IGB NEWS

Upcoming Events
Monthly Profiles
Happenings at IGB
Image Of The Month
Research News
Department Announcements

Volume 13 Number 7

UPCOMING EVENTS

Genomes at Home
DNA To Drugs
November 14, 2020, 2:00 p.m.
Join via Zoom

What new ideas can we gain from watching animals? This week we'll be looking at the movement of wild animals and how their impressive survival skills could give us invention ideas to improve or enhance our own lives.

Genomes at Home
Personalized Health
November 21, 2020, 2:00 p.m.
Join via Zoom

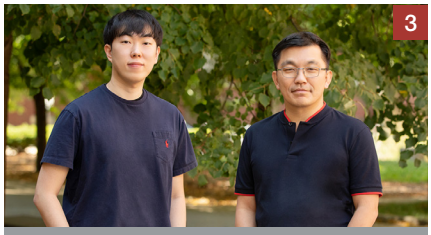
For our last day, we're going to be doing some folding. But not with paper! We'll be folding DNA structures.

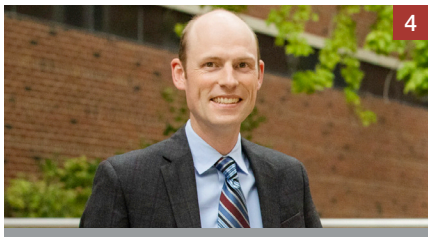
IGB Pioneers Seminar - GNDP
Skin Stem Cells: Coping With Stress
December 8, 2020, 12:00 p.m.
Join via Zoom

Elaine Fuchs, PhD
The Rockefeller University
Rebecca C. Lancefield Professor,
Investigator Howard Hughes
Medical Institute

FEATURED NEWS


2
Lassogen raises $4.5M in seed round for novel therapeutics


3
Octopus-inspired sucker transfers delicate tissue grafts, biosensors


4
Monthly Profile: Erik Nelson

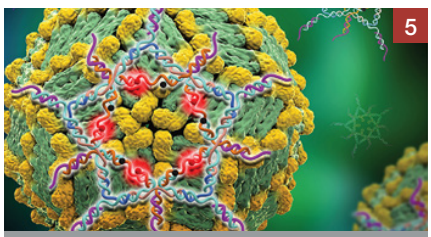
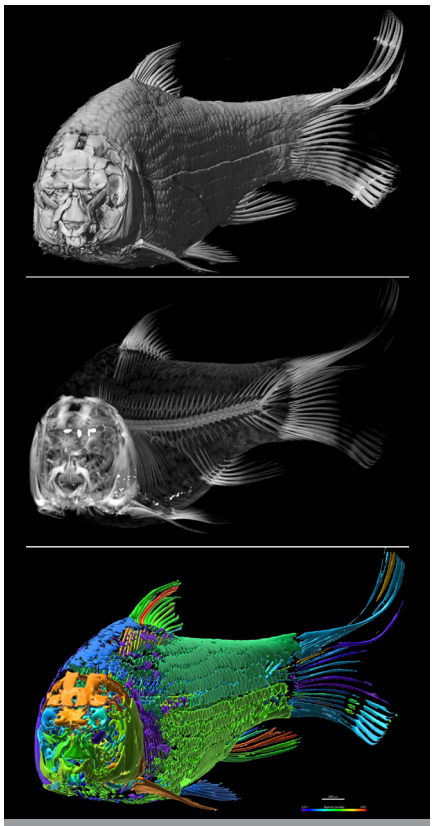

5
On the Grid: Happenings at IGB

IMAGE OF THE MONTH



This month's image shows a Shorthead Redhorse, *Moxostoma macrolepidotum*. The species is commonly found in large creeks and rivers across most of Illinois. The image sequence from top to bottom shows 3D volume rendering at different opacities/modules to show external surface (top), internal skeleton (middle) and psuedocolored Isosurface objects with range of ellipticity (prolate, color coded) from Xray CT data. The sample was scanned using the NSI X5000 High Resolution MicroCT and rendered in 3D using Imaris 3D in IGB's Core Facilities.

IGB News

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

FEATURE

Lassogen raises $4.5M
in seed round to develop novel therapeutics

Although small molecule drugs and antibodies continue to be the standard for cancer treatment, a new class of therapeutics—lasso peptides—may prove effective, especially for disease targets that thwart traditional approaches. Combining the power of antibodies and small molecule drugs, the San Diego-based startup Lassogen is developing lasso peptides as a new therapeutic modality. Now, with $4.5 million raised in a seed round, the company moves one step closer to demonstrating the power of lasso peptides for treating human diseases such as cancer and autoimmune disorders.

Lassogen was founded by CEO Mark Burk, PhD, along with co-founder Kent Boles, PhD, and academic co-founders and advisors Professor of Chemistry Douglas Mitchell (MMG, University of Illinois, pictured above) and Professor of Pharmaceutical Science Tracy Handel (University of California San Diego).

"For a long time, people have been interested in cyclic peptides as therapeutics as there are certain things you can't do very well with standard classic molecule drugs," said Mitchell. "My group here at Illinois was looking at a very unusual class of macrocyclic peptides called lasso peptides. I presented our work at some conferences and this initiated discussions with Mark, after which our relationship was formalized."

Lasso peptides, as the name suggests, form unique structures that resemble a lasso, rendering them completely heat and protease stable. Their shape and volume also allow them to easily engage the binding pockets of important receptors, overcoming many of the limitations presented by antibodies and small molecule drugs.

"Lasso peptides are sort of in this Goldilocks zone where they're not too big or too small," said Mitchell. "They are also globular, unlike most other cyclic peptides. Further, you can boil a lasso peptide and they retain their biological activity and chemical structure. This stability and rigidity have big implications for how they can function in the body."

In order to find lasso peptides in nature, Mitchell recruited University of Illinois undergraduates to write a discovery algorithm that allowed them to define and catalog lasso peptides found in microbial genomes. Although restrictive to archaea and bacteria, lasso peptides were found to be common and fairly distributed within those domains. What was once a bottleneck is no longer the case, as close to 5,000 lasso peptides have been discovered.

With a total of $5.1 million raised since 2019, Lassogen plans to focus its efforts in immuno-oncology, including development of agonists or dual antagonists of cell surface receptors called GCPRs.

"Lassogen has strategically targeted GPCRs that are not exploited medicinally by other therapeutic modalities," said Mitchell. "There are G protein-coupled receptors that are involved in various types of cancer where there is good validation that modulation of that target could be beneficial for stopping tumor growth or enabling the immune response to eliminate the tumor. We have lasso peptide-based compounds that modulate these targets, and we are exploring ways to exploit the vast potential of lasso peptides in cancer."

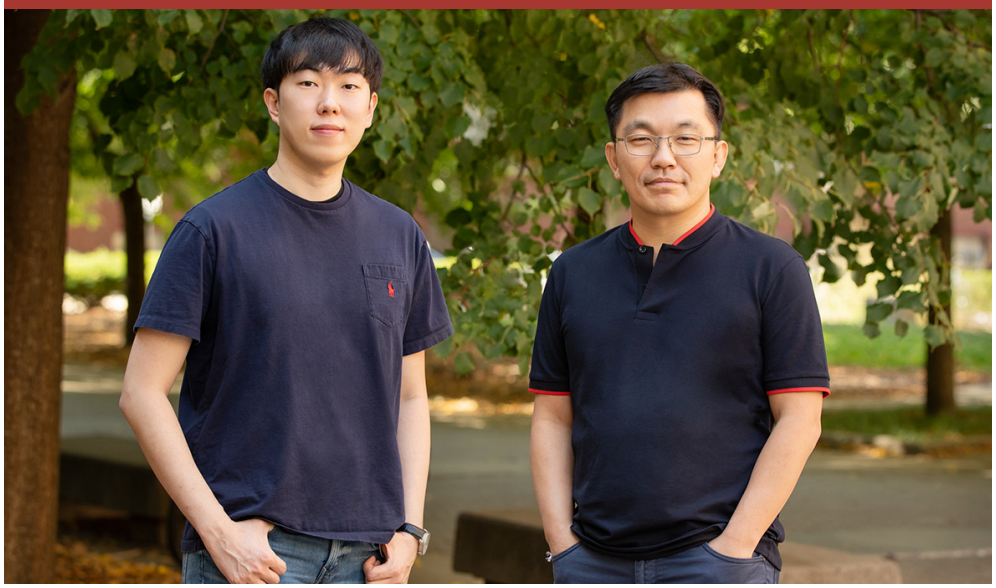
Lassogen also has a federally funded collaborative project with Mitchell at Illinois to develop a production strategy that would allow enzymatic creation of any desired lasso peptide. Their strategy would allow programming of a substrate to become compatible with an enzyme that would normally not process it, thus enabling discovery and optimization for anticancer research or other therapeutic areas.

"Lasso peptides have solved a paradox where pathways are selective and promiscuous at the same time," said Mitchell. "You can retain the part that endows selectivity, but then stick something on the other half of the peptide that is unnatural or natural to make these huge combinatorial libraries that select for the activities that you want."

As an academic collaborator and consultant, Mitchell will continue working with Lassogen in exploring and honing the chimeric strategy. In addition, some applications are currently underway to work on coronaviruses, where protein-protein interactions are key.

"The things that we develop and learn in my lab have value to Lassogen and there are specific larger projects that we want to do together," said Mitchell. "These compounds are underexploited and underleveraged, and in my opinion, too interesting to not pursue." ■

Written by Alisa King-Klemperer.
Photo by Julia Pollack.



Octopus-inspired sucker
transfers thin, delicate tissue grafts, biosensors

Thin tissue grafts and flexible electronics have a host of applications for wound healing, regenerative medicine and biosensing. A new device inspired by an octopus's sucker rapidly transfers delicate tissue or electronic sheets to the patient, overcoming a key barrier to clinical application, according to researchers at the University of Illinois at Urbana-Champaign and collaborators.

"For the last few decades, cell or tissue sheets have been increasingly used to treat injured or diseased tissues. A crucial aspect of tissue transplantation surgery, such as corneal tissue transplantation surgery, is surgical gripping and safe transplantation of soft tissues. However, handling these living substances remains a grand challenge because they are fragile and easily crumple when picking them up from the culture media," said study leader Hyunjoon Kong (M-CELS leader/EIRH/RBTE), a professor of chemical and biomolecular engineering at Illinois.

Kong's group, along with collaborators at Purdue University, the University of Illinois at Chicago, Chung-Ang University in South Korea, and the Korea Advanced Institute for Science and Technology, published their work in the journal Science Advances.

Current methods of transferring the sheets involve growing them on a temperature-sensitive soft polymer that, once transferred, shrinks and releases the thin film. However, this process takes 30-60 minutes to transfer a single sheet, requires skilled technicians and runs the risk of tearing or wrinkling, Kong said.

"During surgery, surgeons must minimize the risk of damage to soft tissues and transplant quickly, without contamination. Also, transfer of ultrathin materials without wrinkle or damage is another crucial aspect," Kong said.

Seeking a way to quickly pick up and release the thin, delicate sheets of cells or electronics without damaging them, the researchers turned to the animal kingdom for inspiration. Seeing the way an octopus or squid can pick up both wet and dry objects of all shapes with small pressure changes in their muscle-powered suction cups, rather than a sticky chemical adhesive, gave the researchers an idea.

They designed a manipulator made of a temperature-responsive layer of soft hydrogel attached to an electric heater. To pick up a thin sheet, the researchers gently heat the hydrogel to shrink it, then press it to the sheet and turn off the heat. The hydrogel expands slightly, creating suction with the soft tissue or flexible electronic film so it can be lifted and transferred. Then they gently place the thin film on the target and turn the heater back on, shrinking the hydrogel and releasing the sheet.

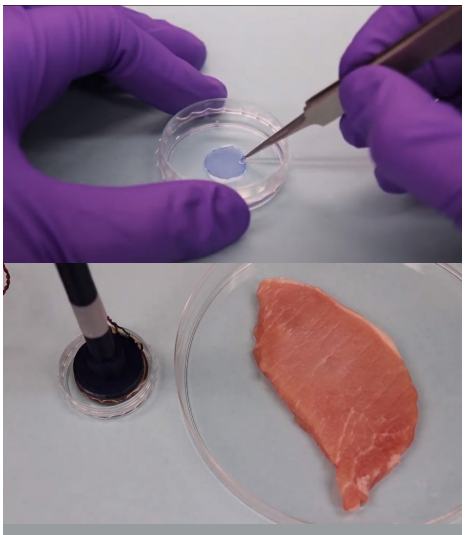
The entire process takes about 10 seconds.

Next, the researchers hope to integrate sensors into the manipulator, to further take advantage of their soft, bio-inspired design.

"For example, by integrating pressure sensors with the manipulator, it would be possible to monitor the deformation of target objects during contact and, in turn, adjust the suction force to a level at which materials retain their structural integrity and functionality," Kong said. "By doing so, we can improve the safety and accuracy of handling these materials. In addition, we aim to examine therapeutic efficacy of cells and tissues transferred by the soft manipulator."

The National Science Foundation, the National Institutes of Health, the Department of Defense Vision Research Program and the Jump Applied Research in Community Health through Engineering and Simulation endowment supported this work. ■

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



A soft, octopus-sucker-inspired device can transfer thin, fragile sheets of cells, tissue or flexible electronics in about ten seconds.

MONTHLY PROFILE

Erik Nelson is a Professor of Molecular and Integrative Physiology whose lab investigates how hormones and metabolic factors can impact tumor progression, with the goal of using their research information to develop novel therapeutics for the treatment of cancer.

Erik Nelson

Preventing and treating breast cancer via Era of Hope Award

Professor of Molecular and Integrative Physiology Erik Nelson (ACPP) has won a $4.5M Era of Hope Scholar Award from the United States Department of Defense (DoD) Breast Cancer Research Program (BCRP). This prestigious award supports individuals early in their careers who have demonstrated significant potential to effect meaningful change in breast cancer research. Recipients of the Era of Hope Scholar Award are leaders and visionaries in their respective field who go beyond conventional thinking to change the current landscape of breast cancer research and therapy.

Approximately 1 in 8 women will be diagnosed with invasive breast cancer in their lifetime as it continues to be the second leading cause of cancer-related deaths in women in the United States. The DoD, in collaboration with several experts, has identified several areas of current shortcomings in the areas of breast cancer management, diagnosis, and therapy. Nelson will spearhead a collaborative and interdisciplinary research team to address several of these key areas.

"The American Institute for Cancer Research has previously funded our work on tumor dormancy and the funding from that source allowed us to develop the data necessary to move on to the next step and secure this award," said Nelson. "What we plan on working on is multi-fold but one of the big things is determining why and how breast cancer cells can lay dormant for years and then suddenly re-emerge. The other aspect of that is we're trying to eliminate the mortality associated with metastatic breast cancer, which accounts for more than 90% of all breast cancer-associated deaths."

Nelson's two-fold approach involves leveraging cholesterol homeostasis to design better treatments for metastatic disease and to prevent metastatic recurrence. Previous work by Nelson's group found that cholesterol was important for regulation of cancer and immune cells, providing the basis for why recurrence develops sooner in patients with high cholesterol levels. In subsequent work, they found that a metabolite of cholesterol, 27-hydroxycholesterol (27-HC), was in fact the causal link.

"With cancer cells, 27-HC seems to be able to activate the estrogen receptor, which for 60-70% of breast cancer patients, drives proliferation," said Nelson. "We also found that it acted on a type of immune cell called a myeloid immune cell. This led to a highly immune-suppressive environment that prevented immune cells from mounting an effective response against cancer."

"I look forward to asking some big questions and starting to translate our studies into meaningful change for breast cancer patients."

One aspect of the project includes a collaboration with Professor of Chemistry Paul Hergenrother (ACPP theme leader/MMG) to develop strategies in inhibiting the synthesis of 27-HC as well as developing drugs that target key biological regulators of cholesterol metabolism. Other collaborators include Professor of Biochemistry David Kranz (ACPP), Professor of Electrical and Computer Engineering Stephen Boppart, Professor of Computer Science Saurabh Sinha (BSD/CABBI/GNDP/GSP), Professor of Bioengineering Wawrzyniec Dobrucki (RBTE), Professor of Food Science & Human Nutrition William Helferich, and Professor and Chief of Clinical Breast Radiotherapy Service Wendy Woodward (The University of Texas MD Anderson Cancer Center).

"We are working with bioengineers because we found that various metabolites can induce the secretion of cancer cell extracellular vesicles, but we don't know how to regulate or drug them," said Nelson. "We are also working with William Helferich to determine if the cooking process of high-cholesterol foods contributes to the promotion of breast cancer metastasis. Cholesterol is amenable to lifestyle interventions and so we want to develop ways to change the diet by looking at cooking style."

Nelson's project also involves cancer research advocates, who are typically cancer survivors or caregivers of someone with cancer. Advocates provide unique perspectives to researchers and help inform patient-centered research. Here at Illinois, Nelson co-leads a Cancer Research Advocacy Group along with Professor of Food Science & Human Nutrition Zeynep Madak-Erdogan (CGD/GSP), working with advocates Sarah Adams, Lea Ann Carson, and Renaé Strawbridge. Outside of Illinois, Nelson has also recruited Jamie Holloway from a cancer research advocacy group in Georgetown.

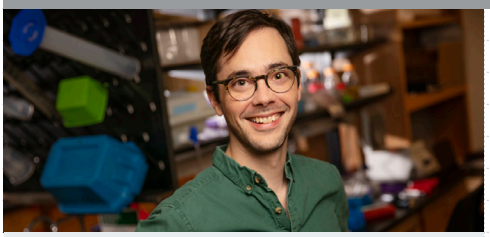
"Current therapies for metastatic disease are not very effective and our goal is to change that," said Nelson. "I look forward to asking some big questions and starting to translate our studies into meaningful change for breast cancer patients."

The views expressed in this article/news release are those of the author and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government. ■

Written by Alisa King-Klemperer.
Photo by L. Brian Stauffer.

ON THE GRID
HAPPENINGS AT THE IGB

AWARDS



CHRISTOPHER BROOKE

Christopher Brooke, Assistant Professor of Microbiology (IGOH) was named the 2020 Forty Under 40 Man of the Year by Central Illinois Business Magazine, for leading efforts to produce viral transport media (VTM) supporting COVID-19 testing across the state of Illinois.

FAN LAM

Fan Lam, Assistant Professor of Bioengineering (GNDP) received a National Institute of Biomedical Imaging and Bioengineering Trailblazer R21 Award, for his research on molecular imaging of the brain.

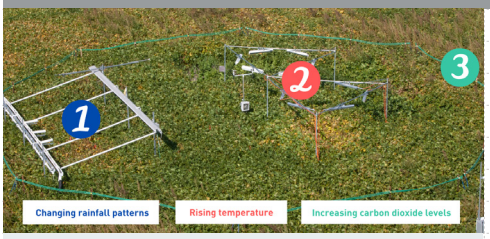
CARL GUNTER

Carl Gunter, Professor of Computer Science (GSP leader) was named the George and Ann Fisher Distinguished Professor in Engineering.

NAVEEN NARISETTY

Naveen Narisetty, Assistant Professor of Statistics (MME) received an NSF CAREER award for his work on how statisticians and data scientists can more efficiently work within the Bayesian framework for real world applications.

CLIMATE

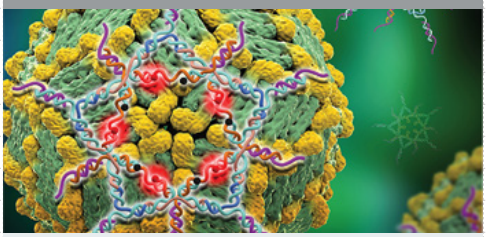


30 YEARS OF EXPERIMENTS SIMULATE FUTURE CROP CLIMATE RESPONSE

Over the past 30 years, a network of 14 long-term research facilities spanning five continents has simulated future levels of carbon dioxide (CO2) to forecast the impact on crops. Importantly, these 'Free-Air Concentration Enrichment' (FACE) experiments are conducted outside in real-world field conditions to capture the complex environmental factors that impact crop growth and yield.

A review published in *Global Change Biology* synthesizes 30 years of FACE data to grasp how global crop production may be impacted by rising CO2 levels and other factors. The study portends a less optimistic future than the authors' previous review published 15 years ago in *New Phytologist*. "There are likely genetic solutions, should society decide to act on these--however, time is short," said co-author Stephen Long (BSD/CABBI/GEGC), Ikenberry Endowed University Chair of Crop Sciences and Plant Biology. Read the full article here.

CENTER NEWS



CENTER FOR GENOMIC DIAGNOSTICS (CGD)

CGD was awarded its third NIH R01 grant in a collaboration with Stanford and Huntsman Cancer Institute, for the detection of miRNA in the serum of advanced prostate cancer patients. The Center plans to apply the research towards therapy effectiveness monitoring.

CGD was also recently approved for the establishment of the Center for Pathogen Diagnostics, in collaboration with Zhejiong University, China.

OUTREACH

GENOMES AT HOME

From the creators of Genome Day . . . Genomes at Home! A series of hands on activities that can be done on Zoom from the comfort of your own home. Designed for elementary and middle school children, activities will be led by IGB scientists live on video and cover topics including the environment, energy use & production, health, and fundamental research at the IGB in an approachable manner for all ages.

Join us every Saturday at 2:00pm from October 17 to November 21 via Zoom
Meeting ID: 865 1546 8256, Password: 713702

November 14, 2020 - DNA to Drugs

November 21, 2020 - Personalized Health

DEPARTMENT ANNOUNCEMENTS

BIOECONOMY

Part of IGB's mission is to stimulate the bioeconomy of the state of Illinois. Here, we feature innovation from IGB researchers.

PATENT AWARD

Hergenrother and co-inventors awarded patent continuation for novel strategy for anticancer and antibacterial drug development

Congratulations to Professor of Chemistry Paul Hergenrother (ACPP leader/MMG) and his co-inventors for their recent continuation of their patent Complex and Structurally Diverse Compounds. The invention provides a novel, general, and facile strategy for the creation of small molecules with high structural and stereochemical complexity. This strategy is important for the development of anticancer and antibacterial drugs.

IP @ IGB

Dr. Cecilia Gentle, the IGB's Economic Development Fellow, is available for consultations about the invention process and reporting inventions to the Illinois Office of Technology Management. Contact Dr. Gentle at gentle2@illinois.edu. ■

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.

Janzen, A., Bataille, C., Copeland, S. R., Quinn, R. L., Ambrose, S. H., Reed, D., Hamilton, M., Grimes, V., Richards, M. P., le Roux, P., & Roberts, P. (2020). Spatial variation in bioavailable strontium isotope ratios (87Sr/86Sr) in Kenya and northern Tanzania: Implications for ecology, paleoanthropology, and archaeology. *Palaeogeography, Palaeoclimatology, Palaeoecology,* 560, [109957]. https://doi.org/10.1016/j.palaeo.2020.109957

Barwinska-Sendra, A., Garcia, Y. M., Sendra, K. M., Baslé, A., Mackenzie, E. S., Tarrant, E., Card, P., Tabares, L. C., Bicep, C., Un, S., Kehl-Fie, T. E., & Waldron, K. J. (2020). An evolutionary path to altered cofactor specificity in a metalloenzyme. *Nature communications*, 11(1), [2738]. https://doi.org/10.1038/s41467-020-16478-0

Žurauskas, M., Barkalifa, R., Alex, A., Marjanovic, M., Spillman, D. R., Mukherjee, P., Neitzel, C. D., Lee, W., Medler, J., Arp, Z., Cleveland, M., Hood, S., & Boppart, S. A. (2020). Assessing the severity of psoriasis through multivariate analysis of optical images from non-lesional skin. *Scientific reports*, 10(1), [9154]. https://doi.org/10.1038/s41598-020-65689-4

Holland, R. L., Bosi, K. D., Harpring, G. H., Luo, J., Wallig, M., Phillips, H., & Blanke, S. R. (2020). Chronic in vivo exposure to Helicobacter pylori VacA: Assessing the efficacy of automated and long-term intragastric toxin infusion. *Scientific reports*, 10(1), [9307]. https://doi.org/10.1038/s41598-020-65787-3

Lee-Thacker, S., Jeon, H., Choi, Y., Taniuchi, I., Takarada, T., Yoneda, Y., Ko, C. M., & Jo, M. (2020). Core Binding Factors are essential for ovulation, luteinization, and female fertility in mice. *Scientific reports*, 10(1), [9921]. https://doi.org/10.1038/s41598-020-64257-0

Tabatabaei, S. K., Wang, B., Athreya, N. B. M., Enghiad, B., Hernandez, A. G., Fields, C. J., Leburton, J. P., Soloveichik, D., Zhao, H., & Milenkovic, O. (2020). DNA punch cards for storing data on native DNA sequences via enzymatic nicking. *Nature communications*, 11(1), [1742]. https://doi.org/10.1038/s41467-020-15588-z

Juma, E. O., Allan, B. F., Kim, C. H., Stone, C., Dunlap, C., & Muturi, E. J. (2020). Effect of life stage and pesticide exposure on the gut microbiota of Aedes albopictus and Culex pipiens L. *Scientific reports*, 10(1), [9489]. https://doi.org/10.1038/s41598-020-66452-5

Barakat, R., Lin, P. C., Park, C. J., Zeineldin, M., Zhou, S., Rattan, S., Brehm, E., Flaws, J. A., & Ko, C. M. J. (2020). Germline-dependent transmission of male reproductive traits induced by an endocrine disruptor, di-2-ethylhexyl phthalate, in future generations. *Scientific reports*, 10(1), [5705]. https://doi.org/10.1038/s41598-020-62584-w

Lee, M. J., Collins, J. D., Harwood, S. A., Mendenhall, R., & Huntt, M. B. (2020). "If you aren't White, Asian or Indian, you aren't an engineer": racial microaggressions in STEM education. *International Journal of STEM Education*, 7(1), [48]. https://doi.org/10.1186/s40594-020-00241-4

Adeniba, O. O., Corbin, E. A., Ganguli, A., Kim, Y., & Bashir, R. (2020). Simultaneous time-varying viscosity, elasticity, and mass measurements of single adherent cancer cells across cell cycle. *Scientific reports*, 10(1), [12803]. https://doi.org/10.1038/s41598-020-69638-z

Suthers, P. F., Dinh, H. V., Fatma, Z., Shen, Y., Chan, S. H. J., Rabinowitz, J. D., Zhao, H., & Maranas, C. D. (2020). Genome-scale metabolic reconstruction of the non-model yeast Issatchenkia orientalis SD108 and its application to organic acids production. *Metabolic Engineering Communications*, 11, e00148. https://doi.org/10.1016/j.mec.2020.e00148 ■

ILLINOIS

IGB News is published by the IGB Communications Office.
Contact Nicholas Vasi (nvasi@illinois.edu)
www.igb.illinois.edu 20.104