UPCOMING EVENTS

Science at the Market
October 22, 2016, 8:00 a.m. - 12:00 p.m.
Market at the Square, Lincoln Square, Urbana, IL
Join us on Saturday for Science at the Market, where IGB members will engage audiences of all ages to learn about DNA, genomes and biology.

Fox Family Innovation and Entrepreneurship Lecture
The Practical Application of Human Cells and Tissue in Surgical Procedures
November 8, 2016, 12:00 p.m.
612 Carl R. Woese Institute for Genomic Biology
Tom Cycyota
AlloSource, President and Chief Executive Officer

Genome Day
November 12, 2016, 1:00 p.m. - 5:00 p.m.
Orpheum Children's Science Museum
346 North Neil Street
Champaign, Illinois 61820
Learn about science and experiments in a fun and exciting environment at IGB's annual Genome Day!

Lecture and Book Signing
The Art of Yellowstone Science
November 16, 2016, 3:00 p.m.
612 Carl R. Woese Institute for Genomic Biology
Bruce W. Fouke, PhD
Professor of Geology & Microbiology
University of Illinois, Urbana-Champaign

Reception and Public Lecture
Natural History Photography Around the World
November 16, 2016, 6:00 p.m.
612 Carl R. Woese Institute for Genomic Biology
Tom Murphy
Wildlife Photographer

FEATURED NEWS

Genome-editing proteins ride a DNA zip line

New research theme to develop precision medicine tools

Monthly Profile:
Ting Lu

On the Grid: Happenings at IGB

IMAGE OF THE MONTH

This month’s image, Investigating the Long-Term Effects of Short (<1 s) Exposure to Fluorescent Excitation Light on Force Relaxation in Cells, used the Zeiss Apotome Fluorescent Microscope with a Zeiss Axioobserver Z1 built-in reflected light shutter. The inward-outward-inward bead fluctuations that were displayed showed how localized cell forces continue to oscillate long after exposure to green fluorescent excitation light. Image courtesy of Samantha Knoll, Sivaguru Mayandi, and Taher Saif

IGB News
Share your news with the IGB. Send ideas on stories, articles, and features to nvasi@illinois.edu.
For gene-editing proteins to be useful in clinical applications, they need to be able to find the specific site they’re supposed to edit among billions of DNA sequences. Using advanced imaging techniques, University of Illinois researchers have found that one class of genome-editing proteins rapidly travels along a strand of DNA like a rider on a zip line – a unique behavior among documented DNA-binding proteins.

TALE proteins can be programmed to recognize and bind to specific regions of DNA for applications in synthetic biology or clinical gene therapy. The zipline behavior that the new study uncovered is different from what researchers have seen in any other proteins that bind to and travel along DNA.

“Among the classes of known DNA-binding proteins, TALE proteins appear to behave in a unique way in terms of target site search,” Schroeder said. “Understanding the search mechanism is helpful in moving toward clinical applications. A major goal is to design these proteins to find a specific target site with minimal off-target binding.”

Using single-molecule imaging techniques, the Illinois team watched how TALE proteins moved along a DNA template that didn’t contain the proteins’ target sequence, a process known as nonspecific search. They expected that TALEs would bind to the DNA backbone and rotate around the double helix, like a nut on a bolt – as do nearly all documented proteins that move along DNA searching for a target site. Instead, they found that the protein wrapped around the helix and slid back and forth, like a rider on a zip line.

“We uncovered a new search process for DNA-binding proteins that doesn’t fit into previous binding classifications,” said Cuculis, now a consultant at the Boston Consulting Group. “We performed several experiments to test these theories, and the results were unexpected based on current thinking about how proteins move along DNA in search of a target site or gene.”

The unusual mechanism could hold advantages for researchers looking to develop TALE proteins for new biomedical applications, Cuculis said. For example, it could be used as a delivery mechanism, like a passenger riding a zip line to a destination, with the TALE protein acting as the hook.

“It opens up more avenues for this protein to be used,” he said. “Because of how well TALEs hook onto the DNA, there’s a potential to attach larger payloads to the proteins. Right now it’s mainly used for gene editing, but based on this work, there may be potential to attach something much larger to deliver to a target site.”

Now that they have detailed how TALE proteins work in vitro, the researchers are beginning to study them at work in live cells.

“It’s providing more fundamental insight into the mechanism behind gene editing,” Schroeder said. “Research is always more interesting when nature behaves in a way we don’t expect, because it enables us to look at things from a new perspective. The hope for this work is ultimately to develop new and optimized systems for genome engineering.”

The Carl R. Woese Institute for Genomic Biology and the David and Lucile Packard Foundation supported this work. Schroeder and Zhao also are affiliated with the department of chemistry and the Center for Biophysics and Quantitative Biology.

The paper “TALE proteins search DNA using a rotationally decoupled mechanism” is available online. DOI: 10.1038/nchembio.2152.

Written by Liz Ahlberg Touchstone. Photo by L. Brian Stauffer

Schematic of single-molecule assay showing dual-tethered DNA templates with a fluorescently labeled TALE. Single proteins were imaged by TIRF-M.
Force triggers gene expression by stretching chromatin

How genes in our DNA are expressed into traits within a cell is a complicated mystery with many players, the main suspects being chemical. However, a new study by University of Illinois researchers and collaborators in China has demonstrated that external mechanical force can directly regulate gene expression. The study also identified the pathway that conveys the force from the outside of the cell into the nucleus.

Identifying the ways mechanical forces send signals within cells has applications not only in fundamental cell biology, but also for cancer, stem cells and regenerative medicine, said mechanical science and engineering professor Ning Wang, who led the study with cell and developmental biology professor Andrew Belmont. The researchers published their work in the journal Nature Materials.

"Each cell in your body has the same DNA, but tissues behave very differently because genes are expressed differently," Wang, an affiliate of IGB's Regenerative Biology & Tissue Engineering research theme, said. "There is so much we don't know about gene expression. I think this work is the beginning to unravel some of the unknowns.”

Researchers have long known that forces, both external and internal, can affect cell behavior. But the question loomed as to whether the forces themselves triggered changes in gene expression, or if the forces triggered a chemical-signaling pathway within the cell.

"Cells only have two ‘senses’ to interact with their environment,” Wang said. “They cannot see or hear, but they can ‘feel’ mechanical forces and ‘taste’ chemical signals. Many studies have detailed chemical-signaling pathways, but it’s important to understand how the mechanical forces affect the cell as well. Mechanical signaling is as important as chemical signaling, and this study shows it’s a direct pathway.”

The researchers stuck tiny magnetic beads to proteins attached to the external membranes of hamster cells. They were able to change the direction and angle of the force the beads exerted while maintaining a consistent magnitude of the force, and found that the external force directly caused regions of chromatin in the nucleus to stretch out. Chromatin is the condensed DNA and protein mixture that makes up chromosomes. Using advanced imaging techniques, the researchers found an increase in transcription of the genes in the stretched regions.

"Work extending back decades has correlated chromosome decondensation with increased gene expression, but it has been extremely difficult to distinguish cause and effect,” faculty member of the Biosystems Design research theme Belmont said. "Does gene activity cause chromatin to decondense, or does decondensation actually drive increased gene expression? Here, we saw chromatin stretching directly drive increased gene expression, which provides a mechanically based mechanism for cells to sense their environment.”

The degree of stretching and therefore gene expression varied based on the direction of the force in relation to the cell’s cytoskeleton, the internal framework of protein tubes that supports the cell.

"The actin in the cytoskeleton forms bundles. When the force is perpendicular to the bundles, it’s like plucking violin strings,” Wang said. “It’s incredibly tense, and the signal is transferred through the cytoskeleton to the nucleus and stretches the chromatin. Doing it the other way, along the string direction, there isn’t much vibration, so a force of the same magnitude has less effect. The effect gets stronger the closer the angle gets to 90 degrees.”

The researchers were able to follow the force and identify the pathway that it travels along the cytoskeleton to the chromatin in the nucleus. Knowing the pathway is important, Wang said, because researchers can now explore mechanical signaling in more detail and perhaps develop ways to harness it for gene regulation or identify targets for cancer therapies.

For example, Wang’s group has published several studies detailing the unique mechanical properties of tumor-repopulating cells – cancer cells that evade standard drug therapies and tend to slip away to metastasize in new locations. He hopes that this study opens new avenues of attack to disable tumor-repopulating cells with fewer side effects than traditional cancer treatments.

Now that they’ve detailed how forces affect stretching of the chromatin, the researchers are beginning to look at how forces affect chromatin compression and what that means for gene expression. They are also probing further into other factors regulating gene expression when the chromatin is stretched.

"When we apply these forces, why are some genes activated while some are not? We think there are factors that inhibit, so that some genes are not ready to be force-activated,” Wang said.

The National Institutes of Health supported this work.

Written by Liz Ahlberg Touchstone. Photo by L. Brian Stauffer
Some people see physical systems and biological systems as sharply contrasting—the carefully engineered and the organically chaotic. When Ting Lu (BCXT/BSD/MME) considers the circuitry of a supercomputer or the genomic architecture of a bacterial cell, he sees echoes of the other in the structure of each.

“The understanding of biology is still far behind compared with physical systems,” Lu said, “but there are certain similarities; for instance, in physics or engineering, systems are often highly modular, from the gene, to protein, to pathway, to tissue, they have hierarchical structures, and similarly in computer systems, from circuit, to device, to computer, to network computer . . . basically, I want to see how I can use physics or engineering tools to understand how living systems work.”

Lu’s scientific goals extend further than that. A true engineer, he wants not only to understand living systems, but to construct them. His research is in the realm of synthetic biology, the design of novel biological systems. Lu’s work focuses on bacteria, and aims to create individual strains or more complex microbial communities that could carry out a desired function, such as synthesizing a biofuel or improving digestive health.

In Lu’s view, what may be the greatest challenge of working with living systems, the complexity of their existing functions, is also one of their greatest advantages.

“If you make a robot, you just have the robot. Someday you can maybe make a robot that is able to make another robot,” Lu said, explaining what drew him to this area of science. “Bacteria look to me like a very fancy sports car; they are tiny but have a very unique and powerful capacity already. So we are not able to fully operate this fancy sports car, but I am trying to make some small modifications, and hopefully we can use them to get somewhere.”

Lu’s academic background helps him bridge the worlds of microbiology and engineering. After earning an undergraduate degree in physics at Zhejiang University and a PhD in biophysics at the University of California, San Diego, he moved to Harvard University and into the world of synthetic biology. Working with Professors of Biological Engineering Jim Collins and Ron Weiss, Lu explored the complex mechanisms that control gene activity, and how they can be tuned to produce a desired function.

“I like the beauty of physics, to find some simple and general rule behind complex behaviors,” Lu said. “During my graduate years, I really became fascinated by the biology of the organism, of biological systems, the complexity behind that.”

One practical application of this interest is an extension of his postdoctoral work; learning to parse the molecular language of a single cell, and using it to write a new set of instructions and create new functionality. For example, recent work from Lu’s laboratory clarified what induces a type of soil-dwelling bacteria, Clostridium, to produce butanol during fermentation. Further work could eventually produce custom-designed bacteria that mass-produce butanol and other biofuels to replace petroleum.

Lu’s second major effort relates to the higher biological level of organization, the connections between individual bacteria sharing an ecological niche.

“Bacteria are single-celled, but they are highly social. They are very much like human beings: they can cooperate, and their interactions actually lead to very complex communal behavior that cannot be understood from single cells,” Lu said. “Communal behavior is very important for human health and the microbiome, and also relates to environmental situations like soil microbiology.”

Working with his colleagues in the Biosystems Design and Microbiome Metabolic Engineering research themes at the IGB, Lu is pursuing a research goal that parallels his work on networks of genes. He studies how individual bacterial cells interact with each other, sending out chemical signals to influence each other’s function in an attempt to cooperate or to compete for space.

By exploring the mechanisms through which bacteria communicate with one another and coordinate their functions and behaviors to survive within a group, Lu hopes that someday soon, researchers will be able to construct custom microbial communities. An engineered probiotic, for example, could support digestion of a poorly tolerated food, improve nutrient absorption, or help prevent a food-borne illness.

It is appropriate that a scientist who is drawn to the surprisingly complex communal lives of bacteria also has an appreciation for Illinois’ collaborative research environment. Since joining the university and the IGB in 2011, Lu has formed strong partnerships with his fellow theme members.

“The IGB is really designed in a way to facilitate collaboration and get people to work together . . . there was no reason why I should not join,” Lu said. “It is very unique, and we are really appealing because we foster that collaboration.”

Written by Claudia Lutz. Photo by L. Brian Stauffer
ON THE GRID
HAPPENINGS AT THE IGB

IN MEMORIAM

DR. SHARON GRAY
1985-2016

University of Illinois at Urbana-Champaign
B.Sc. Integrative Biology, 2006
Ph.D. Plant Biology, 2013

It is with great sadness that we learned Sharon Gray, a postdoctoral student in plant biology at UC Davis and a former member of the Genomic Ecology of Global Change theme working with Prof. Andrew Leakey at the IGB, was killed on October 4, 2016 after a civil unrest altercation in Ethiopia. Sharon was traveling to begin a new research project in the area with charitable organizations including the Netherlands Institute of Ecology when protesters attacked her car.

Sharon was a promising young scientist who was warm-hearted, kind, and highly respected among her peers. She was one of our first participants in the OLLI Citizen Scientist program and led by example in both her research and her interaction with others.

Our deepest condolences to the Gray family, to Sharon’s husband Cody Markelz who was also a member of the Leakey group, and to her friends, colleagues, and fellow researchers here at Illinois and at UC Davis. She will be missed.

A memorial page has been created at the School of Integrative Biology. If you have additional photo memories you would like to share please send to jeff@life.illinois.edu.

IGB DIRECTOR REAPPOINTMENT

Swanlund Chair of Entomology and Neuroscience Gene E. Robinson has been reappointed Director of the Carl R. Woese Institute for Genomic Biology, following the completion of a five-year review.

Vice Chancellor for Research Peter Schiffer remarked in his announcement “By any measure, the Institute has been remarkably successful under Gene’s leadership and has seen more than 50% growth in sponsored research activity. Gene has been a tireless advocate for the scientific, educational, philanthropic and economic development activities of the Institute, establishing new research directions and working to deeply engage with the campus and the community.”

We congratulate Dr. Robinson on his reappointment and look forward to working with him for many years to come!

ENTREPRENEURSHIP LECTURE SERIES

Tuesday, November 8
12:00 pm
IGB Conference Center Room 612

The entrepreneurship lecture series is an opportunity for students, academics and professionals in the life sciences, engineering and other disciplines to gain insight about entrepreneurship and innovation. The next lecture in the series, titled “The Practical Application of Human Cells and Tissue in Surgical Procedures” will be presented by Tom Cycyota, President and Chief Executive Officer of AlloSource. For more information, please contact Courtney Cox, outreach fellow, at Cox22@illinois.edu.

JESSICA SAW

Jessica Saw, MD Program, Mayo Medical School / Graduate Student, Molecular and Integrative Physiology (Wildman Lab) has received a Scholar Award from the ARCS Foundation, a national organization which recognizes outstanding graduate and undergraduate students around the country in science, engineering, mathematics, and biomedical fields.

REBECCA STUMPF

Rebecca Stumpf, Associate Professor of Anthropology (BCXT/CGRH) has been named a University Scholar, a program created to recognize the university’s most talented teachers, scholars and researchers.
**GENOME DAY 2016**
Saturday, November 1, 1:00pm - 5:00pm
Orpheum Children’s Science Museum
346 North Neil Street
Champaign, Illinois 61820

Volunteer here!

Learn about science and experiments in a fun and exciting environment at IGB’s annual Genome Day. Primarily for children in grades K-4, all members of the community are welcome and will benefit from the day. Exhibits and activities are designed to present concepts about the environment, energy use and production, health, and fundamental research at the IGB in a friendly and engaging manner.

**ANNUAL IGB HALLOWEEN PARTY**
Thursday, October 27
4:30pm - 6:00pm, Array Café

IGB members and your families: please join us for the Annual IGB Halloween Party! We’ll have a kid friendly haunted crawl, crafts, games, prizes, and a ton of candy. As always we’ll hold a costume contest for both children and adults (winners announced around 5:30pm).

If you’d like to volunteer please contact Darci Edmonson at darci@illinois.edu for more information.

**NEW ARRIVALS**
Noah Dibert has joined the IGB as a Media Programming Specialist. Noah previously worked with the Port Angeles School District as the Webmaster and also provided technology support. He graduated from Columbus College of Art & Design with a BFA in Advertising/Graphic Design.

**EVENT**
**DROP BOXES FOR SANGER SEQUENCING AND FRAGMENT ANALYSIS SAMPLES**
Drop boxes for Sanger sequencing and fragment analysis samples will be available in four campus locations as of Monday, September 19. Samples will be picked up from the drop boxes at 3:00 p.m., Monday-Friday, and results will be available by 5:00 p.m. the next business day. Samples will not be picked up on weekends and campus holidays.

To use the drop boxes, please put your Core order form in a sealed bag along with your samples and primers (https://unicorn.biotech.illinois.edu/). The drop boxes are for Sanger sequencing and fragment analysis samples only. Please email Leslie Benson or Kim Schneider at dna-seq@illinois.edu, or call 217-265-6814 with any questions. Please note, all samples for Illumina sequencing should be delivered to the sequencing lab after coordination of the submission with the DNA Services Director or Assistant Director: Alvaro Hernandez (aghernan@illinois.edu) or Chris Wright (chwright@illinois.edu).

**DROP BOX LOCATIONS**
Carl R. Woese Institute for Genomic Biology
1206 West Gregory, Urbana
Room 1201, directly inside mail room/central receiving

Chemical and Life Sciences Laboratory (MCB)
601 South Goodwin, Urbana
Room C107, directly outside CLSL Life Sciences Storeroom

Newmark Civil Engineering Laboratory
205 North Mathews, Urbana
Room 1126, outside mail room/receiving area

Vet Med Basic Sciences Building
2001 South Lincoln, Urbana
Room 1828, directly inside mail room/central receiving

**PUBLIC LECTURES AND BOOK SIGNINGS**
Wednesday, November 16
3:00pm Bruce W. Fouke
“The Art of Yellowstone Science”

4:00pm Book signing

6:00pm Reception

7:00pm Tom Murphy
“Natural History Photography Around the World”

Join us for two amazing lectures from Bruce Fouke and Tom Murphy, authors of “The Art of Yellowstone Science: Mammoth Hot Springs as a Window on the Universe” on Wednesday, November 16. Visit artofyellowstonescience.igb.illinois.edu for more info.

**ART OF YELLOWSTONE SCIENCE**
INTELLECTUAL PROPERTY & COMMERCIALIZATION: THE OFFICE OF TECHNOLOGY MANAGEMENT

Thursday, October 20, 2016 at Noon in IGB room 612, you are invited to a Lunch and Learn Session on “Intellectual Property and Commercialization.” This talk is open to all students, including graduate students and postdocs as well. Please bring your friends along if they are curious about these issues. Pizza will be provided. If you would like to attend, please RSVP.

As UIUC OTM Technology Managers, it is helpful for us to attend conferences and symposia to stay abreast of new developments and innovations in related technology areas, network to identify potential Licensee’s of University technologies, and share University innovations with the global community. The FierceBiotech Drug Development Forum in Boston, MA on September 19-21, 2016 is an example of one such event. The meeting brought together several Pharma, Biotech, Venture Capital, and Licensing representatives to discuss issues relevant to the drug industry. A few interesting panel discussions and highlights are below.

- The Genomics Package (Panelists from Synlogic, Foundation Medicine, Broad Institute, Molquant, Inc.)
  - Need for standardization across genomic datasets; particular need for annotation of genomes
  - CRISPR important but other editing tools are welcomed
  - RNA is dynamic, has advantage over DNA
  - Epigenetic markers are very exciting
- Innovative Drug Delivery Technologies (Panelists from Boehringer Ingelheim, Merck, Teva Pharmaceuticals)
  - Benefits of drug delivery technologies- safety, efficacy, overcome abuse, marketing and regulatory exclusivity
  - Formulation, devices, physical state of the drug are all new drug delivery technologies
  - TEVA actively looking for drug delivery mechanisms
  - Trelyst (Contract Development and Manufacturing Organization)- silicone based drug delivery company shared about challenges and long-term investment necessary to bring to market
- The Current State and Future of Big Data (Panelists from Takeda, Merck, Bayer)
  - Issue- making data useful for actual drug development to predictive drug responses in patients
  - Cybersecurity still a big issue and always will be
  - Takeda has history of non-traditional partnerships, i.e. Gates Foundation for data management and software

OTM Tip of the Month: If the University supports the patenting of a disclosed technology, the University will lead the filing of the application(s), working with patent attorneys, and making the financial investment.

Where can I learn more about the OTM?
The Lunch and Learn Session on Thursday, October 20, 2016 at Noon in IGB room 612. Please RSVP at https://illinois.edu/ib/sec/2270788.

The OTM is located in 319 Ceramics Building and for more information about OTM’s mission, activities, and services, please visit our website - otm.illinois.edu. This website contains links to disclosure forms as well as the inventor’s handbook, an easy-to-follow guide to patenting your inventions. If you have other questions about the patentability of your technology, please contact our Technology Managers RK Narayanan at rkn@illinois.edu and Lisan Smith at lisan@illinois.edu.

OTM will be featuring a monthly column on IP and Commercialization in the IGB newsletter. We look forward to discussing the issues facing the technology transfer field and their impact on academic research.

The Office of Technology Management (OTM) is dedicated to protecting and promoting U of I’s inventors and their inventions, to commercialize the IP, and to bring the innovations to public use.

BUSINESS OFFICE

ANNUAL CHARITABLE FUND DRIVE

The 2016 Campus Charitable Fund drive is underway September 19th – November 11th. Please consider contributing! Take a moment to read the brochure by visiting the website at www.ccfd.illinois.edu.

A few things you might want to remember: **We encourage everyone to give by on-line payroll deduction.**

If you are giving by payroll deduction, please remember to type in the annual amount you wish to donate. There is no limit to the number of agencies that you may select, but the minimum ANNUAL donation is $24.00 ($2 per month).

When making a one-time donation, make your check(s) payable to the umbrella organization(s) listed on the Pledge Form, not to designations within the umbrella. If you have any questions throughout the campaign, please contact either Jacinda King at 244-2276 or jkking@igb.illinois.edu. The deadline is November 11, 2016.

COMMUNICATIONS

SPEAKING TO THE MEDIA

As many IGB members are approached for interviews or news coverage regarding their work at the IGB, a short guide is available to assist you on speaking and interacting with the media.

Available on the home page of the IGB website under IGB Resources at www.igb.illinois.edu, the guide is also available for direct download from this link.
RECENT PUBLICATIONS

Please include your connection to the IGB in your author byline when submitting publications, as it will greatly help track potential newsworthy items and increase the possibility of coverage.


Price, N. P. J., Labeled, T. A., Naumn, K. E., Bowman, M. J., Berhow, M. A., ... Bischoff, K. M. (2016). Quinovosamycins: New tunicamycin-type antibiotics in which the α, β,1,1'-linked N-acetylglucosamine residue is replaced by N-acetylglucosamine. Journal of Antibiotics, 69(8), 637-646. DOI: 10.1038/ja.2016.49


