## 

IGB 2023 ANNUAL REPORT





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The Carl R. Woese Institute for Genomic Biology represents the collaborative and multidisciplinary environment that the University of Illinois prides itself in. We are all inspired by the cutting-edge research that serves as a beacon to researchers across the globe.

> **ROBERT J. JONES** CHANCELLOR, UNIVERSITY OF ILLINOIS URBANA-CHAMPAIGN

#### 2023 ANNUAL REPORT | DIRECTOR'S MESSAGE



Ever since the Carl R. Woese Institute for Genomic Biology was established seventeen years ago, it has occupied a unique position within the University of Illinois Urbana-Champaign campus, fostering highly interdisciplinary research within its lab spaces and cultivating a distinctive culture of team science.

As the IGB's influence has grown, so has the need to enhance our visibility and our connectivity within the university ecosystem and beyond. To this end, we unveiled a redesigned website this year, aligning the IGB's brand and vision with that of the campus. This year's Annual Report theme pays homage to this notable step in the IGB's development, and underscores our deep connections to the Illinois community.

As you peruse the pages of this year's Annual Report, you will be greeted with the same striking style and vibrant colors that permeate our new online presence, offering a seamless walk through the IGB's scientific endeavors. The revamped design not only harmonizes with the aesthetics of the university but also serves as a symbolic bridge, unifying our voices and embracing the university's pillars of Innovation, Community, Momentum, and Discovery.

The structure of this year's report departs from tradition by casting a spotlight on each of the IGB's fifteen research themes, reminding us of the variety of prolific research programs that the IGB hosts. Within these pages, we celebrate not only the latest achievements of our longstanding themes, but also the pioneering strides of our newest themes. All our researchers are actively confronting scientific grand challenges with insightful combinations of technology and genomic

biology, exemplifying the institute's unwavering commitment to innovation and progress.

Some of this work is aided by the IGB's own microscopy Core Facilities, which house technological marvels that continue to propel our groundbreaking research. The Core's Minflux microscope, one of only three in existence across the United States, played a pivotal role this year in securing a prestigious \$30 million U.S. National Science Foundation Science and Technology Center grant in collaboration with the Beckman Institute for Advanced Science and Technology that aims at creating detailed whole-cell models to transform our understanding of how cells function.

We take great pride in the partnerships forged by the IGB within and beyond our university this year. The establishment of the Chan Zuckerberg Biohub in Chicago, a collaboration between our university, the University of Chicago, and Northwestern University, signifies a monumental leap towards tackling significant scientific challenges in human biology on a global scale, and the IGB is a key campus pillar in this collaboration.

In tandem with our academic pursuits, we also reaffirm our steadfast dedication to public engagement, and broadening diversity, equity, and inclusion activities. Our commitment is illustrated with new programs such as the Wikipedia edit-a-thon to highlight overlooked scientists and the latest entry to our Genomics For<sup>™</sup> program—Genomics for Faith Leaders. In addition, the launch of our Team Science Leadership Program serves as a testament to our dedication to nurturing collaborative leadership among faculty across the university.

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As we reflect on the accomplishments of this past year and set our sights to the future, I am filled with gratitude for the dedication and contributions of our researchers, staff, and partners, whose efforts have strengthened our connections across the university and beyond. Together, we continue to push the boundaries of scientific exploration, striving towards a brighter future for society through our collective efforts.

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GENE E. ROBINSON DIRECTOR, CARL R. WOESE INSTITUTE FOR GENOMIC BIOLOGY

#### 2023 ANNUAL REPORT

### **IGB Strategic Partnerships**

### The IGB collaborates with partners on diverse, robust initiatives that serve to drive our research portfolio and leverage our interdisciplinary structure.

### A African BioGenome Project

A coordinated pan-African effort to build capacity and infrastructure to generate, analyze, and deploy genomics data for the improvement and sustainable use of biodiversity and agriculture across Africa.

TECHNOLOGY + SOCIETY

### Chan Zuckerberg Biohub Chicago (CZ Biohub Chicago)

The CZ Biohub Chicago is a biomedical research center that brings together leading Chicagoland scientific and technology institutions with the goal of solving grand scientific challenges on a 10- to 15-year time horizon.

( HEALTH + WELLNESS ) ( TECHNOLOGY + SOCIETY )

### A Genomics and Eco-evolution of Multi-Scale Symbioses (GEMS)

GEMS focuses on the classical species interaction between clover and honey bee pollinators as a model to understand the impact and dynamics of the myriad of microbes nested within them. GEMS takes an integrative approach to understand how molecular interactions impact the ecosystem.

### TECHNOLOGY + SOCIETY

### A High Performance Biological Computing (HPCBio)

HPCBio was created to address the need for a structure that could supply infrastructure, user support and training, and R&D capability in computational genomics to the Illinois research community. HPCBio provides a single, straightforward point of access, open to researchers from all campus units, helping them to find solutions to their biomedical data management and analysis problems.

TECHNOLOGY + SOCIETY

### Microbial Systems Initiative (MSI)

The goal of the MSI is to sustain a vibrant microbial sciences research and training enterprise at Illinois. Microbial systems research addresses critical problems in health, agriculture, energy, and many other sectors. The MSI carries out ongoing activities to build collaboration across disciplines, provide world class training opportunities, and build environments of inclusive excellence.



### Molecule Maker Lab Institute (MMLI)

MMLI is an interdisciplinary initiative with leaders in artificial intelligence and organic synthesis intensively collaborating to create frontier AI tools, dynamic open access databases, and fast and broadly accessible small molecule manufacturing and discovery platforms. Advanced AI and machine learning methods enable the MMLI to achieve AI-enabled synthesis planning, catalyst development, molecule manufacturing, and molecule discovery.

TECHNOLOGY + SOCIETY

### Personalized Nutrition Initiative (PNI)

PNI is a campus-wide initiative under the leadership of the Office of the Vice Chancellor for Research and Innovation, in partnership with the IGB and the College of Agricultural, Consumer and Environmental Sciences, to facilitate transdisciplinary collaborative efforts across campus to answer fundamental questions regarding how nutrition modulates health and disease across the lifespan and to translate that information to clinical care and to the public.



## IGB Featured Stories

2023 ANNUAL REPORT



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### Anticancer Discovery from Pets to People (ACPP)





The Anticancer Discovery from Pets to People theme provides successful anticancer therapies in dogs and cats that translate to clinical trials in human subjects.

EST. 2016 —

### Approximately 39.5% of all humans in the US and more than half of the dogs over the age of 10 develop cancer at the same rate.

Researchers have found that both share similarities at the cellular and molecular level, and that these naturally occurring cancers in dogs provide a unique model for treatment research compared to mouse models with artificially induced cancers. Members of the Anticancer Discovery from Pets to People theme have been working with dogs and cats with cancer to discover new treatments that can help reduce tumors in these beloved companions and be used to treat cancer in humans.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | ACPP

### CAR-T immune therapy attacks ovarian cancer in mice with a single dose

AUGUST 1, 2023



Abdominal organs in mice were treated with CAR-T and stained to look at different immune cells and antibodies.

go.igb.illinois.edu/CART23

CAR-T immune therapies could be effective against solid tumors if the right targets are identified, a new study led by University of Illinois Urbana-Champaign researchers suggests. The researchers successfully deployed CAR-T in a mouse model of ovarian cancer, a type of aggressive, solid-tumor cancer that has eluded such therapies until now.

"Even with an advanced stage tumor model, even with a single dose, we saw strong anti-tumor effects," said Diana Rose Ranoa, first author of the study. "There are still a lot of questions to be answered, but this study shows that CAR-T can kill this type of cancer once it recognizes the right target."

T cells are the white blood cells in the immune system that recognize and attack specific foreign invaders to the body. CAR-T therapies use special molecular receptors, called chimeric antigen receptors, that bind to cancer biomarkers. These CARs help a patient's own T cells target the cancer in their body as though it were an outside invader.

While such therapies are effective against blood cancers such as leukemia and lymphoma, cancers that produce solid tumors have remained difficult to treat with CAR-T immune therapies, said study leader David Kranz.

"There aren't the same type of targets for these receptors on solid tumors that there are in blood cancers, and it's very difficult to find a target that isn't found in healthy tissues as well," Kranz said. "The

#### PEOPLE MENTIONED

Diana Rose Ranoa, postdoctoral researcher (ACPP)

David Kranz, professor emeritus of biochemistry (ACPP)

FUNDED BY NIH other factor is that solid tumor cells have their own way of suppressing the immune response to evade recognition by T cells and other immune cells. A lot of work is being done to try to overcome those two barriers—finding good targets and finding the right kind of CARs that could recognize those targets."

In the new study, the researchers focused on a carbohydrate found on the surface of solid tumor cells, but not healthy cells. They developed CAR molecules with varying affinity for the molecule and tested them first in ovarian cancer cell cultures, and then in live mice with ovarian cancer tumors.

They found that the receptors with the highest affinity for the carbohydrate were highly effective at helping T cells find and destroy the cancer, shrinking or eliminating tumors after just one intravenous or injected dose—and continuing to work for months after the initial dose, extending the lives of the mice.

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The researchers hope this and other distinctive factors of the study design may give their treatment greater potential for clinical translation to humans.

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"Setting up our model in immunocompetent mice allowed us to show how the CAR-T cells behave in the presence of an intact host immune system and to demonstrate that these CARs do not have toxic effects against healthy tissues. The treatment is very specific to the tumor," Ranoa said. "And now we have this CAR that we've demonstrated can kill mouse ovarian cancer—and it has been engineered to recognize the same target in human cancers. So human studies are the logical next step for this line of research."



From front left: Diana Rose Ranoa, Claire Schane, David Kranz (front center), Amber Lewis, and Edward Roy.

The researchers plan to test their CAR-T regimen against human cancer cells cultures, as well as continue searching for other possible targets for solid-tumor cancers and the CARs that could find them.

"In this mouse model there was such a potency that it hopefully can be translated to human patients," Kranz said. "To get something so specific against the tumor that doesn't have major side effects for the patient, that's the holy grail."

The study was published in the Journal of ImmunoTherapy for Cancer.

### Team discovers rules for breaking into Pseudomonas

go.igb.illinois.edu/Pseudomonas23

Researchers reported in the journal *Nature* that they have found a way to get antibacterial drugs through the nearly impenetrable outer membrane of *Pseudomonas aeruginosa*, a bacterium that—once it infects a person—is notoriously difficult to treat.

By bombarding *P. aeruginosa* with hundreds of compounds and using machine learning to determine the physical and chemical traits of those molecules that accumulated inside it, the team discovered how to penetrate the bacterium's defenses. They used this information to convert an antibacterial drug that previously had no activity against *P. aeruginosa* into one that did.

"Pseudomonas is still the most difficult to treat gram-negative infection, and gram-negative infections are very challenging to treat in general," said Paul Hergenrother, who led the work. Earlier studies of *P. aeruginosa* focused primarily on antibiotics, testing which ones could kill or weaken the bacterium.

"We took a different approach—testing a variety of nonantibiotic compounds and tracking which ones accumulated inside. We then used machine learning to make sense of the chemical traits that were common to the accumulators," Hergenrother said.

This approach revealed that, among other traits, compounds with a positive charge on the surface and those with more hydrogen-bond-donor surface area were more likely to accumulate inside *P. aeruginosa*.

The researchers then modified an existing antibiotic drug, fusidic

Left to right: Myung Ryul Lee, Paul Hergenrother, Morgan Gugger. (Study lead author Emily Geddes, not pictured.)

### PEOPLE MENTIONED

Paul Hergenrother, professor of chemistry (ACPP leader/ MMG)

FUNDED BY NIH acid, to create a derivative form, called FA prodrug, that included the features identified in the machine-learning exercise. The experiment was found to be successful.

## Team identifies key driver of cancer cell death pathway that activates immune cells

go.igb.illinois.edu/necrosis23

Scientists have identified a protein that plays a critical role in the action of several emerging cancer therapies. The researchers say the discovery will likely aid efforts to fine-tune the use of immunotherapies against several challenging cancers.



Left to right: Chengjian Mao, Xinyi Dai, David Shapiro, Junyao Zhu, and Erik Nelson.

"Most anticancer drugs cause cancer cells to shrivel up and die in a controlled process known as apoptosis. But apoptosis does not usually strongly activate immune cells," said David Shapiro, who led the research with Santanu Ghosh. "The protein we identified, a sodium-ion channel known as TRPM4, is critical for cancer therapies that promote this type of cell death, called necrosis."

Unlike apoptosis, necrosis strongly signals the immune system to target and cleanup the remains of the dying cells, Shapiro said.

Previously the researchers developed two drugs— BHPI, and a more effective agent called ErSO—that spur necrosis in solid tumors, dramatically shrinking and often eradicating primary and metastatic tumors in mice.

The researchers screened breast cancer cells by knocking out each of the roughly 20,000 individual genes in the cancer cells and then treating the altered cells with BHPI or ErSO. Cells that resisted treatments with these agents revealed which genes were essential to the drugs' effectiveness.

TRPM4 emerged as a key driver of the process of necrosis in the treated cancer cells. By targeting the TRPM4 pathway in solid tumors, scientists may further enhance the necrosis-inducing anticancer therapies available to fight such tumors.

The findings were reported in the journal Cancer Research.

### PEOPLE MENTIONED

David Shapiro, professor of biochemistry

Santanu Ghosh, former graduate student

FUNDED BY NIH, Illinois, DOD, Susan Komen Foundation, and BCRF

### Biosystems Design (BSD)







The Biosystems Design theme engineers microorganisms and plants to help overcome hurdles in health and sustainability.

EST. 2015 -

### Microorganisms like yeast, bacteria, and viruses, can be harnessed and used for a variety of purposes.

For example, many microorganisms produce useful biomolecules or antibiotics that can be used in medicine, such as penicillin. Using synthetic biology, researchers in the Biosystems Design theme can alter the genetic material of microorganisms—both prokaryotes and eukaryotes to a limited extent, enabling them to take on new characteristics. The bioproducts from these engineered organisms can help increase drug production, create new medical treatments, and improve the quality and yield of crops, all of which can enhance human health and increase sustainability.

**IGB** Research Themes АСРР BSD CABBI CAIM CGD cis EIRH GEGC GNDP GSP IGOH мме MMG M-CELS RBTE

### 2023 ANNUAL REPORT | IGB FEATURED STORIES | BSD

# AI predicts enzyme function better than leading tools

MARCH 3, 2023



Contrastive Learning-enabled Enzyme Annotation (CLEAN) outperforms the leading state-ofthe-art tools in accuracy, reliability and sensitivity.

go.igb.illinois.edu/Clean23

A new artificial intelligence tool can predict the functions of enzymes based on their amino acid sequences, even when the enzymes are unstudied or poorly understood. The researchers said the AI tool, dubbed CLEAN, outperforms the leading state-of-the-art tools in accuracy, reliability, and sensitivity. Better understanding of enzymes and their functions would be a boon for research in genomics, chemistry, industrial materials, medicine, pharmaceuticals, and more.

"Just like ChatGPT uses data from written language to create predictive text, we are leveraging the language of proteins to predict their activity," said study leader Huimin Zhao. "Almost every researcher, when working with a new protein sequence, wants to know right away what the protein does. In addition, when making chemicals for any application—biology, medicine, industry—this tool will help researchers quickly identify the proper enzymes needed for the synthesis of chemicals and materials."

The researchers published their findings in the journal *Science* and have made CLEAN accessible online.

With advances in genomics, many enzymes have been identified and sequenced, but scientists have little or no information about what those enzymes do, said Zhao.

Other computational tools try to predict enzyme functions. Typically, they attempt to assign an enzyme commission number—an ID

#### PEOPLE MENTIONED

### Huimin Zhao,

professor of chemical and biomolecular engineering (BSD leader/CABBI/ CGD/MMG)

FUNDED BY NSF code that indicates what kind of reaction an enzyme catalyzes—by comparing a queried sequence with a catalog of known enzymes and finding similar sequences. However, these tools don't work as well with less-studied or uncharacterized enzymes, or with enzymes that perform multiple jobs, Zhao said.

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"We are not the first one to use AI tools to predict enzyme commission numbers, but we are the first one to use this new deep-learning algorithm called contrastive learning to predict enzyme function. We find that this algorithm works much better than the AI tools that are used by others," Zhao said.

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"We cannot guarantee everyone's product will be correctly predicted, but we can get higher accuracy than the other two or other three methods."

The researchers verified their tool experimentally with both computational and in vitro experiments. They found that not only could the tool predict the function of previously uncharacterized enzymes, it also corrected enzymes mislabeled by the leading software and correctly identified enzymes with two or more functions.

Zhao's group has made CLEAN accessible online for other researchers seeking to characterize an enzyme or determine whether an enzyme could catalyze a desired reaction.

"We hope that this tool will be used widely by the broad research community," Zhao said. "With the web interface, researchers can



Pictured, from left: Tianhao You, Haiyang (Ocean) Cui, Huimin Zhao, and Guangde Jiang.

just enter the sequence in a search box, like a search engine, and see the results."

Zhao said the group plans to expand the AI behind CLEAN to characterize other proteins, such as binding proteins. The team also hopes to further develop the machine-learning algorithms so that a user could search for a desired reaction and the AI would point to a proper enzyme for the job.

"There are a lot of uncharacterized binding proteins, such as receptors and transcription factors. We also want to predict their functions as well," Zhao said. "We want to predict the functions of all proteins so that we can know all the proteins a cell has and better study or engineer the whole cell for biotechnology or biomedical applications."

## From A to Z: An alternative base modification for mRNA therapeutics

go.igb.illinois.edu/AtoZ23

A team of researchers from the University of Illinois Urbana-Champaign have incorporated a newly discovered base, called base Z, into mRNA to create Z-mRNA that has improved translational capacity, decreased cytotoxicity and drastically reduced immunogenicity compared to unmodified mRNA.

The results from this new research, led by Huimin Zhao was published in the journal *iScience*.

Unmodified mRNA contains four bases— A, G, C and U. In this research A, which can form three hydrogen bonds with U, was replaced with Z. Base Z differs from other modified bases because it does not come from the human body.

"Traditional wisdom is that modified bases should ideally come from the human body so that any mRNA modified by such a base would mimic mRNA in the human body and bypass immune surveillance," said Meng Zhang.

However, base Z mRNA demonstrated low immunogenicity—the ability of cells to provoke an immune response and generally considered to be an undesirable physiological response—and reduced cytotoxicity when tested in cultured cells.

To demonstrate the application of their Z-mRNA in vivo, the team developed a Z-mRNA-based COVID-19 vaccine. They tested this Z-mRNA vaccine, alongside the modified mRNA vaccine used by



Graphical abstract representing the research: base Z replaces base A in mRNA. Base Z-mRNA was used to create a COVID-19 vaccine, tested in mice.

PEOPLE MENTIONED

Huimin Zhao, professor of chemical and biomolecular engineering (BSD leader/CABBI/ CGD/MMG)

**Meng Zhang**, former graduate student

FUNDED BY Illinois and NIH Moderna and Pfizer, in mice, and they found that the Z-mRNA vaccine could induce a substantial and antigen-specific immune response. Although the potency of the Z-mRNA vaccine was not as strong as the current standard, the team believes Z-mRNA could be further improved through systematic engineering efforts.

## How do methanotrophs handle the toxic effects of hydrogen sulfide?

go.igb.illinois.edu/H2S23

Methanotrophs—organisms that grow by consuming methane—seem to be perfect for alleviating global warming, since methane accounts for about 30% of this effect. However, drilling sites, where the natural gas is mostly composed of methane, also contain hydrogen sulfide which inhibits the growth of methanotrophs. In a new study, researchers have discovered that the methanotroph *Methylococcus capsulatus* Bath has an enzyme that helps it grow in the presence of small amounts of H2S.

*M. capsulatus* Bath is currently used commercially to make single cell proteins that are used in animal feed.

### PEOPLE MENTIONED

**Sichong Pei**, former graduate student

FUNDED BY Shell International Exploration and Production, Inc

First, the researchers used different concentrations of H2S to see what concentrations were inhibitory. Although *M. capsulatus* Bath could grow with 0.1% H2S, the growth rate decreased at 0.5% and 0.75% concentrations, and they were completely inhibited at 1% H2S. The researchers then grew the bacteria with different concentrations of H2S and looked at the changes in RNA and small molecule levels. They found that at 0.75% H2S the bacteria switch from using the calcium dependent methanol dehydrogenase *mxaF* to the lanthanide-dependent methanol dehydrogenase *xoxF*.

Although these bacteria have *xoxF*, they primarily depend on *mxaF* because it is more efficient. However, the researchers showed that when these bacteria are exposed to sulfide, they switch to using *xoxF*. "Previously, this switch was only seen when researchers added lanthanide," said Sichong Pei. "I believe that there is an intriguing mechanism behind the switch and this is just one piece of the puzzle."

The study was published in Applied Microbial and Cell Physiology.

### The Center for Advanced Bioenergy and Bioproducts Innovation (CABBI)





The Center for Advanced Bioenergy and Bioproducts Innovation engineers crops to help feed the world and create sustainable sources of fuel.

— EST. 2017 -

In November 2022, the human population reached 8 billion and is expected to keep growing, necessitating efficient agriculture to grow enough food and sustainable sources of fuel to power the world.

To help with this problem, the Center for Advanced Bioenergy and Bioproducts Innovation was established in 2017 with funding from the U.S. Department of Energy. CABBI seeks to create a new generation of bioenergy crops, biofuels, and bioproducts that are sustainable, resilient, and cost-effective. CABBI also uses predictive models to figure out how to grow the right plants in the right locations to maximize yield while minimizing the cost of resources.

**IGB** Research Themes



2023 ANNUAL REPORT | IGB FEATURED STORIES | CABBI

### DOE Renews CABBI Five More Years

MARCH 17, 2023



Researchers in the Feedstock Production focus on high-yielding grasses, such as sorghum (pictured), throughout the rain-fed eastern U.S., including on marginal soils.

go.igb.illinois.edu/CABBI5

The U.S. Department of Energy has committed another round of funding to the University of Illinois Urbana-Champaign to lead the second phase of its Bioenergy Research Center—one of four largescale DOE-funded research centers focused on innovation in biofuels, bioproducts, and a clean energy future for the country.

The DOE announced a five-year extension of funding for the Center for Advanced Bioenergy and Bioproducts Innovation, to a total of \$237.9 million for the period from 2017 to 2027. CABBI is a collaboration between the university's Institute for Sustainability, Energy, and Environment, the IGB, 11 academic departments across the Illinois campus, and 20 partner institutions across the nation.

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"To meet our future energy needs, we will need versatile renewables like bioenergy as a low-carbon fuel for some parts of our transportation sector," U.S. Secretary of Energy Jennifer M. Granholm said in the DOE news release.

XIXIX

"Continuing to fund the important scientific work conducted at our Bioenergy Research Centers is critical to ensuring these sustainable resources can be an efficient and affordable part of our clean energy future."

"Energy independence has become an increasingly important security issue for the U.S., and CABBI will continue to provide breakthroughs toward a new generation of sustainable, costeffective biofuels and bioproducts that will replace fossil fuel-based products," Andrew Leakey said. "This grant represents a massive investment in CABBI and its diverse team of scientists. We are committed to help push the U.S. toward a new bio-based economy."

During Phase II, CABBI researchers will continue to develop fuels and products by integrating three highly interconnected DOE priority areas:

### Feedstock Production

Led by Emily Heaton, scientists use the "plants as factories" paradigm, in which biofuels, bioproducts, and foundation molecules for conversion are grown directly in crops that are resilient and productive.

### $\wedge$ Conversion

Led by Huimin Zhao, experts continue to develop unique tools, yeasts, enzymes, and processing methods to efficiently produce diverse, high-value molecules such as biodiesel, jet fuels, and alcohols.

### ∧ Sustainability

Led by Wendy Yang, researchers provide a holistic and systems-based approach to assess the economic and ecological sustainability of CABBI feedstocks, biofuels, and bioproducts at scales that range from the field to the biorefinery to the bioeconomy.

"Our economy and society will be strengthened by enhancing the productivity, resilience and sustainability of our agricultural system," Leakey said, "And CABBI will help lead the way toward the cutting-edge scientific discoveries and technologies needed to sustainably and profitably produce fuels and chemicals using plants and microbes."



CABBI leadership, March 2023.

#### PEOPLE MENTIONED

### Andrew Leakey,

professor and head of plant biology (CABBI leader/GEGC)

### Emily Heaton, professor of

regenerative agriculture (CABBI)

### Huimin Zhao,

professor of chemical and biomolecular engineering (BSD leader/CABBI/ CGD/MMG)

### Wendy Yang,

associate professor of plant biology and geology (GEGC)

Gene Robinson, IGB Director (GNDP)

FUNDED BY Doe Said Gene Robinson: "The IGB has over 15 years of experience in successfully addressing grand challenges by transdisciplinary integration of the life sciences, physical sciences, social sciences, and engineering, and we are proud to host the CABBI team. Our partnership with iSEE has been a successful one for five years, and we look forward to five more years of breakthrough discoveries."

## CABBI develops eco-friendly enzyme to create key chemical building blocks

go.igb.illinois.edu/Ecofriend23

Using energy from light to activate natural enzymes can help scientists create new-to-nature enzymatic reactions that support eco-friendly biomanufacturing—the production of fuels, plastics, and valuable chemicals from plants or other biological systems.

### Applying this photoenzymatic approach, researchers have developed a clean, efficient way to synthesize crucial chemical building blocks known as chiral amines, solving a longstanding challenge in synthetic chemistry.

The team focused on hydroamination, a complex chemical reaction that can be used to produce chiral amines, which have wide applications in the synthesis of agrochemicals and other products. The team developed a photoenzymatic system that can control unstable nitrogen-centered radicals in a reaction known as enantioselective intermolecular radical hydroamination, which until now had been a major challenge in chemistry.

The findings, published in *Nature Catalysis*, have practical applications for CABBI's research to develop efficient methods for transforming leaves and stems from bioenergy grasses into high-value manufacturing products. Fatty acids that CABBI researchers derive from plant biomass can be readily converted into the unsaturated compounds used in this study, and therefore could potentially be upgraded into chiral amines.

More broadly, the discovery of this new photoenzymatic system demonstrates in principle that chiral amines—precursors for other valuable molecules—can be produced from fatty acidderived material in the lab, thus offering a promising platform for biomanufacturing. It will enable further investigation into upgrading fatty acids into chiral amino acids, which can be used for production of agrochemicals and other molecules and materials.



From left, Haiyang Cui, Zhenghi Zhang, Huimin Zhao, and Wesley Harrison.

FUNDED BY DOE

## New pipeline makes valuable organic acid from plants, saving money and emissions

go.igb.illinois.edu/orientalis23

In a breakthrough for environmentally friendly chemical production, researchers at CABBI have developed an economical way to make succinic acid, an important industrial chemical, from sugarcane.

The researchers created a cost-effective, end-to-end pipeline for this valuable organic acid by engineering a tough, acid-tolerant yeast as the fermenting agent. Succinic acid is a widely used additive for food and beverages and has diverse applications in agricultural and pharmaceutical products.



Issatchenkia orientalis.

The study, published in *Nature Communications*, builds on years of research on succinic acid production by using *Issatchenkia orientalis*, an unconventional yeast ideal for making organic acids. *I. orientalis* has the unique ability to thrive in low-pH, or acidic, conditions. Most organisms require a neutral pH environment to survive, including *Saccharomyces cerevisiae*, a more conventional yeast, or *Escherichia coli* bacteria.

These microorganisms require the addition of a base to neutralize the toxic acidic conditions so they can continue making succinic acid. But that generates side products, such as gypsum or calcium sulfate, which have to be separated out to purify the product, driving up processing costs.

With *I. orientalis*, however, "the organism lives happily at a pH of 3 to 4," so the additives are not required, said co-author Huimin Zhao. "That significantly reduces costs."

Researchers plan further scale-up studies soon to support commercialization of the succinic acid production process. The work will also be a template for production of other chemicals, including 3-hydroxypropionic acid, used in disposable diapers and sealants.

#### PEOPLE MENTIONED

Huimin Zhao, professor of chemical and biomolecular engineering (BSD leader/CABBI/ CGD/MMG)

FUNDED BY Doe



As experiments grow more technologically advanced, so too does the data that researchers collect. The scale of data and the integrative models necessary to analyze it require interdisciplinary collaborations.

The Center for Artificial Intelligence and Modeling brings together biologists, machine learning scientists, and computational modelers, to share their expertise. First, biologists generate new data through experiments. Then computational modelers build mechanistic models to understand the physical processes behind that data essentially the reasons behind the patterns. Subsequently, computer scientists train machine learning and AI to learn these patterns and use them to make predictions.



### 2023 ANNUAL REPORT | IGB FEATURED STORIES | CAIM

# Predicting the response of fungal genes using FUN-PROSE

NOVEMBER 20, 2023



The heatmap showing the activation of genes as predicted by the FUN-PROSE model.

go.igb.illinois.edu/FUNPROSE23

Signals from the environment set off a cascade of changes that affect different genes in different ways. Therefore, traditionally it has been difficult to study how such signals influence an organism. In a new study, researchers have developed a machine learning approach called FUN-PROSE to predict how genes react to different environmental conditions.

Cells, regardless of the organism, fine-tune their reaction to their surroundings using mRNA. First, they use proteins called transcription factors that sense changes and then bind to the DNA sequence—called a promoter—in front of genes. This attachment can either stop the formation of mRNA from the gene or it can increase the amount of mRNA being made. The mRNA then serves as a template to produce proteins responsible for various functions in the cell. This mechanism allows cells to rapidly reallocate resources to processes necessary for survival.

Studying how promoters are controlled is one of the oldest challenges in genomics, and yet researchers still continue to grapple with it. The biggest problem is that different transcription factors can bind to the same promoter sequence and do so in different arrangements under various environmental conditions. Moreover, while there is some evidence that transcription factors tend to bind to specific sequence motifs in promoters, not all of them have been extensively studied. In recent years, researchers have turned to artificial intelligence to help them solve these challenges. "Genes have an average level of expression, and previous machine learning models were unable to measure how the levels change under different conditions," said Sergei Maslov. "We were interested in understanding how specific genes react to changes in pH, temperature, and nutrients."

The researchers developed a model called FUNgal PRomoter to cOndition-Specific Expression, or FUN-PROSE, to predict how baker's yeast *Saccharomyces cerevisiae* and the less studied fungi *Neurospora crassa* and *Issatchenkia orientalis* would react to environmental changes.

To develop the model, the researchers first had to identify promoter sequences and transcription factors for the three species. Then, they trained the model to learn what promoter motifs are recognized by transcription factors in different conditions. According to Veronika Dubinkina, this process involved a commonly used approach of scanning for protein regions that are known to bind DNA.

Finally, the model learned how to integrate all the information to calculate how much mRNA is made in a particular condition compared to the average level of mRNA. The researchers then compared the results obtained from FUN-PROSE to RNA-seq data, which measures fluctuating mRNA levels, from all three fungi. They found that their model was very close to predicting what actually happens in these organisms.

In addition to evaluating its performance, the researchers elucidated how the model makes its predictions.

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"Even with its black-box nature, we were able to understand how our model looks at promoters and saw that it had learned to search for known sequences," said Simon Liu. "Being able to interpret the trained model is essential to validating its logic as well as using it to discover new regulatory knowledge."



From left, Ananthan Nambiar, Sergei Maslov, Veronika Dubinkina, and Simon Liu.

### PEOPLE MENTIONED

Sergei Maslov, professor of bioengineering and physics (CAIM co-leader/CABBI)

**Veronika Dubinkina**, former graduate student

**Simon Liu**, former undergraduate

FUNDED BY DOE, Illinois, San Simeon Fund, and Gladstone Institutes The researchers are now interested in testing their model on other organisms. "In principle, there are no limitations to our technique it should work on any organism. However, in animals, for example, genes are controlled in more complicated ways, which will require significant changes in the model architecture and much more training data" Maslov said. "Still, it would be interesting to see how well this model does."

The study was published in PLOS Computational Biology.

## Researchers design AI method to predict metabolomic profiles of microbial communities

go.igb.illinois.edu/mNODE23

Measuring the concentrations of metabolites produced by microbes, a process called metabolomics, is difficult and expensive. In a new study published in *Nature Machine Intelligence*, researchers have developed a machine learning algorithm called mNODE, which can predict metabolite concentrations based on the species composition of the microbial community.

"In our earlier mechanistic models, we tried to model all of the processes of what is produced and who produces what," said Sergei Maslov. "But those processes are really complicated, and you need to know hundreds of parameters for each microbial species.

The new machine learning method can bypass some of those limitations and if you have enough data, you can predict metabolite concentrations without knowing all of those nitty gritty details."

The researchers named the new method mNODE, which stands for Metabolomic profile predictor using Neural Ordinary Differential Equations. First, mNODE was systematically validated using synthetic data generated by models. These models contained ecological data with known interactions between microbes and metabolites. Then, it was applied to real data from various environments. The microbe-metabolite interactions inferred from mNODE were confirmed by comparing them to the results from metabolomics experiments and genomic evidence.

The researchers say mNODE can not only use microbial composition to predict metabolomic profiles, but it can also incorporate some dietary information to enhance the accuracy of its predictions. They said that although this needs more development, it could be a great tool towards personalized nutrition in healthcare.



The architecture of mNODE.

#### PEOPLE MENTIONED

Sergei Maslov, professor of bioengineering and physics (CAIM co-leader/ CABBI)

FUNDED BY NIH

## Single model predicts trends in employment, microbiomes, forests

go.igb.illinois.edu/Pop23

Researchers report that a single, simplified model can predict population fluctuations in three unrelated realms: urban employment, human gut microbiomes, and tropical forests. The model will help economists, ecologists, and public health authorities predict and respond to variability in multiple domains.

The findings were detailed in the Proceedings of the National Academy of Sciences.

The model, which goes by the acronym SLRM, does not predict exact outcomes, but generates a narrow distribution of the most likely trajectories, said James O'Dwyer who developed the model with Ashish George.

The model divides each population into discrete sectors—for example job types such as healthcare, agriculture or retail trade and assigns a "generation time" to each.

"Generation time is the lifetime of a tree or microbe, or the time a person spends in a given employment sector," George said. "It is measured in hours for microbes, years for job types, and decades for forests." Analyzing the systems in terms of generation time for each sector revealed similarities in how all three systems behave.

"We found a good description of the majority of the data with this model," O'Dwyer said. "We compared it with some other alternative models, and it performed better."

"This is the first effort to unify predictions for fluctuations across these domains using the same model," George said. "This advance will not only aid in developing new prediction methods, but also motivate the cross-pollination of concepts and techniques across these seemingly disparate fields."

### PEOPLE MENTIONED

James O'Dwyer, professor of plant biology (CAIM)

Ashish George, postdoctoral researcher

FUNDED BY Simons

Foundation Grant and McDonnell Foundation Grant

### Center for Genomic Diagnostics (CGD)



WA.



The Center for Genomic Diagnostics employs new technologies to diagnose and treat diseases at a lower cost.

EST. 2016 —

All cells secrete unique biomarkers, which are essentially molecular signals that can relay how the cells are faring. By measuring these biomarkers, doctors can easily diagnose ailments and recommend personalized and effective treatments.

Genomic sequencing to detect these biomarkers has traditionally been expensive, but researchers at the Center for Genomic Diagnostics have been working to develop inexpensive and minimally invasive technologies that can detect and measure biomarkers within a sample quickly and effectively. These new technologies include both handheld personal devices and simple portable systems that can be used in doctor's offices with the ability to streamline diagnosis, treatment, and health monitoring inexpensively.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | CGD

### ER-positive breast cancer presents differing metabolic signatures in African American, white women

**SEPTEMBER 11, 2023** 



"Although the tumors are often caught at earlier stages, patients from lower-income neighborhoods such as Chicago's South Side are more likely to have poor outcomes. That suggests there are some biological factors driving these differing effects." –Zeynep Madak-Erdogan

go.igb.illinois.edu/ComplexE23

New research found the most common form of breast cancer presents differing metabolic signatures in the blood of African American women with estrogen receptor-positive breast cancer compared with non-Hispanic white women. The scientists also identified a protein—negative elongation factor complex E—that was linked with higher mortality rates among African American women with estrogen receptor-positive breast cancer.

The findings, published by *Nature Scientific Reports*, may help explain some of the molecular processes driving higher rates of the disease—especially more aggressive forms of it—in African American women. ER-positive breast cancer accounts for about 70%-80% of all breast cancer cases, and African American women are 40% more likely to die from it than white women, said Zeynep Madak-Erdogan, a co-author of the paper.

"Overall, we are pretty good at managing the disease, early diagnosing cases with mammography and treating them with drugs that were developed several decades ago," Madak-Erdogan said. "Although the tumors are often caught at earlier stages, patients from lower-income neighborhoods such as Chicago's South Side are more likely to have poor outcomes. That suggests there are some biological factors driving these differing effects."

The study population included African American women and non-Hispanic white women ages 20-79 who were recruited at three hospitals in the Chicago area in 2018-19.

#### PEOPLE MENTIONED

Zeynep Madak-Erdogan, professor of nutritional sciences (CGD/ EIRH/GSP)

Ashlie Santaliz-Casiano, postdoctoral researcher

FUNDED BY NIH, Illinois, USDA
The team collected blood samples from 102 patients who were newly diagnosed with ER-positive breast cancer in stages 1-3, and 148 healthy women served as the control group. The samples were collected from control group participants at the time they enrolled in the study and from the patients with ER-positive breast cancer prior to breast surgery or other cancer treatment.

The team analyzed 83 metabolites in the women's blood and found that African American women with ER-positive breast cancer had decreased circulating levels of amino acids—including the antioxidant methionine—compared with women in the healthy control group. Conversely, non-Hispanic white patients with the disease had significantly higher levels of fatty acids compared with African American women and those in the healthy control group.

The team hypothesized that methionine might be needed in greater volume to support increased DNA methylation—a mechanism that controls which genes get expressed—in African American patients with the disease.

Hypermethylation is a possible biological mechanism that might explain poorer disease outcomes in African American women, Madak-Erdogan said. Aberrant hypermethylation in DNA can occur in the promoter and enhancer regions of cancer-related genes, including tumor suppressors, silencing their expression.

"Using the Pan-Cancer Atlas, a database of 33,000 tumors classified by genetic similarity maintained by the Cancer Genome Atlas Program, we mapped the metabolites to epigenetic regulatory systems," said Ashlie Santaliz-Casiano, first author of the study. "We identified 291 genes associated with methylation activities that were expressed at higher rates—15 of them at statistically significant levels—in African American women with ER-positive breast cancer."



New research, led by Zeynep Madak-Erdogan, found that estrogen receptor-positive breast cancer presents differing metabolic signatures in the blood of African American women and non-Hispanic white women.

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Poorer survival rates among African American women with the disease—but not non-Hispanic white women—were associated with higher expression of NELFE, a protein complex that regulates enzymes involved in transcriptional activities for downstream target genes, she said.

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"The current standard screening is mammography, but it requires costly, dedicated equipment, as well as technicians and other trained professionals," Madak-Erdogan said. "If we could come up with a test to diagnose breast cancers earlier, especially those with potentially worse outcomes, that might be useful in clinics with limited resources."

# Microelectronics give researchers a remote control for biological robots

go.igb.illinois.edu/Biobot23

First, they walked. Then, they saw the light. Now, miniature biological robots have gained a new trick: remote control.

The hybrid "eBiobots" are the first to combine soft materials, living muscle and microelectronics, said researchers at the University of Illinois Urbana-Champaign, Northwestern University, and collaborating institutions. They described their centimeter-scale biological machines in the journal *Science Robotics*.

Study co-leader Rashid Bashir and his group have pioneered the development of biobots, small biological robots powered by mouse muscle tissue grown on a soft 3D-printed polymer skeleton. They demonstrated walking biobots in 2012 and light-activated biobots in 2016. The light activation gave some control, but practical applications were limited by the question of how to activate light pulses outside of a lab setting.

The answer to that question came from John Rogers, a pioneer in flexible bioelectronics, whose team helped integrate tiny wireless microelectronics and battery-free micro-LEDs. The researchers can send a wireless signal to the eBiobots that prompts the LEDs to pulse. The LEDs stimulate the light-sensitive engineered muscle to contract, moving the polymer legs so that the machines "walk." The



Remotely controlled miniature biological robots have many potential applications in medicine, sensing, and environmental monitoring.

### PEOPLE MENTIONED

Rashid Bashir, professor of bioengineering and Dean of the Grainger College of Engineering (CGD/M-CELS)

John Rogers, professor of materials science and engineering at Northwestern University micro-LEDs are so targeted that they can activate specific portions of muscle, making the eBiobot turn in a desired direction.

The integration of electronic sensors or biological neurons would allow the eBiobots to sense and respond to toxins in the environment, biomarkers for disease and more possibilities, the researchers said.

# Researchers target prostate cancer with new, rapid biomarker detection method

go.igb.illinois.edu/TRAP23

The pivotal role of microRNA in diagnosing and monitoring cancer is well known by today's researchers. "There have been a lot of studies in recent years linking the presence and concentration of specific microRNA sequences to clinical outcomes for people with advanced prostate cancer," said Brian Cunningham.

Yet, the methods for detecting this pivotal biomarker in cancer diagnostics remain cumbersome, costly, and inaccessible to many. In collaboration with Huntsman Cancer Institute and Stanford University, Cunningham's team has been leading a project to improve upon microRNA detection methods for prostate cancer. In a recent study, published in the journal *Angewandte Chemie*, the team presents their new method of microRNA detection and quantification that dramatically improves upon current methodology.

The new method provides results in just ten minutes —compared to hours for traditional PCR testing and provides a promising new pathway toward accessible point-of-care scenarios for cancer patients. The new method, named Target Recycling Amplification Process, links one gold nanoparticle to one microRNA fragment, and uses a visualization method also created by the team—Photonic Resonator Absorption Microscopy—to detect microRNAs as they are repeatedly released and redetected in a recycling process.

The new amplification method in tandem with PRAM allows researchers to effectively detect very small traces of microRNA molecules in a swift manner—which has the potential to greatly improve the efficacy and accessibility of cancer diagnostics and treatment monitoring.

From left, Brian Cunningham, Xiaojing Wang, and Skye Shepherd.

#### PEOPLE MENTIONED

Brian Cunningham, professor of electrical and computer engineering (CGD leader/MMG)

FUNDED BY NIH and Illinois

FUNDED BY NSF and NIH

## Metabolism

# Center for Indigenous Science (CIS)





The Center for Indigenous Science uses Indigenous Science frameworks to provide alternative scientific models, promoting research that is ethical, sustainable, and community-focused.

Olfactory Signaling Pathway

Disease

Science has the potential to solve major societal and environmental problems, but most scientific views and methods come from predominantly white models and stem from colonial ideas and values.

Although Indigenous science frameworks are the oldest models of science in the Western hemisphere, they are underrepresented in academic spheres. To make matters worse, benefits derived from such models are not equally distributed throughout society, prompting the need for ones that are inclusive and equitable. The Center for Indigenous Science aims to provide a welcoming environment where Indigenous peoples can work together with scientists across the Illinois campus, to promote research that is ethical, sustainable, and community-focused.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | CIS

# Study links epigenetic changes to historic trauma in Alaska Native communities

SEPTEMBER 7, 2023



A Manhattan plot displaying specific regions of DNA across each human chromosome.

go.igb.illinois.edu/EpiTrauma23

Researchers investigated the relationship between historical traumatic events experienced by Alaska Native communities and epigenetic markers on genes that previous studies have linked to trauma. The study found a similar pattern among Alaska Native participants, with specific differences observed in those who reported experiencing the most intense symptoms of distress when reflecting on historic losses.

The study also found that individuals who strongly identified with their Alaska Native heritage and participated in cultural activities generally reported better well-being. The new findings were detailed in the *International Journal of Health Equity*.

The study is the result of a close collaboration between the scientists and members of two Alaska Native communities. The Native Nations guided the design and interpretation of the study and retain control of all of the data, in accordance with principles of Indigenous data sovereignty, said Ripan Malhi.

While DNA sequence remains stable throughout the lifespan, small chemical modifications to specific genes can turn up or turn down the expression of those genes, said Mary LaVanne.

"These epigenetic modifications are often studied in response to severe changes in lived environments," LaVanne said. "Epigenetic alterations can persist throughout the lifespan and are sometimes maintained over multiple generations."

#### PEOPLE MENTIONED

Ripan Malhi, professor of anthropology (CIS co-leader/GNDP/ GSP/IGOH)

Mary LaVanne, former

postdoctoral researcher

FUNDED BY NSF Native communities in Alaska have experienced centuries of disruptive violence, disease and displacement, largely resulting from colonial expansion into the Americas and centuries of mistreatment well beyond the colonial era.

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"At the age of six, I was kidnapped and taken from my grandparents, supposedly to an orphanage," said Rosita Worl. She was taken to a Presbyterian boarding school, which used a system of mass punishment on children who "misbehaved," requiring the other students to collectively beat them with wooden paddles.

### 

To better understand how such experiences might affect gene expression, the research focused on one type of epigenetic change called DNA methylation. The study looked at whether people's feelings of sadness, anger or anxiety when reflecting on traumatic events coincided with specific changes in DNA methylation. The second element of the study looked for evidence that Alaska Native cultural identification correlates with well-being.

"Participants completed surveys on cultural identification, historical traumas and general well-being," Malhi said. Questions included the frequency of thoughts of historical traumas and losses and the symptoms experienced when reflecting on those events.

The surveys took place in community clinics and centers including Alaska Native cultural centers, with community counselors on hand



The study team included, from left, Alida de Flamingh, Rosita Worl, Alyssa Bader, Ripan Malhi, Chuck Smythe, Mary LaVanne and Mason Auger.

and available to participants. The team also collected blood samples from the 117 Alaska Native participants to investigate methylation at more than 850,000 sites across the genome.

The study found associations between the symptoms that arose when participants reflected on traumatic events in their own community's history and DNA methylation of specific genes. Some of the methylated genes had been previously implicated in similar studies of traumatized groups, such as children in a Russian orphanage and people with major depression or PTSD.

The findings are not proof that the historical traumas are causing the differences seen in DNA methylation, LaVanne said. But they add to the evidence suggesting that traumatic events leave a physical—as well as psychological—imprint on those affected and their descendants. The study also speaks to the factors that help people remain resilient and thrive.

"I always tell our kids, we come from strong people. We've survived rises of the sea, lowering of the seas, advances of the glaciers, retreats of the glaciers, suppression of our culture—we've survived it," Worl said. "But, we have those who are still wounded."

# Illinois researchers, Native American tribes working together to curate, increase access to oral histories

go.igb.illinois.edu/DorisDuke23

Researchers at the University of Illinois Urbana-Champaign are working with Native American tribes across the country to digitize oral histories and ethnographic materials collected from tribal members and to make them accessible online.

Illinois is one of seven universities that are part of the Doris Duke Native Oral History Revitalization Project to increase the accessibility of first-person narratives collected in the late 1960s and early 1970s.

Bethany Anderson, Jenny Davis, and Christopher Prom are leading the project at Illinois. Since the revitalization project began in early 2021, the researchers and several student workers have been reviewing the materials and determining what tribes were documented. They have worked closely with the Northern Arapaho, Eastern Shoshone, and Hopi tribes, among others.

Once the project is finished, tribes from around the country will be able to look at the materials online and have access to pieces of their histories. The



Left to right: Jenny Davis, Christopher Prom and Bethany Anderson are leading the project at Illinois.

PEOPLE MENTIONED

Bethany Anderson, natural and applied sciences archivist

Jenny Davis, associate professor of anthropology (CIS co-leader)

## researchers will invite tribal representatives to come to campus and see the full collection, and tribes will be given original materials or copies of them.

"Building relationships and working through the complexities of the materials takes time. Folks need time to review these materials and talk about them. This is not the sort of work that can be rushed," Anderson said. "We see these as long-term relationships, beyond the bounds of the project."

## Winners of the Center for Indigenous Science Scholarship announced

go.igb.illinois.edu/CISS23

The Center for Indigenous Science is a collaboration between the American Indian studies program and the IGB. The Center aims to collaborate with the Indigenous Nations to bring forth initiatives that support tribal sovereignty and address Indigenous needs in health, history, and the environment.

The new CIS scholarship was awarded to Indigenous graduate students at the University of Illinois Urbana-Champaign who are pursuing projects in line with Indigenous Science. The scholarships range from \$2,000-\$8,000. "The award denotes the University's commitment to expanding the community of Indigenous scholars whose work enriches their fields of studies and community-based knowledge," said Jacki Rand. The winners include Sahara Zitlali Vilchis, Elle Sawyer, Jalyn LaBine, Cordarro Mejia, and Joshua Diaz.

"Supporting Indigenous students in STEM and related fields is one of our central goals at the Center. This is a great start as we work to expand opportunities and support in the future" said Ripan Malhi. Christopher Prom, associate dean for digital strategies for the University Library

### PEOPLE MENTIONED

Jacki Rand, associate professor of American Indian studies and the Associate Vice Chancellor for Native Affairs (CIS)

Ripan Malhi, professor of anthropology (CIS co-leader/GNDP/ GSP/IGOH)

Elle Sawyer, graduate student

**Jalyn LaBine**, graduate student

**Cordarro Mejia**, graduate student **Joshua Diaz**,

graduate student Sahara Zitlali Vilchis, graduate student

# Environmental Impact on Reproductive Health (EIRH)





The Environmental Impact on Reproductive Health theme explores the effects of environment, diet, and stress on reproductive health and fertility. Exposure to dangers in the environment, especially during pregnancy, can have long-lasting and devastating health impacts on maternal and child health.

There is growing concern that endocrine disrupting chemicals, widely used in plastics and personal care products, are a contributor to reproductive disorders and infertility. Evidence also suggests that stress and diets high in saturated fats lead to impaired reproductive function as well as maternal obesity. Research within the Environmental Impact on Reproductive Health theme aims to address how exposure to EDCs, high fat diets, and stress impacts pregnancy outcomes and reproductive health.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | EIRH

# Study models the causes of insomnia in menopausal women

MARCH 13, 2023



go.igb.illinois.edu/Menosleep23

One of the most common symptoms that women experience during menopause is sleep disruption. Although this change is thought to be associated with depression, hot flashes, and fluctuating hormone levels, few studies have investigated whether they actually influence sleep. In a new study, published in *Journal of Women's Health*, researchers have modeled what factors influence sleep in menopausal women.

The quality of women's sleep declines as they progress into menopause. Concerningly, women who report sleep difficulties also report reduced quality of life and overall health. "Women experience incredible amounts of discomforting symptoms during menopause. It is a concern because the effects can be so debilitating and can last for years," said Megan Mahoney.

Most researchers have previously hypothesized that changes in reproductive hormone patterns cause poor sleep quality and depression in midlife women. During aging, the decrease in the hormones estradiol and progesterone and increase the levels of follicle-stimulating hormones could cause insomnia. Furthermore, hot flashes can also make it harder for women to fall asleep and stay asleep. However, past studies have not conclusively shown what the underlying causes of sleep deprivation are.

Studies on menopausal women only go back three decades, in part because the symptoms are not lethal. However, researchers now have access to bigger datasets, allowing them to better understand the numerous manifestations of menopause.

The researchers used data from the Midlife Women's Health Study, which was designed to identify which risk factors can cause

#### PEOPLE MENTIONED

### Megan Mahoney,

associate professor of psychology (EIRH)

### Jodi Flaws,

professor of comparative biosciences (EIRH co-leader/MME)

FUNDED BY NIH and Illinois menopausal symptoms among midlife women. Over 700 women participated in the four-year study.

In the initial clinic visits they completed questionnaires regarding their medical history and submitted blood and urine samples. For the next three years they returned to the clinic once a year and completed follow-up questionnaires regarding their menstrual cycles, health status, lifestyle, depressive symptoms, and sleep, and submitted blood and urine samples.

The researchers then used a Bayesian network analysis to model the most likely reason for self-reported insomnia in midlife women. They tested several factors, including hormone concentrations and hot flashes, to see how these may be interacting to influence sleep disruption.

"Surprisingly, we did not find that hormone levels can predict sleep disruption. We did, however, find that women who have hot flashes at night also have insomnia. Moreover, women who had insomnia in the fourth year of the study also had it in the first year. The same was true for depression," Mahoney said.

## 

"The bottom line is that some of these symptoms don't necessarily go away over the course of menopause. When women go to the doctor, if they address these problems in the early phase of their menopause, they can address long-term problems."

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The researchers would like to understand if there are lifestyle factors, such as high cholesterol, that can predict insomnia in menopausal



From left, Jodi Flaws, Megan Mahoney and Rebecca Smith found that nocturnal hot flashes can serve as a predictor of insomnia in menopausal women.

women. If so, exercise and diet could go a long way to help. They are also interested in learning the extent to which exposure to environmental chemicals leads to sleep disruption.

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"Women are continuously exposed to phthalates through their use of personal care products and plastics. We need to examine the associations of these endocrine disruptors and sleep disruptions and insomnia," said Jodi Flaws. "Such studies will serve as a foundation for strategies to prevent or treat sleep disruptions and ultimately improve women's health."

# Di-isononyl phthalate disrupts pregnancy in mice, study finds

go.igb.illinois.edu/DiNP23

We are constantly exposed to phthalates in our environment through plastic products such as storage containers, medical devices, packages, fabrics, and toys. Specifically, di-isononyl phthalate is inevitably becoming a part of our lives. Unfortunately, the impact of DiNP on the establishment and maintenance of pregnancy is largely unknown. In a new study, researchers used mice to understand how DiNP affects pregnancy.



Arpita Bhurke and Indrani Bagchi are studying how di-isononyl phthalate affects the reproductive system of women (Jodi Flaws not pictured).

The researchers chose a DiNP dose that humans are exposed to on a daily basis. They exposed pregnant female mice to DiNP orally for their first week of pregnancy, which is analogous to the first trimester in humans. Using tissue-staining techniques, the researchers found that DiNP exposure impairs the formation of blood vessels in both the maternal tissue and the placenta.

"In mice, these maternal blood vessels are formed after the first week of pregnancy and they have been exposed to DiNP before this development happens," said Indrani Bagchi. "As a result, the tissue formation is effected and it creates a ripple effect, impairing embryo growth."

The researchers found that pregnant mice that had been exposed to DiNP had smaller litter sizes and shorter gestation periods.

PEOPLE MENTIONED

Indrani Bagchi, professor or reproductive biology (EIRH co-leader)

FUNDED BY Nih Mice that were fed corn oil instead of DiNP produced an average of 16 pups per litter, whereas DiNP-fed mice produced 11 pups, and on average the pups weighed less. Additionally, instead of delivering their litter in 20 days, DiNP-fed mice were giving birth 18-24 hours earlier.

The study was published in Reproductive Toxicology.

# Team streamlines DNA collection, analysis for elephant conservation

go.igb.illinois.edu/EleDNA23

A new DNA-collection approach allows scientists to capture genetic information from elephants without disturbing the animals or putting their own safety in jeopardy. The protocol, tested on elephant dung, yielded enough DNA to sequence whole genomes not only of the elephants but also of the associated microbes, plants, and parasites—at a fraction of the cost of current approaches. The researchers reported their findings in the journal *Frontiers in Genetics*.

A team led by Alida de Flamingh, left, and Alfred Roca developed a new, more efficient approach to obtaining DNA from wild animals.

"We combined existing methodologies in such a way that we are now able to use noninvasive samples to generate genome-scale data," said Alida de Flamingh who led the work with Alfred Roca. "This allows us to assess wildlife populations without having to dart, capture, or immobilize animals."

De Flamingh used postcard-sized data-collection cards that have been treated to prevent the samples from degrading. Previous research has shown that once samples are smeared on the cards, they can be stored for months without refrigeration.

By running the sequence data obtained from the cards through genomic databases, the team found a treasure trove of information. The researchers even detected the DNA of butterflies and other arthropods that interact with the dung after it is deposited.

"It's really beneficial to get an idea of everything that's in there because now you can start asking questions, not only about elephant genomes but also about things like their health, their diet, and whether there are pathogens or parasites present," de Flamingh said.

#### PEOPLE MENTIONED

Alida de Flamingh, postdoctoral researcher (EIRH/ GNDP)

Alfred Roca, professor of animal sciences (EIRH/GNDP)

FUNDED BY IFAW, University of Pretoria, and USFWS

# Genomic Ecology of Global Change (GEGC)







The Genomic Ecology of Global Change theme develops new crops and management methods to maintain agricultural ecosystems in the face of a changing climate.

— EST. 2007 —

Agro-ecosystems, which consist of the plants that are used for food, fiber, fuel, clean air, and fresh water, are especially vulnerable to the fluctuations in their environment.

Researchers in the Genomic Ecology of Global Change theme study how changes in gene networks affect plants when they are challenged by elements of global change, including elevated atmospheric carbon dioxide and ozone, increased drought, and altered interactions with insects and plant pathogens. Theme researchers also work to formulate mathematical models that can predict how plants will respond to these changes and make suggestions on how to manage and improve the health of various agro-ecosystems.

**IGB** Research Themes ACPP BSD CABBI САІМ CGD GEGC CIS EIRH GNDP GSP IGOH ΜМΕ MMG M-CELS RBTE

#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | GEGC

# New study indicates C4 crops less sensitive to ozone pollution than C3 crops

NOVEMBER 15, 2023



The SoyFACE research facility near Champaign, IL. The effects of elevated ozone on C3 and C4 bioenergy grasses were investigated at this location.

go.igb.illinois.edu/C4tolerant23

Ozone in the troposphere negatively impacts crop growth and development, causing significant decreases in crop yield worldwide. This airborne pollutant does not come directly from smokestacks or vehicles, but instead is formed when other pollutants, mainly nitrogen oxides and volatile organic compounds, react in the presence of sunlight. In an increasingly polluted atmosphere, understanding what plants are tolerant of O<sub>3</sub> is critical to improving crop productivity and resilience.

In a collaboration between the Feedstock Production and Sustainability themes at CABBI, researchers have studied the effects of elevated O3 on five C3 crops (chickpea, rice, snap bean, soybean, wheat) and four C4 crops (sorghum, maize, *Miscanthus* × *giganteus*, switchgrass). Their findings, published in *Proceedings of the National Academy of Sciences*, indicate that C4 crops are much more tolerant of high O3 concentrations than C3 crops.

"Understanding the tolerance of C4 bioenergy crops to air pollutants will help us deploy them strategically across landscapes around the world," said Lisa Ainsworth.

Both C<sub>3</sub> and C<sub>4</sub> crops are major sources of food, bioenergy, and ethanol production worldwide. The difference between C<sub>3</sub> and C<sub>4</sub> plants lies in the carbon-fixation pathway they use during photosynthesis: C<sub>3</sub> plants convert CO<sub>2</sub> and sunlight into a 3-carbon molecule, whereas the first photosynthesis product of C<sub>4</sub> plants is a 4-carbon molecule. Additionally, the C<sub>4</sub> photosynthesis pathway

#### PEOPLE MENTIONED

Lisa Ainsworth, USDA ARS, professor of plant biology (GEGC)

Shuai Li, postdoctoral researcher (CABBI)

FUNDED BY DOE starts in mesophyll cells that comprise the surface of the leaf, and then moves into bundle sheath cells that are deeper in the plant. This spatial separation is not present in the C3 photosynthesis pathway. Scientists have historically assumed that C4 plants are less sensitive to O3 pollution than C3 plants, but that assumption had not been thoroughly researched until this study.

## 

"Variation in size and growing season length means that it is difficult to do side-by-side comparisons of the response of C3 and C4 crops to ozone in the field" said Shuai Li, primary author on the paper. "This limits accurate comparisons of the O3 sensitivity of C3 and C4 crops."

## 

By synthesizing available literature and unpublished data from crops grown with increased O<sub>3</sub> pollution in open-air field experiments over the past 20 years, authors performed a comprehensive analysis of the impact of O<sub>3</sub> on crop physiology and production in five C<sub>3</sub> crops and four C<sub>4</sub> crops.

"We focused on field experiments and quantified crop responses to increases in O<sub>3</sub> pollution and showed that C<sub>3</sub> crops are more sensitive to elevated ozone," Li said.

The differences could be due to leaf anatomical features, stomatal conductance, and/or metabolic rates between the C3 and C4 crops. In C3 plants, reactive oxygen species from O3 degradation can damage the mesophyll cells where photosynthesis occurs. In C4 plants, however, the spatial separation of the C4 photosynthesis pathway helps prevent O3 from infiltrating the bundle sheath cells



Lisa Ainsworth on scene at the field trials.

where sugars are made. In addition, C4 crops generally have lower stomatal conductance than C3 crops, potentially resulting in less O3 uptake in C4 crops. These factors likely account for C4 plants' superior tolerance of O3.

Ozone pollution is increasing in many parts of the world. This study quantitatively showed that O3-induced reductions in plant function and productivity are more severe in C3 crops than in C4 crops, likely because O3 interacts differently with the C3 and C4 photosynthesis pathways. Based on this finding, agricultural lands in polluted environments can be managed to have improved overall performance. C4 crops, particularly bioenergy feedstocks, can maintain productivity in regions with high O3.

# Illinois researchers create 3D images of C4 plant cellular components

go.igb.illinois.edu/ROGUEC4

A team from the University of Illinois Urbana-Champaign has quantified the plant cell properties in two C4 species, including cell shape, chloroplast size, and distribution of cell-to-cell connections called plasmodesmata, providing information that can change how people model photosynthesis thanks to their 3D reconstructions.

"Our motivation for this project was to provide critical missing baseline information about C4 plant cell structure," said Moonsub Lee, who co-led this work for a research project called Renewable Oil Generated with Ultra-productive Energycane. "We quantified information about the cells involved in C4 photosynthesis that we believe will reduce gaps in understanding."

ROGUE is a research project that aims to create an abundant and sustainable supply of oil that can be used to produce biodiesel, biojet fuel, and bioproducts with support from the U.S. Department of Energy. Much of ROGUE's work focuses on two C4 plants, energycane and miscanthus. Lee and his colleagues believe by quantifying cellular structures they can improve modeling and eventually, production.

Their work, published in *New Phytologist*, contains detailed cellular structures, opening the door for more analysis than was possible with previous 2D images. Their findings extend current perceptions of mesophyll cell shape, finding a more intricate structure than the bundle sheath cell which is closer to a simple cylinder.



Leaf cross sections obtained from confocal laser scanning microscopy with the Airyscan system.

> PEOPLE MENTIONED

Moonsub Lee, postdoctoral researcher (GEGC)

FUNDED BY DOE "This work was our initial attempt at 3D quantification and visualization of C4 plant structures," said Lee. "The images we were able to observe with these microscopy techniques have facilitated new ideas and questions that we are excited to explore."

# RIPE researchers model 'link' between improved photosynthesis and increased yield

go.igb.illinois.edu/RIPElink23

A team from the University of Illinois Urbana-Champaign has modeled improving photosynthesis through enzyme modification and simulated soybean growth with realistic climate conditions, determining to what extent the improvements in photosynthesis could result in increased yields.

"Having higher photosynthesis doesn't necessarily mean higher yield; the yield is impacted by seasonal climate conditions," said Yufeng He.

Realizing Increased Photosynthetic Efficiency, which is led by Illinois, is engineering crops to be more productive by improving photosynthesis, the natural process all plants use to convert sunlight into energy and yields.

The team used the BioCro modeling framework to simulate soybeans in Illinois fields under normal and elevated CO2 conditions, paying specific attention to two important parameters that affect the plant canopy's photosynthetic process: Jmax and Vcmax. They wanted to determine the effect of boosting these photosynthetic processes at the canopy level, rather than just at the leaf level, and determine if the effects could lead to higher yields under a range of climate conditions.

The team found that the overall returns in plant photosynthesis and pod biomass (yields) were affected when plants were simulated in a high CO<sub>2</sub> environment. They also found that correlations between increased photosynthesis and increased yield were dependent on the climate conditions at different stages of soybean growth. Their findings were published in *Field Crops Research*.

The next steps for the researchers involve adding specific data from African plant cultivars and environmental conditions and incorporating more detailed mechanistic models to apply the findings to crop growth in Sub-Saharan Africa.



The researchers used the BioCro modeling framework to simulate soybeans in Illinois fields.

#### PEOPLE MENTIONED

**Yufeng He**, postdoctoral researcher (GEGC)

### FUNDED BY

Bill & Melinda Gates Foundation, FFAR, and U.K. Foreign, Commonwealth & Development Office Gene Networks in Neural & Developmental Plasticity (GNDP)





The Gene Networks in Neural and Developmental Plasticity theme uses gene expression to explain why animals are highly diverse, even though the fundamentals are conserved across species.

EST. 2007 -

All animals share certain fundamental similarities in their forms and behavior, despite their extreme biological diversity. This is likely because gene expression for fundamental traits are similar across species.

Scientists think that minor alterations in these regulatory networks give way to diversity. Understanding the structures of these conserved gene regulation networks, and how modification leads to biological diversity both between and within species, are major challenges and the focus of the Gene Networks in Neural and Developmental Plasticity theme. To address these questions, GNDP researchers examine conserved behaviors and key developmental events in a diverse set of animal models, and develop genome-scale datasets from these animals.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | GNDP

# Icefish species underwent genetic changes during migration to temperate waters

FEBRUARY 21, 2023



go.igb.illinois.edu/Icefish23

Many animals have evolved to tolerate extreme environments, including being able to survive crushing pressures of ocean trenches, unforgiving heat of deserts, and limited oxygen high in the mountains. These animals are often highly specialized to live in these specific environments, limiting them from moving to new locations. Yet, there are rare examples of species that once lived in harsh environments but have since colonized more temperate settings. Angel Rivera-Colón explored the genetic mechanisms underlying this anomaly in Antarctic notothenioid fish.

Antarctic notothenioids have evolved to live in freezing waters due to antifreeze glycoproteins they produce in their cells. These bind to any ice crystals that form, preventing them from growing and the cells from freezing. Icefishes also are the only vertebrates that have adapted to live without hemoglobin in their blood cells.



Angel Rivera-Colón (left) and Julian Catchen.

Hemoglobin is a protein in blood cells that helps increase oxygen uptake and results in the red coloration of cells. Normally animals need hemoglobin to get enough oxygen, but in the cold, oxygen-rich waters around Antarctica, icefishes have developed morphological changes, such as bigger hearts for pumping blood, that they no longer need hemoglobin to get enough oxygen.

Despite this extreme specialization, the pike icefish have escaped Antarctica and now live in warmer, less oxygenated, South American waters. "The movement of this species to warmer waters posed an interesting evolutionary mystery that I wanted to try to solve," Rivera-Colón said.

To understand how the genome of the fish changed as it migrated into warmer waters, Rivera-Colón compared the genetics of the pike icefish to that of an Antarctic species of icefish, *Champsocephalus gunnari*. The team took tissue samples collected by collaborators and fishermen from southern Chile, South Georgia, and the Sandwich Islands to sequence the genomes.

After comparing the genomes, they found that while the genome was highly conserved between the species, there was divergence in areas of the pike icefish genome associated with the physiology that would need to change as the fish moved to warmer waters.

Researchers found the pike icefish genome displayed chromosomal inversions—when part of the chromosome becomes flipped in orientation. "We know that inversions and other chromosomal changes can be very important for mediating adaptive processes as well as creating barriers between species," explained Rivera-Colón. "So finding them here suggests that they could be important for adaptation to the warmer environment in South America."

In addition to evolving to live in warmer waters, the pike icefish would've also needed to adapt to a different light environment. The sea around the Antarctic is dark much of the year, and the surface ice blocks much of the light. But in temperate waters, pike icefish experience a more normal day-night cycle. The team is currently examining gene expression in related fish to see how their physiology and circadian rhythms have adapted to these new light cycles.

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"I think one of the really interesting aspects of this study is that it challenges how we tell stories about 'why evolution acted the way it did'," Julian Catchen described. "Selection pushed an organism to the extreme in this direction, and then the environment shifted, and now it's being pushed in a different direction."

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#### PEOPLE MENTIONED

Angel Rivera-Colón, former postdoctoral researcher (CIS/ GNDP)

Julian Catchen, associate professor of evolution, ecology, and behavior (CIS/ GNDP)

### FUNDED BY NSF

Rivera-Colón added, "Our study just goes to show that this specialization for extreme cold is not an evolutionary dead end, and it helps explain how these transitions happen in nature."

The study was published in Molecular Biology and Evolution.

# Combined use of alcohol and THC can affect rat brains, study finds

go.igb.illinois.edu/Ratcombo23

The increased legalization of cannabis over the past several years can potentially increase its co-use with alcohol. Concerningly, very few studies have looked at the effects of these two drugs when used in combination. In a series of studies, published in *Behavioural Brain Research and Neuropharmacology*, researchers used rats to understand how brain structure and behavior can change when cannabis and alcohol are taken together.

Most researchers have studied the effects of either alcohol or THC (delta-9-tetrahydrocannabinol),

the primary psychoactive drug in cannabis, alone. However, when people, especially adolescents, use these drugs, they often do so in tandem. Even when researchers study the co-use of these drugs, it involves injecting the animals with the drugs, which does not mirror what happens in humans.

"It's rare that a person would have these drugs forced upon them. Also, other studies have shown that the effects of a drug are very different when an animal chooses to take it compared to when it is exposed against its will," said Lauren Carrica. "Our study is unique because the rats have access to both these drugs and they choose to consume them."

The researchers exposed young male and female rats to recreational doses of THC that was coated on Fudge Brownie Goldfish Grahams and a sweetened 10% ethanol solution. The control group of rats were fed cookies and sweetened water. The researchers took blood samples from the rats and tested their memories.

"The effects were more pronounced in females and they had higher levels of chemicals that are produced when THC is broken down. Even so, the influence of THC on memory was modest," Carrica said. "These volitional, low-to-moderate doses of alcohol, THC, or both drugs did not induce long lasting, serious cognitive defects."

Although there were modest differences in behavior, the group still wanted to check whether anything had changed in the signaling pathways in the brain, especially at higher levels of THC. In the



From left, Linyuan Shi, Joshua Gulley, Lauren Carrica, and Nu-Chu Liang showed that the combined use of alcohol and THC can affect rat brains more than either drug alone.

### PEOPLE MENTIONED

Lauren Carrica, graduate student

Linyuan Shi, graduate student

Joshua Gulley, professor of psychology (GNDP)

FUNDED BY NIH second paper they did so by injecting alcohol-drinking or nondrinking adolescent rats with THC. They investigated whether drug exposure during adolescence could change the ability of the brain to undergo synaptic plasticity as an adult. To do so, they sacrificed the rats and measured the electrical signals generated in the brain.

"We found that alcohol and THC together significantly reduced, and in some cases prevented, the ability of the prefrontal cortex in drugexposed rats to undergo plasticity in the same way that the brains from control animals can," said Linyuan Shi.

The researchers are now interested in understanding which neurons are involved in the response to the drugs. "Our ultimate goal is to harness our knowledge of these changes to develop treatment approaches for reversing cognitive dysfunctions that are associated with long-term drug use and addiction," said Joshua Gulley.

# Fish brains provide insight into the molecular basis of decision-making

go.igb.illinois.edu/Fishchoice23

How do animals make decisions when faced with competing demands, and how have decision making processes evolved over time? In a publication in *Biology Letters*, Tina Barbasch and Alison Bell explored these questions using threespined stickleback fish.

Sticklebacks are a powerful model for investigating these questions because of their complex life history and reproductive behavior. During the breeding season, male sticklebacks establish territories to build nests to attract females. Males must simultaneously defend their territories from other males, court females that enter their territory with performative swimming motions, called 'zig-zags', and ultimately provide care for offspring if they can successfully court a female.

To explore the underlying molecular mechanisms of decision making, Barbasch exposed male stickleback to one of three stimuli: a female stickleback (courtship treatment); another male stickleback (territorial intruder treatment); or both a male and female stickleback (trade-off treatment). Some male sticklebacks were left alone as a control. Aggressive behaviors (biting) and courtship behaviors (zig-zags) were quantified, and then the brains of the male stickleback were dissected to look at gene expression using RNA sequencing.



Three-spined stickleback male (left) inspects an intruder introduced to his territory inside a glass flask.

### PEOPLE MENTIONED

**Tina Barbasch**, postdoctoral researcher (GNDP)

Alison Bell, professor of evolution, ecology, and behavior (GNDP leader)

FUNDED BY NIH and NSF Barbasch found that, when faced with a trade-off, males generally prioritized territorial defense over courtship. There was also substantial variation across males in how they responded, suggesting that there might be different strategies that males employ when faced with a trade-off. Furthermore, the gene expression results identified groups of genes that were differentially expressed across each of the experimental treatments relative to a control. Of particular interest are the genes that are only present in the trade-off treatment, because they suggest that males have a unique molecular response when faced with conflicting demands.

"We performed gene ontology analysis on these 'trade-off genes' to look into what the identity and function of these genes might be," described Barbasch. "Preliminary results suggest the 'trade-off' genes may be related to the dopamine response pathway, which modulates reward and motivation in the brain, or neurogenesis, which is important for cognition."

Ultimately, these findings highlight the importance of exploring the molecular basis of animal behavior, as Bell outlines. "Animals are living really complicated lives, across many taxa. This suggests that the mechanisms that are driving complex decision-making are probably really ancient and animals have been managing complex decisions for a long time," she said.

# Sentinel warning calls may be universally understood across continents

go.igb.illinois.edu/Sentinel23

Animals often use vocalizations to warn of nearby danger to others. While this information is generally intended for members of the same species, other species can eavesdrop on the warnings to use the information for their own benefit. For example, the family Paridae, which are a group of birds that consist of chickadees, tits, and titmice, are known as sentinels because their alarm call for danger, which fittingly sounds like "chicka-dee-dee-dee," is understood by most other bird species in their mixed-species flocks.



A tufted titmouse observing its surroundings.

Sentinel calls are so readily understood as a signal for danger that researchers wondered whether species that have never heard the call would still get the message. The team sought to test if bird communities across three different continents could understand calls for danger from a sentinel they had never encountered before—the dusky-throated antshrike. Antshrikes are birds widely distributed across Central and South America that often act as sentinels in their mixed-species flocks.

The researchers presented playbacks of warning calls of the dusky-throated antshrike, along with warning calls of a local Paridae sentinel and controls, to flocks of wintering birds in North America, Europe, and Asia, and measured their behavioral responses. Birds across all three continents responded equally as strongly to the unfamiliar antshrike's warning calls as they did to familiar, local sentinel's warning calls. This finding suggests there is something to sentinel calls that makes them so universally recognizable. For messages that contain important information, such as a warning call for danger, evolution likely converges on similar sounding calls that help get across the message as quickly as possible, according to the researchers.

"Sentinel species are not very well defined," said Jonah Dominguez. "There's lots of birds that we don't typically think of as sentinels being classified as them in the literature, and others that probably are sentinels that are being overlooked. I want to figure out if there's a common thread between them, and whether the term should be used on the species level or more on a flock level."

The study was published in Biology Letters.

#### PEOPLE MENTIONED

Jonah Dominguez, graduate student (GNDP)

### FUNDED BY

NSF, Illinois, the Ministry of Education, Science, and Technological Development of Serbia, and the Basic Scientific Research Projects of Liaoning Provincial Department of Education grant

# Genomic Security and Privacy (GSP)





The Genomic Security and Privacy theme studies advancing technologies with the aim of protecting the privacy and security of genomic information.

— EST. 2019 —

# Over the past decade, advances in genomic technologies have enabled increased access to genomic information in a single biological sample.

For example, many individuals have become interested in learning about their ancestry and understanding how their DNA can influence their health. However, in such situations, it is important to maintain privacy and uphold the ethics surrounding sample collection. The Genomic Security and Privacy theme focuses on these problems by working with research areas that depend on genomic samples and helps oversee the ethics and security aspects of the information. These projects may additionally involve individual privacy and confidentiality of industrial and government data.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | GSP

# Protecting genomic privacy through phone apps

MARCH 1, 2023



go.igb.illinois.edu/Privapp23

Police are increasingly using genomic databases in their investigations. Concerningly, they often do so without a warrant requirement. A paper co-written by Illinois faculty presents possible technological solutions, such as phone applications, that will ensure Fourth Amendment protections of consumer's genomic data.

Over the past few years, many individuals have become interested in analyzing their data through genomics companies, such as 23andMe or Nebula Genomics. The process involves submitting a DNA sample to the company, which sequences the DNA and makes the resulting data available online through a password-protected website. Through these services, the consumers can learn about underlying health conditions or their family history. However, in all these cases, the companies control the data and the analysis tools, decreasing the user's privacy.

"According to the third-party doctrine of the Fourth Amendment, if you disclose information to a third party, they can turn over that information to the government," said Jacob Sherkow. "Genomic data is problematic because it can be inferred through familial sequencing. By our estimates, the genome of essentially every single person in the U.S. of European ancestry can be inferred because of these sequencing companies."

While many of us may want to help police investigations, allowing them to use our genetic data is problematic, according to Sherkow. "Disclosing genomic information necessarily implicates your relatives in a way that does not apply to other information such as your bank records," Sherkow said. "In addition to making you more susceptible to warrantless searches, it also contributes to a dystopian situation where everybody can be uniquely identified regardless of consent."

#### PEOPLE MENTIONED

Jacob Sherkow, professor of law (GSP)

**Carl Gunter**, professor of computer science (GSP leader)

Natalie Ram, professor of law at the University of Maryland Carey School of Law

FUNDED BY NIH To better protect the security and privacy of genomic technology, the researchers are developing a computational system. "The idea is that if you upload your genome to a third-party website, it will not be considered private. However, if I send you a program that analyzes your data on your computer, your privacy is protected," said Carl Gunter.

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"It's like a home pregnancy test—you take it home and find out the answer. Nobody else needs to know unless you choose to tell them."

## 

Cell phone apps are a perfect example of how the computational tools can be sent to the data: they are capable of computing large amounts of data and are private. Although these apps work well for testing whether the users have an underlying health condition, they do not work as well for familial searches.

"Apps can help people answer most of the genomics-related questions they may have. On the other hand, finding relatives requires access to a large database, creating privacy complications," Gunter said. "However, people have been working on this problem and it can be solved using secure hardware, encryption, and using trusted third parties."

The GSP theme is currently working on this problem through different projects. They are also conducting surveys to understand whether the public is open to using these apps to learn about their genetic information. The researchers are hopeful that since most of us have used apps, people will be open to getting information through an app of their choice. The theme is also focused on developing these apps. So far, they have used artificial intelligence to develop apps that range from simple tests—like testing for sprinter's



Jacob Sherkow, left, and Carl Gunter are interested in developing new ways to protect genomic privacy.

gene, which is associated with power athletes—to complex tests, such as predicting the progress of macular degeneration.

The work was done in collaboration with Natalie Ram and was published in 96 Southern California Law Review.

# New initiative to improve forensic science practices in Illinois

go.igb.illinois.edu/ITE23

The landscape of forensic DNA has shifted in recent years to not only include different types of genetic data, but also expand how DNA can help improve the science and the investigations. Such a shifting landscape requires new investigative strategies, and to this end, the Illinois State Police and the University of Illinois Urbana-Champaign are partnering to combine distinct but complementary skills and resources.

"ISP leads one of the largest forensics laboratory systems in the world and we always strive to be one of the best," said Brendan Kelly. "The partnership between ISP and the University of Illinois will put ISP on the cutting edge of forensics that advances investigations and brings justice to victims."

The new ISP-Illinois initiative, housed at the IGB, is called the Investigative Technology Exchange. This partnership hinges on the exchange of ideas, data, skills, and research from both ISP scientists and Illinois researchers to solve the current challenges in forensic science. The applications of genetics approaches to forensic investigations are seemingly endless, but each new application must be carefully vetted, said Cris Hughes, appointed director of the Investigative Technology Exchange.

"Forensic science approaches at accredited public laboratories tend to be scientifically conservative because there are such high standards of quality assurance, and rightly so. As a result, new technology is taken up slowly in public labs compared with private companies," Hughes said. "Yet this is a benefit because this allows us time to critically address the broader implications of the technologies."



From left, Brendan Kelly, Cris Hughes, Robin Woolery, and Matthew Davis.

#### PEOPLE MENTIONED

**Brendan Kelly**, Illinois State Police Director

Cris Hughes, clinical associate professor of anthropology (GSP)

# Polygenic risk scores need better regulation, study argues

go.igb.illinois.edu/PGS23

Polygenic risk scores are used to predict an individual's risk for particular conditions using data from multiple genes. Although the scores may be able to provide valuable insight into disorders, without a healthcare professional, they can be misused. In an article published in the *Journal of the American Medical Association*, researchers from the IGB and Harvard Medical School argue for increased regulation of genetic tests, specifically in regard to PGSs.



Genetic tests, like 23andMe, sequence DNA samples and provide information about ancestry.

In more traditional direct-to-consumer genetic tests, like 23andMe, consumers provide their genetic samples, which are sequenced by a company. The information returned to consumers is based on data from individual genes. "These tests tell you about a range of traits from ancestry to whether you have mutations in a specific gene," said Jacob Sherkow. "There is a clear line from which specific gene is being looked at and, in some cases, what you can do about it when you get a result. It is similar to going to an actual health care provider."

However, for most diseases, a variety of genes contribute to disease risk. PGSs combine the different variations of genes a person has and calculate a "risk score" of developing a particular condition. Because these algorithms are often opaque, consumers receive little information about how their scores might be calculated.

The authors recommend that the FDA reevaluate their regulatory guidelines and police PGSs the same way they regulate direct-to-consumer tests, and that Congress delineate what aspects of genetic testing should be regulated by the FDA. PEOPLE MENTIONED

Jacob Sherkow, professor of law (GSP)

# Infection Genomics for One Health (IGOH)





The Infection Genomics for One Health theme works to describe microbial communities and their genes across different natural and man-made environments.

– EST. 2016 —
## Microbial communities are ubiquitous across all agricultural, industrial, and natural systems, and directly impact human health and disease.

Predictive models for the movement of genes, genomes, and microbes across these interconnected ecosystems are urgently needed to address immediate and critical threats, including antimicrobial resistance and disease transmission, and maintain healthy microbial communities. The Infection Genomics for One Health theme aims to identify gene dynamics of microbes across ever-changing ecosystems, and create a framework that can describe and predict microbial interactions and gene movement. This data can then be used to determine what factors influence microbial transmission, resistance, and symbiotic interactions in different environments.



### 2023 ANNUAL REPORT | IGB FEATURED STORIES | IGOH

## Researchers design educational course to address tick-borne diseases

JANUARY 2, 2023



Female American Dog Tick, Dermacentor variabilis.

go.igb.illinois.edu/TickIQ23

Anyone who enjoys taking walks through the woods or grassy fields when the weather is warm knows that checking for ticks afterward is a must. Ticks can spread numerous diseases to humans as well as to our pets, and some of these diseases can be life-threatening. However, getting a tick-borne disease tested and confirmed by physicians can often be tricky.

"This is something you hear all the time if you work with tick-borne diseases, or TBDs," said Rebecca Smith. "We often hear from people that had Lyme disease talk about how hard it was to get doctors to understand, to listen, and to diagnose them. It got us thinking, what do doctors in Illinois actually know about tick-borne diseases?"

Smith explored this question through a study in *One Health*. Her two goals were to find out how much doctors knew about ticks and TBDs, and to use the data from the study to design a training program to better educate doctors on ticks and associated diseases.

To examine how much medical professionals knew about ticks and TBDs, the team designed web-based surveys that utilizes the KAP model, which assesses the participants' knowledge, attitudes, and practices in this regard. Questions were designed in collaboration with the Illinois-Tick Inventory Collaboration network, which includes researchers in the College of Veterinary Medicine, the Carle-Illinois College of Medicine, and the Illinois Natural History Survey-Prairie Research Institute. The survey included questions about types of diseases, the ticks that can carry those diseases, symptoms, treatment, feelings of risk, preventative practices, training, and more.

#### PEOPLE MENTIONED

Rebecca Smith, professor of epidemiology (IGOH)

FUNDED BY CDC These surveys were then passed around to local hospital associations resulting in 346 participants. The researchers found that while physicians were relatively knowledgeable about diagnosis and treatment of Lyme disease, they did not know much about other diseases. The researchers found only one factor that influenced how knowledgeable participants were about TBDs, and that was how recently they had completed training on the topic, if ever at all. Many practitioners had not had any training on ticks except for medical school, meaning the information they received was likely not comprehensive and now out of date.

"We are on the leading edge of range expansion for three of the four vector ticks that live in the state," said Smith.

## 

"With all of those ticks expanding their range, it might be that physicians haven't heard about the diseases that they carry because it just wasn't an issue when they started practicing in the area."

## 

In response to the troubling findings, Smith's team is designing a continuing education course that will inform practitioners on current ranges of ticks and risk of disease, as well as practices they can implement into their care to increase prevention of TBDs. A similar course is already offered for veterinarians, and has found to be effective towards diagnosis and treatment of TBDs in pets. The course was created in partnership with Carle, and opened in February 2023.

"We want to get the training out there so physicians can get people to a diagnosis faster," explained Smith. "Once it's out we will start fine-tuning how often practitioners will need to take it so they can



Rebecca Smith is designing training programs to better educate doctors on ticks and associated diseases.

have updated information as things progress." Smith hopes that this educational course will prompt more tick training programs to be made for other areas of the country, where seasonality and habitat can result in completely different tick species and TBDs to watch out for. With the introduction of this training, doctors and practitioners in Illinois can be better prepared to handle the increase in incidence of TBDs.

## Genetic sequencing uncovers unexpected source of pathogens in floodwaters

go.igb.illinois.edu/Flood23

Researchers report in *Geohealth* that local rivers and streams were the source of the *Salmonella enterica* contamination along coastal North Carolina after Hurricane Florence in 2018—not the previously suspected high number of pig farms in the region. These findings have critical implications for controlling the spread of disease caused by antibiotic-resistant pathogens after flooding events.

The study, led by Helen Nguyen and Yuqing Mao, tracks the presence and origin of *S. enterica* from environmental samples from coastal North Carolina using genetic tracing.

The study reports that because human and animal fecal genetic markers are often found in flood waters, it is commonly assumed wastewater sources, septic systems, and livestock farms are responsible for spreading antibiotic-resistant bacteria into the environment. However, no studies have conclusively identified contaminant source points.

Three weeks after Hurricane Florence, Nguyen's team collected 25 water samples from water bodies downstream of the swine farms in agricultural production areas in North Carolina, 23 of which contained *S. enterica*.

The team genetically traced the bacteria's origin to the many small local rivers and streams in the area—meaning that these pathogens have already established themselves in the natural environment.

"With climate change bringing warmer temperatures—in which bacteria thrive—and more frequent tropical storms, the importance of our findings needs to be realized by policymakers," Nguyen said. "Agricultural and human wastewater should not be the only source considered when designing mitigation plans to prevent the spread of pathogenic bacteria."



Yuqing Mao, left, and Helen Nguyen.

#### PEOPLE MENTIONED

Helen Nguyen, professor of civil and environmental engineering (IGOH)

Yuqing Mao, graduate student

FUNDED BY Illinois, Allen Foundation and EPA

## Are honey bees, wild bees still in trouble?

go.igb.illinois.edu/Beestress23

A new report reveals that U.S. beekeepers lost roughly half of the honey bees they managed last year. Adam Dolezal, who studies how environmental stressors affect bees, spoke to Diana Yates about the current status of bees in the U.S.

## ^ Honey bee populations have been faltering since at least 2006. Why can't scientists and the beekeeping community address and solve whatever is causing the massive die-offs?



Adam Dolezal studies the factors affecting native bees and honey bee health.

### PEOPLE MENTIONED

Adam Dolezal, professor of entomology (IGOH)

**Diana Yates**, editor of life sciences at the News Bureau

While scientists and beekeepers have made progress understanding what causes problems in bee health, finding solutions is more difficult because the problems are complex, variable, and interact with each other. Nutrition and climate change affect bees and beekeeping in ways we don't yet fully understand.

## Are wild bees also suffering the same dramatic losses? If so, why?

We do know that wild bees are also facing habitat loss, pesticide exposure, and disease pressure that puts them at risk, too. If anything, their losses may be more dramatic than those seen in honey bees. While the deaths of 50% of honey bee colonies may seem staggering, beekeepers can and do manage these losses to keep our honey bee population stable and effective. But our native bees are precious wildlife that can't be easily managed.

## ^ What potential remedies are available now?

Keeping honey bees fed and disease-free is important. Researchers also try to improve honey bee colony survival through the development of hive-monitoring technologies or indoor facilities for overwintering large numbers of colonies.

## Microbiome Metabolic Engineering (MME)







The Microbiome Metabolic Engineering theme seeks to understand the positive effects of the microbiome on human health and how harmful environmental factors reduce those effects.

EST. 2016 -

Trillions of microbes reside within the human digestive system, processing food and maintaining overall health. This microbial community contains millions of genomes, each of which encodes for molecules whose functions are unknown.

Although it is clear that the gut microbiome interacts both with the host and the host's environment, the underlying mechanisms of how it does so in different environments is poorly understood. Researchers within the Microbiome Metabolic Engineering theme use their expertise in physiology, biochemistry, ecology, and systems biology to address these questions by studying human-microbiome interactions and identifying unique pathways that relate to health, nutrition, and the environment.



### 2023 ANNUAL REPORT | IGB FEATURED STORIES | MME

## Engineered yeast used to influence gut microbiome of mice

AUGUST 1, 2023



Lysozyme, an antimicrobial protein that mammals naturally produce in milk, tears, and saliva.

go.igb.illinois.edu/Lysozyme23

Microbial engineering has been found to be a useful strategy for improving human health, but the mechanisms underlying this improvement are still unclear and difficult to test. However, a team of researchers hopes that their study, published in *Microbiology Spectrum*, will provide a platform that will make mechanistic studies on the microbiome more feasible.

The study was conducted by the labs of Yong-Su Jin and Michael Miller, along with first author Jungyeon Kim.

The researchers utilize a genetically engineered strain of *Saccharomyces boulardii* as their delivery vehicle to deliver bioactive proteins into the gut. The yeast is commonly used as a probiotic, and the researchers say that it's not only easy to genetically engineer, it also moves quickly through the gut, unlike other options for vehicles.

The goal of the study was to genetically engineer the yeast to produce lysozyme, an antimicrobial protein that mammals naturally produce



From left, Michael Miller, Jungyeon Kim, and Yong-Su Jin.

in milk, tears, and saliva. The engineered yeast was then fed to mice for 2 weeks, and the microbiome of these mice was compared to mice fed either wild-type unengineered yeast or a saline solution.

First, the researchers measured the presence of lysozyme in the gut and fecal matter of the mice fed the engineered yeast, to verify that the yeast was producing and delivering lysozyme into the gut. After verifying this, they measured the gut microbiome and fecal metabolome of the mice across all three treatment groups.

When the researchers examined the mice fed the lysozyme-secreting yeast, they found the structure of their gut microbiome and diversity of their fecal metabolome was significantly altered compared to mice fed saline or wild-type yeast. The researchers concluded that the lysozyme secretions by the yeast had indeed impacted the gut microbial community.

"What's cool is that we show that our engineered *S. boulardii* is able to produce proteins in the gut that significantly affect the microbiome," said Miller. "The bigger picture is that lysozyme is just a starting point. We can engineer the yeast to make any bioactive protein that we want, and have them deliver that cargo functionally to the gut."

The researchers say that the activity of the yeast could be improved, as they may not have had enough sugar or nutrients to proliferate fully within the gut. However, for a follow-up study the researchers added a new genetic pathway to the yeast that will allow them to utilize lactose, the sugar found in milk. The lactose can then be fed to the mice alongside the yeast to provide a new fuel source for the newly engineered yeast. The researchers have already found that doing so dramatically increases lysozyme production in the gut.

In the future, the researchers are hoping to figure out how to deliver specific quantities of a target protein into the gut. Jin says the ultimate goal of their research would be to utilize engineered yeast in "in-food fermentation," such that the yeast that's already in foods people enjoy, like baked goods, milk, and alcohol, would produce additional proteins that help maintain healthy gut microbiomes.

## 

"My vision is to use this engineered yeast in food," said Jin. "We already use yeast for making bread, wine, beer, and such. But if we create these fermented foods using engineered microorganisms designed to be helpful for the gut microbiome, we can enjoy the benefits of the engineered microorganism simply through the consumption of food."

#### PEOPLE MENTIONED

Yong-Su Jin, professor of bioengineering (BSD/CABBI/ MME)

### Michael Miller, professor of food microbiology

(MME co-leader/ IGOH)

## Jungyeon

Kim, former postdoctoral researcher in Jin's lab and current assistant professor at Seoul National University

### FUNDED BY

Korea Institute of Planning and Evaluation for Technology in Food, Agriculture, Forestry, and Fisheries, the Ministry of Agriculture, Food, and Rural Affairs, and USDA

## Illinois-led team puts cows and microbes to work to reduce greenhouse gases

go.igb.illinois.edu/CGI23

As we hurtle toward crucial tipping points on a warming planet, an international team of scientists is recruiting a surprising ally to make a powerful dent in greenhouse gas emissions: the cow. Animal sciences researchers from the University of Illinois Urbana-Champaign are driving a new project to reduce methane production resulting from rumen fermentation in beef and dairy cattle. The 3-year, \$3.2-million project is part of the Greener Cattle Initiative, led by the Foundation for Food and Agriculture Research.



Targeting methane production in cows may correct climate trajectory more quickly than controlling carbon dioxide alone.

## "Our challenge is to reduce enteric methane emissions by about 30 to 40% with the technologies we have," said project leader Rod Mackie.

The project involves six research hubs around the world, all tackling the challenge of enteric methane. Mackie, along with Josh McCann, will start by tracking hydrogen production and utilization during fermentation. They will take rumen microbial communities from beef cattle that naturally produce more or less methane to explore potential adjustments they can make to the system with promising inhibitor compounds. Later, they will bring their findings back into cows.

Mackie said the project is the beginning of a longer-term endeavor to find enteric methane solutions. But by the end of three years, the goal is to be able to recommend specific amounts of inhibitors that don't hinder or even improve production performance.

Beyond that? "What we'd like is to have ruminants save the planet within 10 years," Mackie said. "That would be amazing."

## New role of small RNAs in Salmonella infections uncovered

go.igb.illinois.edu/SmallRNA23

In a new paper, published in the *Journal of Bacteriology*, researchers investigated the role of small RNAs in *Salmonella* infections.

The bacteria infect humans by using a needle-like structure, called a type 3 secretion system. The genes that encode this system are found on a region of DNA known as the *Salmonella* pathogenicity PEOPLE MENTIONED

Rod Mackie, professor of animal sciences (MME)

Josh McCann, professor of animal sciences island 1. SPI-1 is controlled by an extensive regulatory network. Three transcription factors: HilD, HilC, and RtsA, all control their own and each other's DNA expression. They also activate another transcription factor, HilA, which activates the rest of the SPI-1 genes.

"We didn't know how environmental factors affect gene regulation in *Salmonella*. That's when researchers started looking at small RNAs," said Sabrina Abdulla.



Cari Vanderpool, left, and Sabrina Abdulla.

Small RNAs play a crucial role in determining how genes function in bacterial cells. In this paper, the researchers looked at the sRNAs that regulate the *hilD* mRNA, specifically a sequence called the 3' untranslated region. In bacteria, the 3' UTRs are usually 50-100 nucleotides long. However, the 3' UTR of the *hilD* mRNA is 300 nucleotides long.

The researchers determined that the sRNAs Spot 42 and SdsR can both target the 3' UTR, and they do so in different regions.

"We found that when the sRNAs are deleted, the bacteria cannot survive in the host," Abdulla said.

"We want to extend our studies in two directions: how the sRNAs influence *hilD* mRNA levels and how sRNAs participate in regulating expression of other important SPI-1 genes," said Cari Vanderpool.

### PEOPLE MENTIONED

Sabrina Abdulla, graduate student

Cari Vanderpool, professor of microbiology (MME co-leader/ IGOH)

FUNDED BY NIH and Illinois

## Mining Microbial Genomes (MMG)





The Mining Microbial Genomes theme identifies undiscovered microbial sources with medical potential for new antibiotics and other beneficial drugs.

## Widespread overuse of antibiotics has led to a decline in the efficacy of these drugs because many pathogens are becoming increasingly resistant to them.

Currently, 70 percent of antibiotics, and more than half of all medicines, are derived from microbially-produced natural products—small molecules with unique properties. Ironically, many pharmaceutical companies are scaling back or eliminating metabolite screening programs despite evidence suggesting that a multitude of useful microbial products await discovery. The Mining Microbial Genomes research theme searches through microbial genomes to find new metabolites. The goal of the theme is to learn how these molecules are produced in microorganisms and identify uses for the new metabolites discovered.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | MMG

# **\$9.5M** award to study emerging pathogens, better understand influenza-antibody interactions

JANUARY 26, 2023



go.igb.illinois.edu/EPI23

Aquatic birds, especially ducks, can carry influenza viruses, but they don't often become severely ill. This led scientists to wonder how their immune systems could act as a reservoir for a highly infectious and pathogenic virus, while the birds remain relatively unharmed. Additionally, could the immune system be engineered to thwart transmission to other animals and humans, ultimately preventing future pandemics?

Four faculty at the University of Illinois Urbana-Champaign, plus a collaborator in Colorado, will attempt to answer these questions as part of an ambitious project funded by the Howard Hughes Medical Institute. HHMI will provide \$9.5 million over three years to the Illinois and Colorado project, which was one of 13 selected by the institute as part of its \$100 million Emerging Pathogens Initiative.

"There are a lot more influenza viruses in birds than there are in humans, and so there's a lot more variation. When the viruses spill over (to other animals or humans) they're incredibly lethal and so that's not something we want to see happen," said Wilfred van der Donk.

The Illinois and Colorado team includes Beth Stadtmueller, Nicholas Wu, Wilfred van der Donk, Angad Mehta, and Jenna Guthmiller. The work and the platforms developed by the group in the coming years will be applicable to other avian viruses or other host-virus relationships scientists want to better understand and prevent from spreading, added Stadtmueller. She investigates the structural, biochemical, and biophysical mechanisms of proteins and complexes involved in immunity.

#### PEOPLE MENTIONED

Wilfred van der Donk, professor of chemistry (MMG leader)

Beth Stadtmueller, assistant professor of biochemistry (MMG) The group's first aim is to develop ways to purify antibody-producing cells from ducks to get a better understanding of their antibody repertoire. "Nothing much is currently known about the antibody repertoire in ducks. So, we are excited to have this opportunity to explore its molecular features and potentially leverage them to address public health issues," Wu said.

Mehta and his lab will then take these observations and translate them into human systems. "Overall, our efforts could inform biologics development, diagnostics, and vaccine design," he said.

The influenza virus enters its host through mucosal routes, e.g. the nasopharynx and lungs and gut. Researchers will undertake several different engineering approaches to address the myriad ways the influenza virus invades its hosts. Stadtmueller and her lab are especially interested in mucosal antibodies.

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"The antibodies secreted into those regions have unique and poorly understood structures," she said. "In targeting flu, we're really excited thinking about how these structures can support clearance of viruses and also how they're functioning in the nasopharynx and lungs as opposed to the gut."

## 

The business part of antibodies is a series of loops that are hypervariable, and our immune system selects the ones that bind tightly to a molecule of the pathogen, van der Donk explained. Those loops could be mimicked with circular peptides, thus creating antibody-like molecules. His lab created a library of two million polycyclic peptides.



From left, Nicholas Wu, Beth Stadtmueller, Wilfred van der Donk, and Angad Mehta.

Nicholas Wu, assistant professor of biochemistry (IGOH/MMG)

Angad Mehta, professor of chemistry (MMG)

Jenna Guthmiller, assistant professor of immunology and microbiology at the University of Colorado Anschutz Medical Campus The information obtained regarding the antibodies from ducks and human cells could be used to design the cyclic peptides against avian influenza, van der Donk said.

Ultimately, the implications for their work could extend beyond influenza. The antibody evolution and engineering platforms developed during these studies are expected to be "modular," Mehta said, so they can be readily repurposed for targeting other emerging pathogens. In addition, these platforms can be potentially adapted to develop biologics for treating other diseases like cancer.

## New antifungal molecule kills fungi without toxicity in human cells, mice

go.igb.illinois.edu/AmB23

A new antifungal molecule, devised by tweaking the structure of prominent antifungal drug Amphotericin B, has the potential to harness the drug's power against fungal infections while doing away with its toxicity, report researchers at the University of Illinois Urbana-Champaign and collaborators at the University of Wisconsin-Madison. They reported their findings in the journal *Nature*.

"Fungal infections are a public health crisis that is only getting worse. So let's take one of the powerful tools that nature developed to combat fungi, and turn it into a powerful ally," said research leader Dr. Martin Burke.

Burke's group has teamed up with Chad Rienstra's group at Wisconsin-Madison to show how AmB kills fungi and human kidney cells. Following this, the team synthesized and tested derivatives that could potentially work. Enabled by collaborators and facilities at the IGB and Dr. Timothy Fan, the researchers tested the most promising derivatives. One molecule, dubbed AM-2-19, stood out from the rest.

## "This molecule is kidney-sparing, it is resistance evasive, and it has broad spectrum efficacy," said Arun Maji, the co-first author of the paper.

"This work shows the power of pursuing drug discovery in an interdisciplinary academic environment, especially the excitement of the IGB environment, and we're quite hopeful this could be the first of many great frontier drug discovery stories with IGB continuing to build its impact over the campus in a very positive way," said Burke.



Pictured, from left: Agnieszka Lewandowska, Jonnathan Marin-Toledo, Martin Burke, Timothy Fan, Arun Maji and Corinne Soutar.

#### PEOPLE MENTIONED

Martin Burke, professor of chemistry (MMG)

Chad Rienstra, professor of biochemistry at University of Wisconsin-Madison

**Timothy Fan**, professor of veterinary clinical medicine (ACPP/ CGD)

**Arun Maji**, postdoctoral researcher

FUNDED BY Nih

## Researchers discover new class of ribosomal peptides

go.igb.illinois.edu/RiPPS23

Living organisms produce a myriad of natural products which can be used in modern medicine and therapeutics. Bacteria and other microbes have become the main source for natural products, including a growing family called ribosomally synthesized and post-translationally modified peptides, or RiPPs. The labs of Douglas Mitchell and Huimin Zhao have been working in tandem to identify and analyze new RiPPs that could be good candidates for drug development and therapeutics.



From left, Huimin Zhao, Shravan Dommaraju, and Hengqian Ren.

In a paper, published in *Nature Communications*, co-first authors Shravan Dommaraju and Hengqian Ren reported the discovery of a unique, novel class of RiPPs, which they have named "daptides." Unlike most peptides which have one positively charged and one negatively charged end, or "terminus," daptides instead have two positively charged termini.

The researchers explained that while this change in termini may seem small, the positive charge of both termini gives daptides the potential to interact with negatively charged objects, such as cell membranes. Their next steps are to understand the enzyme functions of the daptides, and use bioinformatics analysis to see if there are other combinations of genes associated with daptide production. Directions for further studies include exploring potential therapeutic uses for daptides and the ecological role that daptide production has for the bacteria that make them.

### PEOPLE MENTIONED

**Douglas Mitchell**, professor of chemistry (MMG)

Huimin Zhao, professor of chemical and biomolecular engineering (BSD leader/CABBI/ CGD/MMG)

Shravan Dommaraju, graduate student

Hengqian Ren, postdoctoral researcher

FUNDED BY NIH

## Multi-Cellular Engineered Living Systems (M-CELS)





TECHNOLOGY + SOCIETY

The Multi-Cellular Engineered Living Systems theme creates machines made of living cells that could serve as a solution to challenging real-world problems.

## For years, artificial systems—such as robots and machines—have been used for industrial applications, making a tremendous impact on society.

However, steady progress made by scientists could replace artificial systems with Multi-Cellular Engineered Living Systems, which are composed of living cells and extracellular matrices and are able to perform new functions that are absent in natural systems. Two research programs, bio-hybrid robots and biological processors, form the foundation of the M-CELS research theme. M-CELS focuses on developing in silico, cellular, and artificial components that are used in the assembly of biomachinery and computing processors, along with studying the genomics and proteomics of engineered living systems.



### 2023 ANNUAL REPORT | IGB FEATURED STORIES | M-CELS

## Illinois chosen to co-lead new Chan Zuckerberg Biohub in Chicago

OCTOBER 5, 2023



The CZ Biohub Chicago is the first institution to expand the CZ Biohub Network.

go.igb.illinois.edu/CZIChi23

The University of Illinois Urbana-Champaign was chosen to colead the Chan Zuckerberg Biohub Chicago—a new biomedical hub—with researchers from Illinois, the University of Chicago, and Northwestern University. The three-university team was selected as part of a competitive application process for a research initiative explicitly focused on measuring human biology. Illinois' strength in interdisciplinary collaboration was an important asset identified in the proposal.

The center brings together leading scientific and technology institutions with the goal of solving grand scientific challenges on a 10- to 15-year time horizon. This state-of-the-art lab and administrative facility is built from the ground up, with specialized rooms, engineering equipment, and a space to host scientific presentations.

The Biohub's main focus is on engineering technologies to make precise, molecular-level measurements of biological processes within human tissues, with the ultimate goal of understanding and treating the inflammatory states that underlie many diseases.

50% of all deaths can be attributed to inflammation-related diseases such as ischemic heart disease, stroke, cancer, chronic kidney disease, and autoimmune and neurodegenerative conditions. Understanding inflammation requires the ability to measure a myriad of interactions at the molecular and cellular level in 3D living tissue, a capability that does not currently exist.

"Our role in the CZ Biohub Chicago is further evidence that our university is working at the leading edge of advancing human health," said Robert J. Jones. "When we unite our expertise with the collective strengths of our world-class research university partners, the horizon for innovation in health expands exponentially. The partnership between our three institutions is strong and growing, and that translates directly and rapidly into impact for the people of Illinois."

The CZ Biohub Chicago is the first institution to expand the CZ Biohub Network, and builds on the successful collaborative model of the first Chan Zuckerberg Biohub in San Francisco. Together, members of the CZ Biohub Network partner to develop science and technologies that help us understand how cells and tissues function and increase our understanding of human health and disease.

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"We are excited to scale this successful model of collaborative science into a larger network by welcoming the new Biohub in Chicago," said Priscilla Chan.

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"This institute will embark on science to embed miniaturized sensors into tissues that will allow us to understand how healthy and diseased tissues function in unprecedented detail. This might feel like science fiction today, but we think it's realistic to achieve huge progress in the next 10 years. I look forward to the advances in science and technology that this new Biohub will spur in studying how tissues function to understand what goes wrong in disease and how to fix it."

"Impactful interdisciplinary collaboration doesn't just happen-it must be nurtured in deliberate ways," said Gene Robinson. "Our campus knows how to do grand-challenge, team-science research,



Priscilla Chan, Shana Kelley, and JB Pritzker at the CZ Biohub Chicago Launch.

### PEOPLE MENTIONED

**Robert J. Jones**, Illinois Chancellor

Priscilla Chan, Chan Zuckerberg Initiative Co-Founder and Co-CEO

### Hyunjoon Kong,

professor of chemical and biomolecular engineering (M-CELS leader/ EIRH/RBTE)

## Martha Gillette,

professor of cell and developmental biology (GNDP/ M-CELS)

Gene Robinson, IGB Director (GNDP)

FUNDED BY Chan Zuckerberg Initiative at scale. This will be an incredible, transformational opportunity for our research community."

Several Illinois faculty members play a significant role in Biohub Chicago, including Joon Kong and Martha Gillette. The IGB will serve as the campus "satellite" for the Biohub, while many other campus units, such as the National Center for Supercomputing Applications, the Beckman Institute for Advanced Science and Technology, the Cancer Center at Illinois, the Holonyak Micro and Nanotechnology Laboratory, the Materials Research lab, the IBM-Illinois Discovery Accelerator Institute and C3.ai Digital Transformation Institute, are involved with Biohub Chicago activities.

## New drug delivery method can reverse senescence of stem cells

go.igb.illinois.edu/Senescence23

As we age, our bodies change and degenerate over time in a process called senescence. Stem cells, which have the unique ability to change into other cell types, also experience senescence, which presents an issue when trying to maintain stem cell cultures that produce biomolecules for therapeutic use.

Instead of removing older cells from the culture, preventing the cells from entering senescence in the first place is a better strategy, according to Ryan Miller.

While treating the cells with antioxidants can delay senescence, current methods of antioxidant delivery have many shortcomings, including large variation in the amount of drug release over time and between cells. However, a study by the labs of Hyunjoon Kong and Hee-Sun Han, describes a new method of delivering antioxidants to stem cells that is reliable, long-lasting, and minimizes variation.

The new method utilizes antioxidants in the form of polymerstabilized crystals. By using microfluidics, a technology that allows researchers to work with incredibly small amounts of fluid, the researchers can create crystals that are all the same size and dosage, minimizing variation and extending release of drugs between cells.



Confocal images of mesenchymal stem cells showing senescent cells producing unwanted biomolecules.

### PEOPLE MENTIONED

**Ryan Miller**, postdoctoral fellow

Hyunjoon Kong, professor of chemical and biomolecular engineering (M-CELS leader/ EIRH/RBTE)

Hee-Sun Han, assistant professor of chemistry (GNDP/IGOH) Increased duration of the drug's efficacy means that stem cell cultures can be kept out of the senescence state for longer, which leads to a larger harvest of the needed biomolecules for therapeutics.

The study was published in Advanced Functional Materials.

FUNDED BY NSF, National Research Foundation, Alzheimer's Association, and NIH

## Researchers reveal real-time glimpse into growth habits of nanoparticles

go.igb.illinois.edu/Nanos23

For the first time, researchers have observed the process of nanoparticles self-assembling and crystalizing into solid materials. In new videos produced by the team, particles can be seen raining down, tumbling along stairsteps, and sliding around before finally snapping into place to form a crystal's signature stacked layers.

Led by Qian Chen, the study used liquidphase transmission electron microscopy and computational modeling to gain an unprecedented view of the self-assembly process at nanometer resolution. The team said these new insights could be used to design new materials, including thin films for electronic applications.

Before this work, researchers used microscopy to watch micron-sized colloidal particles—10 to 100 times larger than nanoparticles—self-assemble into crystals. There are also extensive theories on atomic, molecular, or ionic building blocks, which are 10 to 100 times smaller than nanoparticles. However, the researchers said a knowledge gap existed at the intermediate nanoscale.

Recent advances to improve liquid-phase TEM have made it possible to view nanoparticles in real time as they form solid materials. Chen's team spent years optimizing the process to ensure the electron beam could view the particles without damaging them.

In the experiments the particles collided, sticking together to form horizontal layers, then stacking vertically to form the layer-bylayer crystalline structure. They further visualized crystal formation with advanced computer simulations, verifying the universal trend of distinctive assembly structures from different-sized particles.

The findings were published in the journal Nature Nanotechnology.



Qian Chen, left, onscreen researchers Ahyoung Kim, Binbin Luo and Ahyoung Kim, and Chang Liu, seated, collaborated with researchers at Northwestern University to observe nanoparticles self-assembling and crystalizing into solid materials for the first time.

### PEOPLE MENTIONED

Qian Chen, professor of materials science and engineering (M-CELS)

FUNDED BY DOE and NSF

## Regenerative Biology and Tissue Engineering (RBTE)





The Regenerative Biology and Tissue Engineering theme develops organ regeneration techniques in animals and aims to translate these to humans.

— EST. 2007 —

Organ malformation, damage, and failure are the most common causes of human morbidity and death. The goal of the Regenerative Biology and Tissue Engineering theme is to develop the knowledge base and technologies needed to replace or regenerate human tissues and organs.

RBTE scientists use stem cells and developmental approaches to investigate how organs form and regenerate. They use the knowledge gained from those studies to regenerate tissues and organs in a series of model organisms and then translate their research into humans. With this multi-faceted approach, RBTE scientists are making major strides toward developing regenerative technologies that will positively impact millions of lives.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | RBTE

## Mitochondrial protein plays key role in glioblastoma and therapeutic resistance

OCTOBER 17, 2023





Mice that have the mutation EGFRvIII and no CHCHD2, right, have decreased tumor burdens compared to the control mice that only have the EGFRvIII mutations.

go.igb.illinois.edu/Glio23

Glioblastoma is the most common type of brain tumor that affects adults and, unfortunately, still remains incurable. In a study published in the *International Journal of Oncology*, researchers have demonstrated that a specific mitochondrial protein plays an important role in glioblastoma, and can therefore be used as a potential target to reduce tumors.

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"One of the major challenges with glioblastoma is that it spreads invasively throughout the brain. We're interested in understanding what drives this process in order to identify new therapeutic strategies," said Brendan Harley.

## 

In the current study, the researchers focused on the mitochondrial coiled-coil-helix-coiled-coil-helix domain containing protein 2—also known as CHCHD2. The complicated name refers to the structure of the protein, whose subunits are coiled together like rope strands.

The researchers first looked at The Cancer Genome Atlas glioblastoma database to see whether they could spot any patterns that related CHCHD2 levels to cancer. Out of 577 samples, they

#### PEOPLE MENTIONED

### Brendan Harley,

professor of chemical and biomolecular engineering (RBTE leader/EIRH)

Rex Gaskins, professor of immunophysiology (RBTE)

FUNDED BY NIH and Illinois found that the CHCHD2 genes had higher expression in tumor cells, compared to non-tumor tissue, and was higher in advanced cases of glioblastoma.

"We learned that in humans the gene encoding CHCHD2 was closely linked to the gene encoding the epidermal growth factor receptor, or EGFR, on chromosome 7. A mutated version of this protein is found in over 50% of glioblastoma patients," said Rex Gaskins.

When the results from the database showed that CHCHD2 expression was highest in the patients who harbored the mutation known as EGFRVIII, the researchers realized that understanding the interaction between these two proteins can be crucial to understanding glioblastoma progression.

To confirm their hypothesis, the researchers looked at the effects of CHCHD2 on tumor growth in mice. They compared mice that had CHCHD2 and the mutated version of EGFR to mice that did not contain CHCHD2, but still had mutated EGFR. The first group of mice survived for an average of 17 days, whereas the second group survived for 25 days. The researchers found that the mice that died earlier had more tumor growth infiltrating the surrounding brain tissue.

Although it is evident that these proteins are interacting with each other, it is unclear how they affect glioblastoma progression. The authors have proposed several mechanisms, based on their experiments.

The first possibility is that CHCHD2 decreases the sensitivity of mutated EGFR to cytotoxic drugs. Patients with glioblastoma only survive for 15-20 months, despite being subjected to an arsenal of treatment procedures, including chemotherapy with the drug temozolomide. The researchers used this drug and tested cells that had the mutated EGFR protein and CHCHD2 and cells that only had EGFR. They saw that when cells did not contain CHCHD2, they were more sensitive to temozolomide. The researchers believe that this result highlights CHCHD2 as a potential therapeutic target.



From left, Brendan Harley, Rex Gaskins, Andrew Steelman, and Payton Haak studied the role of the mitochondrial protein CHCHD2 in glioblastoma.

Another possibility is that CHCHD2 affects how EGFR stimulates glioblastoma invasion. Using a hydrogel to replicate the tumor microenvironment in the brain, the researchers showed that cells with both CHCHD2 and mutated EGFR were able to grow and invade the surrounding area. This invasion was especially pronounced when the level of oxygen was lower, a condition commonly experienced by glioblastoma cells as they invade from the tumor into the brain.

"This study suggests that the role of CHCHD2 in glioblastoma progression was underappreciated," Harley said. "The idea that this protein can change behavior based on its environment is valuable. We hope that researchers can start identifying new therapeutic strategies based on this key protein."

## Climate-smart cows could deliver 10-20x more milk in Global South

go.igb.illinois.edu/Girolandos

A team of animal scientists from the University of Illinois Urbana-Champaign is set to deliver a potential game changer for subsistence farmers in Tanzania: cows that produce up to 20 times the milk of indigenous breeds.

The effort, published in *Animal Frontiers*, marries the milk-producing prowess of Holsteins and Jerseys with the heat, drought, and disease-resistance of Gyrs, an indigenous cattle breed common in tropical countries. Five generations of crosses result in cattle capable of producing 10 liters of milk per day under typical Tanzanian management, blasting past the half-liter average yield of indigenous cattle.

After breeding the first of these calves in the U.S., project leader Matt Wheeler is ready to bring embryos to Tanzania.

"High-yielding Girolandos—Holstein-Gyr crosses—are common in Brazil, but because of endemic diseases there, those cattle can't be exported to most other countries," Wheeler said. "We wanted to develop a high health-status herd in the U.S. so we could export their genetics anywhere in the world."

Wheeler's team planned to implant 100 half-blood Holstein-Gyr or Jersey-Gyr embryos into indigenous cattle in two Tanzanian locations in March 2023. The resulting calves will be inseminated through successive generations to create "pure synthetic" cattle with five-eighths Holstein or Jersey and three-eighths Gyr genetics.



Herd of quarter-Holstein, three-quarter-Gyr cattle.

PEOPLE MENTIONED

Matt Wheeler, professor of animal sciences (RBTE)

**FUNDED BY** USDA, Illinois, Ross Foundation While the project is still in its early stages, it represents a step toward more climate-resilient animal agriculture, with the goal of bolstering food security in the Global South where climate change is hitting hardest.

## Metabolic glycan labeling approach shows promise for improving dendritic cell vaccines

go.igb.illinois.edu/Dendritic23

Hua Wang and his research group are passionate about developing novel—but simple—solutions to both improve the efficacy of cancer immunotherapies and look ahead to clinical translation. In their recent publication in *Nature Communications*, they outline their exciting findings that the metabolic glycan labeling of dendritic cells results in enhanced DC activation and antitumor efficacy.



Researchers Joonsu Han (left) and Hua Wang.

DCs are essential immune cells which can process and present antigens on the cell surface to initiate and regulate immune responses. DC vaccines are a form of cancer immunotherapy that isolates monocytes from a patient's blood, transforming them into tumor antigen-presenting DCs, which are then administered to the patient to guide the anticancer immune activity.

In the study, the researchers found that the metabolic glycan labeling of DCs enhanced anticancer immune responses.

Joonsu Han, first author on the team's paper, explained, "The dendritic cell vaccine was actually one of the first FDA approved cancer immunotherapies, but the antitumor efficacy is still not great. We found that the metabolically labeled dendritic cells actually improve the activation status of DCs, leading to the enhanced cytotoxic T-cell response of DC vaccines."

Metabolic labeling of DCs could be a powerful tool to improve cancer immunotherapies because the approach is relatively simple and can be applied universally to different DC vaccines.

"I hope this simple technology can have some impact on patients' lives and lead to good outcomes like being able to go home without cancer," said Han.

### PEOPLE MENTIONED

Hua Wang, professor of materials science and engineering (RBTE)

**Joonsu Han**, graduate student

FUNDED BY Illinois and NIH

## Core Facilities Microscopy Suite



Core Facilities provides a variety of services to the IGB and the Illinois campus. The space is meant to encourage innovation by helping scientists with new techniques and approaches that will enable them to achieve their research goals without a significant investment in instrumentation or time.

— EST. 2007 —

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# The IGB Core Facilities is a state-of-the-art resource for biological microscopy and image analysis.

It provides researchers, both from the IGB and across the campus, with the tools and expertise needed to meet their imaging goals. In addition to providing technical assistance in acquiring and analyzing microscopy images, the staff also aid in designing and interpreting experiments.



### 2023 ANNUAL REPORT | IGB FEATURED STORIES | CORE FACILITIES

## Bringing cells to life: A \$30M NSF grant to support whole-cell modeling

SEPTEMBER 12, 2023





The NSF Science and Technology Center for Quantitative Cell Biology will partner with Minecraft, a 3D, open-world video game, to create whole-cell models.

go.igb.illinois.edu/QCB23

Researchers, policymakers, and Minecraft players can look forward to a new research center.

Supported by a \$30 million U.S. National Science Foundation grant, the NSF Science and Technology Center for Quantitative Cell Biology will create whole-cell models to transform our understanding of how cells function. With cutting-edge imaging and simulation tools, the center will advance the study of healthy and diseased cells; accelerate research into gene expression, metabolism, and division; and share science with communities of all ages through a partnership with the popular computer game Minecraft.

This center is one of four Science and Technology Centers funded by a five-year, \$120 million NSF investment. It will be located at the Beckman Institute for Advanced Science and Technology, where Zan Luthey-Schulten and Martin Gruebele conduct their research.

### 

"Now is the right time to start such a moon-shot effort," said Luthey-Schulten. "The computational and experimental capabilities are just at the verge of where this effort is realistic to contemplate, and this PEOPLE MENTIONED

Zan Luthey-Schulten, professor of chemistry is usually when breakthroughs happen. Whole-cell models are now at the transition point between what is possible already and what is not yet possible. This center will make that transition and move beyond it."

## 

A whole-cell model entails a full quantitative description of the physical and chemical processes that define the state of a cell. Because cells exist in space and time, a true whole-cell model considers all spatial and temporal factors—the result is a fully simulated cell in four dimensions.

To create such models, the center will use cutting-edge imaging and simulation tools, including: MINFLUX, a super-resolution microscopy technique that can accurately locate and track biomolecules in living cells; label-free microscopy, which maps a cell's chemical composition with light instead of dye; and cryo-electron microscopy/tomography, which provides information about a cell's shape and the large, complex biological structures within it.

The results will be integrated into 4D whole-cell models that can bring an entire simulated cell cycle to life on a computer. These models can be used to predict a cell's response to mutations, environmental changes, drugs, and pathogens. It can also be used to model genetic processes in the cell.

To inspire the next generation of scientists, the center will partner with Minecraft, a 3D, open-world video game that gives players the ability to traverse, interact with, and manipulate their environment. Game players will be able to simulate and investigate a full living cell, resulting in an interactive and immersive learning experience.



Zan Luthey-Schulten (right) and Martin Gruebele in front of the MINFLUX at the IGB.

Martin Gruebele, professor of chemistry (MMG)

## Diversity, Equity, and Inclusion (DEI)



The IGB values equality and respect for every member of its community. Faculty, students, and staff from different backgrounds bring their lived experiences and unique perspectives together. This diversity is essential to improving the IGB's ability to solve problems and be responsive to societal needs.

EST. 2018 -

## BLACK Landscapes Matter

ALTER HOOD & GRACE MITCHELL TAD

The Diversity, Equity, and Inclusion initiatives are dedicated to creating a more inclusive, diverse, and welcoming environment within the IGB.

The programming is advanced with the help of the DEI Advisory Group, which comprises IGB community members spanning the breadth of IGB, and the DEI Task Force, which gathers more individuals to take action on the Advisory Group's ideas and bring new initiatives to light.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | DEI

## Three projects chosen for the IGB DEI Awards

AUGUST 1, 2023



From left: Emily Terrill (left) and Eva Fischer; Middle: Melissa Flores (left) and Malavika Venu; Right: Christy Gibson.

go.igb.illinois.edu/DEIaward23

The Diversity, Equity, and Inclusion Task Force at the IGB have awarded three projects for their DEI initiatives. Each project was representative of the different facets of IGB's mission to bring science to society, and was awarded with \$4000.

The first project "Frogs in Class: Using amphibians for 'ribbiting' community engagement," was proposed by Eva Fischer's lab. The lab recognizes that science outreach serves as a powerful tool for enriching K-12 science education. Their project will educate participants from local K-12 schools about poison frogs and how to care for them, along with broader learning objectives on model systems and global climate change.

The second project, led by Melissa Flores and Malavika Venu from the Robinson lab, will create an inclusive space for IGB graduate students through programming that promotes a sense of belonging and provides tools to cultivate professional STEM identities. Events will include coffee and community-building lunches, a digital series on graduate student excellence and diversity, and a workshop on microaffirmations.

The third project is a collaboration between Academic Women in STEM, the IGB Postdoctoral Association, and Parkland College, titled "Beyond the R1: Providing Teaching Experiences for Women and Minorities at a Student-Serving/Teaching Institution." The teaching program will provide postdoctoral fellows, students, and professionals from international and historically underserved backgrounds an opportunity to learn about careers at community colleges. Through this program, the organizers hope that they can help the participants

### PEOPLE MENTIONED

**Eva Fischer**, assistant professor of evolution, ecology, and behavior (GNDP)

Gene Robinson, IGB Director (GNDP)

Melissa Flores, graduate student

Malavika Venu, graduate student
see themselves represented by more diverse scientists and educators and enhance diversity at community colleges.

## New committee for the IGB DEI Advisory Group announced

go.igb.illinois.edu/DEIAG23

At the forefront of pioneering research, the IGB is dedicated to addressing pressing societal challenges in areas such as energy, agriculture, medicine, and more. Solving these complex problems hinges on bringing together a diverse group of scientists with unique perspectives and backgrounds.

The IGB values diversity and inclusivity, and is committed to fostering an environment where everyone feels welcomed and respected. To this end, the IGB DEI Advisory Group was established in 2018 to help cultivate a more inclusive, diverse and inviting atmosphere within the IGB community. The DEIAG meets to formulate new DEI initiatives, and those initiatives are then entrusted to the DEI Task Force, which puts them into action. The combined efforts of the advisory group and task force have already led to many new programs, workshops, and seminars since their inception.

The IGB was pleased to announce the new members of the DEIAG: Hee Jung Chung, Aleks Ksiazkiewicz, Sierra Raglin, and Melissa Flores. The chair of the DEI Task Force, Sara Padron Haba, will also serve on the DEIAG, and act as a conduit between the two groups.

The DEIAG will be chaired by newly appointed Director's Faculty Fellow Jessica Brinkworth. As a Director's Fellow, Brinkworth will lead the DEIAG in examining the current DEI landscape at the IGB and proposing new initiatives, which will then be developed in partnership with the DEI Task Force.

#### PEOPLE MENTIONED

#### Hee Jung Chung, associate professor of molecular and integrative physiology (M-CELS)

#### Aleks Ksiazkiewicz,

associate professor of political science and Director of Graduate Studies (GSP)

Sierra Raglin, postdoctoral researcher (IGOH)

Melissa Flores, graduate student

Sara Pedron-Haba, research assistant professor of chemical and biomolecular engineering (RBTE)

Jessica Brinkworth, professor of anthropology (GNDP/IGOH)

FUNDED BY NSF

# Town hall spurs conversation and new ideas for promoting diversity, equity, and inclusion at the IGB

go.igb.illinois.edu/TownHall23

The IGB held a town hall meeting to introduce new changes to improve diversity and inclusion at the IGB. The meeting was led by Gene Robinson and guest moderator Kaamilyah Abdullah-Span, along with co-chairs of the DEI Task Force Julia Pollack



and Sara Pedron-Haba, who moderated questions submitted anonymously online.

"Today marks an important next step in the process to address concerns and improve conditions in the IGB so that everyone feels welcome and connected in every way possible to the important activities that are going on at this research institute," said Robinson in his welcoming address.

The Committee on Diversity (now the DEI Advisory Group), established in 2018, acts as an advisory committee that develops ideas for promoting a more inclusive community. The second committee, the DEI Task Force, established in 2020, is comprised of members of the IGB community, including staff and postdoctoral researchers. The DEI Task Force takes ideas from the Advisory Group and helps bring them into action. Since their inception, they have created multiple programs, workshops, and initiatives to diversify both the science and the scientists at the IGB, and address any inequities that those at the IGB still face.

Proposed changes discussed at the town hall included new DEI trainings for faculty and staff, beginning with theme leaders and office directors, exit surveys for postdocs, faculty and staff, new language in IGB faculty and theme appointment/reappointment letters, and a more transparent process for reporting grievances.

#### PEOPLE MENTIONED

Gene Robinson, IGB Director (GNDP)

Kaamilyah Abdullah-Span, Director of Campus Culture and Climate

**Julia Pollack**, IGB Creative Program Manager

#### Sara Pedron-Haba, research assistant professor of chemical and biomolecular engineering (RBTE)

## Wikipedia edit-a-thon event series seeks to increase STEM representation

go.igb.illinois.edu/Wiki23

Women have made significant contributions in STEM, and have become increasingly prevalent in the STEM community. However, their online visibility, particularly regarding their accomplishments and contributions to science, remains disproportionately low due to factors such as inherent bias. Wikipedia is the 5th most visited website in the world. In recent years it has emerged as a powerhouse of trusted information, largely due to the collaborative nature behind article creation and management on the platform. However, less than 20% of Wikipedia's pages feature women.

To address this disparity, Wikipedia edit-a-thon events have gained traction in universities across the world. These events provide scheduled times for groups to come together and create or edit Wikipedia pages for women and other underrepresented groups.



This fall, the IGB hosted a series of Wikipedia edit-a-thons. This initiative was spearheaded by the IGB DEI Task Force, a group dedicated to creating new programs and initiatives meant to increase dialogues and create change internally towards a more inclusive environment.

## The group was inspired by Jess Wade, who has written more than 1800 Wikipedia pages for minority scientists.

The edit-a-thon series spanned multiple sessions, providing participants with ample opportunities to collaborate and create new pages. Librarians from the ACES FUNK library assisted newcomers in creating Wikipedia pages, and provided suggestions for women, people of color, and other minorities to write about. The participants edited 83 articles, adding over 17,000 words, 233 references, and 22 images. The pages were subsequently viewed by more than 100,000 people.

#### PEOPLE MENTIONED

**Jess Wade**, physicist at Imperial College London

## Outreach and <u>Publ</u>ic Engagement

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The outreach programs introduce community members to transformative research and teach them about how IGB researchers use genomics to solve preeminent problems faced by local and global communities. These interactions help the public understand the work that goes into cutting-edge research and the results that come out of it.

#### — EST. 2009 —

The outreach team helps IGB to fully embody its motto: Where Science Meets Society.

By engaging with the public through programs and events, publications, and citizen science efforts, the team ensures that the work of IGB researchers continues to be relevant and impactful, a force for positive change in the wider world.



#### 2023 ANNUAL REPORT | IGB FEATURED STORIES | OUTREACH

# Genome Day brings the wonders of genetics and nature to life

DECEMBER 6, 2023



Stations at Genome Day. From left: Ecosystem blocks, Feedback, and Build-A-Bird.

go.igb.illinois.edu/GenomeDay23

From microorganisms and DNA extraction to poison frogs and lemon-scented ants, IGB's Genome Day brought science to life across a wide variety of scales. Families, students, science lovers, and local community members explored stations and activities led by IGB faculty, staff, and students.

The annual outreach event took place over two weekends, first at the Lincoln Square Mall and then at the Champaign Public Library. The mission of Genome Day is to communicate research across all fields of biology to the public in an accessible way and motivate people to get more involved in science.

An exciting part of Genome Day was the inclusion of multiple stations with live animals, such as Fun with Frogs and Abund-Ants, allowing the public to observe the behavior and adaptations of different species. Rebecca Carranza, a volunteer at the station, shared her experience at Genome Day.

#### 

"It was really fun! My favorite part was interacting with other community members who shared my love of insects. Seeing them get excited about cool ant facts was really rewarding."

PEOPLE MENTIONED

Rebecca Carranza, graduate student

Among the most popular stations for the younger attendees were Build-A-Bird and Delicious DNA. At Build-A-Bird, attendees built bird models and learned how different adaptations can help organisms in different environments. At Delicious DNA, volunteers helped everyone extract DNA from strawberries. Attendees then had the option to make necklaces with their DNA samples attached.

Throughout the sights and sounds of Genome Day—attendees asking volunteers questions, kids carrying around various scienceinspired crafts, people adjusting microscope lenses, giant Jenga blocks representing animals in a food web toppling over—one thing became clear: regardless of background or expertise level, science brings together communities around a common goal to further knowledge, understand the world around us, and appreciate the incredible discoveries made every day.

## New OLLI workshop focuses on genomics

go.igb.illinois.edu/OLLI23

Over the years, the Osher Lifelong Learning Institute has been partnering with the IGB and the Beckman Institute for Advanced Science and Technology to create several citizen-science programs for people over 50 who are curious about scientific research, but have never had the chance to try it. In 2023, OLLI featured a workshop called "What's in my blood? Genomics Testing and You."

Genomics-based tests are increasingly becoming a part of our lives, including detecting COVID-19 in our saliva, identifying early signs of cancer, assisting the police in solving crimes, and helping us discover our ancestry. The workshop series described how the information in our genomes—the collection of all the DNA instructions found in our cells—is decoded and used by technologies to detect specific genes.

"We work on state-of-the-art technologies and the participants represent the seniors in our community, who are very intelligent. Although they might not necessarily be scientists or engineers, they are curious about these things," said Brian Cunningham.

The 8-week course was offered over Spring 2023 and covered a basic introduction to DNA, the tools used for DNA sequencing, how genetic tests are carried out, how crime is solved through testing, what cancer markers are used for diagnosis, mRNA technology, and how pathogens are detected. Following these sessions, the participants participated in hands-on demonstrations of instruments that have been invented and developed at the university.



OLLI members at a workshop.

#### PEOPLE MENTIONED

#### Brian Cunningham, professor of electrical and computer engineering (CGD leader/ MMG)

# Pollen Power camp inspires new generation of budding young scientists

go.igb.illinois.edu/PollenPower23

Everyone knows about space camp, but have you heard of plant camp? Pollen Power summer camp, hosted by the IGB, offers local middle schoolers a unique experience filled with plant science-based summer fun.



Pollen Power has taken place every summer since 2013, with the goal of exposing middle schoolers to topics in plant biology while providing strong female mentorship, especially to underrepresented groups in STEM. Throughout the week, campers participate in a variety of activities led by members of the IGB and CABBI, aimed at teaching them not only about plants and pollinators, but also about working in a team, communication, and how to look at the world through the eyes of a scientist.

During the week they foraged for leaves, flowers, and insects around campus, examined their findings under the microscope, and then made art using their foraged finds. Campers were also given tours of state-of-the-art campus labs and facilities in the IGB Core, and the ACES plant biology, and Conservatory greenhouses.

Campers were also placed into groups that were each assigned a staff member from Franklin STEAM Academy to closely mentor them. Together, they designed week-long experiments to test the growth rate of cress seeds under various conditions that culminated into a presentation at the end.

"At Pollen Power, students take something they consider an 'ordinary everyday thing' in nature and learn to see it in a new light, leaving them feeling like scientists," said Sarah Choi, the lead organizer of the camp. PEOPLE MENTIONED

**Sarah Choi**, IGB Outreach and Education Coordinator

# STEAM TRAIN pulls into the station for another successful year

go.igb.illinois.edu/STEAM23

An engineered bazooka designed to launch candy, a 3D-printed novel board game, an ecological experiment with fish, and a magnetically powered trebuchet. You may guess that these were all projects designed by undergraduate or graduate students. However, these projects were



the curiosity-driven creations of middle schoolers as part of the STEAM (Science, Technology, Engineering, Arts, and Mathematics) TRAIN (Transdisciplinary Research Across Institutional Near-peers) program, which just completed its third successful year.

STEAM TRAIN, which partners the University of Illinois Urbana-Champaign with the Champaign Franklin STEAM Academy, is organized by Daniel Urban, Zanne Newman, and Melinda Tidrick, and is funded by the University of Illinois' Community Research Partnership Program. The program encourages independent, student-inspired research by allowing middle school students to dream up any kind of science or engineering project they want. Mentors in the program then help guide the design of the project.

At the end of the semester, the teams gathered to show off their final creations or research findings. The teams not only presented their findings, but also discussed potential real work applications of their work, the limitations, and the insights they gained.

"Working with the kids for STEAM TRAIN is always a blast," said Danny Ryerson. "For many of the kids, this is their first opportunity to take charge of a science project and decide what they want to research. This can lead to really driven researchers and some amazing results."

## Students selected for the 2023 Woese Research Scholar Program

go.igb.illinois.edu/WURS23

Tyler Smith and Catherine Koterba, both undergraduates in molecular and cellular biology, were selected as IGB Woese Undergraduate Research Scholars in the summer of 2023.

As a part of the Gaj lab, Smith focused on the gene GPR3 that, when upregulated, leads to the formation of more amyloid beta plagues, which are one of the key causes of Alzheimer's disease. Over the summer Smith focused on the underlying molecular mechanisms using immunohistochemistry to get an estimate of expression levels of GPR3 across treatments in mice. He also performed an additional staining targeting the amyloid beta plaques, to identify if the treatment reduced buildup of common Alzheimer's symptoms. Although the analysis of these results are still ongoing, Smith's work has established a proof of concept for this potential treatment.

Koterba explored the coevolutionary dynamics between the archaea Sulfolobus islandicus, found in hot springs, and one of its common viruses, Sulfolobus super-elliptical virus. To better understand the



Tyler Smith, left, and Catherine Koterba

#### PFOPLE MENTIONED

Tyler Smith, undergraduate in molecular and cellular biology

Catherine Koterba, undergraduate in molecular and cellular biology

Daniel Urban. IGB Senior **Outreach Activities** Coordinator

Zanne Newman, Franklin's Magnet Site Coordinator

Melinda Tidrick, teacher at University Laboratory High School

Danny Ryerson, IGB Outreach Activities Coordinator

infection mechanisms employed by SSeV, Koterba first infected *S. islandicus* with SSeV in the lab. She then verified that there was a viral infection using the polymerase chain reaction. Following this, Koterba quantified the impacts of SSeV infection on host cell growth. Currently, Koterba plans to identify which genetic mutations might be related to viral resistance in *S. islandicus* and continue to look at samples under the microscope to explore how SSeV influences host morphology. These findings will provide crucial insight into the mechanisms underlying SSeV infection and their evolutionary consequences.

# Genomics for Faith connects scientists and faith members in the community

go.igb.illinois.edu/G4Faith23

Scientific advancements in the area of genomics research continue to penetrate nearly all areas of society. Yet most of the public do not have access to the knowledge necessary to understand how this research may affect them. To this end, Genomics for<sup>™</sup>, was developed as a series of educational programs designed to teach basic concepts in biology.



A new program within the series debuted in May 2023 at the Channing-Murray Foundation, where a crowd of scientists, faith leaders, and faith-holding members of the community gathered for a discussion regarding the definition of life and death. Participants were able to ask questions to a panel of community members with diverse backgrounds in research, health, and medicine. The panel and audience members shared unique perspectives on the topics, which stemmed from various experiences, faiths, and backgrounds in science.

The second workshop occurred in September 2023 at the Bahá'í Center in Urbana, where the participants discussed gene editing. They were broken into discussion groups and were given a chance to ask a panel of scientists any questions they had. The panel addressed misconceptions and fears of the technology being misused, and detailed how they were each training the students in their labs to utilize gene editing tools safely and ethically.

Currently, the IGB is planning future Genomics for Faith sessions to branch into other topics of interest that lean more heavily into genomics research. Members of all faith communities are welcome to attend in the future, and sessions are free.

## New program aims to foster collaborations among mid-career faculty

go.igb.illinois.edu/TSLP23

The Team Science Leadership Program offered by the IGB consisted of a series of workshops that brought together faculty from all over campus. The workshops were tailored to mid-career faculty, and focused on leadership training, communication skills, networking, and community building. The ultimate goal of the program was to empower faculty to develop new research ideas and collaborations, particularly between disciplines that might otherwise never have the opportunity to interact.

"Nationwide there is increasing interest in focusing on the professional development of mid-career faculty, and this program addresses this need for our faculty from the unique perspective of multi-disciplinary team science, which is the IGB's calling card," said Gene Robinson.

James O'Dwyer was the driving force behind the program's creation. O'Dwyer explained that after the COVID-19 pandemic, many faculty were eager to renew pre-pandemic connections and build new ones.

"This program builds on what the IGB does best team science at a large scale—to develop new skill sets among our mid-career faculty," said O'Dwyer. "We hope that the program will help build community and enhance the leadership skill sets among our faculty, forming the next generation of leaders in team science at the IGB and Illinois."

After a successful trial run in spring 2023, the TSLP was established as a certificate course in Fall 2023. The workshops were led by experts who discussed different aspects of team science. Experts included experienced faculty on campus, and program officers from federal agencies and private foundations.

#### PEOPLE MENTIONED

James O'Dwyer, associate professor of plant biology (CAIM)

Gene Robinson, IGB Director (GNDP)

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# IGB Numbers from FY23



**Economic Development** 28 24 3 4 Disclosures Patent Licenses Patents FY23 Applications Optioned Issued FY23 FY23 FY23 44 total 39 total 203 total 245 total

#### ∧ Patents:

Transgenic Plants With Increased Photosynthesis Efficiency And Growth; Stephen Long

Queen Monitoring Cage System; Gene Robinson

Saliva-Based Molecular Testing For SARS-CoV-2; Marty Burke, Paul Hergenrother, Tim Fan, Christopher Brooke

### **Publications**

783 papers published, 7 in Science and Nature

To view the full list of publications across IGB's research themes, please visit our website.

igb.illinois.edu

#### ∧ Science

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Our work is made possible by several funding agencies. We are grateful for their support and look forward to our future endeavors.



## **Outreach and Public Engagement**

# The outreach team supports the institute's deep commitment to communicate its research with the public and promote scientific thinking to encourage a new diverse generation of scientists and science-informed citizens.

	Geographic Reach			Primary target age (yrs)				Participant Hours (hrs)		
Events	Campus	Community	Beyond	0-4	5-10	11-20	21+	500	1000	1500
								Corr	munity/F	amily Events
Art of Science										
Birds, Bees & Bats										
Gameday Genomics										
Genome Day										
Homecoming parade										
Science at the Market										
Science Café										
Trivia night										
									K	12 Education
School/group visits										
Field Trips										
STEAM TRAIN										
Pollen Power Camp										
								Prof	essional I	Development
Genomics For										
Professional Skills for Careers in Biosciences										
	Campus	Community	Beyond	0-4	5-10	11-20	21+	500	1000	1500

igb.illinois.edu/outreach

### Awards

## We are proud to celebrate the achievements and recognition of the members of our institute.

**Lisa Ainsworth**, research plant physiologist, USDA Agricultural Research Service; adjunct professor of plant biology and crop sciences (CABBI/GEGC), received Woolhouse Lecture Award, Society of Experimental Biology.

**Rashid Bashir,** Dean of The Grainger College of Engineering and Professor of Bioengineering (CGD/M-CELS), elected to National Academy of Medicine.

**Alison Bell**, Professor of Evolution, Ecology, and Behavior (GNDP leader), appointed Center for Advanced Study (CAS) Associate; received Excellence in Guiding Undergraduate Research award, Office of the Provost.

Ashwini Bedekar, Research Scientist in the Rao lab (BSD/CABBI), received 2023 Innovator Award, Association for Women in Science.

**Isaac Cann**, Professor of Animal Sciences and of Microbiology (MME), elected Fellow of the American Academy of Microbiology.

**Kathryn Clancy**, Professor of Anthropology (EIRH), appointed Center for Advanced Study Associate.

**Brian Cunningham**, Intel Alumni Endowed Chair Professor and Professor of Electrical and Computer Engineering (CGD Leader/MMG), appointed to Editorial Board of Scientific Reports; received 2023 Michael S. Feld Biophotonics Award.

Wawrzyniec Dobrucki, Associate Professor of Bioengineering (RBTE), named inaugural Neil and Carol Ruzic Faculty Scholar, Carle Illinois College of Medicine.

**Jodi Flaws**, Professor of Comparative Biosciences (EIRH co-leader), received Society for the Study of Reproduction Research Award.

**Mattia Gazzola**, Assistant Professor of Mechanical Science and Engineering (M-CELS), appointed Center for Advanced Study Fellow.

**Kaiyu Guan**, Associate Professor of Natural Resources and Environmental Studies (CABBI), received James B. Macelwane Medal, American Geophysical Union; named University Scholar.

**Sara Pedron Haba**, Research Assistant Professor of Chemical and Biomolecular Engineering (RBTE), elected to American Association for Cancer Research Women in Cancer Research Council.

**Cecilia Leal**, Associate Professor of Materials Science and Engineering (M-CELS), named University Scholar.

**Stephen Long**, Ikenberry Chair of Crop Sciences and Plant Biology (BSD/CABBI/GEGC), received honorary doctoral degree, University of Essex.

**Ripan Malhi**, Professor of Anthropology (CIS co-leader/GNDP/GSP/IGOH), appointed Center for Advanced Study (CAS) Associate.

**Helen Nguyen**, Ivan Racheff Professor in Civil and Environmental Engineering (IGOH), named Editor-In Chief of GeoHealth.

**Jason Ridlon**, Associate Professor of Animal Sciences (MME), received 2023 E.L.R. Stokstad Award, American Society for Nutrition.

**M. Taher Saif**, Edward William and Jane Marr Gutgsell Professor of Mechanical Science and Engineering (M-CELS/RBTE), elected Fellow, American Association for the Advancement of Science.

**Charles Schroeder**, James Economy Professor of Materials Science and Engineering and Professor of Chemical & Biomolecular Engineering (BSD), received 2023 Beckman Institute Vision and Spirit Award; elected Fellow, American Association for the Advancement of Science.

**Shannon Sirk**, Assistant Professor of Bioengineering (MME), received Trailblazer R21 Award, NIH National Institute of Biomedical Imaging and Bioengineering.

**Gregory Stephanopoulos**, H. Dow Professor of Biotechnology and Chemical Engineering at MIT and IGB Science Advisory Board member, elected to National Academy of Sciences.

**Cari Vanderpool**, Professor and Associate Head of Microbiology (MME co-leader/IGOH), elected College of Liberal Arts & Sciences Associate Dean for Research.

Huimin Zhao, Steven L. Miller Chair in Chemical and Biomolecular Engineering (BSD leader/CABBI/CGD/MMG), received 2023 D.I.C. Wang Award for Excellence in Biochemical Engineering, American Institute of Chemical Engineers' Society for Biological Engineering.

To view the full list of awards received by the members of our institute, please visit our website.

igb.illinois.edu/awards

#### ACRONYMS

BCRF

Breast Cancer Research Foundation

#### CDC

Centers for Disease Control and Prevention

DOD

of Defense DOE

U.S. Department of Energy

**EPA** U.S. Environmental Protection Agency

**FDA** U.S. Food and Drug Administration

**FFAR** Foundation for Food and Agriculture Research IGB Carl R. Woese Institute for Genomic Biology

IFAW International Fund for Animal Welfare

**NIH** National Institutes of Health **NSF** National Science Foundation

**USDA** U.S. Department of Agriculture

**USFWS** U.S. Fish and Wildlife Service

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