Vol. 7 University of Illinois at Urbana-Champaign

BIOMARKER

INSTITUTE
FOR GENOMIC
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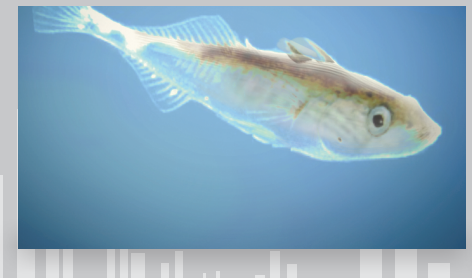
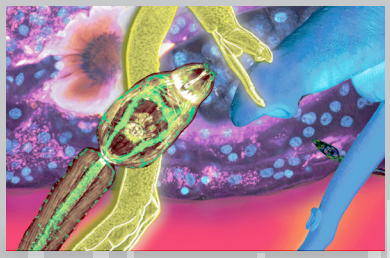
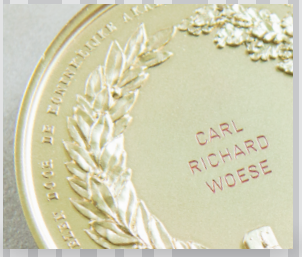
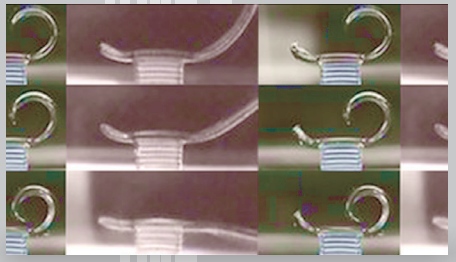




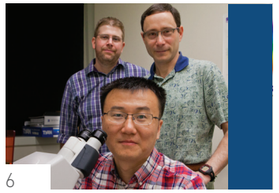


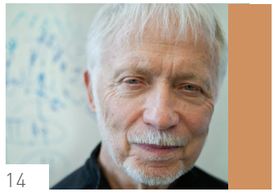


• PIONEERING ADVANCES IN THE LIFE SCIENCES •

Biomarker magazine promotes the interdisciplinary & collaborative research taking place @ the Institute for Genomic Biology (IGB) @ the University of Illinois.

FEATURES





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DIRECTOR'S MESSAGE

Once and Future Biology

A genome is simultaneously a record of an organism's evolutionary past, and a dynamic structure that allows the organism to respond to its environment and prepare for future events. At the Institute for Genomic Biology, we have found and continue to innovate ways to investigate these dual roles of the genome, and to apply insights from these investigations to societal challenges. We are excited to share our latest efforts and plans with you in this issue.

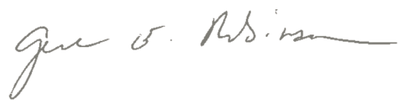
Research that uses the genome as a lens through which to view evolutionary history is in part the legacy of one of the IGB's great researchers and founding members, Carl Woese, who passed away in December 2012. Woese' quest to objectively determine phylogenetic relationships among bacteria, which his ingenious use of ribosomal RNA sequencing made possible, led to his revolutionary discovery of Archaea, the third domain of life. The Institute for Universal Biology at the IGB, a NASA Astrobiology Institute-funded project that Woese helped to found, continues to use genomic data to pursue one of the profound questions that inspired him: how did life originate?

Another IGB research project, based in the new Gene Networks in Neural & Developmental Plasticity research theme, funded by the Simons Foundation, is searching for the origins of genomic mechanisms that enable individual animals to respond to social stimuli. The project will take full advantage of the varied expertise in the theme, combining brain transcriptomic data from a diverse set of animal species with yet-to-be developed bioinformatic tools to construct and compare networks of gene interactions within and across those species. Cross-species commonalities in the genomic response to social situations will reveal just how ancient the roots of our own social behavior may be.

A second new research theme, Biosystems Design, is embarking on an effort to translate our knowledge of transcriptional regulation into new technologies that allow us, for the first time, to engineer the genome of a eukaryotic cell in the same systematic way that we might design and construct a computer. The Carver Foundation grant recently received by the theme will support the development of tools that can then further a broad array of endeavors, including improvement of pharmaceutical production and the enhancement of fuel or food crops.

We hope you enjoy reading about these stories, as well as the others on the pages that follow—of IGB researchers working to identify genomic targets for halting the proliferation of a harmful parasite or enhancing the photosynthetic process of a food crop in order to increase food yields, or to extend other boundaries of current understanding and technology. The past and future success of the IGB is intimately related to the marriage of distinct elements—basic and applied research, biology and informatics, evolution and engineering—to make a powerful new synthesis.

The genome allows us a look into the past, but also inspires visions for what may be to come. Advancing our understanding of genomics will lead to potential solutions to a host of deep biological problems, and in doing so promotes a better future for all the species that share our planet.



Gene E. Robinson
Director, Institute for Genomic Biology

THE IGB'S NEW RESEARCH THEME WAS AWARDED A GRANT FOR ITS FACILITIES FROM THE ROY J. CARVER CHARITABLE TRUST

THE **RIGHT TOOLS** FOR THE JOB

Four thousand years ago, metal working by melting and casting was introduced to Britain. Yet it wasn't until the industrial revolution that technological breakthroughs produced enough cast iron and steel to establish modern-day foundries.

Today scientists at the Institute for Genomic Biology are building a "living foundry" where they will manufacture molecules and materials in an automated, scalable, and high throughput manner using synthetic biology, a new discipline that uses engineering principles to design biological systems more quickly and efficiently.

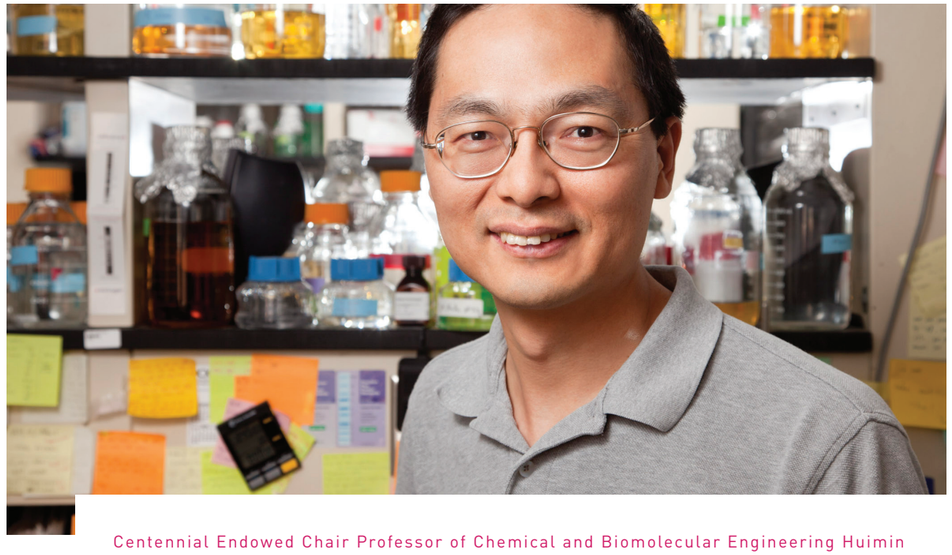
It is the newest "bio-technique" of the biotechnology industry, made possible by recent advances in synthesizing DNA, said Huimin Zhao, a Centennial Endowed Chair Professor of Chemical and Biomolecular Engineering and a faculty member of the Energy Biosciences Institute. In 1970, scientists could synthesize about 75 rungs of the ladder-shaped DNA molecule. In 2008, researchers synthesized more than 580,000 base pairs. Today, almost any gene can be ordered online.

With a $2 million grant from the Roy J. Carver Charitable Trust, researchers will now be able to purchase the research instruments they need to establish a living foundry as part of the new synthetic biology research theme Biosystems Design, led by Zhao, at the IGB.

"Most synthetic biology centers work with bacterial cells, like *E. coli*," Zhao said. "We will be one of the first to develop new synthetic biology tools for plant and mammalian cells. This has the possibility to create huge scientific advances, such as plants with better photosynthetic capacities or gene therapy for diseases like sickle cell anemia and inherited cancers."

To do this, the researchers will have to create new scalable and high throughput technologies that are able to efficiently and cost-effectively construct large DNA molecules, such as pathways and vectors, and alter the expression of multiple genes simultaneously within the cells of plants and animals—technologies that do not yet exist.

The Carver grant will be used to design and build a comprehensive system that will include, but is not limited to, liquid handlers, thermocyclers, incubators, plate hotels, plate readers and a robotic arm. "We can automate a lot of the steps for large-scale DNA construction," Zhao said. "The robotic arm will basically move from one instrument to another. It is highly integrated and automated."



Centennial Endowed Chair Professor of Chemical and Biomolecular Engineering Huimin Zhao is the leader of the newest research theme at the IGB, Biosystems Design.

But it's just a start, Zhao said. "This grant provides us with the basics so that we can be more competitive when we apply for grants because we will already have set up an infrastructure."

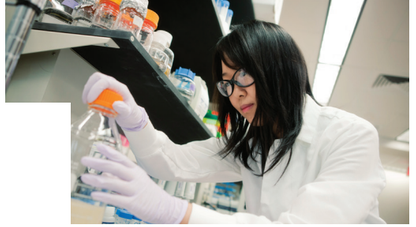
To help them earn additional grants and achieve results, the new research theme will still need to develop more tools such as computational tools for pathway design and genome engineering, and integrated, high throughput detection and analysis tools.

"With the right tools, our research has the potential to vastly improve everything from crop yields to quality of life," Zhao said. "I think this new theme will be doing important work."

Still, Zhao knows that it takes more than equipment to achieve success in the lab. He has recruited talented researchers, including twelve University of Illinois faculty members from seven different departments. With these new tools and top university theme members, coupled with the IGB's interdisciplinary nature, this new theme is off to a promising start.

Roy Carver was an industrialist and philanthropist, famous for his tire manufacturing company Bandag Inc., as well as a University of Illinois graduate (class of '34). The Roy J. Carver Charitable Trust was established after his death to further biomedical and scientific research, as well as children's education and recreation. Grants are dispersed largely to programs in Illinois and Iowa, where he spent the majority of his life.

Various groups at the University of Illinois have received grants from the Carver Trust in the past, including two in 2011 totaling $215,000.



WHAT IS **SYNTHETIC BIOLOGY**?

Imagine what it takes to engineer a car: all the small parts that make up the larger components that make up the engine, gears and other devices that make up a car.

The same is true of biological systems where genes are made of DNA, genes encode proteins, and DNA and proteins are part of cells.

Thus, engineering a cell is sort of like engineering a car, each being assembled from lots of smaller parts and modules.

Of course, that's a pretty simplistic view.

"We all know biology is complex," Zhao said. "In many cases, you can put all the parts together and it will not work. You still have to understand the complexities in the biological systems."

Right now, plant engineering is very tedious. Researchers add a gene and it takes a long time—over several generations—to clone or cross hardy, transgenic plants that express the gene.

Through synthetic biology, it is much faster to create transgenic plants using engineering concepts such as standardization, modularization, and systems integration.

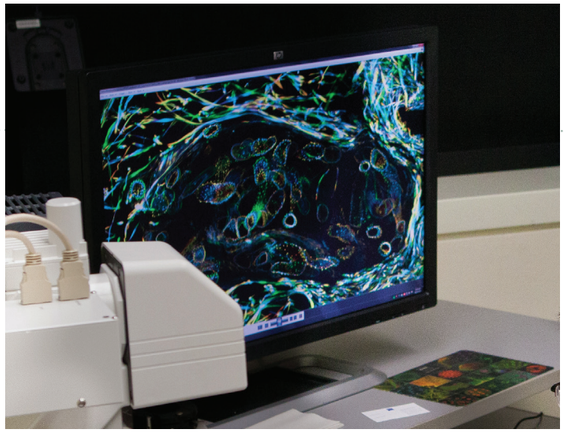
"We try to use engineering principles to design the biological systems more quickly and efficiently," Zhao said. "That's the whole motivation for synthetic biology—to have modules or parts that you can put together to build a cell just like a computer."

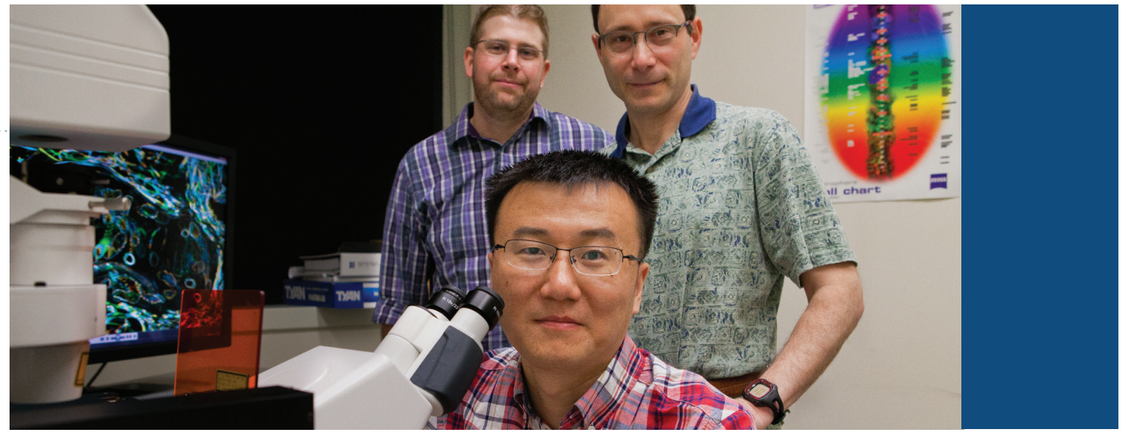
Researchers can use synthetic biology to discover novel antibiotics and anticancer drugs, or produce biofuels and chemicals. They can even engineer cells to do computation by monitoring when a response is triggered by a certain number of molecules entering the cell.

Synthetic biology is the "design, construction, and characterization of improved or novel biological systems using engineering design principles," according to Huimin Zhao's textbook on the subject.

ILLINOIS RESEARCHERS ADVANCE UNDERSTANDING OF **SCHISTOSOME REPRODUCTION**

CHARACTERIZING STEM CELLS IN LARVAL SCHISTOSOMES MAY HELP CONTROL THE PROLIFIC HUMAN PARASITE





IGB Fellow Bo Wang (front) with Phil Newmark (right) and James Collins III (left) are studying the unique mechanisms that allow schistosomes' germinal cells to create thousands of clonal larvae that can then infect humans.

Ancient Egyptian mummies revealed that humans have been hosting parasitic flatworms called schistosomes for more than 5,000 years. Today the parasites continue to plague millions of people across the world, causing roughly 250,000 deaths each year.

The schistosome reproductive cycle results in exponentially more schistosomes each generation. Not only do the adults lay hundreds to thousands of eggs each day, but the larval schistosomes are able to clone themselves thousands of times, with each clone capable of developing into an egg-producing adult.

Researchers at the University of Illinois quickly realized that one key to controlling schistosomes is being able to control their incredibly prolific life cycle. In a recent study published in the journal *eLife*, Illinois researchers have come one step closer to understanding the unique mechanisms that allow schistosomes' germinal cells, stem cells that multiply into other types of cells, to create thousands of clonal larvae that can then infect humans.

THE DISEASE

This work adds to our understanding of the basic biology of schistosomiasis, a chronic disease caused by schistosome parasites that robbed at least 243 million people of their productivity in 2011.

"People don't feel well, and so they are not productive in their work," said James Collins III, a postdoctoral researcher in the Department of Cell and Developmental Biology (CDB) at Illinois. "This disease keeps them from being able to realize their full potential, and in turn, they remain poor and are exposed to more diseases like schistosomiasis, which are ultimately diseases of sanitation. It's a disease of poverty that also perpetuates poverty."

Schistosomiasis can result in abdominal pain, diarrhea, and blood in urine or feces. The parasite's eggs, and not the parasite itself, cause these symptoms and others. The bloodstream carries many of the eggs to the liver and other areas of the body, where they can trigger a massive immune response.

"When you look at people who have a high level of infection, you see many holes in their liver," said Phillip Newmark, a Professor of Cell and Developmental Biology at Illinois, an Investigator of the Howard Hughes Medical Institute, and an affiliate of the Regenerative Biology and Tissue Engineering research theme at the Institute for Genomic Biology. "Where there was an egg, a hole is formed where the tissue has been destroyed by the host immune system's inflammatory response."

THE LIFE CYCLE

Every day for decades, adult schistosomes can lay hundreds to thousands of eggs. Their life cycle starts over when the eggs are excreted from the human host through urine or feces. When the eggs contact water, they hatch out "miracidia" that seek out the snail intermediate hosts.

Inside the correct species of snail, the miracidia become sporocysts, essentially sacs filled with germinal cells, that undergo clonal expansion, making tens to hundreds of thousands of copies of themselves in the form of "cercariae." The fast-swimming cercariae are shed from the snail and search for human hosts who find themselves in cercariae-infested fresh water.

"They are attracted by the fatty acids in your skin," said Collins. "In the lab, you can leave your thumbprint on a plastic petri dish and all the cercariae will swarm to your thumbprint and try to penetrate the plastic."

Once they find a host, they are able to burrow through the skin and enter the bloodstream. Inside the body, they migrate to specific sites in the human host, mature into male or female worms, and find mates with whom they will live, paired together "in copula." If left undetected, they will continue to mass produce eggs for decades.

THE RESEARCH

Illinois researchers are approaching this important problem from a unique perspective, using developmental biology (the study of how organisms grow and develop) and applying the lessons they have learned from studying planarians, non-parasitic relatives of schistosomes.

"When researchers are just focused on targeting diseases and developing drugs, they may wind up limiting their opportunities by not really understanding the biology of the system," Newmark said. "I think fundamental, curiosity-driven research is still vital for developing long-lasting solutions. If anything comes of this, it will be because we were asking very fundamental questions about these parasites, based on our knowledge of their free-living cousins, the planarians."

The team's research was motivated by the idea that stem cells seem to be key to schistosomes' ability to live within humans, but also to their ability to live and clone themselves within their snail hosts.

They discovered that germinal cells possess a molecular signature—a collection of expressed genes—that is similar to that of neoblasts (adult stem cells) that allow planarians to regrow missing body parts. Among these genes, they identified some that are required for maintaining the germinal cell population.

This evidence suggests that schistosome larvae may have evolved by adapting a developmental program used by non-parasitic flatworms in order to rapidly increase their population—essentially giving them the opportunity to reproduce twice within their life cycle, once asexually inside snail hosts and once sexually inside human hosts.

Illinois researchers believe they can apply this newfound developmental knowledge to future studies that may lead to ways to control, or even eradicate, schistosomes. They have already discovered that they can make the reproductive system of a planarian disappear by removing the function of a neuropeptide; eventually, they hope to do the same in schistosomes.

Still, there's much to be learned, says Collins. "We have really only scratched the surface of understanding the basic biology of these organisms. In order to be able to treat this disease, we need to know more about the organisms that cause it. That's one of our main motivations for this work."

First author Bo Wang, a postdoctoral fellow at the IGB, said the obvious next step will be to further characterize these schistosome cells on a genomic level. "We really need to improve our understanding of schistosome stem cells," Wang said. "We still don't understand all the mechanisms that really make them unique, that really make them have this tremendous capacity to proliferate, or reproduce."

The National Institutes of Allergy and Infectious Diseases (NIAID) funded this study. Wang was also supported by the IGB, who sponsored his fellowship.

PROJECT AIMS TO INCREASE PHOTOSYNTHETIC EFFICIENCY FOR SUSTAINABLE YIELD INCREASE

SOLVING THE 'CHALLENGE OF THE CENTURY'

It's been called the holy grail of plant biology, but to the average high school biology student, it's the process by which plants convert light energy into sugar, or photosynthesis.

Scientists believe that improving the efficiency of photosynthesis has the potential to benefit farmers around the world by increasing the productivity of staple food crops by as much as 60 percent.

Researchers at the University of Illinois received a five-year, $25 million grant from the Bill & Melinda Gates Foundation to improve photosynthesis, a unique and promising challenge that has not been solved since scientists first attempted it in the 1960s.

"The Gates Foundation grant reflects the historic excellence of photosynthesis research on this campus," said Gene Robinson, the Director of the Institute for Genomic Biology. "This research will greatly benefit from the cutting-edge approaches that have been developed by our faculty members over the past few years for plant science research."

This grant will be "game changing" said Stephen Long, the project director and a Gutgsell Endowed Professor of Plant Biology and Crop Sciences at Illinois. "This project represents a huge effort to determine and apply the mechanisms of photosynthesis that can contribute to the challenge of this century, food security for all."

The project, called Realizing Increased Photosynthetic Efficiency (or RIPE) will improve photosynthetic properties in rice and cassava, two staple food crops in Africa and Asia where some of the poorest farmers would greatly benefit from the projected yield bump.

But farmers worldwide would profit as well. "What works for those crops should also work in soybean, wheat, barley, potatoes, and other crops," Long said. "It's likely that what we learn from this research can also be applied to crops much more broadly."

To date, conventional breeding methods have not increased photosynthetic efficiency in any crops, so RIPE researchers are turning to computer simulation models of the highly complex photosynthetic system to identify specific target sites for engineering crops.

"Business as usual crop development in the face of accelerating agricultural demand and the challenges of rapid global change will not get the job done," said Don Ort, RIPE associate director and Robert Emerson Professor of Plant Biology at Illinois. "This award invests in the unique strengths at Illinois as well as at our collaborating institutions and holds exceptional promise for broad impact outcomes."

This computational approach has already found two targets that have boosted the productivity of plants compared with those that receive the same amount of water and nitrogen.

According to the U.N. Food and Agricultural Organization, food production will need to increase by 70 percent in order to feed a third more mouths by 2050. It's a goal Long believes will be tough to achieve without this "holy grail" of plant biology—increased photosynthetic efficiency.

"The rapid increases in production that were achieved during the Green Revolution have slowed and will not meet this target," Long said. "Photosynthesis promises a new area, ripe for exploitation, that will provide part of the yield jump the world needs to maintain food security."

Illinois is conducting the study through an international collaboration with other leading research institutions as sub-contractors.

The Bill & Melinda Gates Foundation, a multibillion-dollar non-profit organization, is dedicated to improving the quality of life for billions of individuals worldwide through its awarded grants. The foundation funds research projects to enhance healthcare, reduce extreme poverty, improve educational opportunities, and increase access to technology.

The RIPE project team includes (from left) project director Stephen Long, associate director Don Ort, Martin Parry (Rothamsted Research), Lisa Emerson (Illinois), Christine Raines (University of Essex) and Murray Badger (Australian National University).

STEPHEN LONG: A PIONEER IN PHOTOSYNTHETIC PRODUCTIVITY

GUTGSELL ENDOWED PROFESSOR STEPHEN LONG IS A LEADING RESEARCHER IN PLANT BIOLOGY AND CLIMATE CHANGE

When most people are thinking about retiring, Stephen Long is gearing up to tackle one of the most important projects of his career, improving the efficiency of photosynthesis—a goal that could increase the yield of staple food crops by as much as 60 percent to the benefit of farmers and consumers worldwide.

"It's what interests me," said Long, a Gutgsell Endowed Professor of Plant Biology and Crop Sciences at the University of Illinois and member of the Genomic Ecology of Global Change theme at the IGB. "I couldn't imagine doing anything else. When I lose interest, that will be when I stop. Delivering improved yields through photosynthesis—that's what I want to see accomplished here to really show we can do this on a significant scale."

Long is the project director of "Realizing Increased Photosynthetic Efficiency," or RIPE, a project that is funded by a five-year, $25 million grant from the Bill & Melinda Gates Foundation.

"Everyone knows what a fantastic example the foundation has set in addressing food supply, particularly for poor farmers in Africa and Southeast Asia," he said. "I believe you can see them as really a model supporter of this critically important area of food supply."

Ensuring the world's food supply has always been at the heart of Long's career. He can remember a time before the Green Revolution when food scarcity and famines claimed millions of lives. "I wanted to save the world so I went to study agriculture," he said.

He earned his bachelor's degree in agricultural botany from Reading University, moving on to acquire his doctorate in plant sciences from Leeds University and become a lecturer in environmental physiology at the University of Essex. After more than 20 years at Essex, Long decided to make the 4,000-mile move to the University of Illinois at Urbana-Champaign.

"Illinois has been the world leader in photosynthesis for 50 years," he said. "So if you work in photosynthesis, this is the place you want to be."

At Illinois, he led the establishment of SoyFACE, the Soybean Free Air Concentration Enrichment facility, and served as the first Deputy Director of the Energy Biosciences Institute, a $500 million project funded by global energy company BP to develop sustainable biofuels.

While a doctoral student, Long discovered the first plant in a temperate climate to undergo C4 photosynthesis, a process that allows plants to lose minimal water and maximize sugar production due to modified anatomies and chemical pathways. Later, he discovered that miscanthus, another C4 plant, can be fruitful in a temperate climate, essentially putting the emerging and promising bioenergy feedstock on the map.

"It wasn't actually being considered a crop in the U.S. until we set up our trials here," Long said. "The key thing we really showed was that miscanthus was very productive, considerably more productive than switchgrass, which had really been the major bioenergy crop being considered in the U.S."

On May 3, 2013, Long's lifelong work was recognized when he was elected to the Fellowship of the Royal Society, the world's oldest scientific academy in continuous existence.

"The Royal Society was just a few miles from where I was brought up in London," Long said. "As a Londoner by birth it is a very special honor."

"I guess I've been lucky," says Long. "I love what I do, and I think that's a big factor. I've been lucky enough to work on my hobby for 40 years."

3D-PRINTED SPLINT **SAVES INFANT'S LIFE**

RESEARCH LED BY MATTHEW WHEELER, RIGHT, COULD HELP THIS REVOLUTIONARY TECHNOLOGY SAVE THE LIVES OF COUNTLESS OTHER CHILDREN

Half a millennium after Johannes Gutenberg printed the Bible, researchers printed a 3D splint that saved the life of an infant born with severe tracheobronchomalacia, a birth defect that causes the airway to collapse.

While similar surgeries have been preformed using tissue donations and windpipes created from stem cells, this is the first time 3D printing has been used to treat tracheobronchomalacia—at least in a human.

Matthew Wheeler, a University of Illinois Professor of Animal Sciences and member of the Institute for Genomic Biology Regenerative Biology and Tissue Engineering (RBTE) theme, worked with a team of five researchers to test 3D-printed, bioresorbable airway splints in porcine, or pig, animal models with severe, life-threatening tracheobronchomalacia.

"If the promise of tissue engineering is going to be realized, our translational research must be translated from our laboratory and experimental surgery suite to the hospital and clinic," Wheeler said. "The large-animal model is the roadway to take this device from the bench top to the bedside."

For more than 40 years, pigs have served as a medical research model because their physiology is very similar to humans. In addition to tracheobronchomalacia, pigs have been biomedical models for muscular dystrophy, diabetes, and other diseases. The team chose to use two-month-old pigs for this study because their tracheas have similar biomechanical and anatomical properties to a growing human trachea.

"Essentially, all our breakthroughs in human clinical medicine have been initially tested or perfected in animal models," Wheeler said. "Through the use of animal models, scientists and doctors are able to perfect techniques, drugs, and materials without risking human lives."

First, Wheeler sent a CT scan of a pig's trachea to Scott Hollister, a Professor of Biomedical Engineering at the University of Michigan. Hollister used the CT scan and a 3D CAD program to design and print the splints. These devices were made from an FDA-approved material called polycaprolactone or PCL, which Wheeler has used in more than 100 large-animal procedures.

Next, Wheeler developed a strategy to implement the device and U-M Associate Professor of Pediatric Otolaryngology Glenn Green carried out the surgical procedure. After the splint was placed, the pigs' tracheobronchomalacia symptoms disappeared.

"All of our work is physician inspired," Wheeler said. "Babies suffering from tracheobronchomalacia were brought to ear, nose and throat surgeons, but they didn't have any treatment options. They turned to us to engineer a cure."

KAIBA'S CARE

Kaiba (KEYE'-buh) Gionfriddo was six weeks old when he suddenly stopped breathing and turned blue at a restaurant with his parents. As a result of severe tracheobronchomalacia, his heart would often stop beating, and despite the aid of a mechanical ventilator, he had to be resuscitated daily by doctors.

April and Bryan Gionfriddo believed their son's chance of survival was slim until Marc Nelson, a doctor at Akron Children's Hospital in Ohio, mentioned researchers from the University of Michigan were testing airway splints similar to those used in Wheeler's study.

After obtaining emergency clearance from the Food and Drug Administration, Hollister and Green used computer-guided lasers to print, stack, and fuse thin layers of plastic to make Kaiba's splint.

The splint was sewn around Kaiba's airway to expand his collapsed bronchus and provide support for tissue growth. A slit in the side of the splint allows it to expand as Kaiba's airway grows. In about three years, after his trachea has reconstructed itself, his body will reabsorb the splint as the PCL degrades.

Soon Kaiba's tracheotomy tube will be removed after a year without any breathing crises. His success story provides hope for other children born with this disorder, an estimated 1 in 2,100 births.

"It's not very rare," Wheeler said. "It's really not. I think it's very rewarding to all of us to know that we are contributing to helping treat or even cure this disease."

More data from Wheeler's large animal trials will be essential to show the long-term viability of this procedure before it can be used to save the lives of other children born with this disorder. In future trials, Wheeler plans to add stem cells to the splint in order to accelerate healing.

This translational research was conducted at the IGB, considered by many to be the Midwest region's center for large-animal biomedical models.

"We have a reputation for being excellent in this area," Wheeler said. "We would like to capitalize on the expertise and the facilities that we have here to continue to conduct life-saving research. I'm hoping that this story will encourage more people to come to us and say 'Hey, we'd like to develop this model.'"

'MINING' FOR THE **ORIGIN OF LIFE**

Illinois members of the Institute for Universal Biology, Top, from left: Lee DeVille, Nigel Goldenfeld, Charles Werth. Bottom, from left: Isaac Cann, Rachel Whitaker, Elbert Branscomb, Carl Woese (now deceased), Bruce Fouke, Zan Luthey-Schulten, Rod Mackie. Not pictured: Gary Olsen.

RESEARCH TEAM TO MINE GENOMIC DATA TO INFER UNIVERSAL ASPECTS OF THE EVOLUTION OF LIFE IN DEEP TIME

In the 3.5-3.8 billion or so years leading up to humans walking on two legs and inventing things like microprocessors, life has been continuously evolving from the Last Universal Common Ancestor, called LUCA.

But what happened before LUCA, a small, single-cell organism, came on the scene?

Scientists at the University of Illinois at Urbana-Champaign want to find out. The newly formed Institute for Universal Biology, a NASA Astrobiology Institute (NAI), will study the origin and evolution of life before LUCA on a five-year grant totaling approximately $8 million.

"How does life begin and evolve? Is there life beyond Earth? Why does life exist at all?" asked Nigel Goldenfeld, principal investigator and Swanlund Professor of Physics. "The NAI is the most far-sighted attempt to address these foundational questions that everyone asks at some time in their life. We are thrilled to participate with the NAI in perhaps answering some of the most important questions in all of science."

The goal is to characterize the fundamental principles governing the origin and evolution of life anywhere in the universe using the evolution of life on Earth as a model. This multidisciplinary effort to define and characterize "universal biology" will include the fields of microbiology, geobiology, computational chemistry, genomics, and physics.

Illinois researchers will study the first billion years of life that predated LUCA, using genomics to find signatures of early collective states of life. The group will also perform laboratory work to study in detail how individual cells sense, respond and adapt to changing environments.

The project will also look for signatures of the major transitions that life must make as evolution changes character from being communal to the modern era where organisms' lineages can be traced along the branches of a family tree.

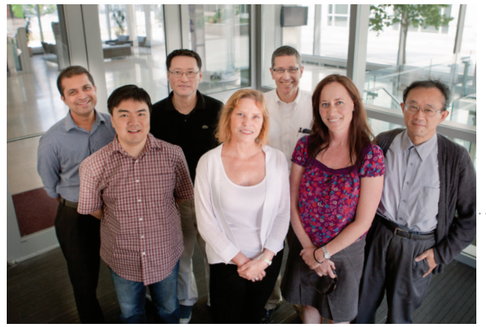
"It is important to develop the field of universal biology, because we may never find traces of life on other planets," Goldenfeld said. "But if we understand that life is generic, maybe even an expected outcome of the laws of physics, then we'll know for sure that we are not alone."

The research will be based at the Institute for Genomic Biology, where Goldenfeld is leader of the Biocomplexity research theme. "This bold research program fits perfectly at the IGB, which was established to help faculty compete for the large grants that are necessary to address grand challenges with a team-based multidisciplinary approach," said Gene Robinson, Director of the IGB. "The NASA award reflects the creativity and vision of the faculty in the Biocomplexity research theme, the IGB, and the campus as a whole."

The grant also funds educational activities related to astrobiology, including a middle school educational program, a class for online learners, and a large, open-access online course for undergraduates. Short web-based videos on astrobiology concepts and findings, called "AstroFlix," will be developed with the grant's support.

Co-investigators on the research team include Elbert Branscomb, Isaac Cann, Lee DeVille, Bruce Fouke, Rod Mackie, Gary Olsen, Zan Luthey-Schulten, Charles Werth, Rachel Whitaker, and Carl Woese (now deceased) from Illinois, Scott Dawson from the University of California, Davis, and Philip Hastings and Susan Rosenberg from Baylor College of Medicine, in Houston.

IGB BIOLOGISTS AND BIOINFORMATICIANS UNITE TO EXPLORE THE **ORIGINS OF SOCIAL BEHAVIOR**



(left) GNDP members Saurabh Sinha, Jian Ma, Fei Wang, Lisa Stubbs, Gene Robinson, Alison Bell, and Yoshi Oono.

An animal's success in nature depends in part on its ability to navigate social situations—to find a mate, defend a territory, or work with others to obtain a meal. Social interactions are also crucial for humans, not only for survival, but for the exploration of space or the complex systems within our own bodies.

A $3 million grant from the Simons Foundation to the Institute for Genomic Biology will fund a multidisciplinary collaborative effort by Gene Networks in Neural & Developmental Plasticity (GNDP) theme members to search for similarities in the ways that the brains of many different species, including our own, produce social behavior. "Our goal," said GNDP Theme Leader and Principal Investigator Lisa Stubbs, "is to tie the truths we extract from each species together, into a fundamental model of how animal brains respond to social stimulus." Stubbs is a Professor of Cell and Developmental Biology.

The project arose naturally from the varied areas of strength and common interests of GNDP. Theme members Alison Bell, Jian Ma, Yoshi Oono, Gene Robinson, Saurabh Sinha, and Fei Wang are also co-investigators. "Our theme was brought together originally because of our shared interest in what regulatory network architecture can teach us about biology," said Stubbs. "We are especially excited about how conserved gene network components are reused, and reshaped, throughout evolution." Now, theme members will be working together to understand how gene networks in the brains of animals respond to social stimuli and develop new ways to compare those network responses.

Stubbs, Bell, and Robinson and their laboratories will be primarily responsible for conducting experiments in mice, stickleback fish, and honey bees, respectively; these animals exhibit interesting social behaviors that are easy for researchers to manipulate. Oono, as well as Ma, Sinha, and their teams will be innovating novel ways to analyze the genomic data produced by the experimental work. Wang and his research group will begin to forge experimental links between new findings and their relevance in the human brain.

Why do GNDP researchers believe that diverse animal species, even humans, may share molecular mechanisms that direct sociality? Inspiration for the project comes from the highly successful efforts of the past several decades to understand how genes direct anatomical development.

The remarkable outcome of this work was the realization that underlying the anatomical diversity observed across animal species are shared sets of genes that direct development. These sets of genes are conserved across many different species. Morphological differences between species are directed by differences in their spatial and temporal patterns of gene expression, rather than differences in gene sequence. This shared genetic "toolkit" directs development of common structures underlying anatomical diversity, such as body segments and appendages.

Just as there is diversity in the physical structure of animals, there is great variation in the structure of their social interactions with other members of their own species. These interactions can often be grouped into the same broad categories—aggression, mate selection, care of young—but the dynamics vary widely between species. A female prairie vole mates with one male for life; in contrast, a female mouse shows no such fidelity, while a female stickleback fish allows herself to be chased away by her mate, and a praying mantis female might make a meal of hers.

On a basic level, though, there are shared principles of social behavior across species, just as there are in anatomy. Animals rely on information from others to guide their behavior during social interactions, and that information, received as primary input, is processed by sets of connected neurons that operate via molecular actions that are deeply conserved, even if the identities of those sets of neurons are not.

IGB researchers will be taking advantage of these commonalities—shared categories of social interactions and conserved brain biochemistry—to ask whether there are also shared gene actions that guide social behavior. Alison Bell, Associate Professor of Animal Biology, described the planned study: "We will measure the response to what we think are comparable behaviors in honey bees, stickleback fish, and mice, and look for responses in the same genes, networks, or pathways in each of these organisms."

The study will initially focus on the brain genomic response to aggressive social encounters. Researchers will expose individual bees, mice, or fish to an intruder, an unfamiliar individual of the same species. They will then use high-throughput RNA sequencing methods to quantify gene expression in brain regions that based on prior work are believed to be involved in producing social behavior. Similarities in the molecular response within the brain of all three species would suggest that the social behaviors of each, although quite distinct, may have evolved from the traits of an ancient common ancestor.

It is possible that some of the same genes, or genes with similar functionality, will be responsive to social stimuli in all three species. Because of the known complexity of brain genomic responses to behavior, however, researchers will probably need more sophisticated ways to identify similarities. Associate Professor of Computer Science Saurabh Sinha said "We will probably realize that the shared molecular basis across the different species is not as simple as a gene or a set of genes being common to all of them and playing a big role, but that there is a more complex notion of molecular similarity."

To do this, researchers will combine experimental data about gene expression and the structure of the genome with computational and statistical methods. Genes called transcription factors produce proteins that work within the cell to help control the activity of many other genes. Sophisticated analyses that take into account experimental data, along with prior knowledge about how genes are regulated, will produce a model of which transcription factors are most important for directing gene activity after a social encounter. These models, called gene regulatory networks, will be developed for the brain genomic response to aggression in mice, fish, and bees.

A novel and valuable aspect of the study will be the innovation of new computational methods that allow the comparison of gene regulatory networks of different species. Sinha identified such methods as one of the important outcomes of the project: "Tools to compare this basic construct of a regulatory network across different species will play a huge role in that act of comparative genomics."

These novel computational methods will enable researchers to detect conservation of molecular mechanisms on a yet-unexplored level of analysis, the level of gene regulatory networks. "The possibility that the same gene networks have been involved in multiple and independent evolutions of social behavior is very exciting because it would provide a new appreciation of the unity of life," IGB Director and Professor of Entomology Gene Robinson said. Professor of Physics Yoshi Oono also emphasized the potential power of the study to yield major evolutionary insights: "The molecules and their organizations responsible for sociality will be recognized to be much older than we now naively expect; they could be older than Metazoa, could go back at least to Filozoa," that is, several hundred millions of years.

Discovering deeply conserved mechanisms of social response will also further efforts to understand human brain function and social behavior. "The findings would also provide new insights into human neurobiology and mental illnesses," Assistant Professor of Bioengineering Jian Ma said. Associate Professor of Cell and Developmental Biology Fei Wang noted the role of his lab in the project, "to use human stem cell-based neural differentiation models to validate and confirm the findings from the animal models," which will begin to test the connection between study results and potential biomedical applications.

The Simons Foundation, in addition to funding basic life and physical science studies, supports a funding initiative for autism research, making the GNDP study with its potential connections to human social behavior particularly aligned with the Foundation's aims. According to Robinson, "If there are gene networks that play a strong role in social responsiveness in different species, these networks might be the ones that get perturbed in mental illnesses that involve social behavior."

Theme members are energized by the freedom and exploration the grant will support: "Here the focus is on the grander vision of getting insights by comparing whatever we learn from each species … the grant allows us some breathing space to really think on a grand scale, which normal projects don't often do," Sinha said.

This energy, and the strong collaborative aspect of the project, will help GNDP continue to establish itself as a theme. "The Simons proposal grew directly out of discussions we had last summer to formulate the focus of our new theme," Stubbs said. "This project is an almost perfect embodiment of our theme."

In addition to the faculty mentioned, many other theme members are playing important roles in the project. Annie Weisner contributed to pilot studies in mice, and Derek Caetano-Anolles will conduct ongoing mouse behavioral and molecular work. Clare Rittschof contributed to pilot studies in bees, and will be joined by Hagai Shpigler and Matt McNeill for ongoing bee behavioral and molecular work. Abbas Bukhari may assist in conducting behavioral experiments in stickleback fish, in addition to his main role performing bioinformatics analyses. Joe Troy will also contribute bioinformatics analyses. IGB Fellow Ken Yokoyama, Charles Blatti, Laura Sloofman, and Yang Zhang will be involved in computational aspects of the project. Former IGB Fellow Qiuhao Qu will help direct work in human stem cells, and Huimin Zhang and Amy Cash-Ahmed will oversee molecular experiments.

CRACKING **HOW LIFE AROSE ON EARTH** MAY HELP CLARIFY WHERE ELSE IT MIGHT EXIST

A UNIQUE THEORY ABOUT HOW LIFE AROSE ON EARTH MAY REVEAL CLUES TO WHETHER IT MIGHT HAVE ARISEN ELSEWHERE IN THE UNIVERSE

Does life exist elsewhere or is our planet unique, making us truly alone in the universe? Much of the work carried out by NASA, together with other research agencies around the world, is aimed at trying to come to grips with this great and ancient question.

"Of course, one of the most powerful ways to address this question, and a worthy goal in its own right, is to try to understand how life came to be on this planet," said Elbert Branscomb, an affiliate faculty member at the Institute for Genomic Biology. "The answer should help us discover what is truly necessary to spark the fateful transition from the lifeless to the living, and thereby, under what conditions and with what likelihood it might happen elsewhere."

While many ideas about this fundamental question exist, the real challenge is to move beyond speculation to experimentally testable theories. A novel and potentially testable origin-of-life theory—first advanced more than 25 years ago by Michael Russell, a research scientist in Planetary Chemistry and Astrobiology at the NASA Jet Propulsion Laboratory—was further developed in a recent paper published in *Philosophical Transactions of the Royal Society B (PTRSL-B)*, the world's first science journal, by Russell, Wolfgang Nitschke, a team leader at the National Center for Scientific Research in Marseille, France, and Branscomb.

Russell's hypothesis proposes that the transition to life was brought about by a peculiar geophysical and geochemical process called serpentinization—a process that played out on and just beneath the surface of our very young planet's ocean floor in the "Hadean" epoch more than 4 billion years ago.

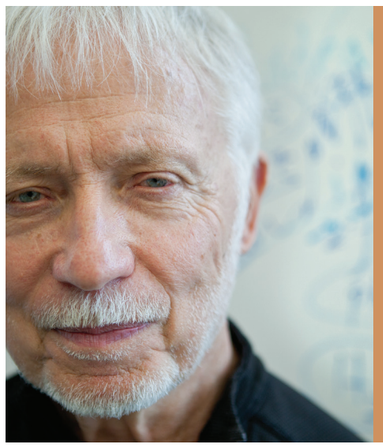
One attractive aspect of the Russell hypothesis is that it provides potential explanations for several seemingly arbitrary and puzzling aspects of how all life on Earth works, including, most notably, how it taps into and exploits sources of energy. This process, quite oddly, involves constantly filling up and depleting a kind of chemical reservoir that is created by pushing a lot more protons onto one side of a membrane than the other—just like pumping water uphill to fill a lake behind a dam.

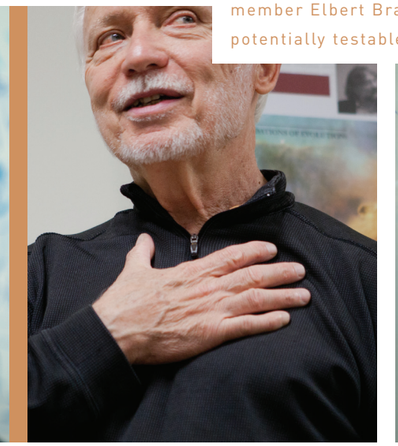
Then, mimicking how hydroelectric turbines are driven by water flowing downhill, these protons are only allowed to flow back "downhill" through the membrane by passing through a turbine-like molecular "generator," which creates, instead of high-voltage electricity, a chemical fuel called ATP, the cell's "gasoline." All cells then burn ATP in order to power their vital processes. The cells of air-breathing organisms, like us, burn ATP by ultimately converting oxygen to CO_2.

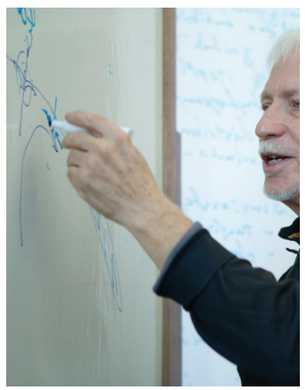
Furthermore, while every bacterial cell has its own proton reservoir system, our bigger cells contain and cultivate herds of ex-bacteria (called mitochondria) that maintain their own reservoir, ATP-producing turbines, etc.—a trick of agricultural domestication at the cellular level that makes it possible not only for multi-cellular organisms to exist but to be huge, fast, and dangerous.

This "reservoir-mediated energy business" is not a minor undertaking of life, Branscomb notes. Every day our bodies produce and consume their weight in ATP molecules. In seconds, each newly made ATP molecule is used. In minutes, the body's entire ATP energy reserve is consumed and regenerated.

"That's why you can't stand to be without oxygen for more than a few minutes," Branscomb said. "We live on a thin, desperate edge to keep our metabolic motors running full blast. Yet in spite of this desperation, the process isn't carried out by using our energy sources directly, but by using the indirect, proton reservoir method. It's an arrestingly strange way of doing business that has made many scientists question why it is this way."







Institute for Genomic Biology affiliate faculty member Elbert Branscomb has further developed a potentially testable origin-of-life theory.

The amazing answer, Russell's model suggests, is because that's how life got launched. "Before there was anything lifelike to take advantage of it, the geochemical process of serpentinization produced 'for free' (along with much else of critical importance) two of the major components of this energy system: cell-like compartments surrounded by membranes and proton concentration differences on each side of the membranes," Russell said.

Thus, according to Russell's hypothesis, first life didn't have to make any of this stuff for itself. It was all a free gift of geochemistry on a wet, rocky, and tectonically-active planet.

"It's only later when life set out to take its act on the road that it had to figure out how to make its own membranes, pump protons uphill across these new membranes, tap into other sources of energy to do the pumping, etc.," Branscomb said. "But once hooked on the free stuff, the trans-membrane proton gradient in particular, life never broke the habit. And here we are, every living thing, still frantically pumping protons as if just staying alive depends on it—which it does."

Also notably, the Russell serpentinization hypothesis is founded directly on modern understandings regarding the physical nature of early Earth. In particular, at the time life arose, the world was almost entirely covered in a great, deep, and weakly-acidic ocean, the atmosphere was relatively oxidized and rich in CO_2, and tectonic processes constantly replenished and destroyed the crusts of the ocean floor, as they still do today. And it is the exposure of newly made ocean crust to the ocean that gives rise to the geochemical magic of serpentinization.

As areas of new ocean crust cool, the still-stressed rock becomes brittle and develops cracks. Seawater gravitates down the cracks where it is heated and reacts chemically with rock minerals to form a highly-alkaline solution rich in hydrogen (H_2) and methane (CH_4), and containing molybdenum, a metal required by all life. This transformed water, or effluent, is then driven back to the surface, at a temperature of about 100 degrees centigrade, where, in Hadean times, it reacted with cooler, mildly acidic ocean water to create precipitates that form massive chimney-like towers similar to chemical gardens.

These highly-structured precipitate chimneys are comprised of a myriad of micro-compartments bounded by semi-permeable mineral membranes. Across these membranes, a pH (i.e. proton) gradient arises between the extremely alkaline (~pH 11) emerging serpentine effluents and the surrounding, relatively acidic (~pH 5.5) ocean.

Magically, this pH gradient is almost exactly the same as the gradient that all living cells constantly recreate with the same strength and the same direction: acidic on the outside and alkaline on the inside.

"It is at least highly suggestive that every living thing is constantly and indeed furiously recreating something equivalent to this ancient ocean effluent membrane-based proton gradient that serpentinization handed life to start with on the rocky floor of the ancient Hadean ocean," Branscomb said. "It was, in part, by exploiting that naturally-given, geochemical proton gradient that the engines required to produce the molecular 'starter kit' of life got going. So suddenly it's obvious why we pump protons and use this silly method—we became dependent on this 'free lunch' energy system when life was born, developed a lot of fancy machinery for using it, and have never severed that umbilicus since."

After Russell proposed this theory, scientists discovered a real-world example of an alkaline hot spring in the North Atlantic Ocean, called the Lost City. This geochemical edifice provides strong and detailed evidence in its structure and chemical properties for Russell's model that origin-of-life expert Nick Lane, a senior lecturer at University College London, has called the only credible theory to date.

One of the most important, and exciting, aspects of Russell's hypothesis is that the key ideas can, in principle, be tested. This paper and its companion paper by Nitschke and Russell in *PTRSL-B* have advanced Russell's hypothesis and brought it substantially closer to experimental testing. To this end, Russell and his collaborators are currently making experimental model systems that recreate the serpentinization process, including the theory's mineralogical membranes and chemical gradients.

Branscomb, a member of the IGB's Biocomplexity research theme, led by Swanlund Professor of Physics Nigel Goldenfeld, was funded in part by the five-year, $8 million grant from the NASA Astrobiology Institute. The grant funds the University of Illinois's Institute for Universal Biology, a NASA Astrobiology Institute, which includes many members of the Biocomplexity theme who are studying the origin and evolution of life.

"We have a sample of only one planet known to harbor life," Goldenfeld said. "Thus it is critical that we be creative in extracting the most information from Earthly life as possible, if we are to ever understand the existence, likelihood, and nature of life elsewhere in the Universe. Russell, Nitschke, and Branscomb's work lays an intriguing foundation for that endeavor, by cleverly bringing together concepts from thermodynamics, geochemistry and biology to advance a major new hypothesis for life's origins."

SCIENCE SKILLS & **BUSINESS** SAVVY

THE CERTIFICATE IN ENTREPRENEURSHIP AND MANAGEMENT PROGRAM

A growing number of young entrepreneurs have taken advantage of a unique offering, made possible by a collaborative effort between the College of Business and the Institute for Genomic Biology. The Certificate in Entrepreneurship and Management (CEM) program offers the opportunity for individuals who have the scientific and high tech skills to do groundbreaking research to master the business skills required to bring their innovations to market.

For five years, the CEM course has provided a program for those in the engineering, life sciences, and related disciplines, graduating more than 100 students. Composed of MD, DVM, PhD students, and postdoctoral associates, these individuals learn the business, economic, and legal issues in scientific and high tech start-up ventures. Classes take place within the IGB's conference spaces, and at the Business Instructional Facility (BIF) in the College of Business. The curriculum faculty include nationally recognized experts in business, law, life sciences, and associated fields.

Students experience an innovative approach as the curriculum is divided into classroom learning with lectures on business fundamentals and experiential learning using the training models provided by the Kauffman FastTrac® TechVenture™ program.

Business lectures are designed to provide non-business students with the strategic framework for making informed business decisions. This section covers four broad-based areas: Business Innovation, Strategy, Leadership, and Structure, with the goal of preparing students to face potential scenarios encountered in the work environment.

The educational modules of the Kauffman FastTrac® TechVenture™ program provides the students with "learning by doing" exercises to help develop an elevator pitch, business plan, and investor presentation, while being trained in how to identify market opportunities, develop business strategies, build their management team, and determine funding required to move their business forward.

Students can participate in the one-year program, averaging 4-6 hours per week, which consists of a lecture component and experiential sessions. Or, students can simply take the one-semester experiential sessions using the Kauffman FastTrac® TechVenture™ program.

The program runs in both the Fall and Spring semesters. For more information about the CEM program, please visit:

http://www.igb.illinois.edu/cem.

(left) Students in the Certificate in Entrepreneurship and Management (CEM) program learn from prominent faculty and industry leaders. (right) Jay Kesan, Director of the CEM Program and Professor in the College of Law.

REMEMBERING CARL WOESE

In the mid-1950s the discovery of the structure of DNA triggered extensive research into deciphering the genetic code. Other scientists rushed to solve the mysteries hidden within the twisted double helix, but Carl Woese believed the more fundamental question was, how did the code get here in the first place?

Perhaps understanding the origin of the translation mechanism of the genetic code could lead to an understanding of how the cell evolved, which could lead to understanding the very origins of life itself.

Professor of Microbiology and a founding member of the Institute for Genomic Biology, Woese was a giant among scientists. Best known for his discovery of Archaea, the third domain of life, his wider work and theories have transformed scientific thinking about the origins of life and the nature of evolution.

Woese thought the first step to understanding the origins of life would be to find a way to determine a phylogenetic tree for all of life. Since at that time biologists divided the living world into eukaryotes (can be multi-celled and have a nucleus) and prokaryotes (single-celled organisms with no nucleus) he thought he might be able to find the organism that existed before the two branches split.

He determined that if there was going to be one place to look, it should be part of the machinery essential to making proteins. The ribosome, he reasoned, forms part of the protein-making machinery at the heart of all cells and every organism has them. Changes that occur in the ribosome can't be so frequent that they are hard to follow and they can't be so rare as to be uninformative.

"He chose the 'Goldilocks' spot," said Nigel Goldenfeld, Swanlund Professor of Physics and longtime collaborator. "Nobody since then has come up with a better idea for a molecule to look at as the proxy for the history of evolution. There are other molecules one could use, but this is the best one because it varies so slowly. He really thought it through. If it was going to be anything, it was going to be the ribosome."

Serendipitously, Frederick Sanger had just developed an early sequencing technique known as oligonucleotide cataloguing. Woese thought he'd try to adapt it and use it to create his phylogeny. And so, in the late 1960s he began to classify life by sequencing the 16S rRNA (ribosomal RNA) gene of as many organisms as he could get his hands on. It took him a year to create his first catalog and nine more before he began to publish his findings.

In those early days, sequencing was mind-numbing, repetitive, solitary, and tedious work. By 1976 he had sequenced the 16S rRNA of about 30 different kinds of bacteria. Today, with computers and automated sequencers, the work that took him thousands of hours would take less than a week.

So while the majority of the scientific community was trying to understand how the genetic code worked, Woese spent more than a decade working in obscurity to figure out where the code came from in the first place.

"He knew what he was asking and why," says Goldenfeld. "It's that kind of very open-minded scientific investigation that made Woese so unique—it's very rare that someone would do that. You have to really convince yourself that this is the right thing to do and be very determined."

Woese's method worked perfectly; it showed a clear difference in the 16S rRNA between eukaryotes and prokaryotes. One of the most revolutionary results of this work was that, for the first time ever, microbes could be objectively catalogued. Bacteriologists had long since given up being able to do anything of the sort. This achievement opened up the world of microbes to further study and analysis.

Meanwhile, his work led Woese to an unexpected discovery the day he analyzed a methanogen. Methanogens, it was thought, were prokaryotes that live in very hot, oxygen-free environments and produce methane gas. They are difficult to grow in the lab, but Woese's colleague Ralph Wolfe had succeeded and offered his methanogen to Woese for his project.

"The big surprise was when we finally did do one of these methanogens . . . uh-oh, it didn't fit into the prokaryote signature," Woese once said.

The methanogen didn't fit with the eukaryotic signature, either. In fact, methanogens share some characteristics with both eukaryotes and prokaryotes. Woese determined that these organisms, which he termed Archaea, were a third form of life that arose separately from prokaryotes and eukaryotes.

Woese did not set out to discover Archaea. They were as much a surprise to him as to the rest of the scientific community. The finding, announced in 1977 in the journal *Proceedings of the National Academy of Sciences* and trumpeted in newspapers and magazines around the world, rocked the scientific community. This was no new species of butterfly or frog, but a whole

new branch of life.

This discovery absolutely transformed taxonomy, phylogeny, and evolution into experimental sciences rather than subjective pursuits. Woese's work also unveiled the great diversity in microbes. We know now that on the tree of life plants and animals are the tiniest twigs, and microbes occupy 90 percent of the branches.

"He was very clever, he understood so much and yet so much was intuitive for him," says Goldenfeld. "There are other, highly technical things that he did that were just brilliant. Some of them I would ask him, 'why did you do this? And how did you have this stroke of insight?' and he'd say, 'I don't know, actually.'"

Woese's groundbreaking approach and paradigm-shifting research findings should have made the University of Illinois the center of this new field of research. But there was strong resistance within the scientific community. He was not invited to speak at conferences; graduate students did not flock to his lab; funding was sparse.

There were many hard years, but gradually the magnitude of this discovery began to be recognized.

Woese received a MacArthur Fellowship (1984); election to the National Academy of Sciences (1988); the Dutch Royal Academy of Science's Leeuwenhoek Medal, the highest honor in microbiology (1992); and the U.S. National Medal of Science (2000). Probably the most important recognition for Woese was the $500,000 Crafoord Prize in Biosciences in 2003 in recognition of his discovery of the Archaea. The Crafoord Prize is the equivalent of the Nobel Prize for his field, for which there is no such prize. He was later elected to the Royal Society in 2006.

When asked about his major contribution, Woese shrugged it off.

"I'm just an average guy," he told one magazine. "I just happen to have a pretty good intuition regarding biology. I may have brought the complete phylogenetic tree into being, but all I am is a midwife. I'm just glad I was there to help bring it in. Do I feel proud about it? Yes, sometimes. But I don't sit around thinking how great I am.

"I come in here every day because I love this stuff, that's all. To be able to study the past, and to look back down the road into what was happening three or four billion years ago—what a privilege!"

Woese was regularly hailed as an intellectual genius, slaving virtually alone for years upon years, and will be remembered wearing his trademark red-plaid flannel shirts and worn out sneakers, doggedly pursuing his research.

Woese, 84, passed away on Dec. 30, 2012, after a long battle with pancreatic cancer. He was a founding member of the IGB and helped to create the Biocomplexity research theme, which develops novel approaches to microbial ecology, evolution, and systems biology in addition to exploring the origin of life and how it evolved from primordial geochemistry. Before his death, he had been selected to be a co-investigator on the Illinois research team of the Institute for Universal Biology, a NASA Astrobiology Institute, as part of a five-year, $8 million grant.

HELP SUPPORT FUTURE SCIENTISTS THROUGH THE CARL R. WOESE RESEARCH FUND

SUPPORTING SCIENTISTS, LIKE WOESE, SUPPORTS FUTURE DISCOVERIES THAT WILL HAVE THE POWER TO REVOLUTIONIZE OUR UNDERSTANDING OF THE WORLD AND OUR ABILITY TO PROVIDE FOR IT

Through its support of future generations of researchers and scholars, the Carl R. Woese Research Fund will continue to impact science just as Woese's insight profoundly changed our basic understanding of biology through his discovery of the third domain of life.

Woese approved this fund in his name before he died from pancreatic cancer complications at the age of 84. Contributions will not only memorialize a world-renowned scientist but will foster the careers of new scientists.

"We especially want to use this fund to create a cadre of Woese Fellows, postdoctoral associates, graduate students, and undergraduates, specially selected for their creativity and interest in interdisciplinary research in the areas of science that were close to Woese's interests," says IGB Director Gene Robinson. "We believe that the honor of being known as a Woese Fellow will help us attract some of the best and brightest students to work at the IGB."

This fund will allow future generations of scientists to follow in Woese's footsteps by melding progressive scientific ideas and innovative state-of-the-art research methods, hallmarks of the IGB since it was established in 2003 with the guidance of Woese.

Donations to the fund will specifically support innovative research in evolution, systems biology and ecosystem dynamics at the IGB.

To make a gift to the Woese Research Fund, send checks made payable to the "University of Illinois Foundation" in care of the Institute for Genomic Biology at 1206 W. Gregory Drive, Urbana, IL 61801. Gifts may also be made online at **https://www.uif.uillinois.edu/Gifts/StartGiving.aspx** by allocating "Carl R. Woese Research Fund" in the "Other - Indicate where to direct donation here" field.

For additional information about giving, please contact **Melissa McKillip**, IGB Director of development at **mmckilli@illinois.edu** or **217-333-4619**.

OUT**REACH** | **REACH** OUT

GENOME DAY

The Genome Day crowd gathers at the Orpheum to enjoy an afternoon of science.

On a clear day in November more than 480 children, parents, and friends of the Institute for Genomic Biology attended the 2nd annual Genome Day, a day of learning about genomes, genes, DNA, and evolution at the Orpheum Children's Science Museum in Champaign.

More than 100 volunteers helped run 15 child-friendly activities related to genetics, including learning how organisms relate to each other on the Tree of Life, or extracting strawberry and banana DNA to make necklaces. Volunteers from SACNAS (Society for Advancement of Chicanos and Native Americans in Science) provided bilingual volunteers for the day.

"Providing families with an opportunity to explore genomics aligns with the Orpheum's mission of inspiring, engaging, and educating children through exploration of science and the arts," said Sonya Darter, Executive Director of the museum, of the first Genome Day. "The IGB is doing some amazing work in life sciences, and providing experiences for families is crucial in creating a platform to get children excited about genomics, and who knows, maybe inspire the next generation of scientists!"

POLLEN POWER! **SUMMER CAMP**

Campers learn of the impact of pollen during their week at Pollen Power! Camp.

Middle school girls learned that pollen does a lot more than help flowers reproduce at Pollen Power!, a weeklong summer camp hosted by the Institute for Genomic Biology at the University of Illinois at Urbana-Champaign.

For a week in July, 27 campers studied past and future plant responses to climate change using pollen, toured state-of-the-art campus research labs and facilities, conducted real-world pollen research, and created video presentations using a green screen and teleprompter.

"This camp was an extraordinary opportunity for these girls to realize not only the potential of this scientific field but also their own potential as students and future scientists," said Lisa Ainsworth, an Associate Professor of Plant Biology at Illinois and member of the Genomic Ecology of Global Change (GEGC) research theme at IGB. "Through this camp, they discovered that they can succeed in a research environment, a lesson we hope they will carry with them throughout their education and as they, hopefully, pursue scientific careers."

SUMMER INTERNSHIP FOR **NATIVE AMERICANS** IN **GENOMICS (SING)**

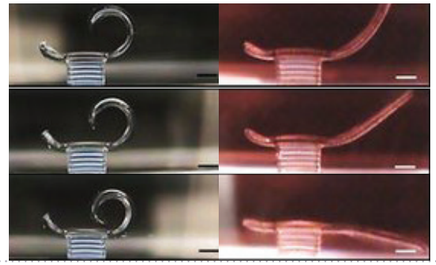
Native Americans discuss genomics as a tool for their communities at the SING workshop.

More than a dozen students from across North America attended the Summer Internship for Native Americans in Genomics (SING) workshop at the IGB in August to discuss the potential, as well as the risks, for genomic research in Native American communities.

During the weeklong workshop, participants learned not only about recent Native American genomic studies and genetic legal cases, but also the skills that are required to conduct real-world genomic research. In addition to a variety of indigenous backgrounds, including Cherokee, Oneida, Native Hawaiian and others, they had a wide range of professional interests to add to the conversation.

"The long-term goal is to increase the number of Native Americans leaders in science," said Ripan Malhi, an Associate Professor of Anthropology at the University of Illinois and an IGB affiliate in the Regenerative Biology & Tissue Engineering research theme. "Diversifying science and the way science is conducted is going to benefit science in general and people with different ancestries."

IGB **RESEARCH BRIEFS**



IGB Director Gives Congressional Testimony on Value of Brain and Behavior Research

Gene Robinson, Director of the IGB, served as one of five witnesses who gave testimony at the House of Representatives Subcommittee on Research and Technology Hearing in Washington, D.C. on the subject "The Frontiers of Human Brain Research." He spoke in support of President Obama's BRAIN initiative, a new research effort to better understand the brain and reveal new methods for treatment and prevention of brain disorders such as Alzheimer's, schizophrenia, autism, and epilepsy.

In his testimony, Robinson used his laboratory's work on the molecular basis of honey bee brain function and behavior as an example to demonstrate the value of basic neuroscience research and how it leads to development of applications in areas such as human health. He stressed the importance of basic research on behavior as well as the brain, the study of diverse animal models, and interdisciplinary collaboration, the latter particularly for the development of new tools for neuroscience research.

Bacteria May Help Lower the Cost of Biofuel

The high production expense of biofuels is in part due to the fact that organisms which are used to ferment biomass are unable to digest hemicellulose, a cell wall component that makes up roughly half of the available plant material. Microbiologist Rod Mackie and Energy Biosciences Institute Deputy Director Isaac Cann have been doing research on an organism that could be used to solve this problem.

The bacterium *Caldanaerobius polysaccharolyticus* contains all of the proteins and enzymes needed to break down xylan, the most common hemicellulose, and then transport the fragments into the cell and metabolize them. All of the genes are located in a single cluster on the microbe's genome. The next step is to develop techniques for transferring this gene cluster, which is quite large, into microbes.

New Grant to Establish Pan-Continental Bioinformatics Research Network in Africa

Victor Jongeneel, Director of the High-Performance Biological Computing (HPCBio) program, also IGB Bioinformatics Director and NCSA Sr. Scientist, is a key participant in a grant awarded by the Human Heredity and Health in Africa Initiative, or H3Africa, to establish a pan-continental bioinformatics network to aid research. Founded in June 2010, H3Africa is a joint initiative of the African Society of Human Genetics, the National Institutes of Health (NIH), and the Wellcome Trust, a UK-based charity organization, to "study genetic diversity in health and disease in African populations." The grant will dispense approximately $2 million dollars per year for five years to cover travel, training, and technical expenses.

"This is a great opportunity for African bioinformaticians to be confronted with real and relatively large scale data," Jongeneel said. "The research projects are going to generate all sorts of very interesting data sets. I think that this project could really be a catalyst to develop capability in bioinformatics on the African continent anchored in good research."

Researchers Work to Put Stem Cells in Their Place

Hyunjoon Kong, Assistant Professor of Chemical and Biomolecular Engineering and IGB faculty member, with Chemistry Professor Steve Zimmerman and Professor and Vice President for Research Larry Schook, have a polymer coating in development that could help an individual's stem cells target inflamed cells to regrow healthy tissue and calm inflammation.

People with chronic diseases like diabetes and multiple sclerosis have inflamed, leaky blood vessels, heightening their risk of heart attack and stroke. The vision of using a patient's own stem cells to regrow healthy tissue, plug the leaks, and calm inflammation could be realized via this polymer coating, which could help stem cells find and adhere to inflamed tissue.

Researchers are testing the ability of the polymer-coated stem cells to repair ruptured blood vessels in mice, with Kong reporting that preliminary results have been positive.

Cells power biological machines

With the aid of a 3D printer, researchers have fashioned soft, quarter-inch-long biological robots out of gel-like material and rat heart cells. When the cells beat, the bio-bots take a step. "After a few days, the cells synchronize and beat spontaneously," says Rashid Bashir, Professor of Electrical and Computer Engineering, Head of Bioengineering and IGB member. With an altered design, the bio-bots could be customized for specific applications in medicine, energy or the environment.

"The idea is that, by being able to design with biological structures, we can harness the power of cells and nature to address challenges facing society," Bashir said. "As engineers, we've always built things with hard materials, materials that are very predictable. Yet there are a lot of applications where nature solves a problem in such an elegant way."

A future goal of the team is to produce bots which move toward a chemical gradient, leading to designs that would be able to identify a specific toxin, and then neutralize it.

Ozone's Impact on Soybean Yield: Reducing Future Losses

Lisa Ainsworth, Associate Professor of Crop Sciences and USDA Agricultural Research Service plant molecular biologist, is performing research to measure the effects of ozone on soybean, determine the mechanisms of response, and attempting to improve soybean tolerance to ozone to then improve soybean yields. At ground level, ozone is a pollutant that can damage crops, especially soybean. Potential increases in background ozone are predicted to increase soybean yield losses by 9% to 19% by 2030. Ainsworth, an IGB faculty member, states that establishing the exposure threshold for damage is critical to understanding the current and future impact of this pollutant.

"Breeders haven't inadvertently bred for ozone tolerance in more modern lines," Ainsworth said. "They're still sensitive to ozone, which means that farmers are still subject to these yearly variations in ozone and are losing yield accordingly."

Biophysicists Measure Mechanism That Determines Fate of Living Cells

A new tension gauge tether laboratory method developed by IGB faculty member and Professor of Physics Taekjip Ha, with postdoctoral researcher Xuefeng Wang, has broad applications for research into stem cells, cancer, infectious disease, and immunology.

"If you went fishing and a fish broke your 30-lb fishing line but not the 40-lb one, you would know that its strength was in the range of 30-40 pounds," explained Wang. "Here we applied the same strategy to measure the molecular tension applied by cells (the fish). Mammalian cells apply a force to activate cell membrane proteins called integrins which mediate cell adhesion. We immobilized ligand molecules (the bait) on a surface through molecular tethers (the fishing line) with defined tension tolerances. After integrin-ligand binding, cells apply a force on the bonds, and we compare this force to the molecular tether strength by observing cell adhesion status."

"This is a very exciting result," says Ha. "With the ability to define the single molecular forces required to make living cells behave as desired, we may be one step closer to a remedy for certain hard-to-cure diseases."

IGB GRANTS

Kou-San Ju
William Metcalf

National Institutes of Health
Discovery and Characterization of Novel Nitroaromatic Antibiotics

Wilfred van der Donk
Taekjip Ha
Christopher Thibodeaux

National Institutes of Health
Single Molecule Studies of Class II Lantibiotic Synthetases

Ripan Malhi

National Institutes of Health
Guiding Indigenous Students in Next-generation Genomic Studies with the Summer Internship for Native Americans in Genomics (SING) Short Course

Elizabeth Ainsworth
Patrick Brown
Andrew Leakey

National Science Foundation
MCA-PGR: Genetic and Genomic Approaches to Understand and Improve Maize Responses to Ozone

Nigel Goldenfeld
Elbert Branscomb
Isaac Cann
Robert DeVille
Bruce Fouke
Roderick Mackie
Gary Olsen
Zan Luthey-Schulten
Charles Werth
Rachel Whitaker
Carl Woese

National Aeronautics and Space Administration (NASA)
Towards Universal Biology: Constraints from Early and Continuing Evolutionary Dynamics of Life on Earth

Huimin Zhao
Christopher Rao

Roy J. Carver Charitable Trust
Illinois Theme for Synthetic Biology

Mayandi Sivaguru

Novus International, Inc.
Analysis of Collagen Organization and Nuclei Morphometry in Tendon from Poultry Birds using Fourier Transform Second Harmonic Generation

Andrew Leakey

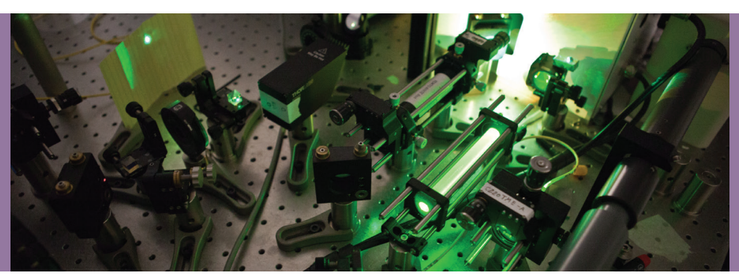
Department of Energy
C4 and CAM Plant Biology Symposium 2013

Bo Wang

Burroughs Wellcome Fund
In vivo Imaging and Functional Genomic Analysis of Stem Cells in Human Parasitic Worm Schistosoma

Gene Robinson
Lisa Stubbs

Simons Foundation
Molecular Roots of the Social Brain



IGB AWARDS

Lisa Ainsworth **(Genomic Ecology of Global Change)** was selected to join the American Society of Plant Biologists (ASPB) Executive Committee as an elected member. Ainsworth was also named as a University Scholar.

Bruce Fouke **(Biocomplexity, Energy Biosciences Institute)** received the 2013 Campus Award for Excellence in Undergraduate Teaching and the 2013 LAS Dean's Award for Excellence in Undergraduate Teaching.

Nigel Goldenfeld **(Biocomplexity)** was named a Center for Advanced Study Professor.

Brendan Harley **(Regenerative Biology & Tissue Engineering)** was awarded a 2013 NSF Faculty Early Career Development (CAREER) Award.

Paul Hergenrother **(Cellular Decision Making in Cancer)** was selected by the University of Illinois as the Kenneth L. Rinehart Jr. Endowed Chair in Natural Products Chemistry.

Victor Jongeneel **(HPCBio)** was appointed to the PubMed Central Advisory Committee of the National Institutes of Health (NIH).

Hyunjoon Kong **(Regenerative Biology & Tissue Engineering)** was named a Centennial Scholar by the College of Liberal Arts and Sciences.

Stephen Long **(Genomic Ecology of Global Change)** was elected to the Fellowship of the Royal Society. Long also received the Marsh Award for Climate Change Research by the British Ecological Society, and was named a Center for Advanced Study Professor.

William Metcalf **(Mining Microbial Genomes, Energy Biosciences Institute)** was selected by the University of Illinois as the G. William Arends Professor in Molecular and Cellular Biology.

Doug Mitchell **(Mining Microbial Genomes)** was awarded a 2012 Packard Fellowship in Science and Engineering from the David and Lucile Packard Foundation. Mitchell was also named one of Genome Technology magazine's Seventh Annual Young Investigators.

Sua Myong **(Cellular Decision Making in Cancer)** received the National Institutes of Health Director's New Innovator Award for 2012. Myong also received the National Medical Scholars Program's 2013 Outstanding Advisors of the Year Award.

Phillip Newmark **(Regenerative Biology & Tissue Engineering)** was named as a University Scholar.

Gene Robinson **(Director)** was elected to the National Advisory Mental Health Council (NAMHC) of the National Institute of Mental Health (NIMH). Robinson was also elected by the Animal Behavior Society as the 2013 Distinguished Animal Behaviorist, and chosen to receive the iBIO Institute's 2013 iCON Innovator Award.

Saurabh Sinha **(Gene Networks in Neural & Developmental Plasticity)** was selected for the Dean's Award for Excellence in Research from the College of Engineering.

Jonathan Sweedler **(Mining Microbial Genomes)** was named a Center for Advanced Study Professor.

Madhu Viswanathan **(Business, Economics, And Law of Genomic Biology)** received a 2013 Campus Award for Excellence in Public Engagement.

Bo Wang **(Regenerative Biology & Tissue Engineering)** received a Career Award at the Scientific Interface by the Burroughs Wellcome Fund.

MORE THAN A **FLIGHT OF FANCY**

A NEW ART EXHIBIT AT MIDWAY AIRPORT FEATURES IMAGES FROM THE INSTITUTE FOR GENOMIC BIOLOGY'S PIONEERING RESEARCH

Midway Airport passengers stuck on dreaded layovers can pass the time by experiencing 12 pieces from the "Art of Science: Images from the Institute for Genomic Biology" art exhibit.

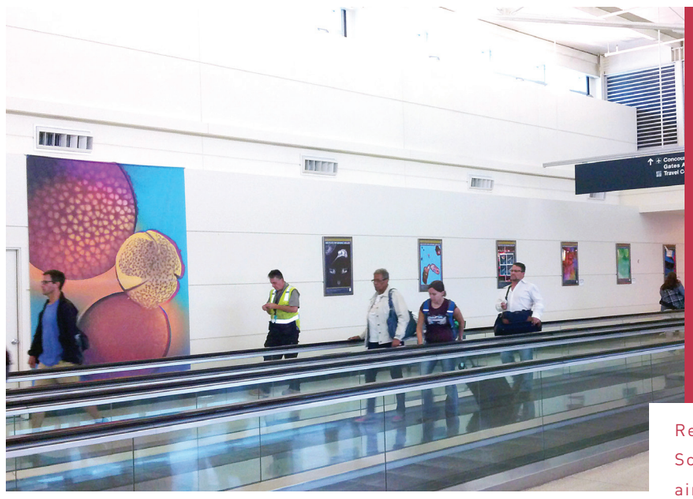
The exhibit, located past security in Concourse A, features images used in the Institute's innovative research projects that address significant problems facing humanity related to health, agriculture, energy and the environment.

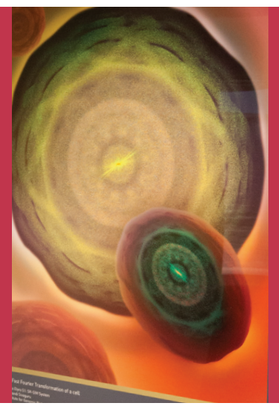
"Art is a really cool way to learn and jumpstart conversations about research," said Kathryn Faith Coulter, the Institute's multimedia design specialist and exhibit's managing artist. "By sparking a natural curiosity through these vibrant images, we hope people will discover how research conducted at the University of Illinois relates to their families, friends, and communities."

The exhibit, which includes two 10-foot banners and 10 pictures, illustrates the microscopic subjects that researchers are able to capture through the Institute's Core Facilities, which provides faculty and students from across the Urbana campus and east-central region resources for biological microscopy and image analysis.

"This exhibit includes images from a variety of scientific disciplines, from coral polyps to kidney stones and human colon cancer cells," said Glenn Fried, Director of Core Facilities. "These images represent much more than art. They represent scientific breakthroughs and discoveries that will impact how we treat human diseases, produce abundant food, and fuel a technologically-driven society."

This exhibit was made possible in part by the Chicago Department of Aviation. Some images from the Art of Science 3.0 exhibit are also on display at the I-Hotel and Conference Center in Champaign. The Art of Science 4.0 exhibit will be held April 3–7, 2014 at the indi go Artist Co-Op gallery, with an opening reception on April 3.





Research images featured in the IGB's Art of Science exhibit can now be seen at Midway airport.

Thank you for your support

SHAPING THE FUTURE OF SCIENCE & SOCIETY

GIVE TO IGB

The Institute for Genomic Biology has been forging new paths in research for nearly a decade, making groundbreaking discoveries in the life sciences. Throughout this time the IGB has consistently placed a premium on intellectual curiosity and student experience, believing that superb facilities and faculty enable not only cutting-edge research, but also the world-class education that is a hallmark of the University of Illinois.

Maintaining this commitment to excellence and innovation means constant renovation of facilities and technologies. The pace and scope of change in the field of genomic biology requires large investments on an ongoing basis, making philanthropic support for the IGB a crucial component.

The IGB brings together world-class researchers and students, laboratory space, materials, and equipment, with all research funded by external sources. Your donation will help us continue shaping the future of science and society, and can be contributed to a specific fund such as those listed below.

For more information, visit
www.igb.illinois.edu
/ABOUT/GIVING
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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 Institute for Genomic Biology. Dr. 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.

Lewin Lecture to Honor IGB Founding Director
The IGB is proud to honor Harris Lewin with its first named endowment. "The Harris A. Lewin Pioneer in Genomic Biology Distinguished Lecture" will recognize the lecture of a world-renowned scientist in the Pioneers in Genomic Biology lecture series. Through his foresight and determination, Dr. Lewin spearheaded the effort at the University of Illinois to create an interdisciplinary campus institute to advance life science research and stimulate economic growth.

The Walk of Life
The double helix – the classically beautiful twisting ladder that forms the shape of DNA – is beautifully depicted within the Walk of Life. Located to the west of the IGB building, adjacent to the historic Morrow Plots, Walk of Life pavers are the perfect way to commemorate anniversaries or special events, or to honor a loved one's special achievements.

STAY CONNECTED WITH THE IGB

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

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