IGB NEWS

Volume 7, Number 8

UPCOMING EVENTS

IGB Seminar (CDMC)

Identifying Barriers to Human iPSC Generation Using High-Throughput Screening

January 27, 2015, 12:00 p.m.
612 Institute for Genomic Biology

Jun Song, PhD
Founder Professor of Bioengineering and Physics
University of Illinois
Department of Bioengineering and Physics

Pioneers in Genomic Biology Seminar Series (ReBTE)

Title to be announced

February 3, 2015, 12:00 p.m.
612 Institute for Genomic Biology

Arthur J. Coury, PhD
Northeastern University
Department of Chemical Engineering

Pioneers in Genomic Biology Seminar Series (GNDP)

Title to be announced

February 10, 2015, 12:00 p.m.
612 Institute for Genomic Biology

David B. Goldstein, PhD
Duke University
Director, Center for Human Genome Variation
The Richard and Pat Johnson Distinguished University Professor

IGB Seminar (ReBTE)

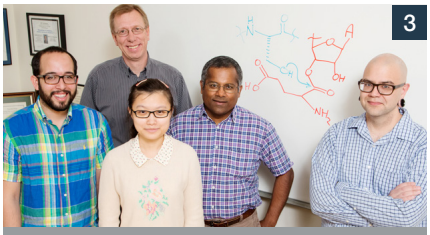
Guiding Stem Cell Fate for Tissue Engineering Applications via Spatiotemporally Controlled Signal Presentation

February 17, 2015, 12:00 p.m.
612 Institute for Genomic Biology

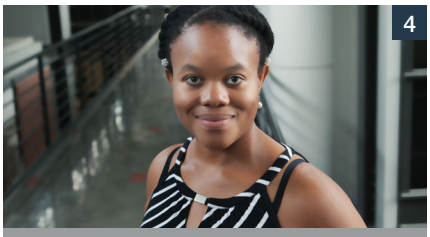
Eben Alsberg, PhD
Case Western Reserve University
Department of Biomedical Engineering

FEATURED NEWS

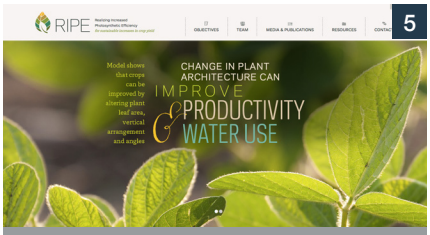
Koala Study Reveals Clues About Origins of Human Genome



Team Discovers How Microbes Build A Powerful Antibiotic

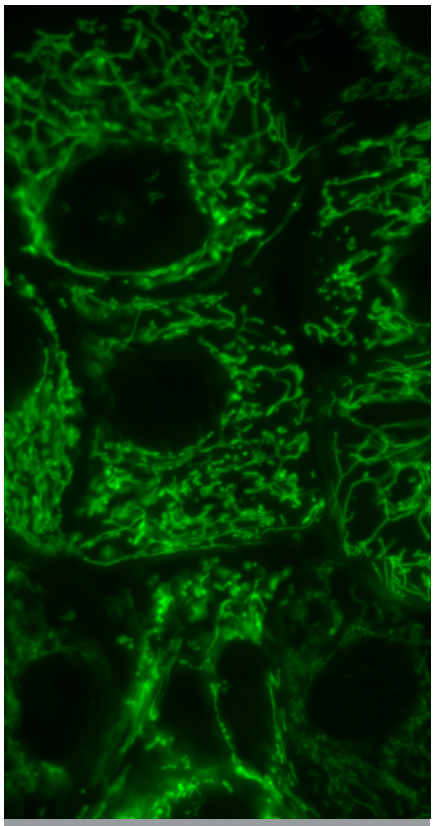


Profile: Princess Imoukhuede



On the Grid: Happenings at IGB

IMAGE OF THE MONTH



This month's image, provided by Matt Leslie of the Rex Gaskins Lab, shows florescent mitochondria-MCF 10A mammary epithelial cells expressing a genetically-encoded redox biosensor targeted to their mitochondrial matrix. The image highlights mitochondrial dynamics and the physical interconnectedness of mitochondria throughout a cell, the full relevance of which is still unknown in cell biology.

IGB News

Share your news with the IGB. Send ideas on stories, articles, and features to *nvasi@illinois.edu*.

Koala Study Reveals Clues
About Origins of the Human Genome

Eight percent of your genome derives from retroviruses that inserted themselves into human sex cells millions of years ago. Right now the koala retrovirus (KoRV) is invading koala genomes, a process that can help us understand our own viral lineage and make decisions about managing this vulnerable species.

In a recent study, published in *Molecular Biology and Evolution*, scientists from the University of Illinois discovered that 39 different KoRVs in a koala's genome were all endogenous, which means passed down to the koala from one parent or the other; one of the KoRVs was found in both parents.

Koalas are the only known organisms where a retrovirus is transitioning from exogenous to endogenous. An exogenous retrovirus infects a host, inserts its genetic information into the cell's DNA, and uses the host cell's machinery to manufacture more viruses. When an exogenous retrovirus infects an egg or sperm cell and the viral genetic information is then passed down to the host's offspring, the virus becomes an endogenous retrovirus (ERV).

Like humans, koalas have evolutionary defenses against endogenization.

"During the early stages of endogenization, there are huge numbers of retroviruses. KoRVs are present all across koalas' genomes, with many thousands or tens of thousands of KoRVs in the population," said Alfred Roca, a Professor of Animal Sciences and member of the Institute for Genomic Biology. "Over time most of them will disappear because these copies of the virus may be present in as few as one individual chromosome. If that one individual happens to not reproduce, or if it reproduces and the other chromosome is passed down, then that ERV will disappear."

In order to end up with 100 ERVs in an organism, the species may have to start with 10,000 ERVs in its ancestors, Roca said. It takes retroviruses, like KoRV, many thousands of years to become a fixed part of the koala genome, like the eight percent of retroviral DNA that all humans share.

The ERVs that are successfully passed down are protected by the koala's DNA repair mechanisms so that their rate of mutation is extremely low. Based on the dearth of mutations in the endogenous koala retroviruses, Roca's team was able to estimate that the KoRVs integrated into the host germ line less than 50,000 years ago. "This is quite recent compared with other ERVs that are millions of years old and have accumulated mutations," said first author Yasuko Ishida, a research specialist in Roca's lab.

(above) Professor of Animal Sciences Alfred Roca, left, with Alex Greenwood of the Leibnitz Institute, Berlin at the San Diego Zoo

In koalas, KoRV has been linked to leukemia, lymphoma, and immune suppression, which can lead to increased susceptibility to chlamydia.

"It seems likely that for thousands of years since this virus integrated, the koala host has suffered fitness effects," Roca said. "It is possible that across species, when a host lineage has been invaded by ERVs, it had to go through this process of adaptation between host and virus, which is a very sad finding. It may be a very long, slow, painful process for the host species, one which human ancestors have gone through and overcome many times in the distant past."

In mammals, retroviral DNA is associated with placental development and has been found to protect hosts from harmful exogenous retroviruses.

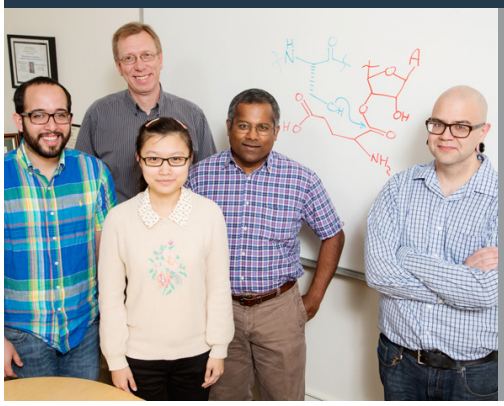
"But once retroviruses become part of the host, they begin to help the host because that is how they survive," Roca said. "They will be better off if they evolve to protect the host. Over time, the detrimental effects go down and the beneficial effects go up."

In the 1900s, koalas were extensively hunted for their fur. In an effort to preserve koalas, a few individuals were moved to an island off the coast of Australia. Years later, the inbred island population was reintroduced to southern Australia. Today some of the southern koalas remain uninfected while almost all northern koalas have dozens of KoRVs in their genomes.

"Which is the lesser of two evils?" Roca said. "Do you try to conserve genetic diversity, which is present in the northern populations along with the retrovirus or do you conserve southern populations that don't have the retrovirus but are horribly inbred?"

Roca's research team included research specialist Yasuko Ishida, graduate student Kai Zhao, and scientific collaborator Alex Greenwood of the Leibnitz Institute in Berlin. Their work was supported by the National Institute of General Medical Sciences. The San Diego Zoo, Columbus Zoo, San Francisco Zoo, and Riverbanks Zoo provided the koala samples. ■

Written by Claire Sturgeon. Photo by Yasuko Ishida.



From left, University of Illinois graduate research assistant Manuel A. Ortega, chemistry professor Wilfred van der Donk, graduate student Yue Hao, biochemistry professor Satish Nair, and postdoctoral researcher Mark Walker

Team Discovers How Microbes Build A Powerful Antibiotic

Researchers report in the journal *Nature* that they have made a breakthrough in understanding how a powerful antibiotic agent is made in nature. Their discovery solves a decades-old mystery, and opens up new avenues of research into thousands of similar molecules, many of which are likely to be medically useful.

The team focused on a class of compounds that includes dozens with antibiotic properties. The most famous of these is nisin, a natural product in milk that can be synthesized in the lab and is added to foods as a preservative. Nisin has been used to combat food-borne pathogens since the late 1960s.

Researchers have long known the sequence of the nisin gene, and they can assemble the chain of amino acids (called a peptide) that are encoded by this gene. But the peptide undergoes several modifications in the cell after it is made, changes that give it its final form and function. Researchers have tried for more than 25 years to understand how these changes occur.

"Peptides are a little bit like spaghetti; they're too flexible to do their jobs," said University of Illinois chemistry professor Wilfred van der Donk, who led the research with biochemistry professor Satish K. Nair. "So what nature does is it starts putting knobs in, or starts making the peptide cyclical."

Special enzymes do this work. For nisin, an enzyme called a dehydratase removes water to help give the antibiotic its final, three-dimensional shape. This is the first step in converting the spaghetti-like peptide into a five-ringed structure, van der Donk said.

The rings are essential to nisin's antibiotic function: Two of them disrupt the construction of bacterial cell walls, while the other three punch holes in bacterial membranes. This dual action is especially effective, making it much more difficult for microbes to evolve resistance to the antibiotic.

Previous studies showed that the dehydratase was involved in making these modifications, but researchers have been unable to determine how it did so. This lack of insight has prevented the discovery, production and study of dozens of similar compounds that also could be useful in fighting food-borne diseases or dangerous microbial infections, van der Donk said.

"Peptides are a little bit like spaghetti; they're too flexible to do their jobs," said van der Donk, who led the research with biochemistry professor Satish K. Nair. "So what nature does is it starts putting knobs in, or starts making the peptide cyclical."

Through a painstaking process of elimination, Manuel Ortega, a graduate student in van der Donk's lab, established that the amino acid glutamate was essential to nisin's transformation.

"They discovered that the dehydratase did two things," Nair said. "One is that it added glutamate (to the nisin peptide), and the second thing it did was it eliminated glutamate. But how does one enzyme have two different activities?"

To help answer this question, Yue Hao, a graduate student in Nair's lab, used X-ray crystallography to visualize how the dehydratase bound to the nisin peptide. She found that the enzyme interacted with the peptide in two ways: It grasped one part of the peptide and held it fast, while a different part of the dehydratase helped install the ring structures.

"There's a part of the nisin precursor peptide that is held steady, and there's a part that is flexible. And the flexible part is actually where the chemistry is carried out," Nair said.

Ortega also made another a surprising discovery: transfer-RNA, a molecule best known for its role in protein production, supplies the glutamate that allows the dehydratase to help shape the nisin into its final, active form.

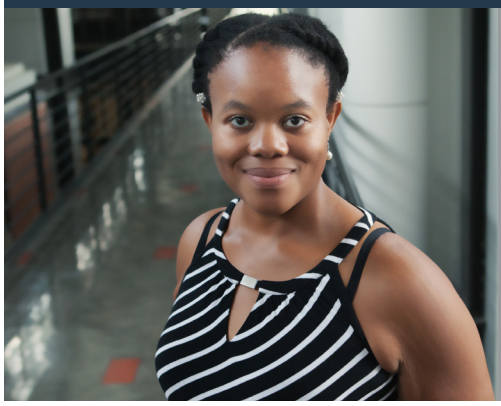
"In this study, we solve a lot of questions that people have had about how dehydration works on a chemical level," van der Donk said. "And it turns out that in nature a fairly large number of natural products – many of them with therapeutic potential – are made in a similar fashion. This really is like turning on a light where it was dark before, and now we and other labs can do all kinds of things that we couldn't do previously."

Van der Donk is a Howard Hughes Medical Institute investigator. He and Nair also are faculty at the IGB.

The National Institute of General Medical Sciences at the National Institutes of Health and the Ford Foundation supported this work. ■

Written By: Diana Yates. Photo by L. Brian Stauffer.

PROFILE



Princess Imoukhuede is an Assistant Professor of Bioengineering, who studies the vascular microenvironment to identify molecular and cellular signaling networks that modulate, inhibit, and promote blood vessel formation.

Princess Imoukhuede:
A Jack-of-all-trades

Princess Imoukhuede, an assistant professor of bioengineering, is not just an interdisciplinary collaborator; she is an interdisciplinary scientist, combining expertise in systems biology, bioengineering, and computational modeling to understand cancer and cardiovascular disease.

"I like to get my hands on a lot of different things," said Imoukhuede, who is a member of the Regenerative Biology and Tissue Engineering theme. "My lab merges experiment with computation to better understand biological processes and methods of targeting disease."

Imoukhuede's research on the formation of blood vessels is akin to controlling war zone supply routes. Her lab is working to increase the number of routes funneling supplies to main operating bases, like the brain and heart, while cutting off supply routes to enemy camps, like tumors and cancers.

She is currently developing models that will provide researchers and clinicians with a "Google Earth perspective" on the widespread impacts of blocking certain routes while developing others.

"My lab is trying to use all the skills we can to fully characterize this complexity," Imoukhuede said. "We want to be able to tailor the therapy to the individual patient so that fewer and fewer people are in the position that many patients are in right now."

To achieve this goal, Imoukhuede's lab partners with mechanical engineers, electrical engineers, clinicians, and many other types of experts.

"I think the future really lies in this type of interdisciplinary approach where people have the expertise to not just look at things in one way, but to work with others who have very different perspectives," Imoukhuede said. "By putting our heads together, we have the ability to answer these tough questions."

"The take home message from this research is that there are a lot of people who care about these very difficult questions," Imoukhuede said. "But it is hard to say what the take home message is for a cancer patient. A patient is going through this—a patient is dealing with this on a day-to-day basis. I hope that more than anything, they know that we not only care about making their lives longer by a couple months—that, of course, is important because the time you spend with your family is very important—but we are looking towards helping people survive this disease."

"My lab is trying to use all the skills we can to fully characterize this complexity. We want to be able to tailor the therapy to the individual patient so that fewer and fewer people are in the position that many patients are in right now."

Imoukhuede was born and raised in Illinois. She attended the Illinois Math and Science Academy, where she participated in research at the Midwestern College of Pharmacy. She went on to earn her bachelor's degree in chemical engineering from Massachusetts Institute of Technology and a doctorate in bioengineering from the California Institute of Technology. Before returning to her home state, she was a postdoctoral researcher in biomedical engineering at Johns Hopkins University. ■

Written by Claire Sturgeon. Photos by Kathryn Coulter.

The Imoukhuede Systems Biology Laboratory has recently published several papers where significant progress has been made in personalizing angiogenesis inhibition cancer treatments.

Imoukhuede, shown above with lab members Jared Weddell (left) and Spencer Mamer, works to better understand the tumor microenvironment and why the same type of tumor may behave differently in people.

ON THE GRID
HAPPENINGS AT THE IGB

AWARDS

MARNI BOPPART

Marni Boppart, Associate Professor in Kinesiology and Community Health (Regenerative Biology & Tissue Engineering) has been elected a Fellow in the American College of Sports Medicine. Among other things, the fellowships recognize "achievement and competence in the related disciplines of sports medicine and a demonstrated contribution to the goals of sports medicine."

BRENDAN HARLEY

Brendan Harley, Professor of Chemical and Biomolecular Engineering (Regenerative Biology & Tissue Engineering) has been elected a 2014 fellow of the American Association for the Advancement of Science. The American Association for the Advancement of Science is the world's largest general scientific society, founded in 1848.

PHILLIP NEWMARK

Phillip Newmark, Professor of Cell and Developmental Biology (Regenerative Biology & Tissue Engineering) was also elected a 2014 fellow of the American Association for the Advancement of Science. Along with Harley, he is one of 401 new fellows advancing science applications deemed scientifically or socially distinguished.

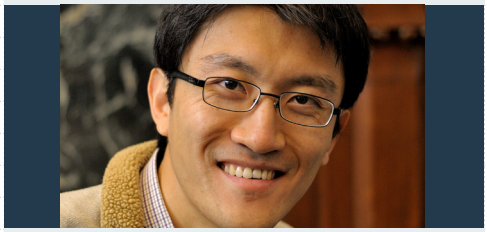
NEW ARRIVALS

ALEK AKSIMENTIEV

Professor Alek Aksimentiev joins the IGB as an Affiliate in Cellular Decision Making in Cancer. He joined the Department of Physics in 2005, and is currently an Associate Professor. His research interests span several areas including nanopore systems for single molecule detection and manipulation, molecular mechanics of DNA processing and the physics of DNA assemblies.

BROOKE HUNT

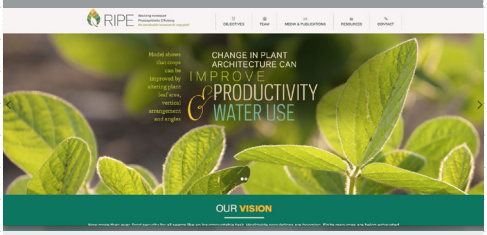
Brooke Hunt joins the IGB Business Office as an Account Technician I, working on monthly financial reports to PIs and approving grant purchases. Brooke previously worked for four years as an Accounts Receivable Clerk at CTF Illinois, which has group homes for developmentally disabled adults. She also attends Parkland College working towards her Business Administration Degree.



SIHAI DAVE ZHAO

Professor Sihai Dave Zhao joins the IGB as an Affiliate in Gene Networks in Neural and Developmental Plasticity. Professor Zhao is an Assistant Professor in the Department of Statistics. He received his Ph.D. in Biostatistics from Harvard University in 2012. His research interests are in the areas of statistical genomics, high-dimensional statistics and survival analysis.

WEBSITE



NEW RIPE WEBSITE LAUNCHED

"Now more than ever, food security for all seems like an insurmountable task. Worldwide populations are booming. Finite resources are being exhausted. By harnessing the major advances in photosynthesis research, crop bioengineering, and computational tools, the RIPE project will realize increased and sustainable yields of staple food crops in developing countries, including rice, legumes, and cassava."

The Bill & Melinda Gates funded Realizing Increased Photosynthetic Efficiency (RIPE) project has launched a new website, giving an excellent overview of the project objectives, team members, and news media, among other information. Visit the site at **http://ripe.illinois.edu/**.

GIVING

YEAR-END DONATIONS

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.

Please contact Melissa McKillip for additional information, *mmckilli@illinois.edu,* 217-333-4619 or visit **www.igb.illinois.edu/content/giving-multiple-funds**

ON THE GRID
HAPPENINGS AT THE IGB

IP @ IGB

REQUIREMENTS FOR PATENTABILITY: WHAT THE RESEARCHER SHOULD KNOW TO PROTECT HIS INTELLECTUAL PROPERTY

Researchers at the Institute for Genomic Biology are making transformative discoveries in the natural sciences. As such, their work may often provide the basis for patents. Here are some helpful guidelines to aid researchers in determining whether their work is patentable.

A patent is a temporally and geographically limited monopoly whereby the patent holder is granted the exclusive right to exclude others from making, using, selling, and offering to sell the patented innovation. The patent grant is intended to encourage the investment of time and resources into the development of new and useful discoveries. In exchange for this limited monopoly, immediate disclosure of the patented information to the U.S. Patent and Trademark Office (USPTO) is required with subsequent disclosure to the public. Once the term of protection has ended, the patented innovation enters the public domain.

At the most basic level, in order for an invention to be patentable, it must be both new and non-obvious. "New" means there is nothing else exactly like it known to the public. "Non-obvious" means that the invention is distinguishable from existing technology and would not be considered obvious to someone skilled in the relevant area of technology.

In order to preserve the newness, or novelty, of an invention, researchers must be conscious of the manner in which they disclose their technology to the public. An invention will not normally be patentable if it was known to the public before it was filed as a patent application; the invention was described in a publication more than one year prior to the filing date; or the invention was used publicly, or offered for sale to the public more than one year prior to the filing date.

In order for an invention to be patentable, it must not only be novel, but it must also be a non-obvious improvement over the prior art. This determination is made by deciding whether the invention sought to be patented would have been obvious "to one of ordinary skill in the art." In other words, the invention is compared to the existing technology and a determination is made whether the differences in the new invention would have been obvious to a person having ordinary skill in the type of technology used in the invention.

Considerations of novelty and non-obviousness are complicated and the Office of Technology Management is here to help you make these determinations. If you have developed technology that you think may be patentable, please contact technology manager, Dr. RK Narayanan at *rkn@illinois.edu* to speak about the invention and how to proceed. ■

ADMINISTRATIVE NEWS

UNIVERSITY LIBRARY

REDESIGNED LIBRARY HOMEPAGE LAUNCHED

If you haven't visited the University Library's homepage (**http://www.library.illinois.edu/**) recently, you should take a look. In late October, the Library launched a redesigned homepage, which features improved usability on mobile devices; and fewer clicks to popular content, like today's hours and study room reservations. The redesign was guided by extensive user testing, but small, iterative improvements will continue to be made as feedback is received. So, if you have comments on the redesigned homepage, please use the feedback link on the right side of the homepage.

Future phases of the project will focus on secondary-level landing pages and unit-level pages. ■

OPERATIONS & FACILITIES

IGB BLOOD DRIVE

The next IGB blood drive will be on **January 23**, from 8 am to 1 pm in conference room 612. Our first blood drive was so successful we would like to make this a continuing event!

IGB BUILDING HOLIDAY SCHEDULE

The IGB building will be closed December 24 thru January 4. This means that all exterior doors will be locked and all card access doors will require entry with a valid IGB prox card. Please take care when entering or leaving the IGB not to allow someone you do not recognize into the IGB. View the full schedule details on the **IGB Operations & Facilities page**. ■

ADMINISTRATIVE NEWS

BUSINESS

HOLIDAY BREAK REDUCED SERVICE DAYS

As we approach the holiday season we are providing a reminder of the upcoming holiday schedule and the accompanying reduced service days.

Wednesday, December 24, 2014	1/2 Gift Day 1/2 Excused Day p.m.
Thursday, December 25, 2014	Christmas Day Holiday
Friday, December 26, 2014	Day after Christmas Designated Holiday
Monday, December 29, 2014	Reduced Service Day
Tuesday, December 30, 2014	Reduced Service Day
Wednesday, December 31, 2014	Reduced Service Day
Thursday, January 1, 2015	New Year's Day Holiday
Friday, January 2, 2015	Reduced Service Day

Reduced Service Days:
It is expected that most units will be closed and most employees will not be working those three days.

Employees may use floating holidays or vacation to cover this time if they do not work.

In addition, non-exempt (eligible for overtime) employees may use accrued compensatory time or take the time excused without pay.

Exempt employees who do not have accrued vacation or floating holidays to cover this time cannot have their pay docked. The unit may require such employees to work or the unit and the employee may make arrangements to account for the reduced service days in an alternative way.

Since the reduced service days are not official holidays, employees who are required to work and those who choose to work will be paid their regular hourly rate of pay. For payroll time reporting purposes, non-exempt staff employees who work should record their time for these three days as regular hours. Exempt employees who are required to work on one or more of these days should not record anything for the days they work, since they record only "exception time" (e.g., vacation or sick leave usage).

If you have any questions, please contact Jacinda King at 244-2276 or *jkking@illinois.edu*. ■

RECENT PUBLICATIONS

Quarterman J, Kim SR, Kim PJ, Jin YS. Enhanced hexose fermentation by *saccharomyces cerevisiae* through integration of stoichiometric modeling and genetic screening. *J Biotechnol*. 2014.

Si T, Xiao H, Zhao H. Rapid prototyping of microbial cell factories via genome-scale engineering. *Biotechnol Adv*. 2014.

Rittschof CC, Bukhari SA, Sloofman LG, et al. Neuromolecular responses to social challenge: Common mechanisms across mouse, stickleback fish, and honey bee. *Proc Natl Acad Sci U S A*. 2014.

Jain A, Arauz E, Aggarwal V, Ikon N, Chen J, Ha T. Stoichiometry and assembly of mTOR complexes revealed by single-molecule pulldown. *Proc Natl Acad Sci U S A*. 2014.

Lane S, Zhang S, Wei N, Rao C, Jin YS. Development and physiological characterization of cellobiose-consuming *yarrowia lipolytica. Biotechnol Bioeng*. 2014.

Monzani PS, Guemra S, Adona PR, Ohashi OM, Meirelles FV, Wheeler MB. MAC-T cells as a tool to evaluate lentiviral vector construction targeting recombinant protein expression in milk. *Anim Biotechnol*. 2015;26(2):136-142.

Kuzawa CW, Chugani HT, Grossman LI, et al. Reply to skoyles: Decline in growth rate, not muscle mass, predicts the human childhood peak in brain metabolism. *Proc Natl Acad Sci U S A*. 2014;111(46):E4910.

Li X, Rui J, Xiong J, et al. Functional potential of soil microbial communities in the maize rhizosphere. *PLoS ONE*. 2014;9(11).

Joachim E, Kim I-, Jin Y, Kim KK, Lee J-, Choi H. Gelatin nanoparticles enhance the neuroprotective effects of intranasally administered osteopontin in rat ischemic stroke model. *Drug Deliv Transl Res*. 2014;4(5-6):395-399.

Sears KE. Quantifying the impact of development on phenotypic variation and evolution. *J Exp Zool Part B Mol Dev Evol*. ;322(8):643-653. ■

ILLINOIS

IGB News is published by the IGB Communications Office.
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www.igb.illinois.edu 14.133