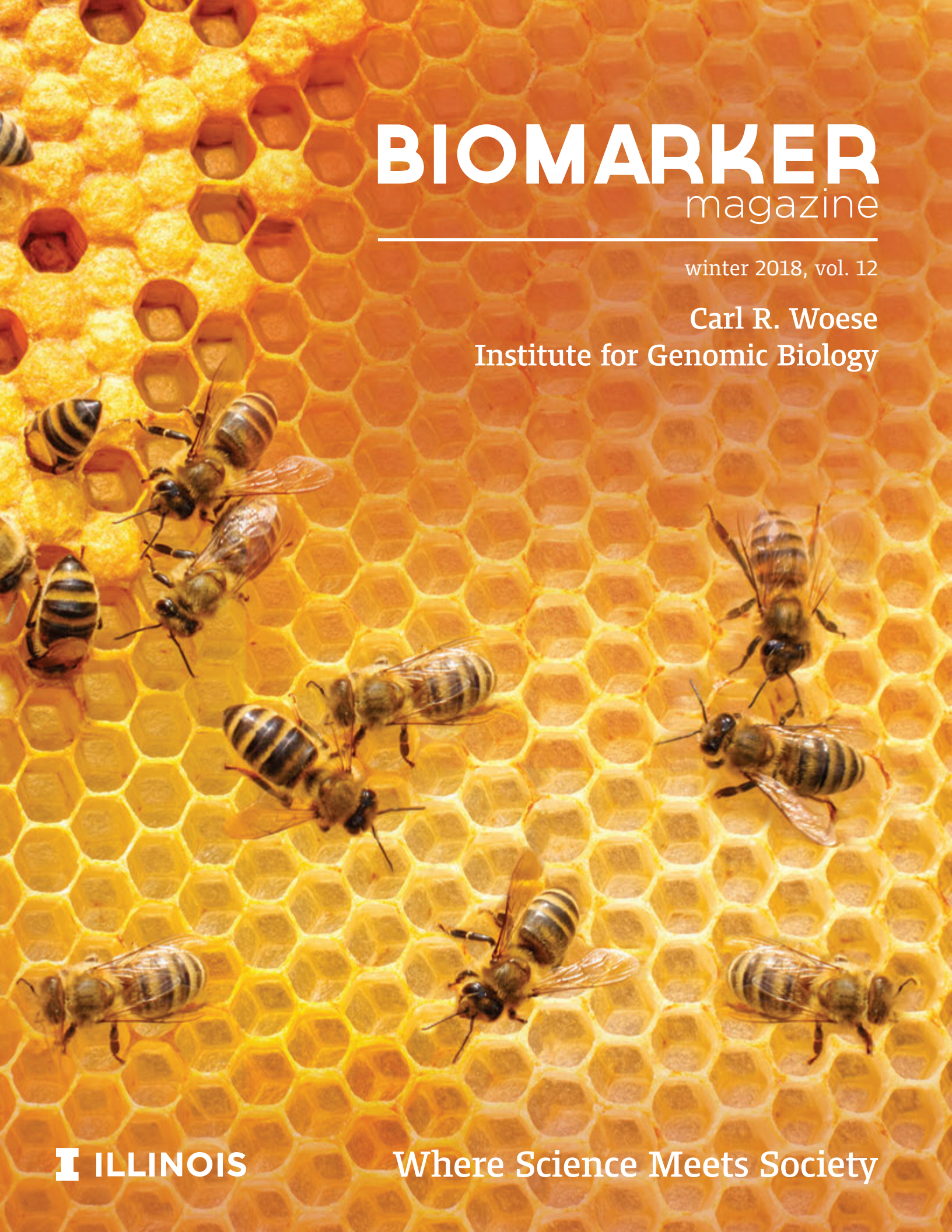

# BIOMARKER magazine

winter 2018, vol. 12

## Carl R. Woese Institute for Genomic Biology

ILLINOIS

Where Science Meets Society

**“Every individual matters. Every individual has a role to play. Every individual makes a difference.”**

—Jane Goodall

## IGB Themes

| | |
|---|---|
| ACPP | Anticancer Discovery from Pets to People |
| BCXT | Biocomplexity |
| BSD | Biosystems Design |
| CGRH | Computing Genomes for Reproductive Health |
| GEGC | Genomic Ecology of Global Change |
| GNDP | Gene Networks in Neural & Developmental Plasticity |
| IGOH | Infection Genomics for One Health |
| MME | Microbiome Metabolic Engineering |
| MMG | Mining Microbial Genomes |
| ONC-PM | Omics Nanotechnology for Cancer Precision Medicine |
| RBTE | Regenerative Biology & Tissue Engineering |

## IGB Strategic Partnerships

| | |
|---|---|
| CABBI | Center for Advanced Bioenergy and Bioproducts Innovation |
| CNLM | Center for Nutrition, Learning, and Memory |
| EBI | Energy Biosciences Institute |

## IGB Funding Agencies

| | |
|---|---|
| DOE | United States Department of Energy |
| NASA | National Aeronautics and Space Administration |
| NCSA | National Center for Supercomputing Applications |
| NIH | National Institutes of Health |
| NSF | National Science Foundation |
| USDA | United States Department of Agriculture |

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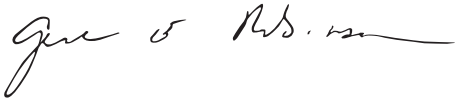
# Director's Message

> "Biological communities are found at every scale and in every domain of life, and the study of one type of community can enhance understanding of others, including our human societies."



Gene E. Robinson

DIRECTOR, CARL R. WOESE
INSTITUTE FOR GENOMIC BIOLOGY

## THE SCIENCE OF THE COLLECTIVE

Just a few decades ago, the first living organism on earth was envisioned as a single cell, an accidentally assembled membrane enclosing a bare minimum of molecular machinery required for replication. Our current understanding of the earliest form of life emphasizes the collective rather than the individual: a mishmash of collaborating, competing, self-replicating molecules with no clear boundaries.

Biological communities are found at every scale and in every domain of life, and the study of one type of community can enhance understanding of others, including our human societies. The strength, resilience and complex environment of collectives and communities is a recurring theme of this year's edition of *Biomarker*, in both the stories of our research accomplishments and of our opportunities to engage with the public.

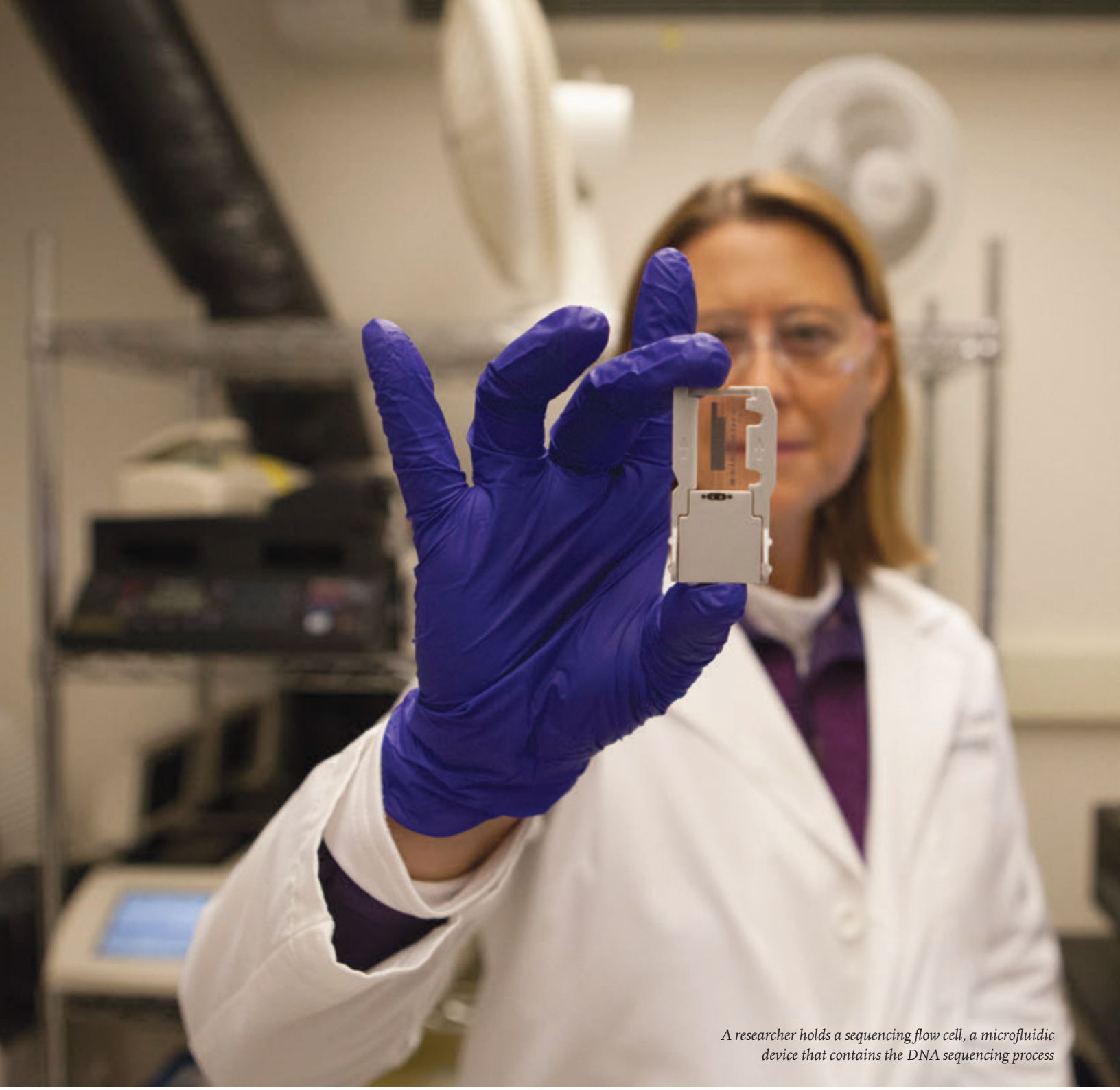
Research from microbes and honey bees reveals that division of labor within a group promotes a diversity of roles and capabilities that allows for more flexible and robust survival strategies. Although separated by evolutionary time on a vast scale, the social networks of resource gathering and consumption in these two types of communities have some striking parallels in their resilience to change.

Communities are sometimes able to accomplish tasks on a scale not possible for individuals. Our story on the conception of the Earth BioGenome Project marks a global research community's ambitious, urgent goal to sequence 1.5 million species representing the diversity of eukaryotic life on Earth. Such a vast endeavor would not be possible without a strong consortium of researchers and institutions to take it on.

In the study of human communities, a collaborative partnership between researchers and groups of interest results in more responsibly-conducted work and stronger science. This year, participants in the Summer internship for INdigenous Peoples in Genomics shared a comprehensive framework for conducting respectful and ethical genomic research in Indigenous communities by engaging with and involving community members.

Other stories from the research community here at the Carl R. Woese Institute for Genomic Biology (IGB) include the successful development of drought-resistant crop plants; new insights into the migratory pathways of humans and their canine companions into the Americas; new strategies for gene editing in yeast; and the creation of a vast library of new compounds to be screened for pharmaceutical potential.

The research we conduct at the IGB is made possible by the collaborative research community that we have worked hard to establish. Thanks to the networks of relationships we have fostered across departments and disciplines, we can span greater breadths of scientific inquiry and tackle larger challenges than would be possible for a single researcher or laboratory working in isolation. Like life itself, while we may explore the benefits of individual action, we return to the collective for our most ambitious endeavors; we continue to believe in the strength of our particular community to do great things.



*A researcher holds a sequencing flow cell, a microfluidic device that contains the DNA sequencing process*

# Decoding the true book of life:

## Earth BioGenome Project aims to sequence genomes of 1.5M species

**"Our task now is to resynthesize biology; put the organism back into its environment; connect it again to its evolutionary past; and let us feel that complex flow that is organism, evolution, & environment united."**

This quote from IGB's visionary namesake, Carl Woese, captures the promise and fascination of an ambitiously holistic approach to biology. It was written in the early days of the genomic era of biology, a time characterized by a shift from research that focused on the singular—the activity of a single gene or the structure of a single protein—to the collective—the actions of many genes influencing one another or the interactions among proteins. This shift was inspired by the rapidly improving capability to sequence, analyze, and manipulate genomes. In a dramatic demonstration of how far the "New Biology" has come, Woese's words were recently used to open a new proposal by an international consortium of scientists to sequence, catalog and analyze the genomes of all known eukaryotic species on the planet.

### A grand proposal for a new era of science

Eukaryotes include all multicellular life on the planet, as well as single-celled fungi, algae and protists, an estimated 10-15 million species in all; the team proposes to sequence 1.5 million of these that have been discovered and described. The undertaking is projected to take 10 years, cost $4.7 billion and require more than 200 petabytes of digital storage capacity.

The proposed initiative, named the Earth BioGenome Project (EBP) and described in a paper in the *Proceedings of the National Academy of Sciences*, would require the cooperation of governments, scientists, citizen scientists and students from around the globe. A similar initiative, the Earth Microbiome Project, has enlisted the support of more than 500 scientists to sequence bacterial and archaeal genomes.

"For the first time in history, it is possible to efficiently sequence the genomes of all known species and to use genomics to help discover the remaining 80 to 90 percent of species that are currently hidden from science," the authors wrote.

The reasons for undertaking such an ambitious project are many, said Swanlund Professor of Entomology and IGB Director Gene Robinson (GNDP), a leader of the proposed effort.

"Genomics has helped scientists develop new medicines and new sources of renewable energy, feed a growing population, protect the environment and support human survival and well-being," Robinson said. "The Earth BioGenome Project will give us insight into the history and diversity of life and help us better understand how to conserve it."

Robinson co-chairs the EBP Working Group with Professor of Evolution and Ecology Harris A. Lewin, former IGB Director and now Vice Chancellor of Research at the University of California, Davis; and W. John Kress, a research botanist and curator at the Smithsonian Institution.

### New technologies expand the scope of genomic exploration

The authors of the EBP proposal compare it to the Human Genome Project, an international scientific research project from 1990 to 2006 that cost roughly $4.8 billion in today's dollars and generated an estimated return-on-investment ratio of 141-to-1.

The Human Genome Project "involved a workforce of more than 47,000 people generating nearly $1 trillion in economic activity," the authors wrote. They suggested that as the biodiversity targeted by their proposed project is globally distributed, the effort and resulting positive economic impact could be as well.

Scientists have so far sequenced fewer than 15,000 species, most of them microbes. However, the cost of genome sequencing has fallen to about $1,000 for an average-sized vertebrate genome and is expected to continue to drop. New technologies, including terrestrial and underwater robots, and an increase in citizen-scientist initiatives and consortiums of scientists focusing on specific groups of organisms are speeding the process of data collection and analysis.

The EBP project will support and promote international protocols for data storage and sharing. A coordinating council with members from Africa, Australia, Brazil, Canada, China, the European Union and the United States will head a global network of collaborators. The council also will include representatives of several current large-scale genomics projects, including the Global Genome Biodiversity Network, the Global Invertebrate Genomics Alliance, the i5K Initiative to Sequence 5,000 Arthropod Genomes and the Genome 10K Project.

### Conserving global biodiversity, ecologically and digitally

A driving force for the project is the threat of extinction of many known and unknown species created by global climate change and human exploitation of ecosystems. Authors of the proposal argued that the sooner the project begins, the more can be done to protect valuable biodiversity. Insight from genomic data could suggest new and effective conservation methods; a genomic record might eventually be used to restore damaged ecosystems.

"The Earth BioGenome Project will make use of existing resources and institutions whose mission is to procure and preserve the world's biodiversity," Robinson said. "For example, the world's botanical garden collections hold more than a third of all plant species . . . The greatest legacy of the EBP will be a complete digital library of life that will guide future discoveries for generations."

The group also aims to establish a worldwide network of specialized research facilities to focus specifically on the impact of global climate change.

"The EBP also will work to establish bio-observatories that use genomics to obtain a baseline understanding of how climate change affects global biodiversity," they wrote, suggesting that these facilities could also become regional resources for the promotion of scientific public engagement and the development of new genomic technologies.

"The EBP is arguably the most ambitious proposal in the history of biology," the authors concluded. "[The resulting] knowledge will guide future discoveries for generations and may ultimately determine the survival of life on our planet." ■

*Stephen P. Long, a professor of crop sciences and of plant biology (center), with postdoctoral researchers Johannes Kromdijk, (left) and Katarzyna Glowacka (right)*

# Scientists engineer crops to conserve water, resist drought

**AGRICULTURE ALREADY MONOPOLIZES** 90 percent of global freshwater, yet production still needs to dramatically increase to feed and fuel this century's growing population. For the first time, scientists have improved how a crop uses water by 25 percent without compromising yield by altering the expression of one gene that is found in all plants, as reported in *Nature Communications*.

The research is part of the international research project Realizing Increased Photosynthetic Efficiency (RIPE), which is supported by the Bill & Melinda Gates Foundation, the Foundation for Food and Agriculture Research, and the U.K. Department for International Development.

"This is a major breakthrough," said RIPE Director Stephen Long, Ikenberry Endowed Chair of Plant Biology and Crop Sciences (BSD/CABBI/GEGC). "Crop yields have steadily improved over the past 60 years, but the amount of water required to produce one ton of grain remains unchanged—which led most to assume that this factor could not change. Proving that our theory works in practice should open the door to much more research and development to achieve this all-important goal for the future."

The international research team increased the levels of a photosynthetic protein (PsbS) to conserve water by tricking plants into partially closing their stomata, the microscopic pores in the leaf that allow water to escape. Stomata are the gatekeepers to plants: When open, carbon dioxide enters the plant to fuel photosynthesis, but water is allowed to escape through the process of transpiration.

"These plants had more water than they needed, but that won't always be the case," said co-first author Katarzyna Glowacka, a postdoctoral researcher who led this research at the IGB. "When water is limited, these modified plants will grow faster and yield more—they will pay less of a penalty than their non-modified counterparts."

In real-world field trials, the team improved the plant's water-use-efficiency—the ratio of carbon dioxide entering the plant to water escaping—by 25 percent without significantly sacrificing photosynthesis or yield. The carbon dioxide concentration in our atmosphere has increased by 25 percent in just the past 70 years, allowing the plant to amass enough carbon dioxide without fully opening its stomata.

"Evolution has not kept pace with this rapid change," Long said. "So scientists have given it a helping hand."

Four factors can trigger stomata to open and close: humidity, carbon dioxide levels in the plant, the quality of light, and the quantity of light. This study is the first report of hacking stomatal responses to the quantity of light.

PsbS is a key part of a signaling pathway in the plant that relays information about the quantity of light. By increasing PsbS, the signal says there is not enough light energy for the plant to photosynthesize, which triggers the stomata to close because carbon dioxide is not needed to fuel photosynthesis.

This research complements previous work, published in *Science*, showing that increasing PsbS and two other proteins can improve photosynthesis and increase productivity by as much as 20 percent. Now the team plans to combine the gains from these two studies to improve production and water use by balancing the expression of these three proteins.

For this study, the team tested their hypothesis using tobacco, a model crop that is easier to modify and faster to test than other crops. Now they will apply their discoveries to improve the water-use-efficiency of food crops and test their efficacy in water-limited conditions.

"Making crop plants more water-use efficient is arguably the greatest challenge for current and future plant scientists," said co-first author Johannes Kromdijk, a postdoctoral researcher at the IGB. "Our results show that increased PsbS expression allows crop plants to be more conservative with water use, which we think will help to better distribute available water resources over the duration of the growing season and keep the crop more productive during dry spells." ■

**"Making crop plants more water-use efficient is arguably the greatest challenge for current and future plant scientists."**

Additional findings to come out of the RIPE project this year included the finding that cassava, a staple crop for over one billion people across 105 countries, has received little attention compared to popular crops like corn and soybeans. Researchers reported in *Food and Energy Security* that breeding cassava has helped the crop withstand pests and disease, but it yields no more today than it did in 1963. Genetic engineering will be required to improve cassava's photosynthesis, a major hurdle for scientists going forward.

In another study, RIPE researchers used a novel screening strategy to identify a more efficient form of Rubisco, an enzyme involved in fixing carbon dioxide en route to creating plant biomass in photosynthesis. The report, published in the *Journal of Biological Chemistry*, showed researchers could improve Rubisco's efficiency and its ability to differentiate carbon dioxide from oxygen. The researchers hope to make similar tweaks to improve the enzyme in crops and increase their growth and yield.


# Respect Indigenous ancestors:

## Scholars urge community engagment

**A RECENT ARTICLE IN THE JOURNAL** *Science* provided guidance for those intending to study ancient human remains in the Americas. The paper, written by Indigenous scholars and scientists and those who collaborate with Indigenous communities on studies of ancient DNA, offers a clear directive to others contemplating such research: First, do no harm.

Scientists studying ancestral remains have similar obligations to those that bind researchers working with living human subjects, the authors wrote. The descendants or people affiliated with those who lived hundreds or thousands of years ago must be consulted before their ancestors are disturbed. Even in cases where the remains were collected long ago and moved far from their original burial place, and even when the surviving lineages are in doubt, scientists ought to consult Indigenous groups living on the land or claiming ancestral ties to the region where the ancestors were found, the authors said.

"Right now, there are inconsistent or no regulations for working with ancient ancestors," said Associate Professor of Anthropology Ripan Malhi (CGRH/RBTE), a co-author of the report. "And there are no requirements for working with descendant or affiliated communities, even though new scientific findings


*Participants of the SING 2018 workshop*

relating to their ancestors can have serious implications for them."

Malhi partners with Indigenous communities to study ancient DNA from individuals found on lands where their descendants still live. Malhi, along with Indigenous scientists, scholars and other scientists who work with Native American and First Nations communities, worked to create the Summer internship for INdigenous Peoples in Genomics (SING), which trains Indigenous scientists in genomics techniques and explores ethical concerns. Not consulting Indigenous communities before analyzing ancient DNA potentially harms those groups, said graduate student Alyssa Bader, who was also a co-author.

"Genetic analyses can reveal information not just about the ancestors, but also their descendants. If genetic variants associated with specific diseases are identified in ancestors, for example, this can influence how we think about disease susceptibility in the descendant community—and that community could be stigmatized," she said.

New findings also may interfere with ongoing treaty negotiations, she said.

"For Indigenous communities involved in negotiating land claims or repatriation, new genetic findings could either bolster or complicate those claims," she said.

Studying ancient DNA without consulting descendant communities is also a missed opportunity, said Concordia University professor Jessica Bardill, the lead author of the article.

"The engagements we highlight show that collaboration with communities not only strengthens the analysis but also can allow for better questions to be asked in the research, informed by community narratives about the ancestors, their lands and their relationships," she said.

For these and other ethical and practical reasons, Malhi said, it's in a scientist's interest to identify and locate potentially affected groups, consult with them about the research and invite them to join the effort, thereby improving the scientist's understanding of the context in which the ancient peoples lived. It also allows Indigenous communities to guide the science and ask research questions that are of interest to them.

"Engaging communities at the outset is critical for understanding their concerns or questions about research involving ancient relatives. Without feedback from the community, scientific interpretations remain one-sided and inherently biased," said Nanibaa' Garrison, a bioethics professor at Seattle Children's Research Institute and the University of Washington School of Medicine, and a co-author of the article.

The NIH and NSF supported this work. ■


*Observations of laboratory-grown microbial communities can provide insights into ecosystem dynamics*

# The way microbes eat could explain their diverse yet stable communities

**A MATHEMATICAL MODEL CREATED BY** IGB researchers could help scientists better understand an intriguing characteristic of microbial communities: their ability to achieve stability despite being so diverse.

Microbial communities are groups of microorganisms that exist in various environments. Though these communities are complex and diverse, they are able to form stable ecosystems.

Stability can be defined as how well the community handles change. Stable communities can resist a change in the nutrient supply or an invasion of a new species. Less stable communities are prone to change in the face of these disruptions.

Sergei Maslov (BCXT/CABBI), a Bliss Faculty Scholar and Professor of Bioengineering, and Akshit Goyal, a visiting scholar from the Simons Centre for the Study of Living Machines at NCBS in Bengaluru, India, previously collaborated on a predictive model to measure microbial community stability based on an economic concept called the "stable marriage problem." They recently created a mathematical model to further understand how microbial communities function and maintain stability.

Their work, published in P*hysical Review Letters*, addresses three signature aspects of microbial communities: diversity, stability, and reproducibility, which is how often a particular species is present in a community.

The goal of their model was to understand which species are universally shared in microbial communities and which species are unique. A key ingredient in their model was a process known as cross-feeding. Microbes consume nutrients and then excrete metabolic byproducts, which return to the shared space of the microbial community and are consumed by other microbes.

They studied these levels of consumption and the ecosystem's maturity, which are both crucial in microbial communities' ability to function.

"We are trying to understand what makes particular states stable, and how many such stable states are out there," Maslov said. "What is the range of perturbations that a state can tolerate before changing it to something else or collapsing altogether?"

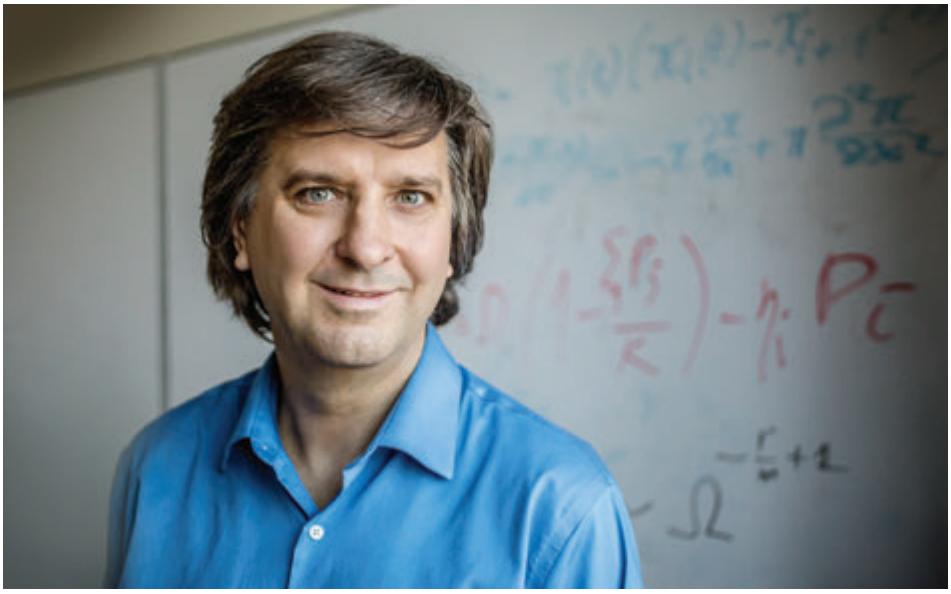
This work has implications for larger ecosystems throughout the world.

"Obviously we want to understand stability from the standpoint that we are perturbing the environment in an unprecedented way," Maslov said. "We want to understand how far we can push before everything collapses."

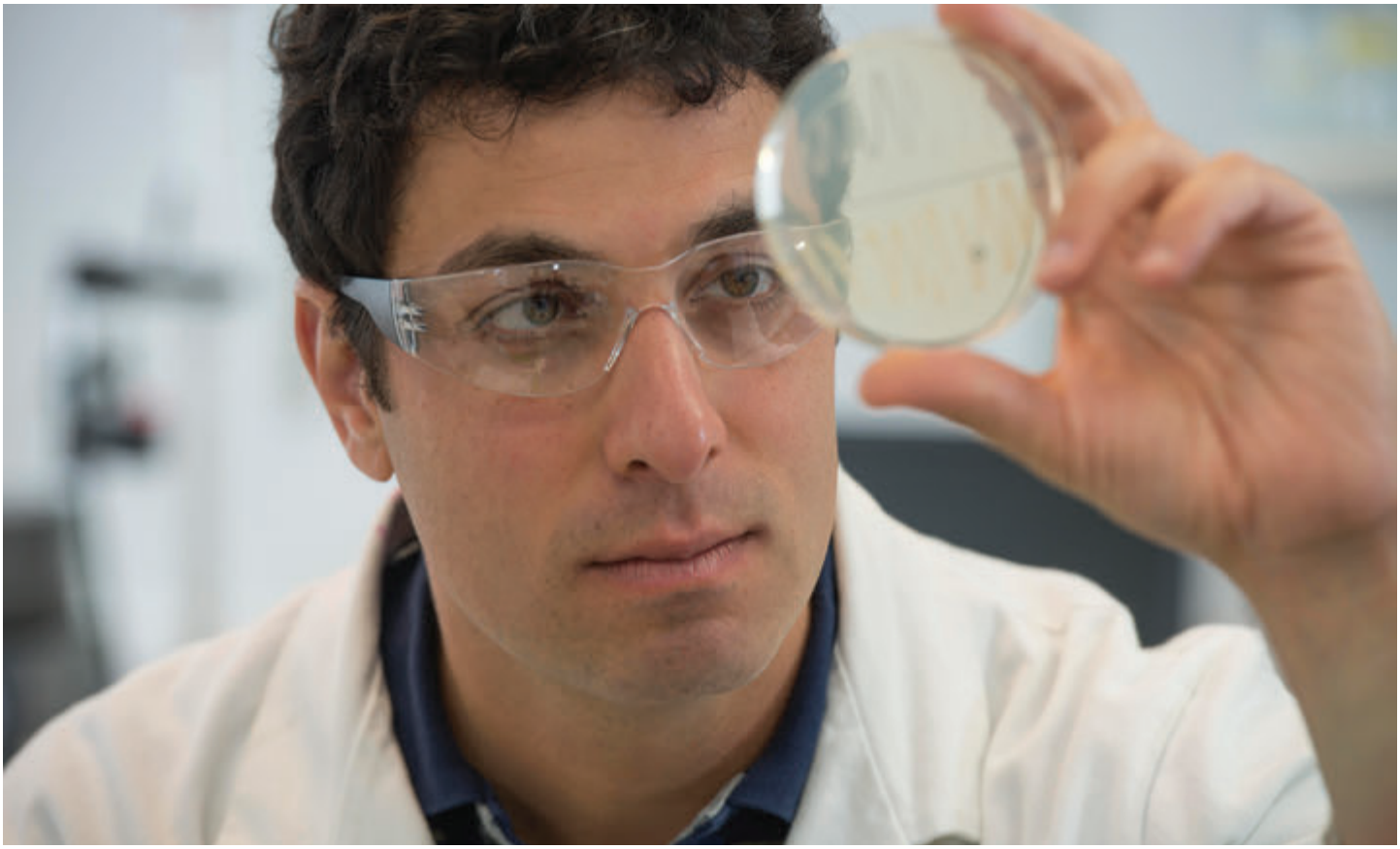
If scientists can understand this better, they can one day learn how to control microbial ecosystems. For example, a soil microbiome could perhaps be changed to a different state by adding microbes or nutrients. But because the systems are so complex and diverse, this is currently impossible.

"That's why our holy grail, in this and future work, is to be able to predictably and reliably control the transitions of the ecosystem from the state it is in to the state we want it to be," Maslov said. "We want to be able to do it without actually having some collapse."

The work was supported by the Simons Foundation and the Infosys Foundation. ■



*Sergei Maslov, Bliss Faculty Scholar and Professor of Bioengineering at the University of Illinois*



*Ali Tavassoli, Professor of Chemical Biology at University of Southampton*

# Study yields million-plus new compounds, pharmaceutical potential

**RESEARCHERS SAY THEY CAN NOW** produce a vast library of unique cyclic compounds, some with the capacity to interrupt specific protein-protein interactions that play a role in disease. The new compounds have cyclic structures that give them stability and enhance their ability to bind to their targets.

The work, reported in the journal *Nature Chemical Biology*, also revealed that one of the newly generated compounds interferes with the binding of an HIV protein to a human protein, an interaction vital to the virus's life cycle.

Most drug-discovery efforts focus on disease-inducing interactions in enzymes and proteins that involve classic "lock-and-key" mechanisms, said Richard E. Heckert Endowed Chair in Chemistry and Howard Hughes Medical Institute Wilfred van der Donk (MMG), who co-led the study with University of Southampton Professor of Chemical Biology Ali Tavassoli. "In most cases, small chemical drugs bind to cavities in enzymes, where the chemical reactions take place. By binding to these crevices, the drugs prevent the enzymes from working."

However, van der Donk noted that many disease processes involve protein-protein interactions that do not fit this model.

"These have long been considered challenging because they do not involve such cavities.


*Wilfred van der Donk, Professor of Chemistry at the University of Illinois*

These protein-protein interactions often are made up of extended surfaces that can be difficult to inhibit with small molecules," he said.

Linear peptides are also problematic. They can be "floppy, like spaghetti, and therefore most of the time are in incorrect orientations to bind," van der Donk said. Cyclic molecules composed of one or more rings of amino acids are more stable and less susceptible to cellular enzymes that tend to chew off the ends of linear peptides. They are thus more likely to successfully bind to their targets.

In the new study, van der Donk and his colleagues made use of an enzyme they discovered from a bacterial species that lives in the ocean.

"This enzyme's natural role is to make about 30 different cyclic proteins, and we tested whether it could make analogs of these natural products in *Escherichia coli*," van der Donk said. *E. coli*, a species of bacterium present in the healthy mammalian gut microbiome, has been used as a drug-producing factory for pharmaceutical products.

The genetic sequences inserted into *E. coli* coded for a series of amino acids recognized by the enzyme. By linking sequence coding for an additional randomized string of amino acids to this "leader sequence," the team was able to generate a library of more than a million unique multicyclic proteins.

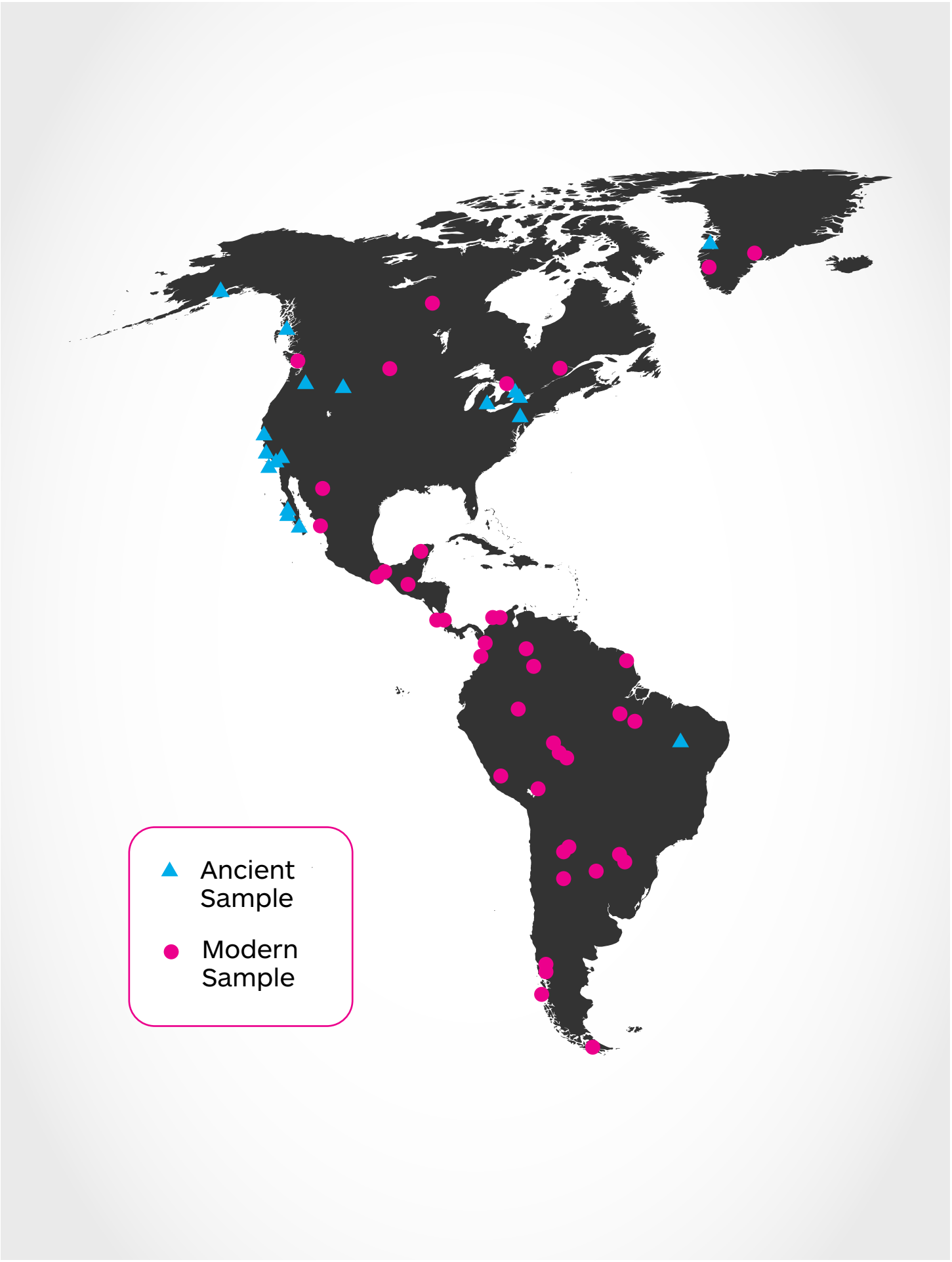
Tavassoli and his colleagues next screened this library in genetically engineered *E. coli* for proteins that could interrupt the binding of the HIV protein to its human host cell target. His team found three potential therapeutic agents, one of which could successfully block the binding activity of the HIV protein in a laboratory experiment.

This drug agent likely will not be used therapeutically, however, as it may have toxic side effects at high doses.

"The real advance here is the ability to generate libraries of millions of potentially therapeutic agents," Tavassoli said. "These could be screened to identify inhibitors of other disease-related processes, which is where its real potential lies."

The NIH, the Howard Hughes Medical Institute and the United Kingdom Engineering and Physical Sciences Research Council supported this research. ■

**"The real advance here is the ability to generate libraries of millions of potentially therapeutic agents."**


Ancient Sample
Modern Sample

# Two ancient populations that diverged in the Americas later reconverged

A GENETIC STUDY OF ANCIENT individuals in the Americas and their contemporary descendants found that two populations that diverged from one another 18,000 to 15,000 years ago remained apart for millennia before mixing again. This historic "reconvergence" occurred before or during their expansion to the southern continent.

The study, reported in the journal *Science*, challenges previous research suggesting that the first people in the Americas split into northern and southern branches, and that the southern branch alone gave rise to all ancient populations in Central and South America.

Associate Professor of Anthropology Ripan Malhi (CGRH/RBTE) and his colleagues use genomic techniques to understand ancient migration patterns in the Americas.

The study showed for the first time that, deep in their genetic history, many Indigenous people in the southern continent retain at least some DNA from the "northerners" who are the direct ancestors of many Native communities living today in the Canadian east.

"It was previously thought that Indigenous South Americans, and indeed most Native Americans, derived from one ancestry related to the Clovis people, who lived about 13,000 years ago," said Cambridge University archaeology professor Toomas Kivisild, who co-led the research with Malhi.

"We now find that all Native populations in North, Central and South America also draw genetic ancestry from a northern branch most closely related to Indigenous peoples of eastern Canada," Kivisild said. "This cannot be explained by activity in the last few thousand years. It is something altogether more ancient."

"We are starting to see that previous models of ancient populations were unrealistically simple," Malhi said.

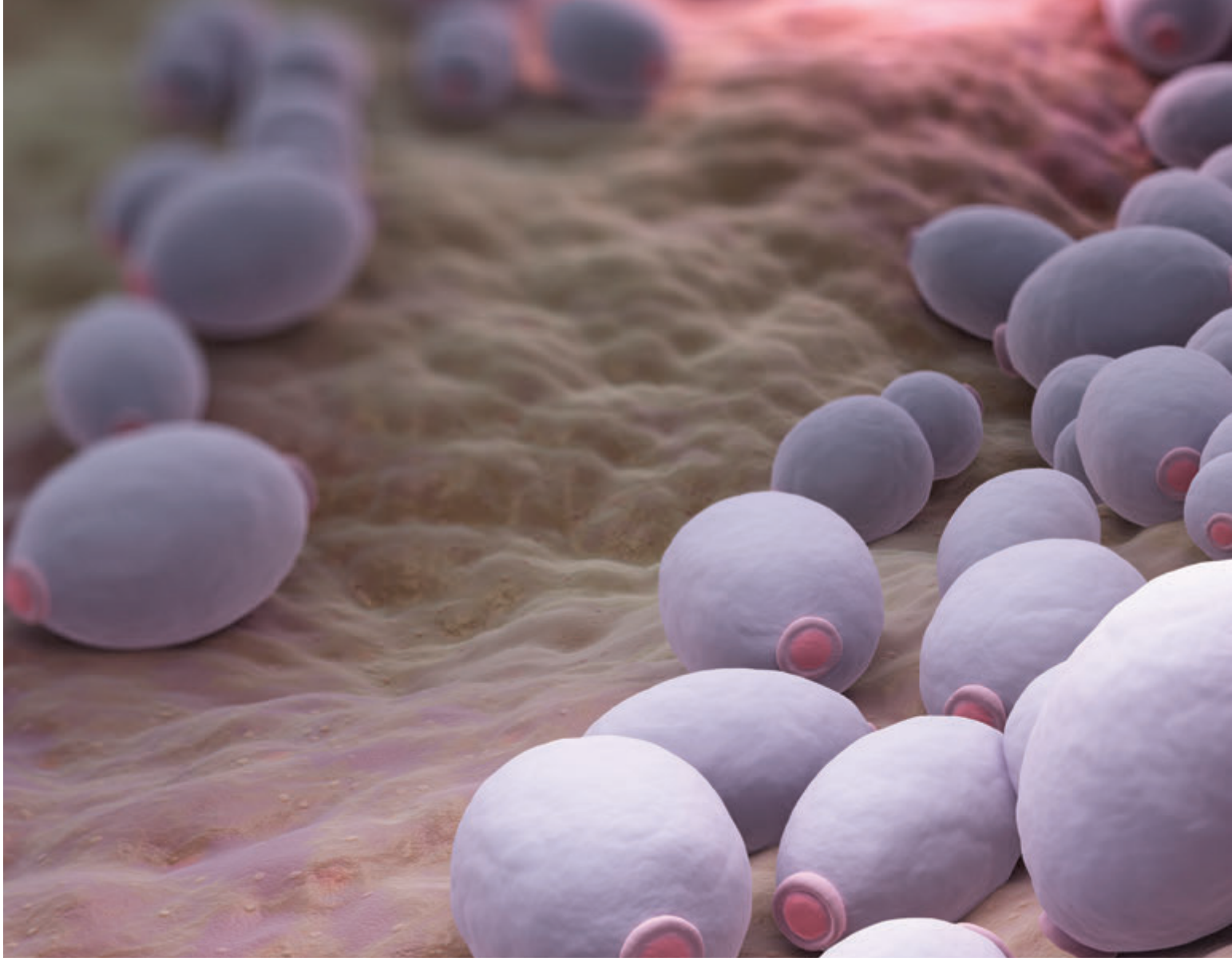
The researchers analyzed 91 ancient genomes from sites in California and Canada, along with 45 mitochondrial genomes from present-day Native individuals. The work adds to the evidence that two populations diverged 18,000 to 15,000 years ago. This would have been during or after their migration across the now-submerged land bridge from Siberia along what is now coastal Alaska, the researchers report.

Ancient genomes from southwest Ontario showed that after the split, Indigenous ancestors representing the northern branch migrated to the Great Lakes region. They may have followed the retreating glacial edges as the most recent ice age began to thaw, the researchers said. Populations representing the southern branch likely continued down the Pacific coast, inhabiting islands along the way.

"The ancient Anzick child from Montana also represents the southern branch and is associated with the Clovis culture, which was once thought to be ancestral to all Native Americans," Malhi said. "The analysis of genomes from ancient peoples from Ontario and California allowed us to identify components of the northern and southern branches in contemporary Central and South American genomes. These components were likely the result of a 'reconvergence' of the two branches deep in time."

The collaborative research effort was supported by the European Research Council, the Natural Environment Research Council, the Economic and Social Research Council, the NSF, the Wellcome Trust, and the European Union Regional Development Fund. ■

*Students participate in the 2018 Summer Internship for INdigenous peoples in Genomics (SING) Workshop, which works with native peoples to study their genetic heritage*



# CRISPR tech "knocks out" yeast genes with single-point precision

**THE CRISPR-CAS9 SYSTEM HAS GIVEN** researchers the power to precisely edit selected genes. Now, researchers have used it to develop a technology that can target any gene in the yeast *Saccharomyces cerevisiae* and turn it off by deleting single letters from its DNA sequence.

Such genome-scale engineering, in contrast to traditional strategies that only target a single gene or a limited number of genes, allows researchers to study the role of each gene individually, as well as in combination with other genes. It also could be useful for industry, where *S. cerevisiae* is widely used to produce ethanol, industrial chemicals, lubricants, and pharmaceuticals.

Understanding and optimizing the genome could create yeast strains with increased productivity, said study leader Huimin Zhao (BSD leader/CABBI/MMG), Steven L. Miller Chair in Chemical and Biomolecular Engineering. Zhao's group published the findings from the study, which was funded by the DOE and the IGB, in the journal *Nature Biotechnology*.

"We want to use microorganisms as cellular factories to make valuable chemicals and biofuels," Zhao said. "The scale we have demonstrated in this study is unprecedented.

*Illustration of* Saccharomyces cerevisiae

CRISPR has been used to introduce point mutations—for example, to address genetic diseases—but *Saccharomyces* yeast has about 6,000 genes, and we want to be able to knock out each of these genes iteratively and find out how they affect the production of a target compound."

Researchers produce "knockout" yeast in which one gene has been deleted or "knocked out," to study how each gene contributes to the function of the cell. When a beneficial mutation is found, they can selectively breed yeast with that characteristic. Leading methods to produce knockout yeast excise the entirety of the targeted gene. This creates unintended problems, Zhao said, because many genes overlap each other. Deleting one gene also deletes portions of others, affecting multiple functions and making it difficult for researchers to truly isolate the effects of a single gene.

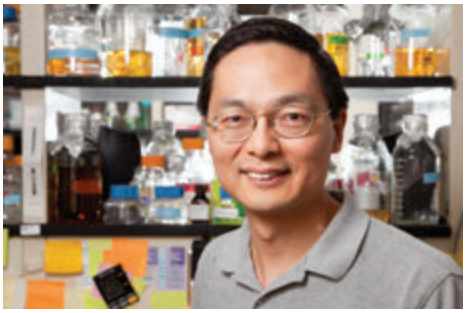
The letters in a DNA sequence correspond to bases, the building blocks that make up DNA strands. Zhao's group harnessed the precision of the CRISPR-Cas9 system to create a technique that allows them to delete just one base in a gene's DNA sequence. Since a cell "reads" DNA three bases at a time, this shifts the reading frame and knocks out the gene. Genes that overlap with the edited one remain unchanged and functional.

"We can introduce just one single base change on the entire chromosome. That makes a minimal disturbance in the function of the neighboring genes, so we can study how important the gene is in its cellular context. That kind of precision has not been achieved before," Zhao said.

Their technique, named CRISPR-Cas9 and Homology-directed-repair Assisted Genome-scale Engineering (CHAnGE), has the advantages of being quick, efficient and low-cost, in addition to its precision. Zhao's group developed a library of knockout yeast, one for each gene in the *S. cerevisiae* genome, and are making it available to other researchers for a $50 handling fee.

"In the past, teams of people would spend several years trying to knock out every gene in a yeast. With CHAnGE, one person can generate a library of yeast mutants covering the entire genome in about a month," Zhao said.

Zhao's group is working to develop libraries for other types of yeast, including ones that produce lipids used in lubricants, biofuels and other industrial applications. ■



*Chemical and Biomolecular Engineering Professor Huimin Zhao*

# Wearable device can predict older adults' risk of falling

**EVERY YEAR, MORE THAN ONE IN THREE INDIVIDUALS** aged 65 and older will experience a fall.

Falls are the most common cause of injury in older adults and can create ongoing health problems. But treatment and awareness of falling usually happens after a fall has already occurred.

As a part of the NIH Women's Health Initiative, researchers wanted to see if they could predict an individual's risk of falling so that preventative measures could be taken to reduce this risk. A new study has now made this prediction a reality.

> **"Being able to predict the fall risk is significant because so many older adults often don't pay attention to the fact that they are unstable until after they fall."**

The study involved 67 women, all over the age of 60, who were tested on their walking ability and asked about the number of falls they had experienced in the past year. Participants also wore a small device with motion sensors that measured their walking patterns for one week.

Bruce Schatz (CGRH), head of the Department of Medical Information Science in the University of Illinois College of Medicine at Urbana-Champaign, was asked to analyze the data from the study. He worked with colleagues from the Women's Health Initiative, including David Buchner from the Department of Kinesiology & Community Health, while supervising graduate students Andrew Hua and Zachary Quicksall, associated with the University of Illinois College of Medicine.

They found that data extracted automatically from the devices could accurately predict the participants' risk of falling. Their findings were published in *Nature Digital Medicine*.

"Our prediction showed that we could very accurately tell the difference between people that were really stable and people that were unstable in some way," Schatz said.

Older individuals fall differently than younger individuals, usually because their bodies are unstable. The researchers used a small device, called an accelerometer, to measure this instability and the user's walking patterns. They combined these measurements with the individual's fall history to determine the risk of falling in the future.

Being able to predict the fall risk is significant because many older adults often don't pay attention to the fact that they are unstable until after they fall. If they know they're at risk, they can do rehabilitation exercises to increase their strength and reduce their chance of falling.

Schatz sees the successful outcome of this research as a sign that, in the future, more wearable devices, or even smartphone apps, will be able to measure walking patterns and warn users of their fall risk.

This research relates to the larger idea of preventative medicine—health care solutions that can warn patients about health problems so they can take action and better manage the problem.

Research like this makes Schatz hopeful that progress is being made, and that a future with successful predictive medicine is on its way.

He predicts that the quality of life among older adults will improve as medicine and health care become more predictive and effective.

"The future is different," Schatz said. "And it's because of projects like this." ■

# Genomic study explores evolution of gentle 'killer bees' in Puerto Rico

**"This could be good news for beekeepers who want to develop a gentle honey bee that is also varroa-resistant."**

A GENOMIC STUDY OF PUERTO RICO'S Africanized honey bees—which are more docile than other so-called "killer bees"—revealed that they retain most of the genetic traits of their African honey bee ancestors, but that a few regions of their DNA have become more like those of European honey bees. According to the researchers who conducted the study, these changes likely contributed to the Puerto Rican bees' rapid evolution toward gentleness, a change that occurred in less than 30 years.

The findings, reported in the journal *Nature Communications*, could lead to advances that will bolster honey bee populations in the Americas, the researchers said.

Africanized bees are the offspring of African honey bees and their European counterparts. In the late 1950s, these aggressive "killer bees" escaped from an experimental breeding program in Brazil. That program had set out to produce a desirable mix of traits from the gentle European bees and their African counterparts, which were more aggressive, disease-resistant and adapted to a tropical climate.

Ironically, what scientists failed to do in the laboratory was eventually accomplished by happenstance. Africanized honey bees arrived in Puerto Rico (most likely on a ship, by accident) in the 1990s, and within three decades had evolved into the gentle yet hardy Africanized bees that dominate the island today. Professor of Biology Tugrul Giray at the University of Puerto Rico first reported on these gentle bees in the journal *Evolutionary Applications* in 2012. Giray is a co-author of the new study.

To gain insight into how the bees became gentle, the researchers sequenced the genomes of 30 gentle Puerto Rican bees, 30 Africanized bees from Mexico and 30 European honey bees from central Illinois.

"The benefit of having these three populations is that you can compare and contrast between the three," said postdoctoral researcher Arian Avalos, who works in the laboratory of IGB Director and Swanlund Professor of Entomology Gene Robinson (GNDP). Professor of Crop Sciences Matthew Hudson (CABBI/CGRH/GNDP) and Guojie

*A researcher holds a honeycomb covered with newly emerged adult honey bees*

Zhang and Hailin Pan of the Chinese Academy of Sciences were also co-authors of the study.

The team discovered that, for the most part, the genomes of the gentle bees resembled those of their Africanized forebears. Specific regions of the DNA, however, had shifted in the gentle bees, reflecting more of their European heritage. These regions appeared to be under "positive selection." This means that something in the bees' environment was favoring these genetic signatures over others.

The scientists hypothesize that the bees evolved to be more docile as a result of living on a densely populated island from which they could not easily escape. Humans likely eradicated the most aggressive bees, enabling their more docile counterparts to multiply.

The new findings offer a bit of hope for the beleaguered beekeeping industry, the researchers said. European honey bees tend to have less genetic diversity than Africanized bees, which carry both European and African honey bee genes. European honey bees also are more susceptible to a host of debilitating parasites and pathogens. Africanized bees are highly resistant to the varroa mite, a parasite of bees that undermines their health and spreads disease, a trait of great potential value to beekeeping.

"Infestation of European honey bees with the mites elicits very little response," said Avalos. "This could be good news for beekeepers who want to develop a gentle honey bee that is also varroa-resistant."

The NSF, the BGI and the University of Illinois supported this research. ■

*Africanized bee populations in Puerto Rico possibly became more docile due to human intervention*

## FAMILY TREE BASED ON GENOMIC SAMPLES

# First dogs in Americas arrived from Siberia, disappeared after European contact

**A STUDY REPORTED IN *SCIENCE*** offers an enhanced view of the origins and ultimate fate of the first dogs in the Americas. The dogs were not domesticated North American wolves, as some have speculated, but likely followed their human counterparts over a land bridge that once connected North Asia and the Americas.

Co-authors of the study include anthropology professor Ripan Malhi (CGRH/RBTE) and his graduate student Kelsey Witt, who is now a postdoctoral researcher at the University of California, Merced.

This is the first comprehensive genomic study of ancient dogs in the Americas that analyzes nuclear DNA, which is inherited from both parents, along with mitochondrial DNA, which is passed down only from mothers to their offspring. By comparing genomic signatures from 71 mitochondrial and seven nuclear genomes of ancient North American and Siberian dogs spanning a period of 9,000 years, the research team was able to gain a clearer picture of the history of the first canine inhabitants of the Americas.

The oldest dog remains in the Americas date to about 9,000 years ago, many thousands of years after people began migrating over a land bridge connecting present-day Siberia and Alaska. The ancient dogs analyzed in this study likely originated in Siberia, the researchers found. The dogs dispersed to every part of the Americas, migrating with their human counterparts.

These dogs persisted for thousands of years in the Americas, but almost completely vanished after European contact, suggesting a catastrophic event likely associated with European colonization.

"By looking at genomic data along with mitochondrial data, we were able to confirm that dogs came to the Americas with humans, and that nearly all of that diversity was lost—most likely as a result of European colonization," Witt said. "Few modern dogs have any trace of these ancient lineages."

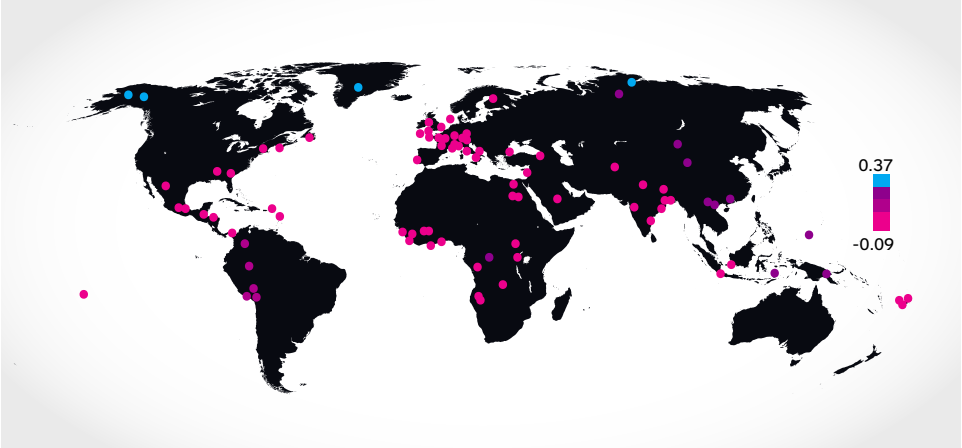
The team also discovered that the genomic signature of a transmissible cancer that afflicts dogs appears to be one of the last "living" remnants of the genetic heritage of dogs that populated the Americas prior to European contact.

"This suggests that this tumor originated in or near the Americas," Witt said.

The new findings reinforce the idea that early human and dog inhabitants of the Americas faced many of the same challenges after European contact, Malhi said.

"It is known how Indigenous peoples of the Americas suffered from the genocidal practices of European colonists after contact," he said. "What we found is that the dogs of Indigenous peoples experienced an even more devastating history and a near-total loss, possibly as a result of forced cultural changes and disease."

This research was funded by the American Kennel Club, the European Research Council, the Illinois State Museum Society, the Leverhulme Trust, the Max Planck Society, Millennia Research, Muséum National d'Histoire Naturelle, the Natural Environmental Research Council, NIH, NSF, the Russian Science Foundation, the Santa Barbara Museum of Natural History, the Social Sciences and Humanities Research Council, the University of Oxford, Wellcome Trust, and the Wenner-Gren Foundation. ■




*A map showing the locations of dog populations obtained from their degrees of relatedness to the pre-Colonial sample, a ~4000-year-old dog from Port au Choix*

# Neighborhood, breast cancer rates in African-American women linked

**"This suggests that the environmental conditions associated with low-income neighborhoods—rather than race itself—increases women's risks of dying from breast cancer."**

**NEIGHBORHOOD CHARACTERISTICS** such as racial composition and poverty rates are associated with increased risks of late-stage breast cancer diagnoses and higher mortality rates among urban black women, a new analysis of recent breast cancer research shows.

Even African-American women living in low-income neighborhoods that are undergoing gentrification and economic improvement may be at significantly greater risk of having distant metastases at the time they are diagnosed with breast cancer, said lead author Brandi Patrice Smith, a graduate student in food science and human nutrition.

"This is enlightening, because an increase in overall neighborhood socioeconomic status should result in better health for residents, not worse health," Smith said. "But because these neighborhoods were still low-income, they didn't have as many resources," such as health care facilities and access to mammography and follow-up care.

The study, which was published in *Hormones and Cancer*, comprised a sample of more than 93,600 black women living in various large cities and urban areas across the U.S.

The dataset included patient information from state breast cancer registries in California, Georgia, Illinois, New York, North Carolina and Texas. Patients, who ranged in age from 19 to 91, were tracked for an average of eight years.

Despite thousands of studies on breast cancer that have shown racial disparities in diagnosis and survival rates, only a small number of researchers have explored how these disparities might be related to various factors in women's living environments, Smith said.

Nearly half of African-American women in the U.S. live in urban areas and about 25 percent reside in low-income neighborhoods, according to the study.

*Zeynep Madak-Erdogan, Assistant Professor of Nutrition (on right); and Brandi Patrice Smith, doctoral student in food science and human nutrition*

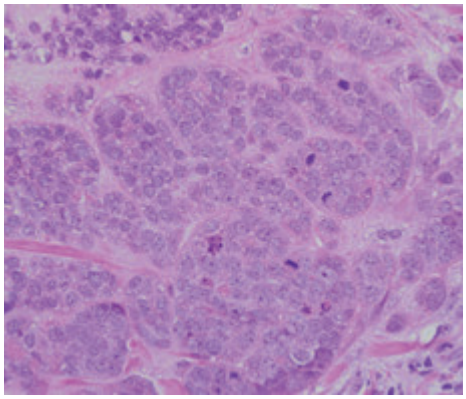
Smith and co-author Zeynep Madak-Erdogan, a professor of food science and human nutrition (ONC-PM), conducted a systematic review of recent breast cancer research to explore possible associations between characteristics of urban neighborhoods and breast cancer rates among African-American women. Among the factors they examined were neighborhood racial composition/segregation, poverty rates and access to mammography.

Residential segregation—which was defined as living in a neighborhood with a predominantly African-American population—significantly increased African-American women's rates of late-stage diagnosis and doubled their chances of dying from breast cancer, the analysis showed. Comparable mortality rates were found among white women who also lived in predominantly African-American neighborhoods.

"This suggests that the environmental conditions associated with low-income neighborhoods—rather than race itself—increases women's risks of dying from breast cancer," Smith said.

Mortality rates and risks of late-stage diagnosis were significantly greater in low-income neighborhoods where women of any race had limited access to mammograms and follow-up care with physicians, Smith said.

The work was funded by the University of Illinois and the U.S. Department of Agriculture. ■



*A cross-section of tissue from an invasive ductal carcinoma, the most common type of breast cancer*

# Reach out and feed someone

## Automated system finds rapid honey bee networks

**BY DEVELOPING A SYSTEM THAT ALLOWS** automated, in-depth monitoring of the social interactions of honey bees, researchers have now uncovered an unexpected property of the bee social network that may someday help us design more effective human and machine communication systems.

The team, which included researchers in computer science, entomology, physics, and mechanical science and engineering from the University of Illinois and Leipzig University, described the work in a new publication in the *Proceedings of the National Academy of Sciences*. Their behavioral monitoring system was designed to take advantage of recent advances in imaging and image analysis. Surprisingly, it revealed that a particular pattern of social interactions, associated with slow spread of information in human communities, appeared to allow for fast spread of information among the bees.

One way to document one-on-one interaction between bees is to spot trophallaxis, a behavior in which one bee requests food and her nestmate responds by offering up a drop of regurgitated sugary liquid. At first glance, trophallaxis looks like one bee grabbing a snack, but this exchange may be rich not only in calories but also information, including chemical signals that the bee offering the food has produced or received from others.

This feature makes trophallaxis a prime behavior to study, but it would be nearly impossible for a human observer to document every occurrence in a colony over an extended period of time. Tim Gernat, a graduate student working in the laboratories of IGB Director and Swanlund Professor of Entomology Gene Robinson (GNDP) and Leipzig University Professor of Mathematics and Computer Science Martin Middendorf, set out to create an automated system that could do just that.

The experimental set-up was a blend of the high-tech and the naturalistic. Colonies of honey bees housed in glass-walled hives were photographed once per second, recording images that included a custom-designed square barcode tag glued to each bee's back. The resulting photo gallery formed a near-complete record of the interactions between colony members over the course of more than a week. For network scientists interested in social interactions, such a thorough record for such a large group represents a new and exciting opportunity.

"I believe the time was right for this kind of work," Gernat said. "High resolution printing exists, high resolution cameras exist, different kinds of barcodes exist . . . what was very difficult, and is still very difficult, is to track the behavior."

Gernat and his colleagues worked to create and refine software that could flag likely exchanges of food between bees.

"The biggest technical challenge was on the experimental side—tracking individual bees and automatically detecting their interactions," said Vikyath Rao, a postdoctoral researcher in the laboratory of Swanlund Professor of Physics Nigel Goldenfeld (BCXT leader/CGRH/GNDP) who contributed to data analysis for the project. Once that challenge was met, the group had a rapid and systematic approach for generating a social network dataset unrivaled in its quality and size.

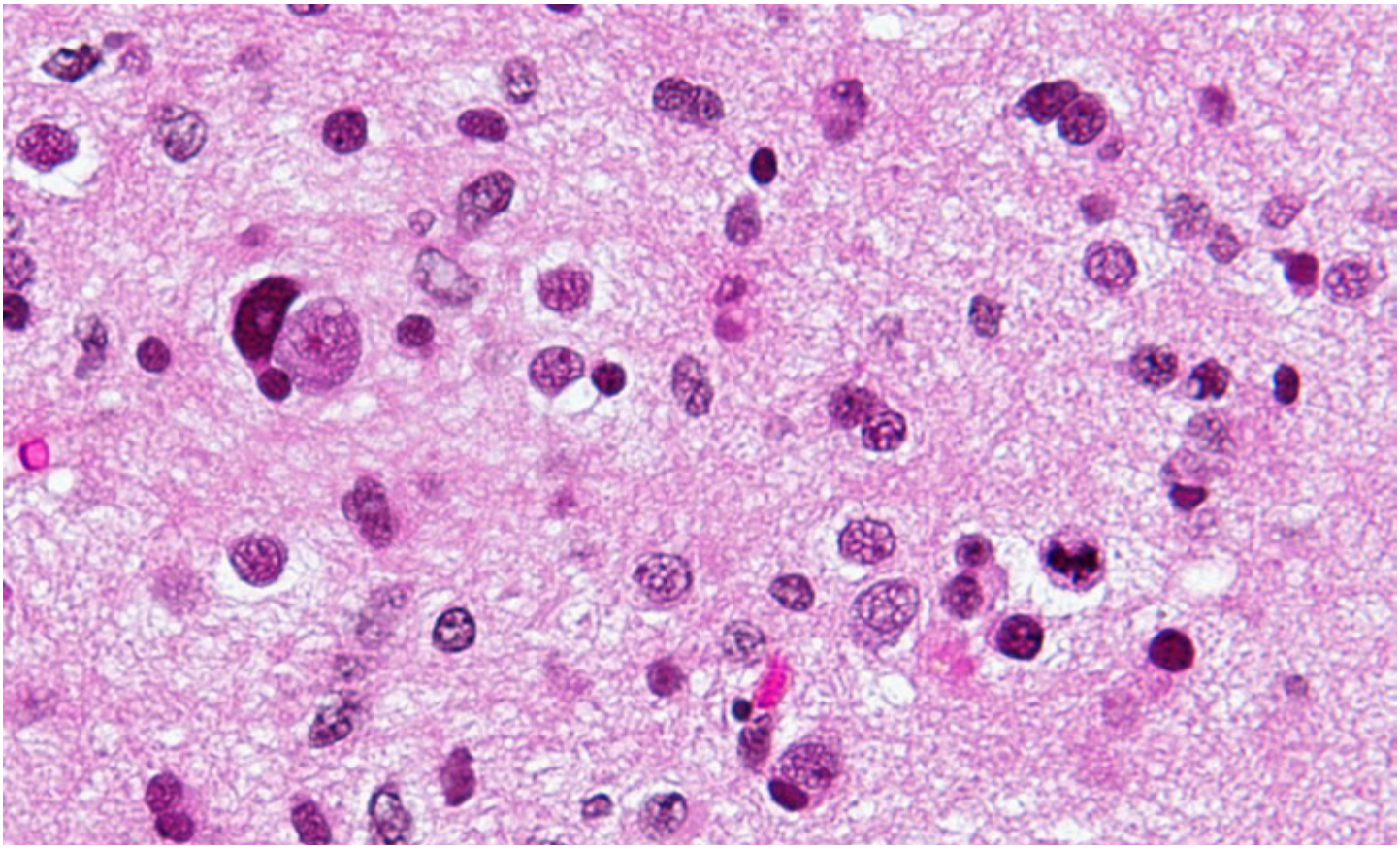
By studying the timing of interactions between bees, the team found that the honey bee social network shared a key feature with human networks as glimpsed from cell phone or social media activity: interactions occurred in a pattern of sporadic bunches and gaps that network scientists describe as "bursty."

This apparent parallel between human and bee social interactions hid a surprise. When the researchers simulated how fast a piece of information (for bees, this could be anything from a chemical signal to a disease-causing pathogen) might spread through the network, they found that this occurred rapidly, unlike the slow spreading found in bursty human networks. This feature was robust to changes in colony demography, even re-emerging in the interaction networks of hives from whom many individuals had been suddenly removed.

This interdisciplinary collaboration is one step in an effort to uncover and be inspired by the secrets of self-organized natural systems.

"The project has opened several promising avenues of future work, beginning with exploring further the underlying principles that make the honey bee network function in such a unique way, and what that might mean for human social networks," Robinson said.

The work was supported by the NSF, the Christopher Family Foundation, the National Academies Keck Futures Initiative, and the NIH. Both Robinson and Goldenfeld are also faculty members in the Illinois Center for Advanced Study. ■



*A cross section of glioma, a cancer targeted by PAC-1*

# Cancer drug starts clinical trials in human brain cancer patients

A drug that spurs cancer cells to self-destruct has been cleared for use in a clinical trial of patients with anaplastic astrocytoma, a rare malignant brain tumor, and glioblastoma multiforme, an aggressive late-stage cancer of the brain.

This phase Ib trial will determine if the experimental drug PAC-1 can be used safely in combination with a standard brain-cancer chemotherapy drug. The trial is approved for patients who have seen their cancer progress after initial treatment. This is an extension of an ongoing human phase I clinical trial of PAC-1 alone in patients with various late-stage cancers. Phase I trials are designed to test the safety of new drugs in human patients.

PAC-1 is unusual in that it is able to cross the blood-brain barrier, a formidable obstacle to most anti-cancer drugs. The drug targets procaspase-3, an enzyme that is overexpressed in many cancer cells, said chemistry professor Paul Hergenrother (ACPP leader/MMG), who discovered PAC-1's anti-cancer effects more than a decade ago.

"PAC-1 restores the activation of procaspase-3 and, because this enzyme is elevated in cancer cells, targets cancer cells over noncancerous cells," Hergenrother said.

After tests in human cell lines and rodents proved promising, Hergenrother and veterinary oncologist Dr. Timothy Fan (ACPP/


*Left to right: Dr. Timothy Fan, Hoover the dog, and Dr. Paul Hergenrother*

ONC-PM), a professor of veterinary clinical medicine, tested PAC-1 in pet dogs with a variety of cancers.

PAC-1 has been evaluated in pet dogs with naturally occurring osteosarcoma, lymphoma and, most recently, glioma—a brain cancer similar to glioblastoma in humans. One 2016 study found that the combination of PAC-1 with a chemotherapeutic agent called doxorubicin saw tumor reductions in four of four dogs with lymphoma and in three of six dogs with osteosarcoma.

The trials in dogs continue and, so far, have found PAC-1 to be safe, with few observable side effects. The researchers report their latest findings in rodents and in dogs with brain cancer in the journal *Oncotarget*.

Certain cancers in dogs are genetically similar to those in humans and respond to the same medications. Dogs also are more similar in size to humans, and can be better models to evaluate how well drug agents perform on larger tumor masses.

The ongoing clinical trial of PAC-1 in human patients with late-stage solid tumors and lymphoma has shown that the drug is well-tolerated at tested doses, said medical oncologist Dr. Arkadiusz Dudek, who chairs an advisory board for Vanquish Oncology, which is funding the clinical trials.

So far, the clinical trials of PAC-1 alone have seen no significant side effects in humans. The team cannot report on clinical outcomes in a phase I clinical trial, since such trials are designed to measure safety, not efficacy.

The human clinical trials will be offered at the University of Illinois Cancer Center in Chicago; the Regions Hospital Cancer Care Center in St. Paul, Minnesota; and Johns Hopkins University School of Medicine in Baltimore. ■

**“PAC-1 is unusual in that it is able to cross the blood-brain barrier, a formidable obstacle to most anti-cancer drugs.”**

# Outreach Events

IGB's recurring outreach programs are a key part of our engagement with the local and regional community. Each time we meet a new attendee, we gain a fresh perspective on the impacts of genomic research on everyday life. This open dialogue with the public enriches our research and helps us to increase its translational value.

## iGEM

This year's International Genetically Engineered Machine (iGEM) team from Illinois was sponsored by CABBI and mentored by CABBI researchers. The team worked together on a research project over the summer in preparation for the iGEM competition, which brings together undergraduate students from across the world to present research in synthetic biology and compete for prizes.

## Art of Science

In the past year, our Art of Science program explored some new mediums, including a monthly wall calendar and events encouraging community members to make their own science-based art. The program is built around images emerging from IGB research, enhanced to emphasize striking visual features and to subtly reflect on the underlying science concepts. In the coming year, we will continue to explore exciting new directions, as well as continuing to showcase Art of Science pieces in our annual and traveling exhibits.

## Genomics for Professionals

Genomics for Professionals is a series of educational programs that targets the needs and interests of specific demographic or professional groups. Over the summer, IGB hosted Genomics for Teachers for 21 middle school and high school teachers. The program informed educators about new genomic research in invasive species, fish, and water quality, and how they can use phenomena related to these topics to design lessons and units aligned to the Next Generation Science Standards. Educators were awarded 6.5 professional development units (CPDUs) and a stipend for attending.


## Pollen Power

In celebration of its sixth year, Pollen Power camp featured an updated design and the latest versions of popular activities. This week-long day camp is offered each July to middle school girls who are curious about plant biology, climate change, and imaging technology. Plant biologists Lisa Ainsworth (CABBI/GEGC) and Andrew Leakey (CABBI/GEGC) organize the camp in collaboration with IGB Core Facilities and IGB Outreach staff; female graduate students act as counselors, and female scientists from around campus give presentations on their work and experiences. As in previous years, this year's attendees learned to operate high-powered microscopes; took field trips to maker spaces, field sites, and a local pollinator museum; and scripted and recorded "weather reports" on the past, present and future climate of Earth. The camp is supported by the NSF and the IGB.

*Pollen Power Summer Camp participants*

# Outreach

## Researchers unite athletics and scientific scholarship for a unique take on science outreach

In the summer of 2018, researchers from the laboratory of Professor of Geology and Microbiology Bruce Fouke (BCXT) partnered with the laboratory of Assistant Professor of Kinesiology Nicholas Burd and the Division of Intercollegiate Athletics to pilot a new element in select summer athletic camps—an afternoon of hands-on science. The effort was funded by a grant from NASA.

The stereotypical division of scholarship and sports conceals the challenging balance of responsibilities faced by student athletes; engaging with scientific research may not receive support as a priority for this demographic. However, scientific concepts, particularly from the biological sciences, may offer valuable insight into the mechanics and health considerations of intense athletic training, and the work ethic and rigor fostered by sports are an asset in scientific research.

The summer camps targeted this overlap in an otherwise unlikely pairing of disciplines by inviting middle school and high school attendees of Illinois sports camps to science workshops at the IGB. In all, over 300 athletes and coaches from five different sports participated.

Students heard talks and engaged in sports-related laboratory experiments that integrated concepts from genomic biology, nutrition, kinesiology, sports medicine, and even astrobiology. A highlight of the camp workshops were discussions in which students related what they were learning to their observations and experiences as athletes.

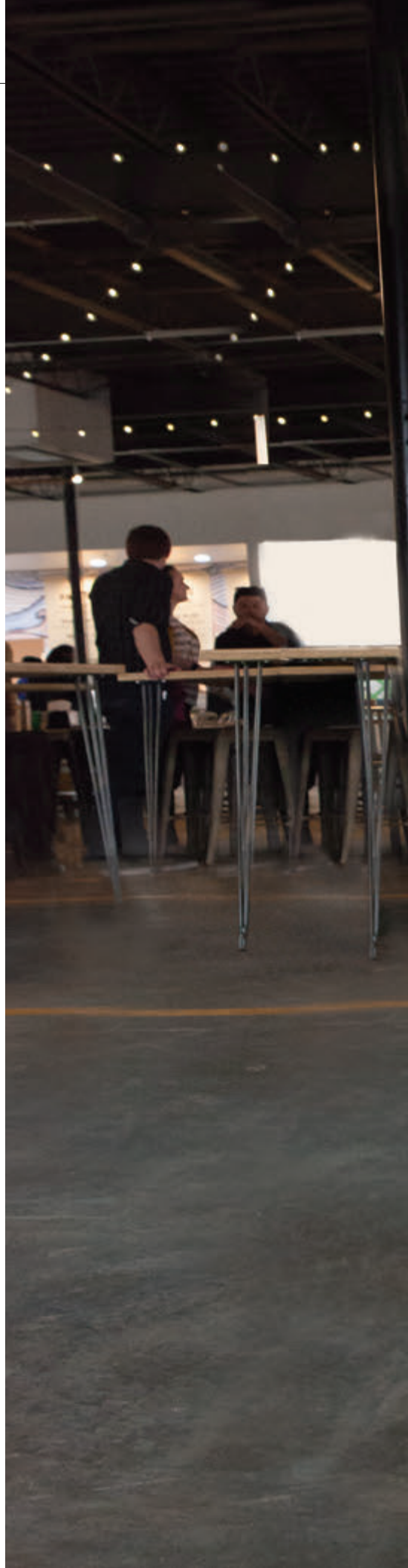
## Unique online course explores the intersection between genomics and the law

At the interface between science and society lies the law. New technologies raise questions about access, fair and appropriate use, and ownership. A new online course developed by the IGB in partnership with the College of Law and the Center for Innovation in Teaching and Learning helps lawyers prepare to grapple with the legal implications of genomic technologies.

The ability to quickly and cheaply sequence a human genome from a sample taken from a coffee cup or to select and insert a desired trait into a common food crop has important legal implications. Does a police officer need a warrant to collect a DNA sample? How strong are the privacy protections for genomic information? Who is liable when a doctor gives medical advice based on mistaken genetic testing? What genomic technologies can be patented?

The new course, "Genomics for Lawyers," addresses these questions and other timely issues through a series of engaging video lectures by Illinois law and science faculty members. The course explores the relationship between genomics and five major legal topics: criminal law, intellectual property and patent law, biomedical ethics, tort law, and privacy. Lawyers who complete the course can earn continued legal education credit.

Since its release, over 3000 students have begun the course, which can be initiated and completed on a self-paced schedule.




*The Art of Science 8.0 opening reception, at new venue Broadway Food Hall in Champaign, welcomed hundreds of art appreciators*

# Awards

## Nutrition scientist Sharon Donovan elected to National Academy of Medicine

Sharon Donovan (MME), a professor of nutrition and the Melissa M. Noel Endowed Chair in Nutrition and Health, has been elected to the National Academy of Medicine (NAM).

Induction into NAM is considered one of the highest honors in the fields of health and medicine. The Academy recognizes individuals who have demonstrated outstanding professional achievements and commitment to service.

A registered dietitian, Donovan and her group conduct basic and translational research in pediatric nutrition, focusing on three areas: optimal intestinal development of neonates, prevention of childhood obesity and determinants of picky eating in 2- to 5-year-old children.

Donovan's work has garnered numerous honors, including awards from the International Life Sciences Institute North America and the American Society for Nutrition. She is an active member of the American Society for Nutrition, serving as that organization's president from 2011 to 2012, and is currently president-elect of the International Society for Research on Human Milk and Lactation.

The NAM is an independent organization of eminent professionals from diverse fields including health and medicine, and the natural, social and behavioral sciences. The academy works to address critical issues in health, medicine and related policy and to inspire positive action across sectors.

## Wolf Prize in Agriculture, National Academy of Medicine for IGB Director Gene Robinson

Swanlund Professor of Entomology and IGB Director Gene Robinson (GNDP) received two significant honors this year, the 2018 Wolf Prize in Agriculture for "leading the genomics revolution in the organismal and population biology of the honey bee" as well as election to the National Academy of Medicine (NAM).

Awarded each year since 1978, the Wolf Foundation awards individuals in the fields of agriculture, chemistry, mathematics, medicine, physics, and the arts rotated among disciplines. Recipients are considered outstanding members in their field. Laureates receive their awards from the President of the State of Israel in a special ceremony held at the parliamentary building in Jerusalem.

"I am deeply honored to receive this award," said Robinson. "The new science of genomics has truly revolutionized how we study all organisms, including honey bees, whose intricate social life enables them to play a vital but often overlooked role in world agriculture as the premier pollinator on the planet."

Robinson's NAM election was in recognition for pioneering contributions to understanding the function of genes in social behavior, evidence of the growing importance of the role behavioral study plays in health and medical research. Having been elected to the National Academy of Sciences in 2005 Robinson is now one of a select community who hold membership in two national academies.

Employing genomics and systems biology to study the mechanisms and evolution of social life using the Western honey bee as a model organism, Robinson's lab has made significant advances in the understanding of the role of genes, hormones, and neurochemicals in the mechanisms and evolution of social behavior, as well as discovering the first gene in regulating the division of labor within honey bee colonies.

## Ruby Mendenhall new assistant deanship, Carle Illinois College of Medicine

Ruby Mendenhall (CGRH/GNDP) was named the Assistant Dean for Diversity and Democratization of Health Innovation at the Carle Illinois College of Medicine.

Mendenhall is an associate professor of sociology, African American studies, urban and regional planning, gender and women's studies and social work at Illinois. She is an affiliate of the Women and Gender in Global Perspectives, the Cline Center for Advanced Social Research, Epstein Health Law and Policy Program, Family Law and Policy Program, the Institute for Computing in Humanities, Arts and Social Sciences.

Professor Mendenhall's insight and experience will enhance the development of a strong medical humanities curriculum thread, training compassionate physician-innovators to be on the forefront of developing new approaches to patient care. Mendenhall aims to democratize health innovation and make the discoveries that will take place at Carle Illinois accessible to everyone. Included in this pursuit is training cohorts of diverse students and creating pipeline programs that will ensure Carle Illinois produces the multifaceted talents required for success in the 21st century.

In her role as assistant dean, Mendenhall will work on health and well-being research, curriculum development, diversity initiatives and translational activities. She will work with faculty, staff and students in the humanities, arts, social sciences, law and other areas to incorporate a breadth of multi-disciplinary research and knowledge into the Carle Illinois curriculum. She will collaborate with community, social, educational, religious, business and governmental partners in breaking down barriers in order to holistically address social determinants of health and decrease health disparities.

## Five Illinois researchers rank among world's most influential

Five faculty members at the University of Illinois have been named to the 2017 Clarivate Analytics Highly Cited Researchers list (previously known as the Thomson Reuters Highly Cited Researchers list), including four from the IGB.

The list recognizes "leading researchers in the sciences and social sciences from around the world," according to Clarivate Analytics. It is based on an analysis of journal article publication and citation data, an objective measure of a researcher's influence, from 2005-15.

The highly cited IGB researchers this year are: crop sciences and plant biology professor Lisa Ainsworth (CABBI/GEGC, highly cited in plant and animal science), crop sciences and plant biology professor Stephen P. Long (BSD/CABBI/GEGC, plant and animal science), chemistry professor Yi Lu (BSD/CABBI/ONC-PM, chemistry), and psychology professor Brent Roberts (GNDP, psychiatry, psychology).

Ainsworth's research focuses on plant metabolism, photosynthesis and molecular variation within species and how those factors contribute to plant responses to global change. A key goal of her work is to maximize crop production in the future.

Long is the Gutgsell Endowed Professor in the departments of crop sciences and plant biology. He uses computational and experimental approaches to improve photosynthetic efficiency, and works to address the effects of climate change on crop yield.

Lu, the Jay and Ann Schenck Professor of Chemistry at Illinois, focuses on the design and engineering of metalloenzymes and their applications as biocatalysts in alternative-energy applications and as sensors and imaging agents to be used in environmental monitoring, food safety and medical diagnostics.

Roberts is a professor of psychology in the field of personality psychology. He studies continuity and change in personality throughout adulthood, with an emphasis on understanding the factors that influence change.

## Walnuts impact gut microbiome and improve health

Diets rich in nuts, such as walnuts, play a role in heart health and in reducing colorectal cancer. According to new research, the way walnuts impact the gut microbiome—the collection of trillions of microbes or bacteria in the gastrointestinal tract—may be behind some of those health benefits.

The study, published in *The Journal of Nutrition*, shows that consuming walnuts not only impacted the gut microbiota and microbial-derived secondary bile acids, but also reduced LDL-cholesterol levels in the adults participating in the study—good news for cardio, metabolic and gastrointestinal health.

"We found that when you consume walnuts, it increases microbes that produce butyrate, a beneficial metabolite for colonic health," said Hannah Holscher (MME), Assistant Professor of Food Science and Human Nutrition and lead author of the study. "So the interaction of walnuts with the microbiome is helping to produce some of these health effects."

The findings also show that walnut consumption led to a reduction in secondary bile acids.

"Secondary bile acids have been shown to be higher in individuals with higher rates of colorectal cancer," Holscher said. "Secondary bile acids can be damaging to cells within the gastrointestinal tract, and microbes make those secondary bile acids. If we can reduce secondary bile acids in the gut, it may also help with human health."

Funding for the study was provided by USDA-ARS and California Walnut Commission.

# Research

## Products of omega-3 fatty acid metabolism may have anticancer effects

A class of molecules formed when the body metabolizes omega-3 fatty acids could inhibit cancer's growth and spread, a new study in mice indicated. The molecules, called endocannabinoids, are made naturally by the body and have similar properties to cannabinoids found in marijuana, but without the psychotropic effects.

In mice with tumors of osteosarcoma—a bone cancer that is notoriously painful and difficult to treat—endocannabinoids slowed the growth of tumors and blood vessels, prevented the cancer cells from migrating and caused cancer cell death. The work, which was supported by the NIH and the American Heart Association, was published in the *Journal of Medicinal Chemistry*.

The researchers, led by Assistant Professor of Comparative Biosciences Aditi Das, found that the endocannabinoids they focused on did kill cancer cells, but not as effectively as other chemotherapeutic drugs on the market. However, the compounds also combated the osteosarcoma in other ways: they slowed tumor growth by inhibiting new blood vessels from forming to supply the tumor with nutrients, they prevented interactions between the cells, and most significantly, they appeared to stop cancerous cells from migrating.

"The major cause of death from cancer is driven by the spread of tumor cells, which requires migration of cells," said study co-author Timothy Fan (ACPP/ONC-PM), a professor of veterinary clinical medicine and veterinary oncology. "As such, therapies that have the potential to impede cell migration also could be useful for slowing down or inhibiting metastases."

## Virus-bacteria coevolution solves diversity paradox by 'killing the winner'

There is remarkable biodiversity in all but the most extreme ecosystems on Earth. When many species are competing for the same finite resource, a theory called competitive exclusion suggests one species will outperform the others and drive them to extinction, limiting biodiversity. But this isn't what we observe in nature. Theoretical models of population dynamics have not presented a fully satisfactory explanation for what has come to be known as the diversity paradox.

Physicists Chi Xue and Nigel Goldenfeld (BCXT leader/CGRH/GNDP) have shed new light on this fundamental question in ecology by improving a popular proposed scenario for diversity known as "Kill the Winner." Their work was supported by the University of Illinois and the NASA Astrobiology Institute for Universal Biology, which Goldenfeld directs.

Goldenfeld and Xue developed a statistical model that accounts for multiple factors observed in ecosystems, including competition among species and simultaneous predation on the competing species. Using bacteria and their host-specific viruses as an example, they showed that as the bacteria evolve defenses against the virus, the virus population also evolves to combat the bacteria. This "arms race" leads to a diverse population of both and to boom-bust cycles when a particular species dominates the ecosystem then collapses—the so-called "Kill the Winner" phenomenon. This coevolutionary arms race is sufficient to yield a possible solution to the diversity paradox.

Goldenfeld and Xue published their findings in *Physical Review Letters*.

## New informatics tool makes the most of genomic data

The rise of genomics, the shift from considering genes singly to collectively, is adding a new dimension to medical care; biomedical researchers hope to use the information contained in human genomes to make better predictions about individual health, including responses to therapeutic drugs. A new computational tool developed through a collaboration between the University of Illinois and Mayo Clinic combines multiple types of genomic information that could help biomedical researchers predict what drugs will most safely and effectively treat individual patients.

The tool was described in *Genome Research* after its development by members of KnowEnG, a Center of Excellence housed within the IGB and established by an NIH Big Data to Knowledge (BD2K) Initiative award to the University of Illinois in partnership with Mayo Clinic. KnowEnG stands for Knowledge Engine for Genomics, representing the center's mission to develop analytical resources for biomedical work with genomic data.

"There was no tool that would exploit all of these [data types] together," said Professor of Computer Science and Willett Faculty Scholar Saurabh Sinha (BSD/GNDP), who co-directs the BD2K Center. "Our end result was testable predictions" about how different genomic features would influence the effectiveness of different drugs, he said.

Sinha and graduate student Casey Hanson created and tested an algorithm that takes in data on gene expression, genomic factors that help control gene expression, and resulting traits (such as drug response) and uses these to predict which genes are most important in determining the latter.

# Research

## In responding to predation risk, secondhand experience can be as good as new

Throughout the living world, parents have many ways of gifting their offspring with information they will need to help them survive. A new study in *Nature Ecology and Evolution* examining the effects of exposure to predators across two generations of stickleback fish yielded a surprising insight into how such transgenerational information is used.

The NIH- and NSF-funded study was led by Laura Stein, who began the work as a doctoral student in the laboratory of animal biologist Alison Bell (GNDP). Stein, Bell, and doctoral student Abbas Bukhari found that when either a stickleback father or his offspring experienced the threat of predation, the offspring responded with the same adaptive strategy—developing to be smaller and more timid. Even if both generations experienced the threat, the developmental differences in size and behavior remained the same.

"The results were not what we had predicted, because models assume that information from different sources is additive," said Bell. "If, say, the developmentally plastic response is to be smaller in response to predation risk and if the generational response is to be smaller in response to predation risk, the models all assume that if those two things are combined together, they should be doubly small … that's not what we found at all."

By comparing levels of brain gene expression across their experimental groups, the researchers determined that paternal experience and personal experience predominantly activated a shared set of molecular responses, perhaps helping to explain on a mechanistic level why either or both were able to produce the same developmental outcomes.

## Study reveals how polymers relax after stressful processing

A new study has found that entangled, long-chain polymers in solutions relax at two different rates, marking an advancement in fundamental polymer physics. The findings will provide a better understanding of the physical properties of polymeric materials and critical new insight to how individual polymer molecules respond to high-stress processing conditions.

The study, published in the journal *Physical Review Letters*, could help improve synthetic materials manufacturing and has applications in biology, mechanical and materials sciences as well as condensed matter physics. The work was supported by NSF and PPG Industries.

"Our single-molecule experiments show that polymers like to show off their individualistic behavior, which has revealed unexpected and striking heterogeneous dynamics in entangled polymer solutions," said co-author Charles Schroeder (BSD), Professor of Chemical and Biomolecular Engineering. "A main goal of our research is to understand how single polymers—acting as individuals—work together to give materials macroscopic properties such as viscosity and toughness."

The team is excited to bring new insight to the understanding of how complex fluids flow and how they are processed and manufactured, especially with polymers that are subjected to intense stress, such as the fluids that are used for 3D printing.

## Long-term estrogen therapy changes microbial activity in the gut, study finds

Long-term therapy with estrogen and related compounds alters microbial composition and activity of the gut, affecting how estrogen is metabolized, a new study in mice found. The study was supported by the USDA, the NIH, the University of Illinois, and Pfizer Inc.

Professor of Food Science and Human Nutrition Zeynep Madak-Erdogan (ONC-PM) and her colleagues found that a microbially-produced enzyme plays a pivotal role in metabolizing synthetic estrogens in the intestinal tract. They shared their findings in *Scientific Reports*.

"Our findings indicate that clinicians might be able to manipulate the gut biome through probiotics to change the half-life and properties of estrogens so that long-term users obtain the therapeutic benefits of estrogen-replacement therapy without increasing their risks of reproductive cancers," said Madak-Erdogan. If the human gut microbiome response resembles that of mice, the results might also help explain individual variation in responses to hormone therapy.

Co-authors of the study included researchers Loretta Auvill, Colleen Bushell (CGRH/GNDP), Kathryn Carlson, Sung Hoon Kim, and Michael Welge (CGRH); postdoctoral research associate Xiaoji Liu; Professor of Chemistry John Katzenellenbogen; Associate Professor of Food Science and Human Nutrition Michael Miller (IGOH/MME); and Assistant Professor of Pathology Rebecca Smith (IGOH).

# Research

## New technique can track drug and gene delivery to cells

Professor of Bioengineering Andrew Smith (ONC-PM) and graduate student Mohammad Zahid have developed a technique to track and map drug and gene delivery vehicles to evaluate which are most effective at infiltrating cells and getting to their targets, insight that could guide development of new pharmaceutical agents. The researchers described their tracking system and their findings on the most effective delivery vehicles in *Nature Communications*.

Gene therapies have shown promise in cell culture and animal studies but have been less effective in clinical trials. This class of pharmaceuticals, called biologics, are different from traditional drugs in that they need to be attached to specialized delivery agents, such as nanoparticles or proteins, to reach their intended cellular targets.

"We have these really great models that tell us how classical drugs work, but there's no model that works for these new biologics that have to have some additional mechanism to deliver to cells. This has been a key missing part of pharmaceutical medicine," Smith said. "If we don't understand the mechanisms of the problem, we can't solve it. Now we can pinpoint why that happens and figure out how to overcome the key bottlenecks, which has never been possible."

Smith and Zahid combined two imaging tools to track and measure how different delivery agents entered human and mouse cancer cells. The researchers used single-molecule imaging, which allows them to observe individual molecules over time, and quantum dots, which act like tiny beacons inside cells. This allowed the researchers to see, count and track all of the delivery agents that entered the cell. Their work was funded by the NIH.

## Study reveals how bacteria steal nutrients from human hosts

Our bodies need nutrients to stay healthy; so do the pathogens that infect us and make us ill. A new study published in *mBio* revealed how a zinc-import system in the bacteria *Staphylococcus aureus* could contribute to their ability to cause infection by allowing the tiny invaders to steal zinc from their host.

"Transition metals such as zinc are essential for all forms of life," said Assistant Professor of Microbiology Thomas Kehl-Fie (MMG), who led the study. "We get these metals from food, while invading bacteria must get them from us."

In order to combat an infection, the body's immune system hoards zinc and other critical nutrients, in an effort to weaken the bacteria. "The host and bacteria are, in effect, engaged in a tug of war for zinc," said Kehl-Fie. "Our immune system tries to remove zinc from sites of infection and the bacteria, while the bacteria use transporters to pull the metal away from the host."

Kehl-Fie and colleagues discovered a new system that enables *S. aureus* to acquire zinc from the human body. The discovery explains how the bacterium is able to grow well even in environments that are very zinc-limited. The study was supported by the NIH, March of Dimes, and the Vallee Foundation.

## Cholesterol byproduct hijacks immune cells, lets breast cancer spread

High cholesterol levels have been associated with breast cancer spreading to other sites in the body, but doctors and researchers don't know the cause for the link. A new report in *Nature Communications* suggested that the culprit is a byproduct of cholesterol metabolism that acts on specific immune cells, altering their behavior so that they facilitate the cancer's spread instead of stopping it.

"Breast cancer impacts roughly 1 in 8 women. We've developed fairly good strategies for the initial treatment of the disease, but many women will experience metastatic breast cancer, when the breast cancer has spread to other organs, and at that point we really don't have effective therapies. We want to find what drives that process and whether we can target that with drugs," said Erik Nelson (ACPP/CGRH), a professor of molecular and integrative physiology who performed the study with postdoctoral researcher Amy Baek.

Baek and Nelson identified new potential drug targets that could inhibit the creation or actions of the dangerous cholesterol byproduct, a molecule called 27HC. Because 27HC acts through the immune system, and not on the breast cancer itself, the researchers believe their findings have broad applicability for solid tumors. They performed experiments looking at colon cancer, lung cancer, melanoma and pancreatic cancer, and found that 27HC increased metastasis for all the tumor types, suggesting that a treatment targeting 27HC could be effective across multiple cancer types.

The NIH and the Susan G. Komen Foundation supported this work.

# Research

## Viruses share genes with organisms across the tree of life

Viruses share some genes exclusively with cells that are not their host, according to a study reported in *Frontiers in Microbiology*. The research adds to the evidence that viruses are agents of diversity and can swap genes with a variety of cellular organisms.

University of Illinois and COMSATS Institute of Information Technology researcher Arshan Nasir led the study with Gustavo Caetano-Anolles (GEGC), a professor of crop sciences, and Kyung Mo Kim, a senior scientist at the Korea Polar Research Institute.

The team analyzed the genomes of organisms and the viruses that infect them. They examined the functional components of proteins, called folds, which can be reliable markers of evolutionary changes over time.

The researchers found hundreds of folds that are present across all superkingdoms of life and in all types of viruses, which suggests they came from an ancient ancestor of all life forms. Some folds, however, occur only within a single superkingdom and the viruses that infect it, suggesting a transfer of genetic material only between those viruses and their hosts.

The data also point to other unknown mechanisms that allow viruses to exchange genetic material with cells.

"While people tend to think only about viruses that infect and kill their hosts, we have known for decades that a virus will sometimes enter into a cell and incorporate its genetic material into the cell without killing it," Caetano-Anolles said.

This research was supported by The Higher Education Commission of Pakistan, the NSF, and the NIH.

## Light green plants save nitrogen without sacrificing photosynthetic efficiency

Scientists have designed plants with light green leaves that allow more light to penetrate the crop canopy to increase photosynthesis and yield. Models show these plants likely require less nitrogen and photosynthesis is hardly affected.

Leaves at the top of the crop canopy absorb more light than lower leaves, but they aren't as efficient with light energy. Researchers wanted to see if moving light energy from the top of the canopy to deeper into the canopy would make the crop canopy more efficient overall.

Published in *Plant Physiology*, researchers tested this idea using a computer simulation that incorporated data from nearly 70 varieties of soybeans with varying levels of chlorophyll. They found that plants with 20 percent less chlorophyll theoretically require 9 percent less nitrogen with no penalty to carbon gain (biomass) and yield.

RIPE Deputy Director Don Ort (GEGC leader/BSD/CABBI), a physiologist with the USDA/ARS Photosynthesis Unit and the Robert Emerson Professor of Plant Biology and Crop Sciences, explained that lower chlorophyll levels lead to more light being lost to reflection.

"We don't get the full benefits of getting light deeper into the canopy where it can be absorbed," he said.

The researchers want to see if these nitrogen savings could be used to fix other photosynthetic bottlenecks as well as other ways to increase light penetration into the canopy. They hope to explore whether lighter green leaves can be combined with changes in leaf architecture, or if leaves can be re-engineered to be thinner and reduce light reflectance and improve transmittance.

This work was supported by RIPE, an international research project funded by the Bill & Melinda Gates Foundation, the Foundation for Food and Agriculture Research, and the U.K. Department for International Development.

## Humans are Sumatran rhinoceros' biggest threat—and last hope

Researchers urged conservationists to translocate the two subspecies of the Sumatran rhinoceros, a critically endangered species, and create a cell bank to preserve the rhinos' genetic diversity.

The species is at the brink of extinction—as few as 100 Sumatran rhinos are left in the wild today, due to poaching and habitat loss from logging.

In the wild, Sumatran rhinos are solitary creatures, only coming together to breed. In such few numbers, it is increasingly difficult for them to find each other in their mountainous habitat. If they aren't able to mate, females develop reproductive diseases that prevent them from breeding successfully.

Researchers analyzed samples taken from Sumatran rhinos in zoos, the wild, and museum specimens to reveal differences in the species' mitochondrial DNA and confirm the classification of three subspecies of the rhinos, one of which is likely extinct. Their findings were published in the *Journal of Heredity*.

Principal investigator Alfred Roca, a professor of animal sciences (CGRH/GNDP), said that although the two remaining subspecies are "probably as different as humans were from the Neanderthals," they should be combined into a single conservation unit.

The researchers recommend bringing them into breeding centers as soon as possible, and preserving their genomes. In the future, scientists could use preserved cell lines to create artificial gametes.

This work was supported by the United State Fish and Wildlife Service Rhinoceros and Tiger Conservation Fund, the International Rhino Foundation, the World Wildlife Fund, the National Science and Engineering Research Council (Canada), and the University of Illinois.

## A new way to do metabolic engineering

A group of IGB researchers, including Steven L. Miller Chair of Chemical and Biomolecular Engineering Huimin Zhao (BSD leader/CABBI/MMG) and visiting research associate Jiazhang Lian, reported a new method in *Nature Communications* that could make the metabolic engineering process more efficient.

Metabolic engineering involves modifying microorganisms to produce valuable products such as biofuels and chemicals. This is achieved by changing or deleting the expression of genes to modify the microorganism's genome. In this process, several targets in the genome are modified in order to achieve specific goals.

These targets are typically tested individually in a series of time-consuming steps, limiting productivity and the yield of the final product. The researchers decided to create a method that combines all of these steps and executes them simultaneously, making the process faster and easier. They based this method on the CRISPR system, a method of genetic manipulation that uses a set of DNA sequences to modify genes within a cell.

By performing these manipulations simultaneously, scientists can explore different combinations of manipulations and discover which combination is best. This new method, called CRISPR-AID, will allow researchers to easily explore all the possible target combinations, opening up thousands of possibilities.

The researchers hope to eventually extend to the genome scale—to be able to test all the genes in an organism at once—which would be a considerable leap in the field of metabolic engineering.

## Scientists monitor crop photosynthesis, performance using invisible light

Researchers reported the first continuous field season to use sun-induced fluorescence (SIF) data to determine how soybeans respond to fluctuating light levels and environmental stresses.

The report was published in the *Journal of Geophysical Research - Biogeosciences* and led by postdoctoral researcher Guofang Miao.

Plants convert light energy into sugars and carbohydrates that become our food and biofuel. But up to 2 percent of the plant's absorbed light energy is emitted as fluorescent light.

Researchers captured this process using hyperspectral sensors to detect fluctuations in photosynthesis over the growing season. They designed this continuous study to better understand the relationship between absorbed light, emitted fluorescent light, and the rate of photosynthesis.

A network of SIF sensors has been deployed across the U.S. to evaluate croplands and other natural ecosystems. Kaiyu Guan (CABBI), an assistant professor of crop sciences and principal investigator of this research, said their ultimate goal is to monitor the photosynthetic efficiency of any field across the world to evaluate crop conditions and forecast yields on a global scale in real time.

"This research advances our understanding of crop physiology and SIF at a local scale, which will pave the way for satellite observations to monitor plant health and yields over vast areas of cropland," said Carl Bernacchi (CABBI/GEGC), an associate professor of plant science.

This work was supported by the NASA New Investigator Award; the Institute for Sustainability, Energy, and Environment; a NASA Interdisciplinary Science Award; and the TERRA-MEPP research project, which is funded by the Advanced Research Projects Agency-Energy within the DOE.

# News

## DOE grants $10.6 million to produce more biodiesel, biojet fuel

The DOE awarded the University of Illinois a $10.6 million, five-year grant to transform two of the most productive crops in America into sustainable sources of biodiesel and biojet fuel. The research project Renewable Oil Generated with Ultra-productive Energycane—or ROGUE—kicked off with a team meeting held in conjunction with the 2018 Genomic Sciences Program Annual Principal Investigator Meeting in Tysons, Virginia.

"The U.S. continues to enjoy cheap, abundant energy but more than 80 percent of which is derived from natural gas, coal, and petroleum," said ROGUE Director Stephen Long (BSD/CABBI/GEGC), Ikenberry Endowed Professor of Crop Sciences and Plant Biology. "Heavy, diesel-powered semi trailers and the aviation industry desire other options, but electric batteries are not feasible, and current biofuel crops cannot meet demands for biodiesel and biojet fuel."

ROGUE will engineer energycane, a bioenergy crop derived from sugarcane, and Miscanthus to produce the oil that is used to create biodiesel and biojet fuel. Their work is guided by computer models, which project that these crops can achieve 20 percent oil content in the plant, a dramatic increase from natural levels of less than a tenth of one percent.

ROGUE is a collaboration among researchers from Illinois as well as Brookhaven National Lab, University of Florida, and Mississippi State University.

## Crop-counting robot earns top recognition at leading robotics conference

Today's crop breeders are trying to boost yields while also preparing crops to withstand severe weather and changing climates. To succeed, they must identify genes for high-yielding, hardy traits in crop plants' DNA. A robot developed by plant scientists, computer scientists and roboticists to help with this task was recognized by the best systems paper award at Robotics: Science and Systems, a leading robotics conference held in Pittsburgh.

"There's a real need to accelerate breeding to meet global food demand," said principal investigator Girish Chowdhary (GEGC), an assistant professor of field robotics in the Department of Agricultural and Biological Engineering and the Coordinated Science Lab. "In Africa, the population will more than double by 2050, but today the yields are only a quarter of their potential."

Crop breeders run massive experiments comparing thousands of different cultivars, or varieties, of crops over hundreds of acres and measure key traits, like plant emergence or height, by hand. The task is expensive, time-consuming, inaccurate, and ultimately inadequate—a team can only manually measure a fraction of plants in a field.

To address this challenge, the researchers developed the 13-inch wide, 24-pound robot named TerraSentia. It is transportable, compact and autonomous, and able to capture each plant from top to bottom using a suite of sensors (cameras), algorithms, and deep learning.

This work was supported by the DOE Advanced Research Project Agency-Energy (ARPA-E) as part of the TERRA-MEPP project at the IGB, a partnership between the University of Illinois, Cornell University, and Signetron Inc. The robot is now available through the start-up company, EarthSense, Inc., which is equipping the robot with advanced autonomy and plant analytics capabilities.

## New NIH-funded research aims to improve prostate cancer outcomes

Researchers led by Bioengineering Assistant Professor Andrew Smith (ONC-PM) recently received a $1.8 million grant from the NIH to develop a new assay technology that could determine the effectiveness of cancer drug treatments and aid in disease prognosis. The team is focusing on detecting nucleic acid-based biomarkers in a single drop of a cancer patient's blood.

"Very few types of cancer can be detected or monitored using bodily fluids," Smith said. "Instead, most cancers require invasive biopsies or imaging tests that cannot monitor changes in real time." Smith's Illinois collaborators include Donald Biggar Willett Professor of Electrical and Computer Engineering Brian Cunningham (ONC-PM leader/MMG) and Assistant Professor of Epidemiology Rebecca Smith (IGOH).

One such example is prostate cancer. Doctors screen for this disease using a 1970s-era blood test for a compound called prostate-specific antigen (PSA) that is produced by prostate tissue, including cancer cells. If a patient's PSA level is high, he has to undergo an invasive and painful biopsy to determine whether cancer is present or not; this procedure does not distinguish well between slow-growing and aggressive forms of the disease.

Smith and his team, which includes researchers from the Medical College of Wisconsin and Mayo Clinic, are taking an entirely different approach. By frequently measuring the concentrations of microRNA biomarkers in a patient's blood during his cancer treatments, they believe they can determine precise therapeutic regimens for each patient. According to Smith, the assay technology they are developing will be the first to read out nucleic acids from a single drop of blood.

# News

## New Woese Undergraduate Research Scholar Lauren Todorov

Lauren Todorov likes to think that life is a web—if you look hard enough, you'll find that everything is connected. She applied this mindset to the research she pursued as this year's Carl R. Woese Undergraduate Research Scholar.

Todorov, a senior in molecular and cellular biology, joined Professor of Geology and Microbiology Bruce Fouke's (BCXT) research group in 2017 and became involved in the lab's research on universal biomineralization, a concept that focuses on the interactions between water, rock, and microbes, and how "life makes rock."

Todorov's research focused on studying coral and several aspects of its biology, ecology and evolution. Studying coral formation can help scientists better understand many processes in the human body and the natural world, including climate change, human arthritis, osteoporosis, kidney stones, and rock formation on earth and in space.

Todorov said the multidisciplinary environment of IGB gave her a unique research opportunity.

"We have technology here that no one else in the world has," she said. "With this coral project alone, I've learned so much that no one in the world can even test or see."

She said the Woese scholarship program will help her discover what research she wants to pursue in the future.

"Research is my passion," she said. "I'm just excited to do that and see where the research takes me."

## CABBI celebrates official launch

The Center for Advanced Bioenergy and Bioproducts Innovation (CABBI), a collaboration between the IGB and the Institute for Sustainability, Energy, and Environment (iSEE), celebrated its official launch as a new DOE Bioenergy Research Center.

More than 100 scientists and staff from Illinois and its 17 partner institutions—as well as government and campus dignitaries including Chancellor Robert J. Jones—attended the celebration, which was emceed by CABBI Director Evan H. DeLucia (CABBI/GEGC), the G. William Arends Professor of Integrative Biology at the University of Illinois at Urbana-Champaign and the Baum Family Director of iSEE.

"The work we will be doing over the next five years will have a major, lasting impact on our nation's energy, economy, and security," said IGB Director Gene Robinson (GNDP). "We already have people in the labs right here at IGB; the work has begun."

Conversion Theme Leader Huimin Zhao (BSD leader/CABBI/MMG), Sustainability Theme Leader Madhu Khanna (CABBI), and Feedstocks Theme Leader Stephen Moose (BSD/CABBI/GEGC) presented their research plans for CABBI, discussing innovative ideas such as incorporating automation in the design process and engineering grasses with increased yield efficiency.

Visiting scholars toured a greenhouse at the Illinois Energy Farm, where Illinois Assistant Professor of Crop Sciences and CABBI researcher Erik Sacks discussed breeding of Miscanthus and energycane. Researchers later visited the Integrated Bioprocessing Research Laboratory, a state-of-the-art facility that will accelerate the commercialization of bioprocessing technologies in renewable chemicals and fuels.

## Alumnus funds graduate students researching brain tissue cultures

Scott Fisher believes learning how to solve a problem can be as valuable as solving one. This belief is what drove him to create a fund that will support IGB research in the area of regenerative biology and tissue engineering.

The fund will aid the research needs of graduate students who are developing technologies to culture brain tissue to learn about brain cancer, traumatic brain injuries and neurological disorders.

Fisher, an alumnus of the University of Illinois and a retired program manager at Ecolab, created the fund to give back to the university and to honor his late wife, Bonita J. Fisher, who was diagnosed with multiple sclerosis. Fisher believes that multidisciplinary research can eventually make advances in curing diseases like this.

The IGB's RBTE theme is working to build a model that will enable researchers to study tissue outside of the brain. Studying brain tissue is particularly difficult because it is unlike any other tissue in the body. The tissue engineering community has struggled to build effective models of brain tissue. After learning about the work of the RBTE theme, Fisher thought it was a perfect fit.

Using cancer cells received from Mayo Clinic, a partner on this project, RBTE researchers are studying a primary culture of brain tissue to analyze brain tumors. Similar approaches are being used, in collaboration with neurobiologists at Rockefeller University, to study traumatic brain injuries and degenerative brain conditions such as multiple sclerosis.

# AWARDS

**Rashid Bashir**
Grainger Distinguished Chair of Bioengineering (ONC-PM/RBTE); Royal Society of Chemistry Fellow; Biomedical Engineering Society's Robert A. Pritzker Distinguished Lecture Award

**Alison Bell**
Associate Professor of Animal Biology (GNDP); University Scholar

**Martin Burke**
Professor of Chemistry (MMG); University Scholar

**Carla Cáceres**
Professor of Animal Biology (IGOH); Fellow of the American Association for the Advancement of Science

**Brian Cunningham**
Donald Biggar Willett Professor of Engineering and Professor of Electrical and Computer Engineering (ONC-PM leader/MMG); Institute of Electrical and Electronics Engineers Photonics Society Distinguished Lecturer Program; Center for Advanced Study Associate

**Sharon Donovan**
Professor of Nutrition and Melissa M. Noel Endowed Chair in Nutrition and Health (MME); National Academy of Medicine

**Brendan Harley**
Professor of Chemical & Biomolecular Engineering (RBTE leader); Campus Distinguished Promotion Award; College of Engineering Dean's Award for Excellence in Research; College of Liberal Arts and Sciences Dean's Award for Excellence in Undergraduate Teaching

**Hannah Holscher**
Assistant Professor of Nutrition (MME); New Innovator in Food and Agriculture Research, Foundation for Food and Agriculture Research

**Paul Kenis**
William H. and Janet G. Lycan Professor and Head of Chemical & Biomolecular Engineering (RBTE); Elio Eliakim Tarika Endowed Chair in Chemical Engineering

**Andrew Leakey**
Professor of Plant Biology (CABBI/GEGC); University Scholar

**Ting Lu**
Associate Professor of Bioengineering (BCXT/BSD/CABBI/MME); American Chemical Society Infectious Diseases Young Investigator Award

**Zaida Luthey-Schulten**
William H. and Janet G. Lycan Professor of Chemistry (BCXT); Fellow of the Biophysical Society

**Olgica Milenkovic**
Professor of Electrical and Computer Engineering (BSD/GNDP/ONC-PM); Fellow of the Institute of Electrical and Electronics Engineers

**Douglas Mitchell**
Professor of Chemistry (MMG); Alumni Research Scholar Professor of Chemistry; Campus Distinguished Promotion Award

**Jeffrey Moore**
Murchison-Mallory Professor of Chemistry and Professor of Materials Science and Engineering (BSD); U.S. Secretary of Energy's Achievement Award; Stephanie L. Kwolek Award, Royal Society of Chemistry

**Stephen Moose**
Professor of Crop Sciences (BSD/CABBI/GEGC); Karl E. Gardner Outstanding Undergraduate Adviser Award, College of Agricultural, Consumer and Environmental Sciences

**Gene Robinson**
(Director/GNDP); Wolf Prize in Agriculture; National Academy of Medicine

**Saurabh Sinha**
Professor of Computer Science (BSD/CABBI/GNDP); American Institute for Medical and Biological Engineering Fellow; University Scholar

**Rachel Smith-Bolton**
Assistant Professor of Cell and Developmental Biology (GNDP/RBTE); I. C. Gunsalus Scholar, College of Liberal Arts and Sciences

**Rebecca Stumpf**
Associate Professor of Anthropology (BCXT/CGRH/IGOH); Center for Advanced Study Associate

**Jonathan Sweedler**
James R. Eiszner Family Endowed Chair in Chemistry (BSD/CABBI/MMG); "Magnificent Tens" Power List, The Analytical Scientist

**Amy J. Wagoner Johnson**
Associate Professor of Mechanical Science and Engineering (CGRH/RBTE); College of Engineering Dean's Award for Excellence in Research

**Dave Zhao**
Assistant Professor of Statistics (CGRH/GNDP); Lincoln Excellence for Assistant Professors Award, College of Liberal Arts & Sciences

**Huimin Zhao**
Steven L. Miller Chair in Chemical and Biomolecular Engineering (BSD leader/CABBI/MMG); Marvin Johnson Award, Biochemical Technology Division of the American Chemical Society

# GRANTS

**Mikel Hernaez**
Chan Zuckerberg Initiative
"Quantization and Compressive Learning Methods for Omics Data"

**Gene Robinson**
**Huimin Zhao**
**Xin Li**
**Ting Lu**
DARPA
"Protecting the National Food Supply: Advanced Bio-Manufacturing to Produce Deployable Pollinating Units"

**Evan DeLucia**
**Donald Ort**
**Vijay Singh**
**Madhu Khanna**
**Stephen Moose**
**Huimin Zhao**
Department of Energy
"Center for Advanced Bioenergy and Bioproducts Innovation"

**Ting Lu**
**Yong-Su Jin**
Department of Energy
"Dissecting the Division of labor in Microbial Consortia for the Production of Biofuels and Chemicals"

**Stephen Long**
**Carl Bernacchi**
**Patrick Brown**
**David LeBauer**
**Donald Ort**
**Vijay Singh**
**Girish Chowdhary**
**Kaiyu Guan**
Department of Energy: ARPA-E
"TERRA-MEPP (Mobile Energy-crop Phenotyping Platform) TERRA PLUS-UP"

**Gene Robinson**
**Saurabh Sinha**
GA State Univ/National Science Foundation
"RCN: The Genetics and Genomics of Social Behavior"

**Stephen Long**
**Donald Ort**
**Yong-Su Jin**
Gates Foundation
"Reinvestment: RIPE: Realizing Increased Photosynthetic Efficiency for Sustainable Increase in Crop Yield"

**Matthew Hudson**
**Liudmila Mainzer**
**Derek Wildman**
**Ravi Iyer**
**Olgica Milenkovic**
**Saurabh Sinha**
Mayo Foundation
"Mayo Clinic Grand Challenge: Computational Methods for Insight into Hypoplastic Left Heart Syndrome"

**Gene Robinson**
Modular Biosciences Inc.
"Modular Biosciences Inc. FUA"

**CheMyong Ko**
**Yuan-Xiang Pan**
National Institutes of Health
"Conversion of ERalpha Cells to ERbeta Cells in a Cell Lineage"

**Paul Hergenrother**
**Timothy Fan**
**Gee Lau**
**William Metcalf**
**Emad Tajkhorshid**
**Christina M. White**
National Institutes of Health
"Predictive Guidelines for Penetrance and Discovery of Broad-Spectrum Antibiotics"

**Paul Hergenrother**
**Timothy Fan**
National Institutes of Health
"Targeted Therapy for Head and Neck Cancer"

**Paul Hergenrother**
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**David Kranz**
National Institutes of Health
"Small Molecule Activators of Procaspases as Anti-Cancer Agents"

**William Metcalf**
National Institutes of Health
"Discovery, Biosynthesis and Bioactivity of Phosphonic Acid Natural Products"

**Amy Wagoner Johnson**
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**Gabriel Juarez**
National Science Foundation
"Convergence: RAISE Engineering Coral Reef Recovery"

**Mayandi Sivaguru**
Pioneer Hi-Bred Intl
"Imaging of Molecules Introduced into Company's Plant Cell Samples"

**Ravi Iyer**
**Carl Gunter**
**Saurabh Sinha**
Sandia National Laboratory
"Security and Privacy for Genomic Data"

**Christopher Rao**
**Roderick Mackie**
University of CA, Berkeley/Shell Oil
"Biological Methane Conversion"

**Paul Kenis**
University of CA, Berkeley/Shell Oil
"Durable Electrodes and Electrolyzers for Efficient Electroreduction of Carbon Dioxide to CO"

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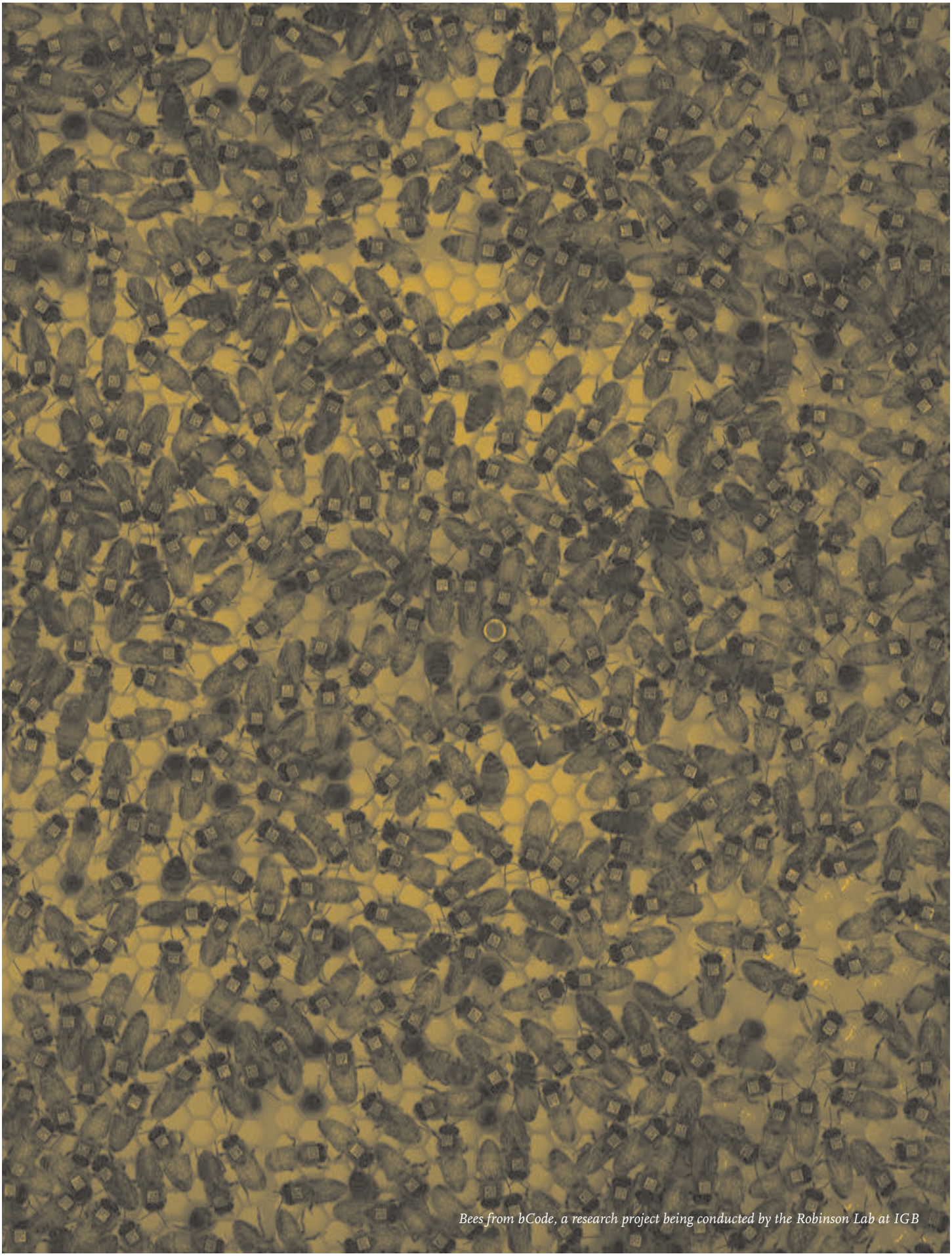
**Derek Wildman**
Women & Infants Hospital Rhode Island
"Inflation Test Validation and Testing Fetal Membranes"



*Bees from bCode, a research project being conducted by the Robinson Lab at IGB*

# Give to the IGB

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

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

## IGB Annual Fund

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

## Carl R. Woese Research Fund

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

## iGEM Undergraduate Team

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

## Stay Connected with the IGB

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