NIH RECORD

May 31, 2019
Vol. LXXI, No. 11

National Institutes of Health

STOKED BY STOCHASTICITY

Betzig Boosts Biology with Better Visuals

BY RICH MCMANUS

While there are those who think necessity is the mother of invention, Nobel laureate Dr. Eric Betzig says dissatisfaction—pure, serial frustration with limits—has prompted him to create sophisticated new microscopes that are allowing biologists to understand the lives of cells at more intimate levels.

Convinced that you can't understand what you can't see, especially in living systems, Betzig, a physicist with appointments at both the University of California, Berkeley, and the Howard Hughes Medical Institute, shared "The Secret Lives of Cells" at a Wednesday Afternoon Lecture on Apr. 24.

Invented around 400 years ago, the microscope was the dominant tool for the study of living systems invisible to the naked eye for some 300 years, he said. From about 1880 to 1980, an era of stagnation settled in. The microscope stalled at a limit of resolution that remained fundamentally constant for a century.

Meanwhile, three new tools—biochemistry, molecular biology and structural biology—flourished, though what they offered tended to be reductionist and inferential, Betzig said.

"Taking a cell down to its screws" has only limited usefulness, in much the same way that seeing photographs of a football game—even at high resolution—would tell a neophyte almost nothing about the rules of the game, if that's all he had to reason from.

SEE **BETZIG**, PAGE 4

Nobel laureate Dr. Eric Betzig speaks at NIH.

Sex Chromosomes Can Trade DNA in Two Regions

BY ERIC BOCK

Dr. Melissa Wilson

The X and Y chromosomes, also known as sex chromosomes, differ greatly from each other. But in two regions, they are practically identical, said Dr. Melissa Wilson, assistant professor of genomics, evolution and bioinformatics at Arizona State University.

"We're interested in studying how the process of evolution shaped the X and the Y chromosome in gene content and expression and how that subsequently affects literally everything else that comes with being a

SEE **WILSON**, PAGE 8

Ray Bosmans (r) lets kids touch his pet Honduran milksnake at Earth Day event.

TYCTWD Celebrates 25 Years

BY DANA TALESNIK

Science talks. Nature walks. How does blood clot? Meet a robot. Hearts, brains, bones, even see a spleen. Earth Day shows us how to be green.

Kids of all ages had a blast learning about the amazing science that happens across

SEE **TYCTWD**, PAGE 6

NIH science explores the "final frontier." See p. 5.

ALSO THIS ISSUE

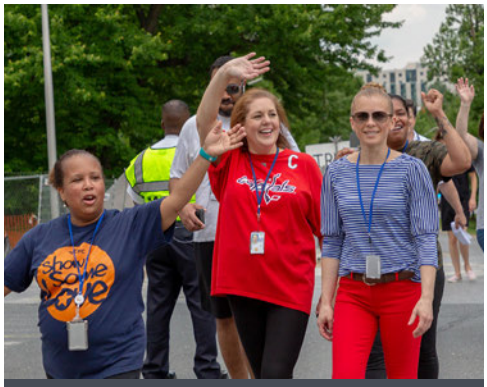
12th Annual Take a Hike Day

June 12

Join the Office of Research Services for the 12th annual Take a Hike Day, a non-competitive and fun walk/run on Wednesday, June 12 from 11:30 a.m. to 1:30 p.m. in front of Bldg. 1, rain or shine.

Activities will begin at 11:30 a.m., followed by opening remarks from NIH leadership. Not on campus? No problem. You can participate in Take a Hike Day at the following off-campus locations: Executive Plaza, Fishers Lane, Rockledge and Shady Grove. New participating locations this year are Rocky Mountain Laboratories and NIEHS Research Triangle Park. To register, visit https://go.usa.gov/xQ4GR.

Fun fact—the *Physical Activity Guidelines for Americans* recommends 30 minutes of moderate physical activity each day. So lace up your walking shoes and take a break from the routine for a walk or jog around the perimeter of the NIH campus (about 3.25 miles). No matter how fast you walk or how far you run, the ultimate goals are to begin or continue a regular habit of physical activity and create a foundation for long-term behavior changes for a healthier lifestyle.



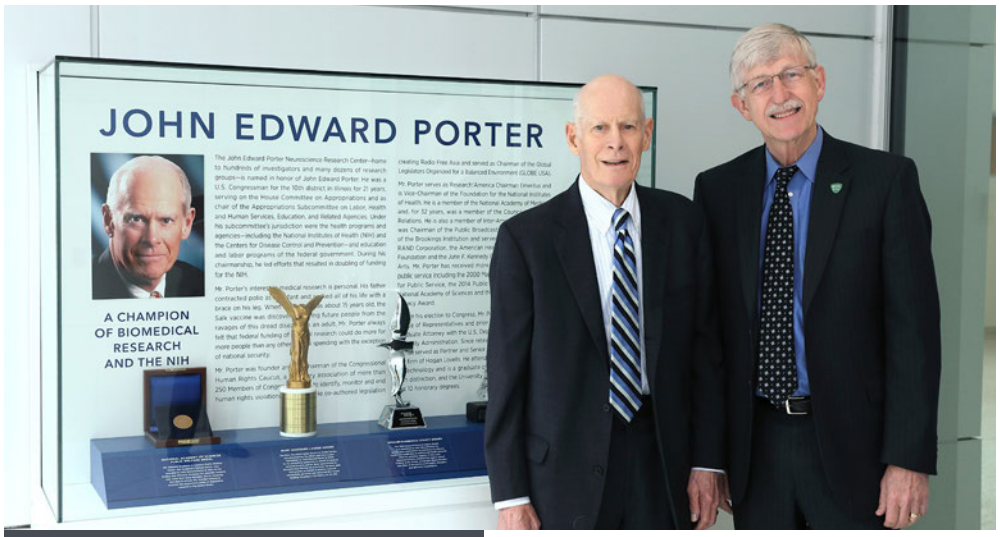
The event last year drew a happy crowd.

More than 16,000 employees have participated in Take a Hike Day over the past 11 years, so let's continue the tradition. Physical activity is always more fun with a partner, so collect your co-workers and register today. Remember to bring your NIH ID badge to get back on campus at the conclusion of the walk/run.

Through the end of June, NIH is highlighting wellness-supporting events through the "Spring into Wellness" campaign. To learn more about NIH-sponsored events that support your financial, social, career, physical and community well-being, visit https://wellnessatnih.ors.od.nih.gov/Pages/springintowellness.aspx.

NLM Talk Features Elhadad, June 12

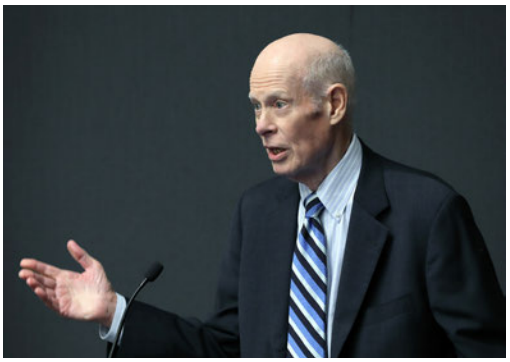
The next talk in the NLM Informatics and Data Science Lecture Series—Advancing Women's Health through Data Science and Personal Health Informatics—will be given by Dr. Noémie Elhadad on Wednesday, June 12 from 2 to 3 p.m. in Lister Hill Auditorium, Bldg. 38A.



Porter Exhibit Dedicated

Former Rep. John Edward Porter returned to NIH on May 9 for the dedication of an exhibit in the building named after him on campus, the John Edward Porter Neuroscience Research Center. Five years ago, the building opened with a symposium and dedication. The recent event unveiled a display case that briefly explains why the facility is named in his honor. Above, Porter is joined by NIH director Dr. Francis Collins. At right, Porter offers brief remarks at the ceremony.

PHOTOS: CHIA-CHI CHARLIE CHANG



She will discuss two issues: how to characterize and discover the different ways endometriosis presents in individuals, essentially phenotyping the disease, and how to support individuals with the disease, considering its heterogeneous presentations.

Elhadad is associate professor and co-interim chair of the department of biomedical informatics at Columbia University and is affiliated with the computer science department and data science institute. Her research is at the intersection of machine learning, technology and medicine.

Dr. Noémie Elhadad

The talk will be broadcast live and archived at http://videocast.nih.gov/. Individuals who need reasonable accommodation to participate should contact Ebony Hughes at (301) 451-8038 or Ebony.Hughes@nih.gov or the Federal Relay (1-800-877-8339).

NAS Elects Two from NIH

The National Academy of Sciences recently announced the election of 100 new members, two of whom are NIH scientists.

Dr. Michael Lenardo

Dr. Michael Lenardo is chief of the molecular development of the immune system section in NIAID's Laboratory of Immune System Biology and director of the Clinical Genomics Program.

Dr. Elaine Ostrander is chief and distinguished investigator of NHGRI's Cancer Genetics and Comparative Genomics Branch and head of the comparative genetics section.

Dr. Elaine Ostrander

NAS is a private, nonprofit institution that was established under a congressional charter signed by President Abraham Lincoln in 1863.

NHLBI Division Celebrates 50th Anniversary

BY ALEXIS CARTER

For 50 years, the Division of Lung Diseases, part of the National Heart, Lung, and Blood Institute, has focused on translating basic scientific research into more effective treatments and patient care.

In April, the division kicked off its golden anniversary with a scientific symposium highlighting the progress and future of a centerpiece of this work—lung imaging. The half-day event included researchers from both the intramural and extramural programs. They discussed how they apply sophisticated imaging techniques to advance the understanding of healthy and diseased lungs at the cellular and molecular level and how this work informs the diagnosis, treatment and management of lung diseases in general.

In welcoming remarks, NHLBI director Dr. Gary Gibbons acknowledged the institute's legacy of excellence in pulmonary science research since 1969 and said he is excited about the breakthroughs yet to come. With technological innovations in imaging, the phrase "chronic lung disease" one day will no longer be needed, he said, noting that he has charged the division leadership with making that a reality sooner than later. With a renewed commitment to the prevention, preemption, remission and reversal of pulmonary disorders, Gibbons said he is sure the watershed moment will come.

Dr. James Crapo of National Jewish Health gave the first talk, highlighting a key finding of the NHLBI-funded COPDGene study he leads as principal investigator. After following a cohort of 10,000 people for 5 years, Crapo said he had identified a group of participants who, after taking a breathing test that measures lung function, showed no obstruction in their airways, even though they still had symptoms of COPD. These participants also had a higher risk of morbidity and mortality, compared to a group who had showed gradual lung tissue damage over time. With this finding, Crapo has a proposal: to include people who have not yet developed airflow obstruction in the diagnosis of COPD as a way to help prevent disease.

Dr. Scott Fraser of the University of Southern California noted his work with the NHLBI-funded Molecular Atlas Lung Development Program consortium. He and his team are building tools that can acquire and analyze microCT images in hopes of defining the anatomy of the developing lung.

Dr. Sanjay Jain of Johns Hopkins University discussed his progress developing molecular imaging tools to better understand bacteria, the infections they cause and the environments that could minimize them. The hope is that this will lead to limiting the overuse of antibiotics.

NHLBI's Dr. Adrienne Campbell-Washburn showed how advances in low-field MRI could greatly improve cardiac and lung imaging and other image-guided procedures that diagnose and treat disease.

Kicking off the second session, Dr. Carmen Priolo of Brigham and Women's Hospital/Harvard Medical School detailed how PET imaging can identify abnormal metabolic processes in preclinical models—and one day in imaging trials—of lymphangioleiomyomatosis (LAM), a rare lung disease mostly affecting women.

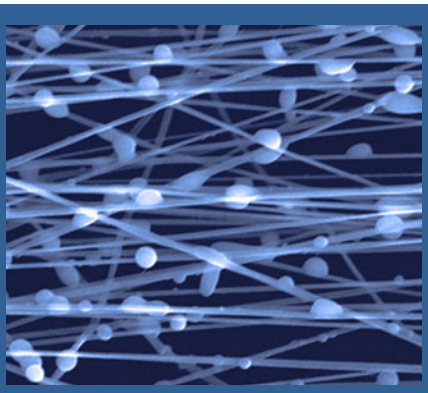
NHLBI's Dr. Marcus Chen illustrated how an ultra-low dose chest CT, when compared to a traditional x-ray, could be used to validate clinical cases of LAM and other lung diseases.

Dr. R. Graham Barr of Columbia University rounded out the symposium by discussing how he uses machine learning and advanced imaging techniques to help understand chronic lung disease in large-scale, long-term studies, including the Multi-Ethnic Study of Atherosclerosis lung study and the Subpopulations and Intermediate Outcome Measures in COPD Study.

Dr. James Kiley, who has directed the Division of Lung Diseases since 1984, ended the event, calling the discussions "a window into the future of pulmonary imaging at all levels.

"It was a phenomenal display of hard work by many people across the country," he said, inviting the audience to stay tuned for more anniversary events to come.

On hand at the symposium were (from l) Dr. Adrienne Campbell-Washburn, Dr. James Crapo, division director Dr. James Kiley, Dr. Scott Fraser, Dr. Sanjay Jain, NHLBI director Dr. Gary Gibbons, Dr. Marcus Chen, Dr. Carmen Priolo, Dr. R. Graham Barr and division deputy director Dr. Gail Weinmann.



ON THE COVER: *Researchers at the Midwest Cancer Nanotechnology Training Center are developing a blood clot-mimicking patch capable of delivering drugs at an implantation site in a controllable manner. The patch, consisting of drug-releasing microparticles bound to directionally aligned microfibers, was formed through a unique electrospinning/electrospraying process. The image shows the 2-6-micrometer-thick microparticles attached to the 1-micrometer-thick microfibers.*

IMAGE: ROSS DEVOLDE & HYUNJOON KONG, NCI

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email editor or phone (301) 496-2125.

Editor: Rich McManus
Rich.McManus@nih.gov

Associate Editor: Carla Garnett
Carla.Garnett@nih.gov

Staff Writers:
Eric Bock • *Eric.Bock@nih.gov*
Dana Talesnik • *Dana.Talesnik@nih.gov*

Subscribe via email: **listserv@list.nih.gov**
Follow: **http://nihrecord.nih.gov/**

The NIH Record is recyclable as mixed paper.

National Institutes of Health
Turning Discovery Into Health

Betzig

CONTINUED FROM PAGE 1

"You have to see the structure in its entirety," Betzig told the packed audience. "You've got to see it in motion or your understanding is going to be limited."

Obsessed with building better microscopes since the early 1980s, he began to assemble a kit of parts from other tech innovations, including personal computers, to control a new-generation microscope; digital cameras, to record images; lasers, whose coherent light could be shaped in space and time; and fluorescent proteins such as GFP (green fluorescent protein).

Mixing these components led to what Betzig calls a "Cambrian explosion" in microscopy. "I was lucky to get in on that in the early days."

A key advance was photoactivation, he said, which enabled researchers to find the locations of molecules precisely. "That's when we advanced from diffraction-limited imaging to super-resolution."

Betzig said he and his chief collaborator Dr. Harald Hess "were terrified of being scooped—the idea seemed so obvious. We were also both unemployed." They built their first super-resolution microscope in the living room of Hess's house.

"We were two physicists who knew zero biology," Betzig admitted, calling Hess the smarter one since, when both left jobs at Bell Labs, Betzig told them they could go to hell while Hess left quietly and was rewarded with some leftover equipment.

The men were lucky enough to get hired at the Howard Hughes Medical Institute's Janelia Research Campus, Betzig recalls.

History of dissatisfaction

"My history is one of getting dissatisfied over and over again with super-resolution and then seeking solutions," he noted. "I said, 'Damn, I've looked at dead stuff all my life. I want to see something living.'"

As techniques accumulated—from high-pressure freezing of cells to whole-cell correlative 3-D focused ion beam scanning electron microscopy to live imaging with single particle tracking (SPT) photo-activated light microscopy (PALM)—advances in seeing "became a tremendous hypothesis generator," said Betzig.

Suddenly, the dynamics of the endoplasmic reticulum became visible. The fusions and fissions that characterize endoplasmic reticulum-mitochondria interactions became apparent. Myosin filaments could be seen in production and embryogenesis could be better studied. The tango of T cells and their antigens could be seen. Science's ideas about how transcription worked were upended.

★ ★ ★

"I will never make a better contribution [to science] than lattice light-sheet microscopy. I never felt more like Galileo than with this microscope."

-DR. ERIC BETZIG

★ ★ ★

"I will never make a better contribution [to science] than lattice light-sheet microscopy," Betzig said. "I never felt more like Galileo than with this microscope...Everyone who comes to us goes away with 10 terabytes (TB) of data and a big smile on their face."

A 'glass half-empty guy'

His collaborators are legion, numbering nearly 200, including many teams at NIH, where he and Hess worked in 2005. They did much of their work inventing PALM in a darkroom in Bldg. 32 with Dr. Jennifer Lippincott-Schwartz.

"If there's one way I would describe the cell nowadays, and my understanding of it as a physicist," said Betzig, "is it's a highly stochastic [unpredictable] system...The smaller you look, the more stochastic it is. The dynamics is an incredibly important part of being able to understand how the cell works."

He admitted, "Being the glass half-empty guy that I am, and the pessimist, I was disappointed with the lattice, despite its successes." Most multi-cellular systems are like a bag of marbles or seeing through a wet windshield, because of their different refraction indices, said Betzig, who seems to work best when most perturbed.

He envisioned two paths to future improvements, both offered by his brethren who study the cosmos. "My take-home message is that microscopists are the retarded step-children of astronomers because we steal everything from them 50 years after they develop it first," he quipped.

One "theft" is eliminating aberrations, such as those posed by the atmosphere for astronomers, who simply put their telescopes in orbit to solve the problem. In the past few years, biologists have used expansion microscopy to get rid of aberrations in their specimens. But that can't be done on live animals.

The second path is adaptive optics, which Betzig likened to "a dynamic pair of

"I find biology beautiful, amazing and incredibly humbling and scary," said Betzig.

PHOTOS: CHIA-CHI CHARLIE CHANG

eyeglasses." His team combined AO technology with the lattice light sheet to study organelle dynamics in 3-D over time, even following cells through mitosis and watching zebrafish spinal cords grow from the inside out.

"I find biology beautiful, amazing and incredibly humbling and scary in the thought that there are 37 trillion cells in your body right now doing that dance," he said, as a video of neutrophil motility in the zebrafish inner ear played on screen. "And each one of those cells has 2 billion molecules that are kind of doing the kind of dance you see in those SPT PALM movies...We really have our work cut out for us, to try to understand these systems. It's amazingly complicated."

As big a boon as new wave microscopy has been to biology, access to such expensive and rare tools is a barrier, Betzig noted. "The ultimate answer is commercialization" to remove the bottleneck.

Making a 'Swiss Army knife'

He and his team have created what they call a "Swiss Army knife," a next-generation lattice-AO microscope measuring 4 feet by 4 feet that can accommodate a range of sample sizes. Betzig said it incorporates, in one box, all of the last 30 years of improvements in microscopy. His colleagues at the Janelia Research Campus are building the first seven of them now, at a cost of about $410,000 a pop, and two more will form the cornerstones of the Advanced Bioimaging Center he is helping to establish at Berkeley.

Each knife will generate about 20 TB of data a week, which sounds great until you consider that data generated 5-6 years ago are just now making it into papers published today, Betzig said. Armies of skilled data analysts will be needed to parse a data tsunami that has already broken over biologists' heads, he said, and big tech companies are raring to display their data-crunching chops.

The ability to see cellular dynamics "with clarity that we could not have imagined 20 years ago, 15 years ago...[is] going to change the way we look at living systems in the future," Betzig concluded.

The complete talk is available at https://videocast.nih.gov/summary.asp?Live=31951&bhcp=1. R

ABOARD THE ISS

NIH Science in Space

Astronaut David Saint-Jacques poses for a picture while he grabs a small black box that's floating in space. The box contains an NIH-funded experiment—including the hardware to run it—that could help scientists on Earth better understand how bone, cartilage and the immune system interact after a knee joint injury. This project is among four from NCATS and one from NCI that blasted off on May 4 to the International Space Station (ISS).

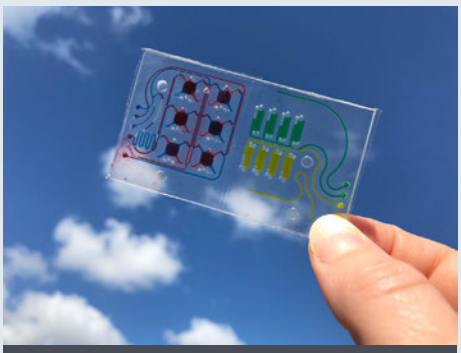
Canadian Space Agency astronaut David Saint-Jacques assists with an NIH-funded experiment on board the International Space Station.

PHOTO: NASA

The NCATS projects are part of the "Tissue Chips in Space" program. Tissue chips are about the size of a thumb drive. They contain tiny chambers where human cells live, grow and do their thing. Scientists use tissue chips to study diseases that affect certain parts of the body. They can also use them to test the potential effects of drugs on organs or tissues.

NCATS launched the Tissue Chips in Space program with the ISS National Lab in 2016 (NIBIB joined in 2017) to rapidly evolve tissue chip technology for addressing critical drug development needs. Late last year, tissue chips made their first space flight.

Space is a great place to use tissue chips. That's because microgravity appears to accelerate disease-like processes, including ones related to aging.



NCATS scientific program manager Dr. Lucie Low holds an example of a tissue chip that launched into space on May 4.

PHOTO: LUCIE LOW

The tissue chips on the May flight mimic lung infection and bone marrow response, bone and cartilage, the kidney and the blood-brain barrier that protects our brain from infections and toxins in the blood. This mission is to understand how the tissues change in reduced gravity and to develop automated versions of the tissue chip technology. On a future mission, the chips will be used to test potential drug therapies on the biological processes similar to disease and aging observed during the initial mission.

Also on board the orbiting lab is a project from the NCI Experimental Therapeutics (NExT) Program's Chemical Biology Consortium. The goal of the project is to crystallize Taspase 1—a protein involved in cancer—in microgravity to better understand its complex, three-dimensional structure. Knowing the structure could help guide the design of potent drugs.—**Emily Marti**

Above, a demonstration on CPR prompts technique practice. At center, NIH director Dr. Francis Collins boosts DNA research in a spirited primer that also featured guitar-playing. At right, Cpl. Alvin Maker shares NIH Police gear.

PHOTOS: CHIA-CHI CHARLIE CHANG, MARLEEN VAN DEN NESTE

TYCTWD

CONTINUED FROM PAGE 1

NIH at the 25th Take Your Child to Work Day. Nearly 4,000 students from grades 1-12 were registered for some 200 activities on and off campus, with plenty more kids in tow, including smaller ones, who participated in the various open-access events.

Around the Clinical Center, an annual favorite is Fantastic Voyage, run by the department of laboratory medicine. Youngsters dressed in scrubs rotated among several tables to learn about blood and microorganisms.

At Fantastic Voyage, DLM technician Teresa Bauch holds up infectious bacteria in a petri dish.

At the microbiology station, kids viewed Lyme ticks and fungi under a microscope, as medical technologist Teresa Bauch showed infectious bacteria growing in petri dishes.

"That stuff is really gross," exclaimed Addie Soper, 6, who learned a lesson in hygiene after seeing the dishes. "I learned to wash my hands because they showed me what they look like before and after you wash them."

Over in the neuroscience MRI lab, NIMH fellows hosted older kids throughout the day.

"When we learn new things, that helps your brain change and develop," said postbac fellow Gabrielle Reimann, whose lab is studying which parts of the brain become activated during learning. Brain regions light up on MRI depending on the amount of blood flowing to them, she explained.

The kids then played a game of guess the fruit or veggie based on its MRI cross-section. Next door, they took turns lying still for a mock MRI scan.

"It was a real experience, learning what would happen if I was in a real MRI," said 5th grader Zorin Petrow, an aspiring space engineer. "And they explained how it works, how the MRI shows the hydrogen atoms moving all around, attracted to the magnet."

Elsewhere in the Clinical Center, some older kids got a close-up look at preserved human organs in NCI's pathology lab.

"Every tumor sample comes through this lab," said medical technologist Patricia Fetsch. "All cancer tissues extracted are studied here."

Pathology resident Dr. Hong Jiang described each sample as some brave kids wearing gloves touched and held different organs. Among them was the brain of a stroke patient, a diseased liver and the black, spongy lung of a smoker with lesions from emphysema.

"After the surgeon cuts out a tumor, our lab tells the surgeon if it's benign or malignant," said Jiang. "We can even tell how fast the tumor is growing when it's fresh...The doctor may then refine treatment based on the sample studied."

The @NIH Twitter account live-streamed a later session of the pathology lab

Kids of all ages enjoy a controlled bubbly explosion conducted by the Science Guys of Baltimore at the FAES Science Fair on the FAES terrace.

presentation. The other Twitter live-stream video event that day was hosted by OD, which gave 25 kids the chance to be investigative reporters at a mock press conference held in Bldg. 31.

The kids met SIPPC, a small robot designed to help babies with mobility issues learn to crawl. Dr. Alison Cernich, director of NICHD's National Center for Medical Rehabilitation Research, introduced the robot and its inventor, Dr. Peter Pidcoe, an NICHD-funded scientist who is director of the engineering and biomechanics lab at Virginia Commonwealth University.

At left, resident game show host (a.k.a. NIH principal deputy director) Dr. Lawrence Tabak keeps a Wilson Hall audience guessing. At right, NIH deputy director for extramural research Dr. Michael Lauer, who is also a cardiologist, discusses stethoscopes and how to hear heartbeats.

Kids learn about and touch preserved human organs while their parents look on in NCI's Pathology lab.

A few kids then got to try out SIPPC, wiggling the leg of a stuffed animal, which moved the light-weight, battery-powered plastic robot.

OD science writer Dr. Tianna Hicklin encouraged the kids to ask questions. It's the job of a good science reporter, she said, to help the public understand complicated ideas by describing the science in plain language.

Soon, many hands went up. Budding reporters asked Pidcoe how he came up with the idea, how long it takes a baby to learn to use SIPPC and—something he hadn't previously considered—whether it could be used for animals.

Many kids especially enjoyed meeting and petting live animals—from turtles and snakes to Spike, the baby gator—brought over from several animal refuge and preservation groups. They were part of the many Earth Day exhibits at Natcher Bldg., which included recycling games, displays with eco-friendly tips and a honeybee exhibit.

Kids of all ages went home inspired, while their grown-ups left work stimulated, but perhaps tired.

Above, NIMH postbac fellow Gabrielle Reimann prepares Zorin Petrow for a mock MRI scan. At right, kids learn all about bloodwork from DLM technician Michael Guyah at the Fantastic Voyage phlebotomy table.

Wilson's lecture was followed by a Q&A chat with NIGMS director Dr. Jon Lorsch. Below, the two gather with college students and postbacs.

PHOTOS: CHIA-CHI CHARLIE CHANG

Wilson

CONTINUED FROM PAGE 1

human," she said at the Apr. 10 NIGMS Director's Early-Career Investigator Lecture in Lister Hill Auditorium, Bldg. 38A.

In humans, each cell contains 23 pairs of chromosomes, for a total of 46. The first 22 pairs look the same in both males and females. The last pair, the sex chromosomes, differ. Typically, females have two X chromosomes, while males have one X and one Y chromosome.

"I say typically because I don't know which one of us is normal and I don't like saying something is normal," she said. "Variations in the sex chromosomes can be pretty typical."

Historically, most clinical research was conducted in men, she noted. "We're finding out that treatments designed for men don't work so well in women." There is, however, a massive sex difference.

The sex chromosomes have been evolving over the past 200 million years, she explained. At first, the chromosomes were identical. Over time, the Y chromosome started to break and rearrange itself. These inversions made it more difficult to recombine with the X chromosome. Now, the X chromosome has about 1,100 genes while the Y chromosome has just 27 unique genes.

And yet, there are two regions called pseudoautosomal regions (PAR1 and PAR2) on the tips of the sex chromosomes that can pair with each other and swap DNA. This is called recombination. Wilson says a sex-determining gene called SRY sits near the boundary of the regions on the Y chromosome. Individuals who inherited the Y chromosome "went on to make testes, and those who didn't made eggs." In some cases, SRY can transfer to the X chromosome.

A deficiency in PAR1 recombination has been linked to Klinefelter syndrome, a genetic condition where males are born with an extra X chromosome. This occurs in about 1 out of every 500 births in the U.S.

There are other sex-linked disorders besides Klinefelter syndrome. One, called Turner syndrome, happens in about 1 in 2,000 or 2,500 females. Those born with the condition have one missing or structurally altered X chromosome. Another is De la Chapelle syndrome, a rare disorder in which individuals have two X chromosomes, but have a male appearance.

Wilson said the field needs to develop new methodologies to analyze the sex chromosomes, recognizing the complications and appreciating the variations.

Wilson's lab is also studying the Gila monster's genome. A black-and-orange lizard native to the southwestern United States and Mexico, Gila monsters have venomous saliva. There's a peptide in the venom that's used to treat type 2 diabetes.

"We'd like to understand what the peptide is doing in the monsters and then can better understand how it works in humans," Wilson said.

Her lecture was followed by a Q&A chat with NIGMS director Dr. Jon Lorsch.

Wilson asserted, "You're not going to be able to do biology without understanding programming in the future," adding that scientists don't have to be expert programmers, but they must understand it.

She credited her scientific success to diligence, good luck and mentors who made sure she had opportunities and built her confidence.

In her lab, Wilson talks about the challenges of research with her students. It's important for them to hear different perspectives and realize that "we're here because we don't know the answer yet" and that being wrong can still lead to interesting data.

Recently, Wilson was interviewed by *Pathways* student magazine, a collaboration between NIGMS and Scholastic, Inc. She called the experience "the coolest thing ever" to get to "be in Scholastic."

Adjei To Give NCI Seminar, June 13

Dr. Alex A. Adjei

Dr. Alex A. Adjei will give the next lecture in the NCI Center to Reduce Cancer Health Disparities' Continuing Umbrella of Research Experiences (CURE) Distinguished Scholars Seminars on Thursday, June 13, 1-2:30 p.m. at the NCI Shady Grove campus, Seminar Rm. 110. The title of his talk is "Successes and Challenges in Early Phase Drug Development for Cancer Therapy."

Adjei is professor of oncology and pharmacology at the Mayo College of Medicine. He is also a consultant in medical oncology at the Mayo Clinic and director of the Early Cancer Therapeutics Program across all three Mayo sites. He is the editor-in-chief of the *Journal of Thoracic Oncology*.

Adjei has spent more than 30 years focused on evaluating mechanisms of drug action and synergistic drug combinations. He has applied his expertise in cancer pharmacology, pharmacogenomics and drug development to advancing the treatment of lung cancer.

To register for the seminar via WebEx visit https://bit.ly/30vthXP. Individuals who need reasonable accommodation to participate should contact Victoria Coan at (240) 276-7659 and/or the Federal Relay Service (1-800-877-8339) at least two days before the meeting.

People eating ultra-processed foods ate more calories and gained more weight than when they ate a minimally processed diet, according to an NIH study.

IMAGE: ISTOCK

Heavily Processed Foods Cause Overeating, Weight Gain

People eating ultra-processed foods ate more calories and gained more weight than when they ate a minimally processed diet, according to results from an NIH study. The difference occurred even though meals provided to the volunteers in both the ultra-processed and minimally processed diets had the same number of calories and macronutrients. The results were published in *Cell Metabolism*.

This small-scale study of 20 adult volunteers, conducted by researchers at NIDDK, is the first randomized controlled trial examining the effects of ultra-processed foods as defined by the NOVA classification system. This system considers foods "ultra-processed" if they have ingredients predominantly found in industrial food manufacturing, such as hydrogenated oils, high-fructose corn syrup, flavoring agents and emulsifiers.

Previous observational studies looking at large groups of people had shown associations between diets high in processed foods and health problems. But, because none of the past studies randomly assigned people to eat specific foods and then measured the results, scientists could not say for sure whether the processed foods were a problem on their own, or whether people eating them had health problems for other reasons, such as a lack of access to fresh foods.

"Though we examined a small group, results from this tightly controlled experiment showed a clear and consistent difference between the two diets," said Dr. Kevin D. Hall, an NIDDK senior investigator and the study's lead author. "This is the first study to demonstrate causality—that ultra-processed foods cause people to eat too many calories and gain weight."

Emergency Treatment Guidelines Improve Survival of People with Severe Head Injury

A large study of more than 21,000 people finds that training emergency medical services (EMS) agencies to implement prehospital guidelines for traumatic brain injury (TBI) may help improve survival in patients with severe head trauma. The findings were published in *JAMA Surgery*. The study was supported by NINDS.

"This demonstrates the significance of conducting studies in real-world settings and brings a strong evidence base to the guidelines," said Dr. Patrick Bellgowan, program director at NINDS. "It suggests we can systematically increase the chances of saving the lives of thousands of people who suffer severe traumatic brain injuries."

Based on scores of observational studies, guidelines for prehospital management of TBI that were developed in 2000, and updated in 2007, focused on preventing low oxygen, low blood pressure and hyperventilation in people with head injury.

Collectively, the studies suggested that controlling those factors before patients arrived at the hospital could improve survival, but actual adherence to the guidelines had not been examined.

The Excellence in Prehospital Injury Care study, led by Dr. Daniel Spaite at the University of Arizona, trained EMS agencies across Arizona in the TBI guidelines and compared patient outcomes before and after the guideline implementation.

All patients in the study experienced head injury with loss of consciousness.

Daily Folic Acid Supplement May Reduce Risk of Gestational Diabetes

Taking a folic acid supplement daily before pregnancy may reduce the risk of gestational, or pregnancy-related, diabetes, according to a study by researchers at NIH and other institutions. The findings appear in *Diabetes Care*.

Folic acid is the synthetic form of folate, or vitamin B9, which is found in leafy green vegetables, nuts, peas, beans and other foods.

The U.S. Preventive Services Task Force recommends that all women of reproductive age take a daily supplement containing 400 to 800 micrograms of folic acid to reduce the risk of conceiving a child with a neural tube defect, a class of birth defects affecting the brain and spinal cord.

Gestational diabetes results when the level of blood sugar, or glucose, rises too high. It increases a woman's chances for cesarean delivery and for blood pressure disorders during pregnancy. It also raises the risk of cardiovascular disease and type 2 diabetes later in life.

In the current study, researchers analyzed data from nearly 15,000 women enrolled in the Nurses' Health Study II, a long-term study of diet, lifestyle factors and disease outcomes among female nurses.

Among more than 20,000 pregnancies, there were 824 cases of gestational diabetes.

Compared to women who did not take a folic acid supplement, those who took less than 400 micrograms were 22 percent less likely to develop gestational diabetes. Those who took 600 micrograms were 30 percent less likely to develop the condition.

"In addition to reducing the risk for neural tube defects, our findings suggest that taking folic acid supplements before pregnancy might provide a low-cost way to reduce the risk of gestational diabetes," said the study's senior author, Dr. Cuilin Zhang of NICHD.

A recently recognized brain disorder that mimics Alzheimer's disease has for the first time been defined with diagnostic criteria.

IMAGE: MAXIPHOTO/ISTOCK

Guides Proposed for Alzheimer's-Like LATE

A recently recognized brain disorder that mimics clinical features of Alzheimer's disease has for the first time been defined with recommended diagnostic criteria and other guidelines for advancing and catalyzing future research. Scientists from several NIH-funded institutions, in collaboration with international peers, described the newly named pathway to dementia, Limbic-predominant Age-related TDP-43 Encephalopathy, or LATE, in a report published in *Brain*.

"While we've certainly been making advances in Alzheimer's disease research—such as new biomarker and genetic discoveries—we are still at times asking, 'When is Alzheimer's disease not Alzheimer's disease in older adults?'" said NIA director Dr. Richard Hodes. "The guidance provided in this report, including the definition of LATE, is a crucial step toward increasing awareness and advancing research for both this disease and Alzheimer's as well."

Alzheimer's is the most common form of dementia, which is the loss of cognitive functions—thinking, remembering and reasoning—and everyday behavioral abilities. In the past, Alzheimer's and dementia were often considered to be the same. Now there is rising appreciation that a variety of diseases and disease processes contribute to dementia. Each of these diseases appear differently when a brain sample is examined at autopsy. However, it has been increasingly clear that in advanced age, a large number of people had symptoms of dementia without the telltale signs in their brain at autopsy.

NIH director Dr. Francis Collins speaks with Linda Katz, widow of Dr. Stephen I. Katz.

PHOTOS: CHIA-CHI CHARLIE CHANG

Former NIAMS Director Katz Remembered

BY GREG LAVINE

Music flowed from Masur Auditorium as more than 400 gathered on May 3 to celebrate the life of Dr. Stephen I. Katz, former director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Katz passed away unexpectedly in December 2018 at the age of 77 while serving as head of NIAMS. His career at NIH began as a researcher at the National Cancer Institute in 1974 before he became the second director of NIAMS in 1995.

The memorial event featured NIH director Dr. Francis Collins, two former NIH directors and several past and present institute leaders. Katz's three children also spoke at the event.

"Steve was many things, and one of them was a musician," Collins said shortly before picking up a guitar to join members of the Affordable Rock 'n' Roll Act band—which Katz had belonged to, as a guitarist—to perform the Beatles' *Eight Days A Week*. The song was one of several the Katz family recorded on a CD titled *Stray Katz*, in a studio session celebrating Katz's 75th birthday. Katz's daughter, Karen, joined the band on stage.

Collins spoke highly of Katz's dedication to mentoring and training to help the next generation of scientists. In recognition of these efforts, Collins said that NIH has created a new R01 program named for Katz.

"We want to encourage risk-taking we believe could be good for us," he said. These grants will target researchers just launching their independent careers who want to explore novel ideas they may not have been able to pursue while working in someone else's lab.

Dr. Robert H. Carter, acting director of NIAMS and longtime colleague of Katz, served as master of ceremonies for the event and shared how the institute pulled together to continue his legacy.

"Steve was the center of the NIAMS universe. The planets revolved around Steve," Carter said. "When he passed, the planets wobbled."

Dr. Elias Zerhouni, NIH director from 2002 to 2008, echoed that sentiment, noting that Katz's passing left an enormous void felt across NIH.

"The NIH forest has many trees, but not all are equal," Zerhouni said. "Steve was a special tree. The roots of his tree ran deep."

Dr. Lawrence Tabak, NIH principal deputy director, was one of several speakers who was recruited to NIH in large part because of Katz's salesmanship. When Tabak arrived at housing on the NIH campus, Katz was one of the first people at the front door, with a bottle of champagne and a loaf of challah bread.

Katz's love for the NIH family went well beyond house calls for new leaders. Mark Katz, Katz's oldest son, remembered that his brother, Ken, and sister, Karen, often found themselves in the presence of NIH employees thanks to their father's generosity.

"Thanksgiving Day would have seemed incomplete without the fellows of the derm branch," Mark said [Katz had been head of NCI's Dermatology Branch].

Collins is joined by past NIH directors Dr. Elias Zerhouni (l) and Dr. Harold Varmus.

While Katz's passion for the NIH community was a consistent theme that ran through the ceremony, Tabak also stressed that the NIAMS director's scientific efforts benefited individuals across the globe through improved medical care.

"There are mensches," Tabak said using a Yiddish term for a person of integrity and honor, "and there are mensch godol, a once-in-a-generation mensch." Godol is a Hebrew word for big.

Dr. Richard Hodes, director of the National Institute on Aging, noted that Katz was a team player who put NIH's goals ahead of his own.

"There was not a competitive bone in his body in the sense that all his competition was directed to common goals," Hodes said. "It was never Steve over anyone else."

Dr. Vivian Pinn, former director of NIH's Office of Research on Women's Health, was among the speakers who experienced Katz's influence. She remembered him for his mentorship and support of both her office and her career.

"Dr. Katz was enthusiastic about promoting women and minority researchers," she said.

Dr. Story Landis, former director of the National

Above, members of the Katz family take in the remembrances. At right, members of the Affordable Rock 'n' Roll Act Band include (from l) Dr. Robert Walker, Dr. John O'Shea, Dr. John Tisdale, Dr. Peter Grayson, Laura Chopp, Dr. Mike Pazin, Karen Katz and Collins.

Institute of Neurological Disorders and Stroke, remarked on how wise, kind and generous Katz was, echoing the sentiments of other speakers.

Karen Katz (c) sings as the ARRA Band plays behind her.

"Steve's door was always open and his interest was genuine," she said. "His advice was heartfelt and honest."

Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, said he recalled first meeting Katz in the halls of the Clinical Center when both were young researchers caring for patients. For complex dermatology-related questions, there was one researcher Fauci turned to for consultation.

"Steve was a consummate physician," he said, "encyclopedic in his knowledge, with an endearing bedside manner."

Dr. Heidi Kong, head of the NIAMS cutaneous microbiome and inflammation section, also benefited from Katz's deep knowledge of dermatology. She noted Katz's influence could be felt around the world, as many of those he mentored from the United States, Asia and Europe are now leaders with their own mentees. The event was broadcast live around the world online, giving his international colleagues and mentees the opportunity to watch.

"I would not be here today at the NIH, doing the research I love, if it had not been for the mentorship of Steve," Kong said.

Dr. Harold Varmus, NIH director from 1993 to 1999, recruited Katz to be NIAMS director. Whether tackling important NIH business or strumming a guitar, Katz was content to be in the background doing vital, if unglamorous, tasks, Varmus recalled.

"He worked for the benefit of institutions, and people affected by them, not for his own ends," he said.

In closing remarks, Carter noted the creation of the Katz Scholar as part of the dermatology training program, and the naming of a conference room in honor of Katz.

Collins and the band closed the event with a Hebrew song, *B'shana Haba-ah*. This was a Katz favorite and one that he taught to Collins. The NIH director noted that a few particular lyrics summed up the spirit of the event.

"Now the torch must be passed in hope and not in sorrow and a promise to make a new start."

A full video version of the event is available at https://videocast.nih.gov/launch.asp?27489.

VRC Needs Healthy Volunteers

Vaccine Research Center researchers seek healthy volunteers, 18-50 years old, for a study evaluating an investigational vaccine that targets HIV. Compensation is provided. There is no risk of infection. To learn how to participate, call 1-866-833-5433, email vaccines@nih.gov or visit http://bit.ly/VRC-018.

Problem Drinkers Needed for Study

If you or someone you know is drinking too much, NIH may be able to help. NIAAA conducts studies on how alcohol affects the body and is looking for new ways to treat alcohol problems. If you qualify, you can receive alcoholism treatment at no cost while you participate in research. Compensation may also be provided. To learn how to participate, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://go.usa.gov/xUx4C. Refer to study 14-AA-0181.

At Risk for Prostate Cancer?

NCI researchers seek men who have a genetic mutation that puts them at a high risk for prostate cancer to join their clinical trial. Eligible participants are 30- to 70-year-old men without prostate cancer and who have a documented gene mutation. Partner with NCI in research to help prevent and find better treatment options for prostate cancer. For more information, call 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010) or email PRPL@cc.nih.gov. Read more at https://go.usa.gov/xEHtD. Refer to study 19-C-0040.

Two Sites Offer Platelet Donation

The NIH Blood Bank and the NIH Donor Center at Fishers Lane need donors to help with a special type of blood donation called platelet donation. There is currently an acute need for platelet donors to support Clinical Center patients.

Two convenient locations are available for platelet donation:

• NIH Donor Center at Fishers Lane, 5625 Fishers Lane, Rockville, Monday-Friday, 7:15 a.m. to 5:45 p.m., Saturday, 7:30 a.m. to 1 p.m.

• NIH Blood Bank, department of transfusion medicine, 1st floor of the Clinical Center, Mondays, 2:30 to 5:30 p.m., Fridays, 7:30 a.m. to 1 p.m.

Call for an appointment at (301) 496-4321 or email nihplatelets@cc.nih.gov.

If you have not donated platelets before and are not sure whether you are eligible, visit https://www.cc.nih.gov/blooddonor/donationtypes/platelets.html to learn more about platelet donation.

Exterior view of the NIH Donor Center at Fishers Lane

Music Fills CRC Atrium This Spring

Top (l), Loudoun Youth Guitars—a group of talented and highly motivated guitar students from several middle and high schools in Loudoun County, Va.—perform mostly classical music. They give concerts throughout the metropolitan area. The NIH Philharmonia (top, r) is an all-volunteer organization including NIH staff, other federal workers and the surrounding community and provides classical music of all kinds. They perform several times a year at St. Elizabeth Catholic Church in Rockville. The orchestra presented movements from Beethoven's Ninth Symphony, including *Ode to Joy*. The Tacy Foundation Youth (r) supports medical facilities with mostly classical music concerts by children and teens from the metropolitan area.

Upcoming concerts include the University of Maryland Jazz Combo on June 6, the Tacy Foundation Youth on June 14 and the NSO Ensemble on July 9, all at 12:30 p.m. in the CRC atrium.

PHOTOS: DEBBIE ACCAME

NINR Launches 'Symptom Science Center,' June 27 in Masur Auditorium

The National Institute of Nursing Research Division of Intramural Research will host a scientific symposium to mark the launch of the NINR-led Symptom Science Center, a trans-NIH resource for the scientific community. "Symptom Science Center: A Resource for Precision Health" will be held Thursday, June 27 from 8 a.m. to 4 p.m. in Masur Auditorium, Bldg. 10.

The symposium will feature a keynote address from NIH deputy director for intramural research Dr. Michael Gottesman as well as an introduction to the Symptom Science Center and scientific panels on cancer-related symptoms, patient-reported outcomes and symptom science at the Clinical Center and symptom clusters in concussions. There will also be a poster session to highlight the innovative research conducted by NIH intramural researchers and trainees.

The event will also be broadcast live and archived at https://videocast.nih.gov. For details and to register, visit https://www.ninr.nih.gov/sscevent.

Webinar on Mobile Health Interventions, June 4

The Office of Disease Prevention will hold a Methods: Mind the Gap webinar with Dr. Eric B. Hekler on "Using Control Systems Engineering to Optimize Adaptive Mobile Health Interventions." It will take place on Tuesday, June 4 at 1 p.m.

Dr. Eric B. Hekler

Hekler will review the need for optimization of adaptive interventions. He is an associate professor in the department of family medicine and public health at the University of California, San Diego. He is also director of the Center for Wireless and Population Health Systems and faculty member of the Design Lab at UCSD.

Registration is available at https://prevention.nih.gov/education-training/methods-mind-gap/using-control-systems-engineering-optimize-adaptive-mobile-health-interventions. The webinar will be recorded and available on the ODP website within about a week.

'Big Read' Author Event, June 7

Author and science journalist Helen Thomson visits NIH to discuss her book *Unthinkable: An Extraordinary Journey Through the World's Strangest Brains* with NIH director Dr. Francis Collins in an informal conversation on Friday, June 7, 1-2 p.m. The event will be held in Masur Auditorium, Bldg. 10 and be broadcast via live videocast. Registration is not required to attend. Afterward, FAES is hosting a meet and greet and reception with the author on the FAES Terrace, 2-3 p.m.

Helen Thomson

The June 7 discussion will be presented in an interview format, with Thomson and Collins talking about the nine cases of extraordinary people with rare neurological disorders featured in the book. By examining these stories, interwoven with discussions on how the brain works, they will explore the complexities and possibilities of all our brains.

The Big Read is presented by the NIH Library and the Foundation for Advanced Education in the Sciences. For questions about the event, email kathleen.mcglaughlin@nih.gov.