell supported this research through student fellowships.

In pig brain development, nature beats nurture

The domestic pig is ideal for drug therapy studies because their bodies are excellent analogues for human newborns. But some critics say they can't be sure those outcomes reflect reality, since the subjects are raised in carefully controlled environments.

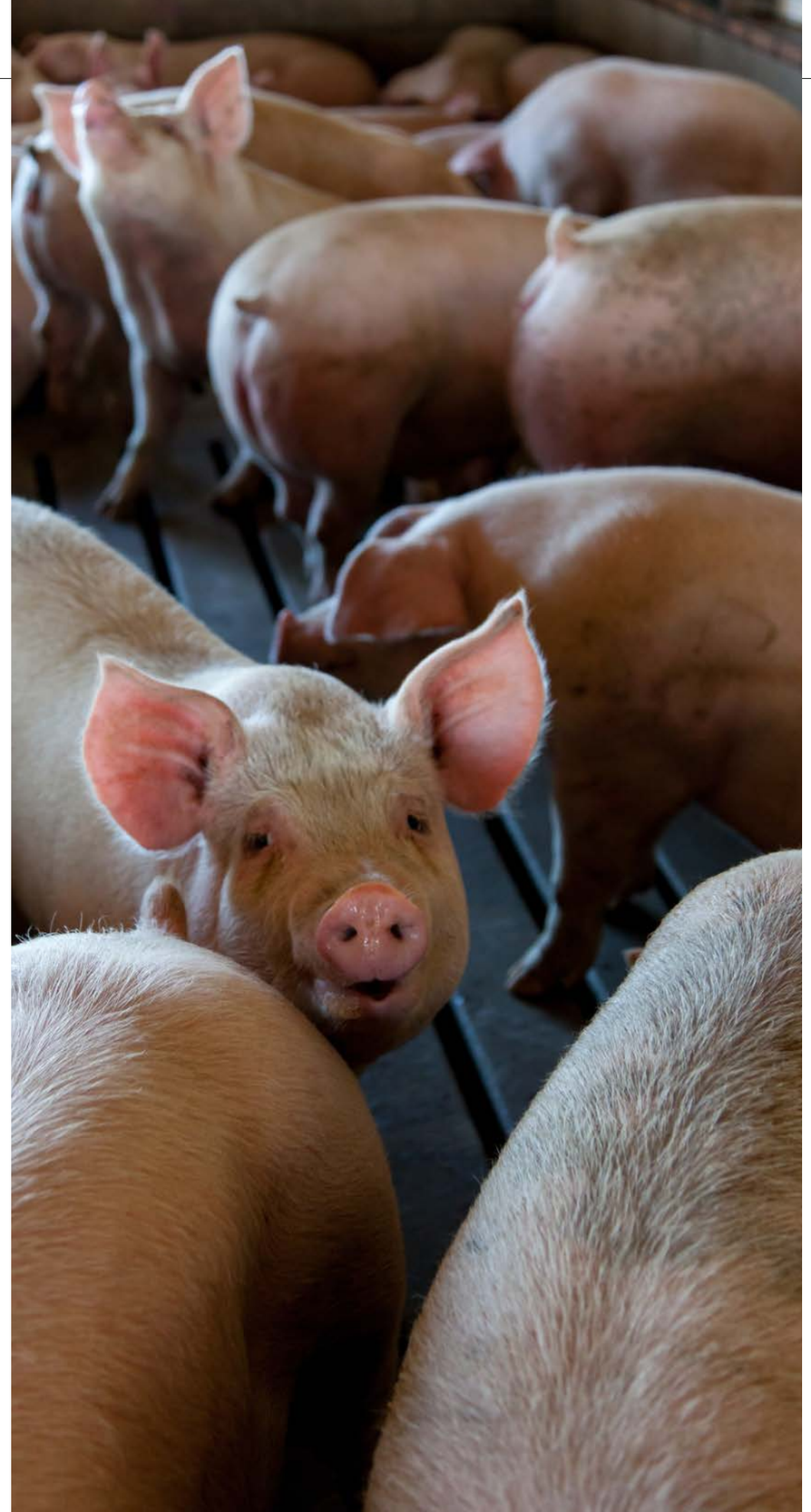
"We now have indisputable evidence to say that the brains of pigs raised in an artificial environment grow and develop in the same way structurally as those of pigs raised by their mother," says Ryan Dilger (GNDP), associate professor in the Department of Animal Sciences and senior author on a new study in *Frontiers in Neuroscience*.

In the study, the research team brought 2-day-old piglets to their facility, which is outfitted with large individual enclosures that let pigs see, smell, and hear others in adjacent pens. Another subset of piglets stayed with their littermates and mothers in farrowing crates on a research farm. At 4 weeks of age, the artificially reared pigs moved back to the farm.

All pigs were anesthetized and scanned in a magnetic resonance imaging machine at 1, 2, 3, 4, 8, 12, 18, and 24 weeks of age. The researchers assessed brain macro- and microstructure of the artificially reared and sow-reared pigs using the new pig brain atlases. Not only did the pigs eat and grow at the same rates in the two rearing environments, their brain development was equivalent overall as well.

"We're mixing the biomedical world with the agricultural world, to ultimately benefit both pig and human nutrition," Dilger said.

Funding was provided by Nestlé.



Research

New microscope discovery combines AI to detect disease, improve treatment

A newly developed laser source and microscope are helping researchers better understand and search for biomarkers indicative of cancer and other diseases, offering new promise for early detection and treatment plans.

The study, co-authored by Carle Illinois College of Medicine professors Stephen Boppart and Saurabh Sinha (IGB Director of Computational Genomics, BSD/CABBI/GNDP/GSP), was recently published in *Cancer Research*.

The technique collects multiple optical signals from cells and tissues without having to add any dyes. "The multimodal imaging approach allows us to visualize the dynamic cells and tissues without disturbing their functions, and not only distinguish and classify different cell types, but also characterize their dynamics and metabolic profiles," Boppart said.

In the study, researchers use the new microscope, combined with AI/deep-learning algorithms, to investigate the tumor microenvironment and search for clues and biomarkers indicative of cancer. The result opens possibilities for better representation and understanding of the evolving cancer landscape.

"By exploring laser-tissue interactions and AI algorithms, we showed a way to capture the intrinsic cellular contrast and to digitally stain and phenotype different cell types in living tissues without physically staining it. This brings great value for potentially advancing living tissue diagnosis and assessment in clinical settings," said Sixian You, lead author and assistant professor at Massachusetts Institute of Technology.

This research was supported in part by grants from the NIH. Lead author, Sixian You, was supported by McGinnis Medical Innovation Graduate Fellowship through the bioengineering department.

Cholesterol metabolite induces production of cancer-promoting vesicles

Scientists working to understand the cellular processes linking high cholesterol to breast cancer recurrence and metastasis report that 27-hydroxycholesterol, a byproduct of cholesterol metabolism, causes some cells to send out cancer-promoting signals to other cells. These signals are packaged in membrane-bound compartments called extracellular vesicles. Reported in the journal *Endocrinology*, the discovery could lead to the development of new anti-cancer therapies, researchers say.

"Extracellular vesicles play an important role in normal physiology, but they also have been implicated before in cancer biology," said study lead Erik Nelson (ACPP), a professor of molecular and integrative physiology. "These particles carry cargo from one cell to another. This cargo is important because it's diverse and acts as a communication network. But very little is known about what regulates the vesicles."

The vesicles contained a unique collection of signaling molecules, the researchers found. And when injected into mouse models of mammary cancer, the vesicles "promoted both breast tumor growth and breast cancer metastasis," Nelson said.

"This is an important study because it establishes that a hormone or a metabolite can regulate these extracellular vesicles," Nelson said. "Understanding how this system works might prove to be therapeutically useful."

This work was supported by the National Cancer Center and the National Institute of Arthritis and Musculoskeletal and Skin Diseases at the NIH, along with the Alzheimer's Association, the American Institute of Cancer Research and the Department of Defense Breast Cancer Research Program.

Research

Deciphering the impacts of small RNA interactions in individual bacterial cells

Bacteria employ many different strategies to regulate gene expression in response to fluctuating conditions in their environments. One type of regulation involves non-coding RNA molecules called small RNAs (sRNAs), which are found in all domains of life. A new study by researchers describes the impacts of sRNA interactions in individual bacterial cells. Their findings are reported in the journal *Nature Communications*. The research team involved collaborations with professor of biophysics Taekjip Ha (Johns Hopkins University) and Illinois professor of chemistry Zaida Luthey-Schulten (BCXT).

Bacterial sRNAs are often involved in regulating stress responses using mechanisms that involve base-pairing interactions with a target mRNA and enhancing or repressing its stability or the amount of protein being made from the mRNA. Hfq, a hexameric RNA chaperone protein, facilitates binding between the RNAs and promotes stability of the sRNA.

The researchers used mathematical modeling and quantitative super-resolution imaging to examine the consequences of changing individual base-pair interactions on kinetic parameters of regulation such as the time needed for an sRNA to find an mRNA target.

"What we found was that individual base-pair interactions had some effect on the regulation, but they were relatively minor effects," said professor of microbiology Cari Vanderpool (IGOH/MME), who co-led the study. "The much bigger effects were due to mutations in the sRNA that disrupted its ability to interact with Hfq. If the sRNA couldn't effectively bind to Hfq, then it was much slower in finding its mRNA target and once found, it came unbound much more quickly."

The NIH and the NSF supported this work.

Unveiling the cause of onion center rot

Since 1983, the bacteria *Pantoea ananatis* has been known to infect several important crops including onions, rice, and corn. It was unclear, however, what molecules were involved. A new study, published in *mBio*, has identified one of the culprits: pantaphos.

"We can inject onions with purified pantaphos and cause onion rot. The injected onions start rotting, and become gross and mushy. It was exciting to see," said Alexander Polidore, a PhD student in the Metcalf lab. "Additionally, bacteria that cannot synthesize this molecule cannot cause onion rot, which means that it is necessary to cause the infection."

Intriguingly, pantaphos has also shown promise as an effective herbicide. "I compared pentaphos to common herbicides, and it was just as good—or even better—against typical weeds such as mustard seedlings," Polidore said.

An important requirement for an herbicide is that it kills weeds, but remains non-toxic to other animals, including humans. Therefore, the researchers tested the toxicity of pantaphos against other organisms. "Although it does not affect other bacteria and fungi, we found that it is moderately toxic to normal human cell lines, but strikingly toxic to glioblastoma cell lines. We were excited because those cancer cells are notoriously hard to kill," Polidore said.

Although pantaphos is somewhat toxic to human cell lines, it is possible that it will not be toxic to whole animals. "Our cell line studies are preliminary and will require follow-up experiments to define the level of toxicity in humans," said William Metcalf (MMG leader), a professor of microbiology.

The study was funded by the NIH.

Research

3D microscopy clarifies understanding of body's immune response to obesity

Thanks to a new analytical technique, scientists are getting a clearer view of the microenvironments found within adipose tissue associated with obesity. This advance may illuminate why some adipose tissues are more prone to inflammation—leading to diseases like type 2 diabetes, cancer and cardiovascular disorders—and help direct future drug therapies to treat obesity.

In a new study, bioengineering professors Andrew Smith (CGD) and Mark A. Anastasio, molecular and integrative physiology professor Erik Nelson (ACPP) and nutritional sciences professor Kelly Swanson detail the use of the new technique in mice. The results are published in the journal *Science Advances*.

Inflammation in adipose tissue presents itself as round complexes of inflammatory tissue called crownlike structures. Previous studies have shown that body fat that contains these structures is associated with worse outcomes of obesity and related metabolic disorders, the study reports.

To get a better view, the team combined a special type of microscopy that uses a 3D sheet of light rather than a beam, a fat-clearing technique that renders tissue optically transparent, and deep-learning algorithms that help process the large amount of imaging data produced.

"Right now, we know that some patients are overweight but metabolically healthy, while others are underweight and metabolically unhealthy," Smith said. "We believe that having the ability to look deep into the microenvironments with fat tissue may unlock some of the reasons why this is."

The NIH and the Beckman Institute for Advanced Science and Technology supported this study.

Researchers hunt for drugs that keep HIV latent

When the human immunodeficiency virus infects cells, it can either exploit the cells to start making more copies of itself or remain dormant—a phenomenon called latency. Keeping these reservoirs latent is a challenge. A new paper, published in the *Proceedings of the National Academy of Sciences*, has found a way to look for chemicals that can keep the virus suppressed into its dormant state.

"The current drug treatments block healthy cells from becoming infected by the virus," said Yiyang Lu, a PhD student in the Dar lab. "The latent reservoir poses a bigger problem because it can start producing the virus at any time. Consequently, patients have to remain on antiretroviral therapy all their lives to prevent a viral rebound."

Using a drug screen, they were able to find five new latency-promoting chemicals, raising the possibility that similar screens can be successfully adapted to study other systems that exhibit variability in gene expression, such as cancer. They are currently working on understanding how the five novel drugs suppress viral reactivation. "We want to test if these drugs have off-target effects in terms of how many other genes they affect in the host cells," Roy Dar (BCXT/GNDP/M-CELS), an assistant professor of bioengineering, said. "We also want to test these drugs in patient samples to see whether these drugs suppress HIV in them."

The study was funded by the NIH, the National Institute of Allergy and Infectious Diseases, and the NSF.

Research

Fast-acting, color-changing molecular probe senses when material about to fail

Materials that contain special polymer molecules may someday be able to warn us when they are about to fail, researchers said. Engineers at the University of Illinois Urbana-Champaign have improved their previously developed force-sensitive molecules, called mechanophores, to produce reversible, rapid and vibrant color change when a force is applied.

The new study led by postdoctoral researcher Hai Qian, materials science and engineering professor and head Nancy Sottos, and Beckman Institute of Advanced Science and Technology director Jeffrey Moore (BSD) is published in the journal *Chem*.

"The color change is the result of stress applied to the bonds that connect the mechanophores to a polymer chain," Qian said. "We are now bonding the mechanophores to polymer chains using a different arrangement scheme, called an oxazine structure. The new structure allows for an instantaneous and reversible color change, so instead of the polymer slowly becoming darker over time, the color changes quickly when the force is applied and disappears when the force is removed."

A long-standing challenge in materials science has been making observations regarding mechanical load and other stresses in materials at the single-molecule level. Although this advancement cannot do this, Moore says the goal is nearer with the development of this new type of mechanophores.

Graduate students Doug Ivanoff and Abigail Halmes and undergraduate student Nathan Purwanto also participated in the study.

The Air Force Office of Scientific Research Center of Excellence supported the research.

Gut bacteria help digest dietary fiber, release important antioxidant

Some species of gut bacteria break down dietary fiber in such a way that it not only becomes digestible, but releases ferulic acid, an important antioxidant with multiple health benefits, according to a new study.

Grains such as rice, oats, rye and wheat are rich in a class of dietary fiber called arabinoxylans, which humans cannot digest on their own. Many gut bacteria have enzymes to break down simple components of arabinoxylans; however, they lack the ability to break down complex ones—including those containing ferulic acid.

Study leader Isaac Cann (MME leader/BCXT), a professor of animal sciences and microbiology, his group, and collaborators at the University of Michigan and Mie University in Japan studied the genomes and digestive activity of bacteria in the intestine. They found that a group of Bacteroides bacteria have several enzymes that break down arabinoxylans, some of which had not been seen or catalogued before. The group published its findings in the journal *Nature Communications*.

Understanding this mechanism of how bacteria in the colon help the body break down dietary fiber and access ferulic acid has applications for personalized nutrition. With the compound's protective activity against certain diseases and its role in modulating inflammation and immune response, patients may benefit from probiotic ingestion of the ferulic acid-releasing bacteria or from consuming a diet rich in arabinoxylan fiber, Cann said.

The NIH and the IGB supported this work.

Genome-editing tool TALEN outperforms CRISPR-Cas9 in tightly packed DNA

Researchers used single-molecule imaging to compare the genome-editing tools CRISPR-Cas9 and TALEN. Their experiments revealed that TALEN is up to five times more efficient than CRISPR-Cas9 in parts of the genome, called heterochromatin, that are densely packed. Fragile X syndrome, sickle cell anemia, beta-thalassemia and other diseases are the result of genetic defects in the heterochromatin.

The researchers report their findings in the journal *Nature Communications*.

The study adds to the evidence that a broader selection of genome-editing tools is needed to target all parts of the genome, said Huimin Zhao (BSD leader/CABBI/CGD/GSE/MMG), a professor of chemical and biomolecular engineering,who led the new research.

CRISPR is a bacterial molecule that detects invading viruses. It can carry one of several enzymes, such as Cas-9, that allow it to cut viral genomes at specific sites. TALEN also scans DNA to find and target specific genes. Both CRISPR and TALEN can be engineered to target specific genes to fight disease, improve crop plant characteristics or for other applications.

"We found that CRISPR works better in the less-tightly wound regions of the genome, but TALEN can access those genes in the heterochromatin region better than CRISPR," Zhao said. "We also saw that TALEN can have higher editing efficiency than CRISPR. It can cut the DNA and then make changes more efficiently than CRISPR."

The NIH and NSF supported this work.

Energycane produces more biodiesel than soybean at a lower costs

Bioenergy from crops is a sustainable alternative to fossil fuels. New crops such as energycane can produce several times more fuel per acre than soybeans. Yet, challenges remain in processing the crops to extract fuel efficiently.

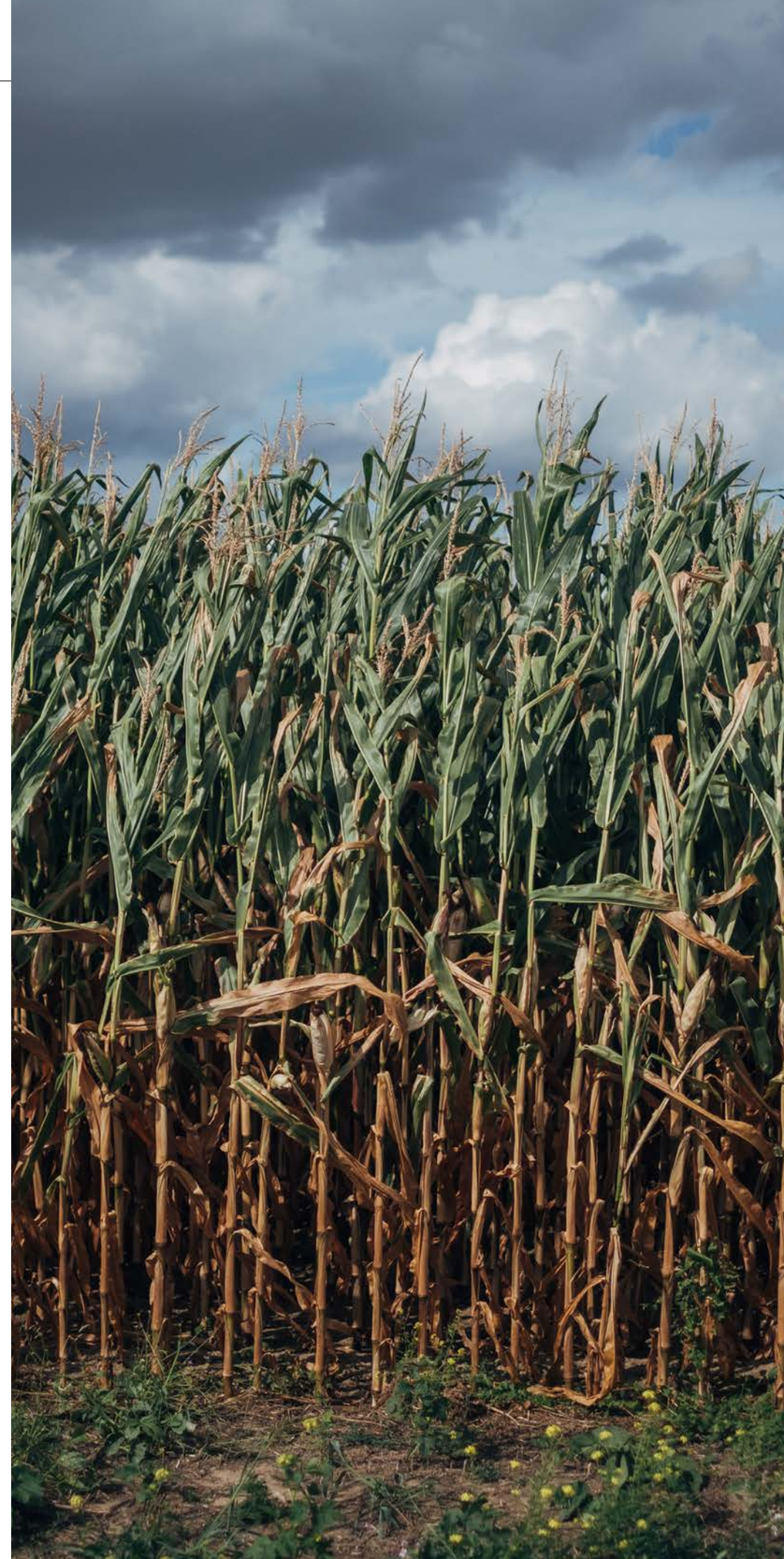
Four new studies explore chemical-free pretreatment methods, development of high-throughput phenotyping methods, and commercial-scale techno-economic feasibility of producing fuel from energycane in various scenarios.

The studies are part of the ROGUE (Renewable Oil Generated with Ultra-productive Energycane) project and focus on bioengineering accumulation of triacylglycerides (TAGs) in the leaves and stems of energycane, enabling the production of much more industrial vegetable oil per acre than previously possible.

"Energycane is attractive in its ability to grow across a much wider geography of the U.S. south east than sugarcane. This is a region with much underutilized land, yet capable of rainfed agriculture," says ROGUE Director Steve Long (BSD/CABBI/GEGC), Ikenberry Endowed Chair of Plant Biology and Crop Sciences.

"Our research shows the potential to produce a remarkable 7.5 barrels of diesel per acre of land annually. Together with co-products, this would be considerably more profitable than most current land use, while having the potential to contribute greatly to the national U.S. goal of achieving net zero greenhouse gas emissions by 2050," Long states.

Partial funding for the studies was provided by the Biological and Environmental Research (BER) program, and the DOE.



News

Advances in Brain Cancer Research Leads to $3M NCI Award

Researchers from the Cancer Center at Illinois, IGB, Mayo Clinic, and Georgetown University are joining forces on a project targeting glioblastoma, the most aggressive form of brain cancer. The team, led by Brendan Harley (RBTE leader/EIRH), professor of chemical and biomolecular engineering, received a $3M grant from the National Cancer Institute for their research which will unite the cell biology, bioengineering, and chemistry behind cancer drug development.

"Glioblastoma patients tend to have tumor re-occurrences within six to seven months of the surgery," Harley said. "It's caused by the cancerous cells that could not be removed. This issue got our team interested in how we can develop better therapeutic treatments."

Harley is an expert in building tissue microenvironments, using bioengineering techniques to recreate the brain tissue. His lab is partnering with the Mayo Clinic and Rebecca Riggins, associate professor of oncology at Georgetown, to provide cell lines engineered to be resistant to temozolomide, the primary chemotherapy used to treat glioblastoma.

The team will be developing a biomaterial that simulates the vascular environment in the brain in order to understand how the tumor microenvironment can promote glioblastoma cell resistance to drugs. They will also explore how they can create a mutated version of temozolomide that can successfully destroy cancerous cells.

"This program is committed to supporting research groups that are pushing the boundaries of tissue engineering technologies for cancer," Harley said. "It connects us to both collaboration opportunities as well as what challenges our colleagues are facing so that we can work together to address them."

iGEM 2021: Designing better enzymes to break down plastic

Polyethylene terephthalate, or PET, is a type of plastic that is widely used for packaging food and beverages, including soft drinks, juices, and water. Although PET is the most recycled plastic in the U.S., its current recycling rate is only 31%. This year's Illinois iGEM team aims to improve that by tweaking PETase—a naturally-occurring enzyme found in *Ideonella sakaiensis*, a bacterium discovered in 2016 as the world's first PET-eating bacterium.

The current PETase enzyme made by *I. sakaiensis* cannot be used for many of the existing recycling conditions. "The majority of PET ends up at landfills. Since it is very hard to degrade PET naturally, we are looking at PETase and trying to optimize how it degrades the plastic," said Mary Cook, a senior in bioengineering.

The team is also hoping to use their research to help the Urbana-Champaign community. "Being involved in your community is a really big part of iGEM," Cook said. "We want to reach out to local places in Champaign to get a better idea of how plastic is recycled and how we can apply our solutions here."

The 2021 team consists of Mary Cook; Jefrin Joseph; Kristin Lai; Suva Narayan; Royal Shrestha; and Angela Yoon. They will also be partnering with the University of Toronto and the University of Texas, Austin since the iGEM teams from those universities are also working on PET plastic. The Illinois iGEM team is sponsored by the IGB and CABBI.

News

Leading New Directions in Cancer Research: The Unanswered Black Box

Hyunjoon Kong (M-CELS leader/EIRH/RBTE), Robert W. Schafer Professor of Chemical and Biomolecular Engineering, approaches cancer research from a perspective that integrates cell engineering and biomaterials. The Kong research team has been working with Georgia Tech University and Massachusetts Institute of Technology over the past 10 years under the NSF Science and Technology Center Grant.

Most recently, the American Association for Advancement of Science published his lab's work on cephalopod-mimicking technology to transfer thin sheets of cell clusters and bioelectronic sensor. The applications of this project are broad, spanning from sensor administration to drug delivery and cell therapies. With regard to cancer discovery, this could change the way that scientists and clinicians administer tests and treatments.

"Many people think that cancer cells are caused by another living system that invaded our body. However, cancer cells are generated from our own cells. Therefore, our immune cells cannot detect the presence of cancer cells making it very difficult to diagnose cancer at the initial stage and further, treat them," said Kong. "Our research will allow people to see how the normal and cancer cells are communicating with each other."

Kong is leading Multi-Cellular Engineered Living Systems (M-CELS) theme within the IGB. He calls this direction an "unanswered black box" that they want to open. They want to interrogate how cell communication influences body, tissue, and pathogen development. Cancer is one of these developments that they are pursuing.

Regeneron Science Talent Search scholar conducts at-home study on crop improvement

In a freshman biology class, a simple demonstration comprises a candle and a plant in an enclosed space. Through the process of photosynthesis, carbon dioxide emitted by the candle is converted into oxygen by the plant, allowing the candle to last longer. For 18-year-old Bailey Goldstein, this experiment sparked his interest in photosynthesis.

This year, Goldstein was named a top 300 scholar in the Regeneron Science Talent Search 2021, the nation's oldest and most prestigious science and math competition for high school seniors. As a top scholar, Goldstein will receive $2,000, and his school will also receive $2,000 to use toward STEM-related activities.

Goldstein's research study aimed to determine if differences in crop yield were due to different non-photochemical quenching (NPQ) mechanisms—employed by plants and algae to protect themselves from high light intensity—and whether NPQ was viable for crop improvement. Due to the COVID-19 pandemic, Goldstein's visit to the IGB was cancelled, but that didn't stop him from conducting research.

"I used an oak tree in my backyard to assess the difference between NPQ in different environments," said Goldstein. "I am able to conclude that this NPQ mechanism does vary with different environments and it is a viable method to improve crop efficiency."

"It's so amazing that all these people at Illinois are coming together, funding this research, conducting this research, and going through all this work for the common good of humanity, and I think it's something to be admired," said Goldstein.

News

New grant awarded to study genomic privacy attitudes

The concept of genomic privacy has recently become important due to the rise of sequencing services, which can inform people about their ancestry or genetic predispositions to health disorders. However, it is unclear what concerns people may have about data privacy. A new grant, awarded by the University of Illinois Urbana-Champaign and IGB, aims to understand these concerns. The $35,000 grant will be used over the course of 18 months, with the option to renew for another 12 months.

"Although broad questions about genomic privacy concerns have been raised in the past, we're trying to understand which particular aspects of genomic privacy are worrying to laypeople," said Stephen Schneider, a research fellow in the Genomic Security and Privacy (GSP) theme at IGB.

The researchers are hoping to sample a population of 1600 people, evenly divided between Caucasian, African American, American Indian, and Latinx communities. "According to the literature, racial and ethnic minorities tend to have more privacy concerns, but it is unclear why. For this reason, we need to build a questionnaire that allows us to examine the difference between racial and ethnic groups," Schneider said.

"We will also be studying whether concerns about genomic privacy will correlate with other concerns, such as financial privacy, in the literature," said Aleksander Ksiazkiewicz (GSP), an assistant professor in political science. "We can then understand if these are generic concerns or whether there is something unique in this context."

New grant awarded to develop better *in vivo* DNA-editing techniques

The NIH has awarded a four-year $2.2 million grant to IGB researchers, which will be used to develop more precise genome editing technologies for gene therapy applications. The team includes Pablo Perez-Pinera (ACPP), an associate professor of bioengineering, Thomas Gaj (BSD), an assistant professor of bioengineering, and Jun Song (ACPP), a professor of physics.

Genomic editing has been a critical tool in furthering research and treating human diseases. Several tools, including the CRISPR-Cas9 system, have enabled researchers to modify the genomic DNA in living cells. However, the current approaches produce double strand breaks in the DNA, which can have undesired consequences. A newer class of DNA editing tools that can overcome these problems is prime editors, which can introduce changes in the DNA without causing double strand breaks.

Although prime editors are able to introduce several types of DNA changes, many challenges remain for their implementation in biomedical applications. The team has proposed to develop a toolset to overcome existing limitations and be able to edit target DNA sequences accurately in specific tissues in living mice, with a particular emphasis on the brain. They hope that this technology will be widely applied in the biotechnology and biomedical fields.

Gene therapies involving DNA editing technologies are poised to change the way that many diseases are treated, including some which were previously considered incurable. The new tools that will be created by this project could become the core components of new gene therapies for numerous disorders, such as Huntington's disease or amyotrophic lateral sclerosis.

News

$2.4M NIH grant will develop biomaterials to repair skulls, promote regeneration

A new research project aims to develop biomaterials that are strong, malleable, and support stem cell growth to transform skull reconstruction surgeries with a $2.4 million grant over five years from the National Institute of Dental and Craniofacial Research, a branch of the NIH.

"Craniofacial bone reconstruction is difficult and time-intensive—relying on bone grafts and ill-fitting, non-regenerative plastic implants; the result is often poor healing and high complication rates," said Brendan Harley (RBTE leader/EIRH), a chemical and biomolecular engineering professor. "Our goal is to improve patient recovery by accelerating bone regeneration."

Led by Harley, the project's interdisciplinary team includes University of California, Los Angeles professor Justine Lee, an expert in bone biology and pre-clinical testing, and Dimension Inx co-founders Adam Jakus and Ramille Shah, also a professor at the University of Illinois Chicago, who offer expertise in 3D printing.

Together, they will create an innovative off-the-shelf biomaterial that can be quickly and easily shaped to fit complex skull injuries—which can result from trauma, birth abnormalities, and surgical treatments for strokes and cancer.

"The porosity required to support cell growth in many biomaterials renders them mechanically weak," Harley said. "Further, many require stem cells to propagate outside the body, which is time-consuming, costly, and impractical."

The new composite biomaterial being developed is fabricated from 3D-printed mesh integrated into a porous scaffold made of mineralized collagen infused with stem cells that can propagate inside the body to promote bone regeneration.

Ting Lu jointly presented with €1 million Future Insight Prize

Ting Lu (BCXT/BSD/CABBI/MME), a professor of bioengineering, received the 2021 Future Insight Prize along with Stephen Techtmann, an associate professor of biological sciences at Michigan Technological University. The prize aims to stimulate innovative solutions to solve some of humanity's greatest problems in the areas of health, nutrition and energy. The prize comes with €1 million ($1.19 million) of research funding to incentivize winners whose work has enabled significant progress towards making this vision a reality.

Lu's research at Illinois focuses on microbial synthetic biology. "Combining experimentation with modeling, my lab harnesses engineered gene circuits to program microbial cell functionalities for a variety of novel biotechnological applications, such as food generation in this case," said Lu.

Techtmann is an environmental microbiologist who studies microbial communities in diverse natural environments. The core of the duo's technology is to utilize a combination of natural and rationally engineered microorganisms for efficient conversion of waste to readily edible food. In addition, they use synthetic biology approaches to augment probiotics to improve food quality by increasing nutritional content, improving the resistance to foodborne pathogens, and adding personalized therapeutic benefits.

With the prize, the duo plan to continue their research by enabling a fully biological solution for PET plastic conversion, augmenting the biosafety and health-promoting contents of food and further expanding the technology to additional plastics and non-edible biomass for food generation.

AWARDS

Lisa Ainsworth
USDA Agricultural Research Service (CABBI/GEGC); Distinguished Senior Research Scientist of the Year, ARS Employee Recognition Program

Rashid Bashir
Professor of Bioengineering and Dean of the Grainger College of Engineering (CGD/M-CELS); Professional Impact Award for Education, American Institute for Medical and Biological Engineering

Alison Bell
Professor of Evolution, Ecology, and Behavior (GNDP leader); Fellow, Animal Behavior Society

Marni Boppart
Professor of Kinesiology and Community Health (RBTE); Fellow, American Physiological Society

Martin Burke
May and Ving Lee Professor for Chemical Innovation and Professor of Chemistry (MMG); Member, American Society for Clinical Investigation

Mohammed El-Kebir
Assistant Professor of Computer Science (IGOH); NSF CAREER Award

Hee-Sun Han
Assistant Professor of Chemistry (IGOH/GNDP); WISTEM2D Scholar Award, Johnson & Johnson

Brendan Harley
Robert W. Schaefer Professor, Chemical & Biomolecular Engineering (RBTE Leader/EIRH); Clemson Award for Basic Research, Society For Biomaterials

Mark Hauber
Harley Jones Van Cleave Professor of Host-Parasite Interactions, Evolution, Ecology, and Behavior (GNDP); Center for Advanced Study Associate

Joseph Irudayaraj
Founder Professor of Bioengineering (CGD/EIRH); Fellow, International Academy of Medical and Biological Engineering; Fellow, Royal Society of Chemistry

Ting Lu
Assistant Professor of Bioengineering (BCXT/BSD/CABBI/MME); Future Insight Prize, Merck KGaA

Korinta Maldonado
Assistant Clinical Professor of Anthropology (IGOH); Immigrant Leadership Award, Champaign-Urbana Immigration Forum

Ripan Malhi
Professor of Anthropology (GNDP/GSP/IGOH); Robert W. Sussman Award for Scientific Contributions to Anthropology

Sergei Maslov
Professor and Bliss Faculty Scholar of Bioengineering (BCXT/CABBI); Fellow, American Institute for Medical and Biological Engineering

Ruby Mendenhall
Associate Professor of Sociology (GNDP); Pearl Birnbaum Hurwitz Humanism in Healthcare Award, Arnold P. Gold Foundation

Satish Nair
Department of Biochemistry Head (MME/MMG); Gregorio Weber Endowed Chair of Biochemistry

Gene Robinson
Swanlund Chair, Professor of Entomology (Director/GNDP); Member, American Philosophical Society

Wilfred van der Donk
Richard E. Heckert Endowed Chair in Chemistry (MMG); National Academy of Sciences

Cari Vanderpool
Professor and Associate Head of Microbiology (IGOH/MME); Fellow, American Academy of Microbiology

Fadi Alnaji
Post-doctoral researcher (Brooke Lab);
Christopher Brooke
Associate Professor of Microbiology (IGOH);
Martin Burke
May and Ving Lee Professor for Chemical Innovation (MMG);
Timothy Fan
Professor of Veterinary Clinical Medicine (ACPP/CGD);
Nigel Goldenfeld
Swanlund Professor of Physics (BCXT leader/GNDP);
Kelsie Green
Laboratory technician (Burke Group);
Paul Hergenrother
Kenneth L. Rinehart Jr. Professor of Chemistry (ACPP leader/MMG);
Sergei Maslov
Professor of Bioengineering and Physics (BCXT/CABBI);
Diana Ranoa
IGB Fellow;
Rebecca Smith
Associate Professor of Epidemiology (IGOH); Presidential Medallion, University of Illinois System

GRANTS

Brendan Harley
Timothy Fan
Paul Hergenrother
National Institutes of Health
"Perivascular Tissue Models to Overcome MGMT-mediated Temozolomide Resistance in Glioblastoma (R01)"

Roderick Mackie
Isaac Cann
U.S. Department of Agriculture
"Congress on Gastrointestinal Function 2021: Microbiology and Nutrition"

Gene Robinson
University of Birmingham/European Research Council
"How Dopamine Affects Social and Motor Ability from the Human Brain to the Honey Bee"

Christopher Brooke
University of Massachusetts Medical School/National Institutes of Health
"Longitudinal Comparison of Multimodal CoV Test Results with Live Virus Shedding"

Rachel Whitaker
Jessica Brinkworth
Korinta Maldonado
Gilberto Rosas
Ellen Moodie
Champaign Urbana Public Health Department/Illinois Department of Health Services
"COVID-19: Champaign County COVID Comprehensive Mobile Health"

Pablo Perez Pinera
Jun Song
Thomas Gaj
National Institutes of Health
"Development of Technologies for Efficient *In Vivo* Prime Editing"

Xing Wang
Brian Cunningham
Louisiana State University/National Institutes of Health
"COVID-19: Detection and Automatic Privacy-Protected Contact Tracing System Designed for COVID-19 (U01)"

Isaac Cann
Roderick Mackie
Wenyan Mei
National Institutes of Health
"Mechanistic Studies to Develop a Polysaccharide Degradation Signature (PDS) and its Application in Improving Host Health (R01)"

Erik Nelson
Stephen Boppart
Wawrzyniec Dobrucki
William Helferich
Paul Hergenrother
David Kranz
Saurabh Sinha
Department of Defense
"Leveraging Cholesterol Homeostasis for the Prevention and Treatment of Metastatic Breast Cancer"

Olgica Milenkovic
Nigel Goldenfeld
National Science Foundation
"COVID-19: Collaborative Research: CIF: Medium: Group Testing for Real-Time Polymerase Chain Reactions: From Primer Selection to Amplification Curve Analysis"

Stephen Long
Donald Ort
Gates Foundation
"RIPE Expanded Field Trials–Gates AG 1"

Ravishankar Iyer
Mayo/National Science Foundation
"Subsidizing Administrative Support of CCBGM Center/Site: Center for Computational Biotechnology and Genomic Medicine (CCBGM)"

Gene Robinson
Sihai (Dave) Zhao
National Science Foundation
"Gut Microbiome Effects on Brain and Behavior"

Brian Cunningham
Xing Wang
Stanford University/National Institutes of Health
"Ultrasensitive HIV Viral Load Quantitation using Designer DNA Nanostructure Capture Probes and Photonic Resonator Interference Scattering Microscopy (R01)"

Illustration by Jillian Nickell

Give to the IGB

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

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

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

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Illustration by Owen Davey

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