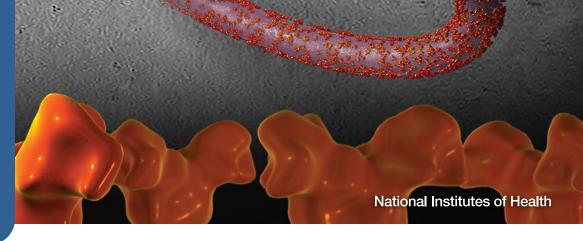


June 29, 2018 Vol. LXX, No. 13



BETTER SUITED FOR BOATS

Bike Day 2018 Celebrates Sans Sun

BY CARLA GARNETT

Not even gray skies and steady showers could dim the devotion or slow the wheels of NIH cyclists on Bike to Work Day 2018. Leading off the celebration at a little after 8 a.m. on May 18 was staunch BTWD supporter and NIH pedaler-in-chief himself.

"I look forward to this event every year," said NIH director Dr. Francis Collins, who estimated 2018 was his 8th or 9th time cycling onto campus for the event. "I always like to mix and mingle with those who are brave enough to get on bikes every day regardless of the weather."

May is National Bike Month. In 1956, the League of American Bicyclists began Bike to Work Day to promote 2-wheeled commuting and reduce traffic and pollution. In the DMV region, the Metropolitan Washington Council of Governments (COG) convenes a committee each year consisting of representatives from Commuter Connections. a transportation organization, and the Washington Area Bicyclist Association to plan the event.

Collins said he had a special reason for participating this year.

"We want to recognize Peter Chines, who was a big part of Bike to Work Day and the NIH bicycle community over the past 20 years," Collins said. "He was a big advocate for the [NIH] Bicycle Commuting Club and he ran the Bike Bucks Program for many years. He also was part of my lab. We lost Peter last summer and we wanted to

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Breast Cancer Treatments Tailored to Individuals

BY ERIC BOCK

Advances in precision medicine are informing oncologists how best to treat patients



with early-stage breast cancer, said Dr. Nancy Davidson at a recent Contemporary Clinical Medicine: **Great Teachers Grand Rounds** lecture in Lipsett Amphitheater.

The approach involves

tailoring therapy to the characteristics of the patient and his or her tumor cells, said Davidson, president of the Seattle Cancer

SEE BREAST CANCER, PAGE 4

ANCIENT BLOODSUCKERS

Biologist Gathers Genetic Clues from Sea Lampreys

BY DANA TALESNIK

Fishermen in the Great Lakes probably wish there were more researchers like Dr. Jeramiah Smith, who studies sea lampreys. These slimy, parasitic little suckers feed on adult fish, wreaking havoc on the lake



Dr. Jeramiah Smith

trout population and often evading control efforts. In some parts of the world, they're a delicacy: elsewhere, a predatory pest. Lampreys also happen to be fascinating fish that offer insights into evolutionary

SEE LAMPREYS. PAGE 8

11th NIH Graduate & Professional School Fair

July 18

The 2018 NIH Graduate & Professional School Fair will be held on Wednesday, July 18 from 8:45 a.m. to 3:30 p.m. at Natcher Conference Center. The fair provides an opportunity for NIH summer interns (especially those in college) and postbacs, as well as other college students in the D.C. area, to prepare for the next step in their careers by exploring educational programs leading to the Ph.D., M.D., D.D.S., M.D./Ph.D. and other graduate and professional degrees. More than 200 colleges and universities from across the U.S. are sending representatives of their graduate schools, medical and dental schools, schools of public health and other biomedically relevant programs in hopes of recruiting NIH trainees.

The day will also include workshops on getting to graduate and professional school; M.D./Ph.D. programs; interviewing; and careers in public health, computational biology/bioinformatics, psychology and dentistry. Exhibits will be open from 9:45 a.m. to 2:15 p.m.

A list of institutions planning to attend and registration information can be found at https://www.training.nih.gov/gp_fair.

Taljaard Speaks in Disease Prevention Series

July 11

The Office of Disease Prevention will hold a Mind the Gap webinar with Dr. Monica Taljaard about stepped wedge cluster randomized design. It takes place at 11 a.m. on July 11.



The presentation will explain the unique characteristics of the stepped wedge cluster randomized design and its implications for sample size calculation and analysis and discuss its strengths and weaknesses compared to traditional designs.

Taljaard is a senior scientist in the clinical epidemiology program at the

Ottawa Hospital Research Institute and associate professor in the School of Epidemiology and Public Health at the University of Ottawa. She has a Ph.D. in epidemiology and biostatistics from Western University and her main research interests are in the design, analysis and ethics of cluster randomized trials.

She will accept questions during the webinar via WebEx and Twitter. Use the hashtag #NIHMtG.

To register visit https://nih.webex.com/nih/onstage/g.php?MTID=ea32481d1330dfa1395a42633f2603441.



Fogarty's Glass Receives Carter Humanitarian Award

The 2018 Jimmy and Rosalynn Carter Humanitarian Award was presented to Fogarty International Center director Dr. Roger Glass (c) by the National Foundation for Infectious Diseases (NFID) on May 10. Glass was recognized for his "lasting contributions to improving children's health worldwide, including novel scientific research for the prevention of gastroenteritis from rotaviruses and noroviruses." Also shown are NFID president Dr. Walter Orenstein (I) with Dr. Mathuram Santosham of Johns Hopkins University, who nominated Glass for the award.





NIDA honorees Dr. Ivan Montoya and Dr. Kenzie Preston

NIDA Staff Receive Awards from CPDD

NIDA Division of Therapeutics and Medical Consequences acting director Dr. Ivan Montoya has received the J. Michael Morrison Award from the College on Problems of Drug Dependence (CPDD), the oldest and largest organization in the world dedicated to advancing a scientific approach to substance use and addiction disorders.

The award is given every other year for outstanding contributions in the area of scientific administration related to substance use and addiction disorders research. The award is named after J. Michael Morrison, a well-liked and respected pharmacologist and research official at NIDA.

CPDD also honored Dr. Kenzie Preston, senior investigator and chief of NIDA's Clinical Pharmacology and Therapeutics Research Branch, with the Marian W. Fischman Lectureship Award. It

was established in 2001 to recognize the contributions of an outstanding woman scientist in drug abuse research and named in memory of Fischman, a respected leader in drug abuse research and an outstanding scientist.

Montoya and Preston were recognized at the CPDD annual meeting on June 10 in San Diego.

Interested in Learning How to Sail?

The NIH Sailing Association (NIHSA), an R&W-supported club, offers a Sailing Basic Training course for NIH employees, contractors, fellows, patients and NOAA employees. The summer course will be offered from July 10 to Sept. 21. For details, visit www.nihsail.org/training/.

The in-class sessions are held on campus; the onboard sessions are held at Selby Bay on the South River near Edgewater, Md. Participants must be able to provide or arrange for their own



transportation to both the in-class and onboard sessions.

If you are interested in the course and would like more information, email nihsabasictraining1@gmail.

com. If you are an experienced sailor and would like to charter NIHSA boats, contact us about joining the club and doing a check-out sail.

NIHSA is always looking for experienced volunteers to help with both in-class and onboard instruction.

CELI: OER Program Aims to Hone Extramural Leadership Skills

BY MANJU SUBRAMANYA

Imagine you are the chief of an integrated review group at CSR, anticipating a boatload of applications for review for a new high-profile NIH initiative and you don't have enough scientific review officers and support staff to handle the onslaught.

As a leader, what would you do under those circumstances?

During last year's Cement Extramural Leadership Institute (CELI) training



program, that is exactly the real-life scenario that one group of participants huddled together to brainstorm. Group members investigated the issue. conducted interviews with key staff and developed strategic recommendations. Their proposal was then reviewed

and critiqued by a panel of NIH leaders to determine if it was likely to be effective.

The group's recommendations to accommodate the rising workload for SROs, given limited hiring? Creative use of staffing resources by calling on recent retirees, detailees, fellows and contractors to pitch in; redistributing some SRO responsibilities to extramural support assistants (ESAs) and in turn handing off some ESA tasks to NIH Pathway Program fellows; increasing and standardizing the number of chartered reviewers on IRGs; increasing use of virtual meetings to decrease time commitment by reviewers, and more.

CELI is designed to expand the leadership and decision-making skills of NIH extramural staff. Piloted in 2017, it is coordinated



through the Office of Extramural Research in the Office of the Director. CELI brought in instructors from The Evaluators' Institute, the University of Maryland and American University to share best and next practices in leadership, business and management. The program also featured discussions by distinguished faculty such as NIH deputy director for management Dr. Alfred Johnson and DPCPSI director Dr. Jim Anderson.

"The goals of the program are to glean knowledge, break down silos, share information across ICs and equip leaders with new strategies and techniques for decision-making," said Rosalina Bray, extramural staff training officer who coordinates the CELI program and other training activities conducted by OER.

The pilot was well-received. "This program has enabled me to build better teams within my department, adjust my thinking to anticipate obstacles and plan strategically for impact," wrote a member of the CELI 2017 cohort.

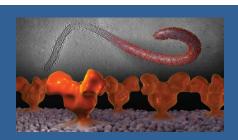
Self-nomination applications are now being accepted for the 2018 CELI program and should be submitted by Friday, July 27. The competitive program is open to NIH GS-13, 14, 15 or Title 42 extramural federal employees, free of charge. The program itself runs from October to December.

The CELI program meets twice a month for 3 months, with participants essentially spending 6 days in session. In addition, participants are expected to review course materials, engage with fellow members online or offline and complete a group assignment.

Bray hopes the CELI program will expand to engage CELI alumni and offer online leadership courses.

"There is an extraordinary need for

advanced leadership opportunities for extramural staff," she said. "We are dedicated to designing high-impact programs to strengthen the competencies and skills of our talented extramural staff and improve the business needs of NIH."



ON THE COVER: Ebola in 3-D. Cryo-electron tomographic image of a virus-like particle displaying Ebola virus surface spikes (top) and visualization of their three-dimensional structure (bottom)

IMAGE: VERONICA FALCONIERI & SRIRAM SUBRAMANIAM, NCI

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Breast Cancer

CONTINUED FROM PAGE 1

Care Alliance, senior vice president of Fred Hutchinson Cancer Research Center and professor of medicine at the University of Washington.

"The incidence of breast cancer is considerably higher in African-American and white women than it is in Hispanics and Pacific Islanders in this country," she said.

There has been a decrease in mortality from breast cancer thanks to early diagnoses and advances in treatment including surgery, radiation and systemic therapies, she noted.

"The disease is largely one—although not exclusively—of older women," Davidson explained. "The mortality from breast cancer goes up over time and is highest in older women."

Traditionally, she said, health care professionals have determined the stage of breast cancer by measuring the size of a tumor, how many lymph nodes are involved and whether or not the cancer has spread to other parts of the body.

Starting this year, doctors began factoring biological markers into the staging system for breast cancer. When a patient first presents symptoms, an oncologist will look at results from a physical exam, any breast images and the results of biopsies and the tumor itself "including the grade and the expression of important proteins." Final staging will be completed after definitive surgery, at which time all the pathological information will be available.

There are several molecular subtypes of breast cancer, Davidson said. One of the most common types across all ethnicities is luminal breast cancer. There are two subtypes: A and B.

Luminal A cancers are usually estrogen receptor-positive, meaning they need the hormone estrogen to grow. Additionally, they are usually HER2 receptor-negative, meaning the HER2 protein involved in cell growth isn't found on the surface of the cancer cell. Luminal B cancers are also estrogen receptor-positive but they may be HER2 receptor-negative or positive.

Detailed information about the type of cancer helps oncologists choose the best therapy for an individual. A patient with early-stage estrogen receptor-positive breast cancer, for example, would be advised to * * *

"The incidence of breast cancer is considerably higher in African-American and white women than it is in Hispanics and Pacific Islanders in this country."

~DR. NANCY DAVIDSON

 \star \star \star

begin what is known as endocrine therapy. The treatment slows or stops the growth of tumors by blocking a woman's ability to produce estrogen or destroying the estrogen receptor or blocking the ability of estrogen to interact with its receptor. In some cases, patients will also receive chemotherapy.

Unfortunately, some patients don't tolerate endocrine therapy. Hot flashes and other symptoms of menopause and other side effects such as a slight increased risk for uterine cancer or thinning of the bone may be factors, depending on the type of endocrine therapy that is used.

"These side effects are important because we are asking our patients to stay on these therapies for long periods of time," Davidson said.

In one study of roughly 9,000 patients with breast cancer, results showed stopping the adjuvant endocrine therapy early or not taking scheduled doses was associated with increased mortality.

"The bottom line was for women who

were less than 60 percent adherent; they had almost a 4-fold greater chance of dying as a consequence of breast cancer," Davidson reported.

If a patient has HER2 proteins on the surface of a tumor, a physician would recommend both chemotherapy and one or more monoclonal antibodies against HER2 that block the function of the protein. There are five FDA-approved anti-HER2 therapies. In rare instances, some of these can be toxic to the heart.

Scientists are also studying bone-targeted treatments as a form of adjuvant therapy in older patients with breast cancer because bones are a common site of breast cancer recurrence.

Newer drug and lifestyle approaches to prevention of breast cancer recurrence are also under study.

Precision medicine will continue to drive much of the work on breast cancer that will ultimately improve patients' lives, Davidson concluded.



"The mortality from breast cancer goes up over time and is highest in older women," said Davidson.

PHOTOS: LESLIE KOSSOFF



Members of last year's Children's Inn's charity Marine Corps Marathon and 10K teams hold up signs with the reasons they joined Team #RunINN4Kids. The inn's charity teams still have openings for runners of all skills and abilities to participate in this year's marathon or 10K.

Runners Can Support Kids at Children's Inn at NIH

The Children's Inn at NIH's Marine Corps charity Team #RunINN4Kids has race slots available for runners of all abilities who want to run the marathon or 10K to benefit NIH pediatric trial participants.

Members of Team #RunINN4Kids benefit from weekly training tips provided by a professional coach, the chance to train with dedicated team members and support children staying at the inn while they are participating in protocols at the Clinical Center. Team members also receive innthemed running gear and are invited to a catered pasta party at the inn the weekend before the race.

"Our team is open to anyone who wants to participate in this great race while supporting pediatric NIH patients staying at the Children's Inn," said Julie Ofrecio, the inn's corporate partnerships and events manager. "We have NIH patients, parents, volunteers and friends of the inn participating on our team and we'd love to have our friends from the NIH join as well!"

Team #RunINN4Kids has race slots for up to 80 runners. Registration deadline is Aug. 17.

Funds raised by the team help provide free lodging and supportive services for children with rare or serious illnesses.

To learn more about the team or sign up, visit https://childrensinn.org/news-and-events/runinn4kids/.

DIFFERENT MINDS

Grandin Inspires in NIEHS Spirit Lecture

Dr. Temple Grandin brought her message about "Developing Individuals Who Have Different Kinds of Minds" to NIEHS recently. The professor of animal sciences at Colorado State University delivered an enlightening 2018 NIEHS Spirit Lecture to a packed auditorium. Grandin has published numerous scientific articles and books on animal behavior and her designs for humane handling of livestock are widely used today. She is also a well-known author and speaker about autism, which she discusses with the authority of a person with autism.

Grandin said she sees the world differently than typical adults. "Everything I think about is a



Temple Grandin credits her mother as her first mentor because she pushed her to get out, do things and work hard. "By the time I graduated high school, I knew how to work," Grandin said.

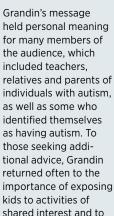
picture," she said. For visual thinkers like her, Grandin emphasized the importance of schools offering classes that foster creativity and teach skilled trades such as art, sewing, woodworking and auto shop. Creative geniuses such as Thomas Edison, Jane Goodall and Albert Einstein would likely have been labeled as autistic today, she suggested. Many of them had unconventional educations and she questioned whether they would have been as successful in today's educational system.

"Too many kids are getting labeled, and I'm worried they are getting screened out," Grandin cautioned. For those who think differently, she believes that early exposure to work experiences is important to success in life. "I was a lousy student in high school, and I wasn't fond of studying until studying became the path to my goal of becoming a scientist," she said.

In her research, visual thinking allows Grandin to better understand animal behavior. For example, she noticed details—such as dangling chains or shadows—that could spook animals. "Animal minds are specific because they are sensory-based and not word-based," she said, explaining how these observations became part of her designs for livestock handling equipment and an animal welfare scoring

system. "Observation is a very important part of science," she reminded the audience. Visual thinkers see details others may overlook. Individuals with autism may be either visual, pattern, verbal

or auditory thinkers or a combination. Scientific advances require different minds working together, she stressed.





Maggie Humble (I), a biologist in the NIEHS mitochondrial DNA replication group, chats with Grandin after waiting in line to get her book signed.

PHOTOS: STEVE MCCAW

work experiences. "We've got to get these kids out doing something," she said, suggesting walking neighbors' dogs on a set schedule, volunteering at church and other tasks appropriate to age and ability levels.

A video of her NIEHS presentation is available at https://youtu.be/JUr9W4I6Y38.-Katie Glenn





At left, cyclists collect their T-shirts and other event items. Nate Marchiano (r), whose commute is 13 miles round trip from Four Corners (Silver Spring), bikes to work at the Clinical Center's transfusion services lab about two times weekly. At right, 2018 Carl Henn Award winner Dr. Vernon Anderson (l) accepts the trophy for years of cycling advocacy as BTWD enthusiasts (from l) Collins, Joe Cox, chief of ORS transportation services, and NLM's Dr. Valerie Virta, BTWD coorganizer, look on.

PHOTOS: MARLEEN VAN DEN NESTE, GERALD JORDAN

Bikes

CONTINUED FROM PAGE 1

do something to honor his memory. We all miss him every day, not only for the amazing contributions he made to the lab and the research we're working on in genetics and genomics, but also for the amazing person he was."

The NIH director cycled about 4 miles from his house to campus with wife Diane Baker, a perennial BTWD enthusiast, and sister-in-law Debra Boterf, who was visiting from Sarasota, Fla. Collins said it was Chines who encouraged him—and taught him the best route—to bike to work.

With many of his lab members clustered under tents in the inclement weather, Collins announced that a memorial plaque honoring Chines will be installed near the bike enclosure at Bldg. 49. The citation recognizes him "for his contributions to bicycle commuting, his impact on genetics, genomics and bioinformatics research and his friendliness to all."

Dr. Valerie Virta, one of BTWD's organizers, presented the seventh annual Carl Henn Bicycle Advocacy Award to 2018



Peter Gracyalny (I) of Silver Cycles performs a little on-site maintenance at Bike to Work Day.

winner NIGMS program director Dr. Vernon Anderson, a past president of NIHBCC and longtime cycling proponent.

A scientific editor in NLM's National Center for Biotechnology Information who's been helping at Bike Day several years herself, Virta said Anderson "has continued the legacy of Carl Henn values for more than 5 years...Under his leadership, NIH has continued to lead the national capital region as the employer with the most BTWD participants."

Anderson also organized numerous other bike events including Car-Free Day and seminars promoting the personal and environmental benefits of cycling, Virta continued.

"No one gets into this business looking for fame and fortune-and this is what constitutes fame and fortune," Anderson quipped with a grin as he accepted the bike statuette. "In the 9 years I've been on campus, the number of bicycle riders and people participating in Bike to Work Day-thanks to Peter and many other volunteers—has grown. There are these occasional breaks in the weather like today that cause the attendance to diminish somewhat, but in fact there are hundreds of people who will still come and ride in all weather...Your continued efforts and your dedication to ride in weather like this is what makes this happen. Thanks to all of you."

About 100 pit stops in the region are listed at the event's website; cyclists register at one of the stations to qualify for a free T-shirt on event day. The stations also provide fruit, bagels and other breakfast-on-the-go items as well as coffee and other beverages. In years past, NIH has owned the COG award for employer with most BTWD participants.

According to Virta, 203 people checked

in at NIH's station this year. Distance-wise, the longest commute to campus is 40 miles round-trip, she noted. The person who has been commuting by bicycle for the longest is Donald White—for 58 years. Top five institutes participating this year were NCI, NIAID, NLM, OD and NIDDK.

At the Bldg. 1 pit stop, you could register your vehicle with the NIH Police or get a bike maintenance check by a local cycle shop. Generally the weather is kind this time of year; the last time the event was drenched was in 2014.



Cycle Day Recycled, Via Video

Since 2010, much of the action on Bike to Work Day has been captured on video camera by Jules Asher (shown above) of NIMH. 2018 was no different. If you opted to stay dry this year but feel you missed out—never fear. Watch all of Asher's BikeToWorkDay@NIH2018 videos:

NIH director Dr. Francis Collins and Henn Award (speeches) https://youtu.be/ KSQ-FHUplyg

Why We Ride (interviews) https://youtu. be/m_QAwW1o5t4

Pit Stop (music video of Bldg. 1 action) https://youtu.be/1FZcDIKesHw

And finally, **Asher's own ride** https://youtu.be/ NcGa8QA1Hb0.







INSPIRING NEXT-GENERATION RESEARCHERS

in an activity alongside NLM Deputy Director Jerry Sheehan.

5th Science Day at NIH Invokes Energy, Passion

BY REBECCA NEWTON

Now in its fifth year, "Science Day at NIH" highlighted an unexpected and recurring theme for the day: passion. Nearly 500 students from 11 area schools recently attended the event at the Natcher Bldg., where they were engrossed in an assortment of science and health care activities and career options.

Co-sponsored by the National Institute on Minority Health and Health Disparities, the National Library of Medicine, Friends of the NLM and Mentoring in Medicine, Science Day seeks to promote diversity in the biomedical workforce. The overarching goal is to inspire students to explore careers in health care and science. The young people—many of them African American or Latino—participated in hands-on activities and presentations about biomedical research career options from a diverse group of scientists and other NIH staff.

After an amusing pep rally, students were welcomed by NLM director Dr. Patty Brennan (via video), NLM Deputy Director Jerry Sheehan, NIMHD director Dr. Eliseo Pérez-Stable and NIH chief officer for scientific workforce diversity Dr. Hannah Valantine.

"You have to have passion for what you do...If you

dislike what you're doing, you will not do a good job," said Pérez-Stable, delighting the audience with a colorful journey through his medical and scientific career.

Panelists Dr. Kelvin Choi of NIMHD, Dr. Nakela Cook of the National Heart, Lung and Blood Institute, Dr. Jeff Day of NLM and Dr. Carla Easter of the National Human Genome Research Institute presented an overview of their respective NIH roles and how passion drove them. Easter also revealed her other passion: Zumba. She even entertained students with a dance move.

During the afternoon, students took in "Lunch with a Scientist," where energetic staff of various careers—librarian, researcher, legislative liaison, information specialist, chemist, program officer, educator, digital asset developer, program director and psychologist—shared their roles at NIH.

Hosted by various institutes and centers, nearly 20 activity tables showed students such presentations as medical illustration, closing a wound, organ party, CPR, radiation safety, headache games and a Cool Spot carnival, among other attractions.

At the event's conclusion, students were able to share what they learned and ask questions. Some expressed their desire to return next year and appreciated the staff for fueling their passion, preparing them to choose a career and providing an overall great day of learning at NIH.

Wentzensen Receives ASCCP Award

Dr. Nicolas Wentzensen, senior investigator and deputy chief, Clinical Genetics Branch, NCI, recently received the Distinguished Scientific Award from the ASCCP (formerly known as the American Society for Colposcopy and Cervical Pathology, now the Society of Lower



Genital Tract Disorders). He received the society's highest honor for his role in leading the Colposcopy Standards project. Colposcopy is a cervical cancer prevention technique in which the cervix is inspected for signs of cancer or precancer. The project is expected to have immediate and lasting benefits for the millions of women in the United States and around the world who undergo cervical cancer screening.

Healthy Volunteers Needed

NIAID researchers seek healthy volunteers, 18-60 years old, for a study at the Clinical Center to examine safety and tolerability of an investigational product targeting Ebola. You cannot get Ebola from this product. Financial compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://clinicaltrials.gov/ct2/show/NCT03478891.

NIMH Conference Explores Mental Health Services Research

In August, the National Institute of Mental Health is hosting the 24th Mental Health Services Research (MHSR) Conference with the theme: What's the Next Big Thing? MHSR is organized every other year by NIMH's Services Research and Clinical Epidemiology Branch. It aims to promote high-priority areas in mental health services research and identify opportunities with potential for significant impact for people with mental disorders.

MHSR is the nation's premier mental health services research conference. It brings together leading researchers, clinicians, advocates and federal and non-federal partners. This year, MHSR will feature state-of-the-art research presented via keynote speakers, thematic panels, discussion groups, papers and posters.

"MHSR is an opportunity to collaborate and network with peers, learn from experts and discuss the latest research in mental health services—research that is crucial to closing the science-to-service delivery gap," said Dr. Michael Freed, one of the conference co-chairs. "This



year's conference will focus on what is driving today's research and how the latest findings can help make a positive impact on the health and well-being of people with mental disorders."

Services research aims to improve access, continuity, quality, equity and value of mental health care and it includes the science of dissemination and implementation—a mission crucial to closing the science-to-service delivery gap.

There is no fee to register, but registration is required. For details or to register, visit www. cvent.com/events/24th-nimh-conference-on-mental-health-services-research-mhsr-/event-summary-cee7c0d7f4e24463acb0568f7d907e63. aspx. Follow MHSR 2018 on Twitter, #MHSR2018.

Lampreys

CONTINUED FROM PAGE 1

biology, tissue regeneration and maybe even cancer.

Smith, associate professor of biology at the University of Kentucky, has loved going fishing since his childhood days. Growing up in eastern Wyoming and the Black Hills of South Dakota, he spent much of his time outdoors in an area with a rich geological past. Fascinated by the abundance of fossils native to the area, he often dreamt of becoming a paleontologist. These interests in the deep history of life ultimately led Smith to study lampreys, considered living fossils that diverged from the vertebrate lineage 600 million years ago.

"They're important in terms of understanding the evolution of basically everything that makes us vertebrates," said Smith at the NIGMS Director's Early-Career Investigative Lecture recently in Natcher Conference Center. The lecture, part of a series designed to inspire undergrads to pursue careers in biomedical research, was followed by a Q&A chat with NIGMS director Dr. Jon Lorsch.

"Because lampreys share the deep ancestry of the rest of other vertebrates," Smith said, "we can reconstruct changes that have, over time, given rise to our own development."

The species has changed little in its outward appearance over the last 340 million years, yet lampreys have unusual traits that continue to intrigue scientists. For example, the lamprey's mouth opens to form a large, sucking disk with razor-sharp teeth. It has no jawbone and its skeleton is mostly cartilage. But it does have a spinal cord



Smith interacts with students following his talk.

NIGMS director Dr. Jon Lorsch (I) and ECI speaker Dr. Jeramiah Smith (r) engages with members of Morgan State University's Student Research Center who attended the lecture.

PHOTOS: CHIA-CHI CHARLIE CHANG

that, if severed, can regenerate itself within several months.

"Lampreys have genes that are homologous to genes we have in our own genome," said Smith. Some of the lamprey's cellular processes, however, such as those that contribute to spinal cord regeneration, may have been lost at some point during the evolution of most vertebrates.

The lamprey also is one of few vertebrate genomes that toss out unwanted genes. By undergoing programmed genome rearrangement (PGR), the lamprey discards 20 percent of its DNA while still an embryo.

This begs the question, quipped Smith, "How does the lamprey manage to re-engineer its genome when it's not a scientist?"

He showed a slide of two balls of cells in a petri dish that thrived and developed into his now 6-year-old twin sons.

"Each one of these cells has the same genome," said Smith. "Each of the cells [in one of the embryos] has exactly the same material as every cell in Jack's body. The amazing thing is: the cells that make [Jack's] hair and his skin and his liver, and the cells that will make my grandchildren, all look very different from one another despite the fact that they share the same genome." That's because these identical cells can turn genes on or off.

Most vertebrates turn off or silence genes chemically but, Smith said,

lampreys shut cells off by disposing of them. What's more, the lamprey has two distinct genomes.

When Smith's lab first sequenced the lamprey genome, they found that many genes, normally present in germline cells (eggs and sperm), were absent from its blood. They continued finding genetic sequences that only existed in the lamprey's

"Because lampreys share the deep ancestry of the rest of other vertebrates, we can reconstruct changes that have, over time, given rise to our own development."

~DR. JERAMIAH SMITH

. . .

reproductive cells but not in any other tissue. There was a second, smaller genome found in all other cells of its body. Studies have used the genome to identify genes that enable lampreys to regrow severed spinal cords. Humans also have these genes, but use them differently.

"What we think we're learning from lampreys is that they delete these genes to regulate their function," said Smith. "These genes are kept in the germline genome over evolutionary time—so they must be important for reproduction at some level—but they're not allowed to be in most of the cell types, so perhaps they're dangerous and that's the way the lamprey regulates these genes."

It's known that turning on certain silenced genes can contribute to development of





ECI speaker Smith (I) and Lorsch chat informally at the event.

cancer. Studies are ongoing to determine whether the lamprey disposes of certain genes to protect itself from this disease.

In one experiment, DNA should have been migrating with the rest of the genome during normal cell division, but instead lagged behind and formed structures that are not typically seen in healthy cells. Thanks to 3-D imaging, Smith's lab could see that, during PGR, as the lamprey shed genes over several cell divisions, in the 7th division there was abnormal material characteristic of aggressive cancer cell types.

"Over evolutionary time, lampreys have done more experiments than us and maybe know a little more about the genes that contribute to the development of cancer," said Smith.

Sequencing lamprey genomes is tough in part because there's repetition in many places, said Smith. Using Cas-9 gene editing, his lab can knock out specific genes to learn more about their role in the lamprey's DNA elimination process and other notable characteristics.

"If an experiment doesn't go as expected, don't get discouraged," Smith told a college student asking for career advice. "See what else it's telling you. In many ways, we move forward from seeing the unexpected."

The student was among 20 undergraduates from Morgan State University in Baltimore who attended as part of the NIGMS-sponsored ASCEND Center for Biomedical Research. The program promotes diversity and entrepreneurship among young scholars.

Smith concluded, "I hope I've given you some sense of the importance of funding basic research that's not necessarily disease focused, but which helps us understand general principles that underlie disease."

NIAMS Labs Welcome Congressional Staff

BY COLLEEN DUNDAS

"Having the opportunity to tour the NIAMS labs, visit where patients are cared for and hear about cutting-edge research from leading investigators was a memorable experience," said Anna Hyde, NIAMS Coalition co-chair and vice president of advocacy and access at the Arthritis Foundation.

Hyde recently joined Capitol Hill staffers to tour the Clinical Center, see inside NIAMS labs and hear from researchers as part of NIAMS

Congressional Tour Day. The biennial event is sponsored by the NIAMS Coalition, an independent consortium of approximately 90 professional and voluntary organizations whose goal is to raise awareness about the institute's research.

NIAMS deputy director Dr.
Robert Carter opened the
morning event by providing an
overview of the NIH and NIAMS
mission and history of research
into the causes, treatment
and prevention of arthritis and
musculoskeletal and skin diseases. NIAMS scientific director
Dr. John O'Shea emphasized
NIAMS's current efforts to
engage and support the next
generation of scientists.

Dr. Timothy Bhattacharyya, head of orthopaedics research in the Clinical Trials and Outcomes Branch, discussed a 5-year multidisciplinary investigation into the cause of the "candle-wax bone" disease—melorheostosis—and how the group identified a genetic cause for the disorder.

Participants next visited a patient exam room in the outpatient clinic. Dr. Heidi Kong, head of the cutaneous microbiome and inflammation section of the NIAMS Dermatology Branch, illustrated how the institute's microbiome studies on healthy volunteers and patients with atopic dermatitis are helping to unravel the complex relationship between microbes and skin disease.

Dr. Mariana Kaplan, chief of the Systemic Autoimmunity Branch, explained how her team's research is revealing clues into the causes of lupus and associated heart attack risk and how a type of immune cell, neutrophils, may contribute to the onset and severity of lupus.

Finally, Dr. Andrew Mammen, head of the muscle disease unit in the Laboratory of Muscle Stem Cells and Gene Regulation, shared a 13-year-old



Dr. Heidi Kong (r) explains, as her research nurse performs a mock procedure, how skin microbiome samples are collected from patients. NIAMS Coalition co-chair Stephanie Hazlett (seated) volunteered for the demonstration.

patient's self-made video story of hope and healing after a life-altering diagnosis. Through this success story, Mammen underscored the importance of continued studies for children with genetic nerve and muscle disorders.

The event offered opportunities for visitors to interact personally with NIAMS researchers and staff. Such small group chats led to discussions on the past, present and future impact of NIH research.



NIAMS deputy director Dr. Robert Carter (seated, second from r) and scientific director Dr. John O'Shea (seated, third from I) with congressional staff, coalition members and NIAMS staff at the recent Tour Day.



Researchers have linked sensitivity to an allergen in red meat to the buildup of plaque in the arteries.

IMAGE: RIBEIROROCHA/THINKSTOCK

Researchers Find Link Between Allergen in Red Meat, Heart Disease

A team of researchers says it has linked sensitivity to an allergen in red meat to the buildup of plaque in the arteries of the heart. While high saturated fat levels in red meat have long been known to contribute to heart disease for people in general, the new finding suggests that a subgroup of the population may be at heightened risk for a different reason—a food allergen.

The study, which is supported by NHLBI, appears in *Arteriosclerosis*, *Thrombosis*, *and Vascular Biology*, a peer-reviewed journal of the American Heart Association.

"This novel finding from a small group of subjects from Virginia raises the intriguing possibility that allergy to red meat may be an under-recognized factor in heart disease," said study leader Dr. Coleen McNamara, a professor of medicine in the Cardiovascular Research Center of the University of Virginia Health System, Charlottesville. "These preliminary findings underscore the need for further clinical studies in larger populations from diverse geographic regions and additional laboratory work."

The number of people with red meat allergies in the United States is unclear, but researchers estimate that it may be 1 percent of the population in some areas. The number of people who develop blood antibodies to the red meat allergen without having full-blown symptoms is much higher—as much as 20 percent of the population in some areas, the researchers say.

High Thyroid Hormone Level in Early Pregnancy Linked to Gestational Diabetes

Women in early pregnancy who have high levels of a certain thyroid hormone may be at greater risk for gestational diabetes, compared to women who have normal levels of the hormone, according to researchers at NICHD. Their study appears in the Journal of Clinical Endocrinology and Metabolism.

The researchers found that pregnant women with the highest levels of the thyroid hormone triiodothyronine (T3) were more than four times more likely to develop gestational diabetes, compared to women with lower levels of the hormone. T3 is produced from the related hormone thyroxine (T4). The researchers also found that a high T3/T4 ratio—which indicates a high conversion rate from T4 to T3—was strongly associated with a higher risk for gestational diabetes.

To conduct the study, researchers evaluated medical records of 107 women with gestational diabetes, comparing them to 214 pregnant women who had not developed the condition. The women had taken part in the NICHD Fetal Growth Study, a diverse sample of more than 2,300 participants.

Study authors note that abnormal thyroid functioning has been linked to miscarriage and preterm birth. Their findings suggest that screening pregnant women for thyroid disease early in pregnancy could help identify women at high risk for gestational diabetes and other pregnancy-related complications.

No Link Found Between Brain Injury, IV Fluid Treatment of Pediatric Diabetic Ketoacidosis

Giving children intravenous (IV) fluids to treat diabetic ketoacidosis—an emergency complication of untreated diabetes—does not appear to worsen the brain swelling that may accompany the condition, according to a study supported by NICHD.

The findings, published in the New England Journal of Medicine, contrast with widespread concern that providing too much IV fluid may result in serious brain injury.

Diabetic ketoacidosis is often the first sign of type 1 diabetes in children who have not yet been diagnosed. Deprived of glucose, the liver converts body fat into ketones, which turn the blood acidic. Untreated diabetic ketoacidosis can be fatal.

The study was conducted at 13 U.S. emergency departments that participate in the Pediatric Emergency Care Applied Research Network. It enrolled more than 1,300 children with diabetic ketoacidosis.

The research team, led by investigators at the University of California, Davis, divided the children into four treatment regimens, varying the amount and rate of IV fluid infusion—from rapid to gradual—and varying the sodium content of the fluid.

Researchers found no difference in brain injury rates among the treatment regimens. Neither the infusion rate nor the sodium content of the fluid significantly influenced neurological outcomes of the children in the study.



People with EoE experience difficulty swallowing and nutritional problems because an accumulation of immune cells scars the esophagus.

IMAGE: DIGITAL VISION/THINKSTOCK

Eosinophilic Esophagitis Due to Missing Protein?

Scientists have discovered that the absence of a specific protein in cells lining the esophagus may cause inflammation and tissue damage in people with eosinophilic esophagitis (EoE). EoE affects as many as 150,000 people in the United States, many of whom are children

People with EoE experience difficult or painful swallowing, vomiting and nutritional problems because an accumulation of immune cells called eosinophils scars the esophagus.

The researchers found that the protein SPINK7 was nearly absent in esophageal biopsies taken from adults and children with active EoE but was prevalent in biopsies from healthy people. In a healthy esophagus, SPINK7 tamps down inflammation and helps preserve tissue structure.

Encouragingly, a licensed drug for emphysema reversed damaging inflammation in tissues lacking SPINK7, the investigators report in a paper posted online June 6 in *Science Translational Medicine*. The researchers received support from NIAID and NIDDK.

Because food contains enzymes that can damage human tissue, the lining of the esophagus normally protects itself by producing its own enzymes that degrade the offending proteins and thus protect the lining.

Researchers led by Dr. Marc Rothenberg at Cincinnati Children's Hospital found that SPINK7 facilitates this protective process. When they silenced *SPINK7*, the gene that codes for SPINK7, in cells derived from esophageal tissues, the research team discovered that large gaps formed between the cells lining the esophagus. These cells also lost barrier functions that ordinarily move food along the digestive tract.

Tissues that did not express SPINK7 also produced high levels of chemical messengers called cytokines that attract eosinophils and produce the same type of inflammation seen in allergic diseases.



NCATS director Dr. Christopher Austin presents Dr. Pamela McInnes with a commemorative plaque in recognition of her leadership on the NCATS Advisory Council and Cures Acceleration Network review board at a meeting May 10.

PHOTO: LISA HELFERT

NCATS Deputy Director McInnes Retires After 29 Years

Dr. Pamela McInnes, deputy director of the National Center for Advancing Translational Sciences, retired May 31 after 29 years of federal service. For the past 4 years, she helped shape and build the new center from the ground up, working with staff, key stakeholders and the broader research community to strengthen NCATS' role as a leader in clinical and translational science.

McInnes' expertise in clinical and translational research, extramural research management, trans-NIH collaborations and public-private partnerships served NCATS well, helping the center overcome many challenges.

"Pamela has been my partner, confidante and advisor in building NCATS for the past 4 years." said NCATS director Dr. Christopher Austin. "It is simply impossible to quantify all the ways that she has contributed to NCATS' development. I can't thank her enough and I wish her all the best in her well-deserved retirement."

Before joining NCATS in 2014. McInnes served as director of the Division of Extramural Research at the National Institute of Dental and Craniofacial Research. There, she was responsible for the institute's extramural research activities, which range from basic through clinical studies, including large and complex clinical and population-based trials.

Prior to her time at NIDCR, McInnes spent 16 years at the National Institute of Allergy and Infectious Diseases, where she served in many capacities, including as deputy director for the Division of Microbiology and Infectious Diseases. In addition, she led the reorganization and oversight of NIAID's Division of Clinical Research as well as the scientific design and implementation of a Challenge Grant Program promoting joint ventures among NIH and biotechnology, pharmaceutical and medical device companies.

The author of numerous peer-reviewed articles and books, McInnes first joined NIH in 1989 as a grants associate in the Office of Extramural Programs in the Office of the Director. Before coming to NIH, she served in academic roles at Louisiana State University Medical Center in New Orleans. McInnes earned her D.D.S. and M.Sc. from the University of the Witwatersrand in Johannesburg, South Africa.

NCATS is conducting a national search for a replacement. In the interim, Dr. Danilo Tagle will serve as acting deputy director.

NIAMS Division Director McGowan Says So Long

Dr. Joan McGowan, director of the NIAMS Division of Musculoskeletal Diseases, has retired. In her 30-year career at NIAMS, McGowan led a program

of research on basic muscle and skeletal biology; orthopaedics, osteoarthritis, bioengineering, tissue engineering and regenerative medicine; muscle physiology and muscle diseases; and osteoporosis and related bone diseases.



and innovated a cross-cutting federal research programs as well

as programs critical to the institute," said NIAMS director Dr. Stephen Katz. "Her career at the NIH has been truly exemplary, with a broad and sustained impact on public health matters and on NIH programs."



Dr. Joan McGowan



McGowan (r) briefs surgeon general Dr. Richard Carmona (I), the Duchess of Cornwall (second from I) and Prince Charles (third from I) during a 2005 royal visit to NIH.

McGowan served as a project officer and an osteoporosis consultant for the Women's Health Initiative, a long-term NIH-supported study that began in 1991 and focused on strategies for preventing heart disease, breast and colorectal cancer and osteoporosis in postmenopausal women. She was the NIH organizer of a Consensus Development Conference on Optimal Calcium Intake in 1994, and one on osteoporosis in 2000.

She co-chaired the federal working group on bone diseases whose members represent federal agencies with activities in osteoporosis and related bone diseases. "Joan was the face of bone research at the NIH for many years," said NICHD's Dr. Karen Winer. "She brought much candor, wisdom and intelligence to her work and appreciated the profound impact of decisions made on the lives of investigators and the many people who depend on their funded projects."

McGowan was the senior scientific editor of Bone Health and Osteoporosis: A Report of the Surgeon General, published in 2004. The following year, during a visit to campus by Prince Charles and his wife, the Duchess of Cornwall, she briefed them on key messages in the report.

McGowan's oversight of musculoskeletal research extended into space when NIH and NASA entered into a 2007 agreement to support research aboard the International Space Station. The initiative, BioMed-ISS, encouraged scientists to use the ISS to answer questions about human health and diseases

McGowan's division played a leading role in the 2015 Common Fund's Molecular Transducers of Physical Activity program (MoTrPAC). An expert roundtable discussion organized from within her division came up with the idea; it came to fruition through NIH-wide organization and leadership. MoTrPAC's co-coordinator, Dr. Maren Laughlin of NIDDK, said, "Joan should be celebrated for scientific leadership and foresight. She was a hands-on leader of the study throughout the NIH design and consortium planning stages, bringing passion for the science to the table in addition to deep NIH organizational and policy experience."

Before joining NIH, McGowan was a faculty member at Harvard Medical School and Massachusetts General Hospital. She received

> her master's degree in nutritional science from Cornell University and her doctorate in biomedical science from Brown University. She graduated from Marymount Manhattan College with a bachelor's degree in chemistry.

In reflecting on her retirement, McGowan remarked. "As gardeners know, it is difficult to prune. I have to cut off some really important and very fulfilling parts of my working life. But I need this to make room for new growth and development. I am not going to turn into a gardener, but more time enjoying nature and time with my family will be welcome!" B



NIH Police's Lt. Lawrence Brown is one of several grillmasters for the awareness event.

PHOTOS: GERALD JORDAN, CARLA GARNETT

Police Celebrate Annual Event Under Soggy Skies

The NIH Police hosted its 26th Police Awareness Day on May 16, under drippy skies, which forced the event to relocate from its usual home on the front lawn of Bldg. 1 to the Bldg. 31A patio. Law enforcement representatives from 13 local, state and federal jurisdictions participated, including the Washington, D.C. Metro Transit Police, the Montgomery County Sheriff's Office, Montgomery County Park Police, the U.S. Department of Commerce NIST Police, Amtrak Police, U.S. Department of Justice (Alcohol, Tobacco and Firearms), U.S. Park Police, Maryland Transportation Authority Police and Maryland State troopers.

National Police Week dates back to 1962, when President John F. Kennedy designated May 15 as Peace Officers Memorial Day. The event has grown over the decades, bringing tens of thousands of law enforcement professionals from across the country to the nation's capital for a service honoring those who have given their lives while wearing the badge. Many groups also take the opportunity to educate the communities they serve on police operations.

NIH's observance this year included K9 demonstrations, a cookout featuring chicken, hotdogs, hamburgers and sausages, personal safety and wellness displays along Bldg. 31's A-wing corridor and various other activities.





At left, the chow line forms. At right, NIH Police Chief Alvin Hinton (I) and Deputy Chief Leslie Campbell (3rd from r) share a light moment with attendees.





Clockwise from above: Washington, D.C. Metro Transit Police officer D. Kayal with bomb-sniffing dog Hugo. NIH Police Cpl. Steven Cradlin and K9 Diesel. Peter Girgenti of Montgomery County Park Police, with search & rescue dog Xena, who's greeted warmly by NIAID director Dr. Anthony Fauci and his special assistant Patty Conrad. And below, with light rain falling, NIH Police Cpl. Christine Fedorisko (I) and K9 Deputy Casey Meiklejohn, along with Odie of the Montgomery County Sheriff's Office, surveil the day's festivities.







Above, in the Bldg. 31A lobby, Lt. D. Moe of NIH discusses safe weapons handling. Below, a Maryland State trooper prepares to take a bite out of...a burger. Several demonstrations, activities and exhibits were forced indoors by the inclement weather.

