

‘UNTHINKABLE’ ‘Big Read’ Delves into Quirky Brains

BY DANA TALESNIK

The brain can perform in unusual ways beyond our imagination that, in some cases, defy explanation.

Graham, for example, believed he was dead. Incredibly, an imaging scan while he was up and about confirmed low brain activity consistent with someone in a coma. Sylvia, meanwhile, never gets a moment’s peace because a continuous hallucination of musical notes plays in her head. And there’s Rubén, who perceives distinct colors when he sees people, hues that don’t exist for him in real life because he’s colorblind.



British author Helen Thomson explores these and other mind-boggling cases in her new book *Unthinkable: An Extraordinary Journey Through the World’s Strangest Brains*. On June 7, she visited NIH to converse with NIH director Dr. Francis

Collins about the people with rare neurological conditions whom she met and interviewed for the book. Hundreds of NIH’ers joined them in Masur Auditorium for the 3rd annual Big Read, the culminating event following book club discussions around NIH.

Thomson, a freelance science journalist long fascinated with the brain, told the crowd that she started amassing peculiar case studies in medical

journals and then reached out to the patients’ neurologists to learn more about these unusual conditions.

The first patient she met, Tommy, inspired her to write the book. On paper,

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Annual hike evokes hoopla. See story, p. 12.

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UNCLOAKING A ‘MAGICAL SUBSTANCE’ Kieffer Dissects Opioid Effects on the Brain

BY CARLA GARNETT

For almost as long as we’ve known about the powerful spell opium can cast on a user, scientists have been trying to learn precisely how the drug operates in the body, particularly in the brain. According to recent Wednesday Afternoon Lecture Series guest Dr. Brigitte Kieffer, researchers are closer than ever to understanding, witnessing, mimicking and perhaps predicting opioids’ work within the gray matter.



SEE **OPIOIDS**, PAGE 4

PRIVATE EYE OF PLUMBING NHGRI, CC Sleuths Uncover an Uncommon Bacteria

Using a cutting-edge NIH genomic center, a sophisticated microbiology lab and cross-disciplinary collaboration, experts at NIH were able to identify the source of a decade-long outbreak of rather uncommon hospital-acquired *Sphingomonas koreensis* infections, said Dr. Sean Conlan at a Biowulf 20th anniversary talk in Bldg. 50 held recently.

“Metagenomic analysis allowed us to



SEE **BACTERIA**, PAGE 8

NIH Again Aims to ‘Knock Out Hunger’

NIH officially kicked off its annual Feds Feed Families (FFF) food drive campaign “Knock Out Hunger” on July 1 by joining federal agencies across the nation to help those in need. NIH has set a 2019 goal of collecting 28,000 pounds of non-perishable food items or the equivalent in monetary donations. The campaign is 6 weeks long, ending on Aug. 9.

Donations collected at NIH will be distributed throughout Maryland, the District of Columbia and Virginia by the Capital Area Food Bank. As part of an ongoing effort to serve the NIH community directly, a portion of NIH donations will be directed to the pantries of the Edmond J. Safra Family Lodge and the Children’s Inn at NIH.

During the drive, place donated items in collection boxes at various on- and off-campus sites. For specific locations and regular updates, visit <https://www.ors.od.nih.gov/FedsFeedFamilies/Pages/default.aspx>. Donation options include non-expired canned and boxed food, baby food and beverages, as well as other items such as soap, toothpaste, tissues, diapers and shampoo.

Eurest Dining Services will again offer its Fighting Hunger Voucher Program for the length of the campaign. Funds collected from vouchers will be used to purchase non-perishable items to help NIH reach its collection goal. Eurest is also offering a new promotion this year, “Keep the Change.” Customers can round up their purchase to the next whole dollar by simply saying, “Keep the Change.” Money collected will be added to the food voucher totals. Vouchers will be available for purchase in any dollar amount at participating Eurest dining locations.

Follow the latest campaign developments via Twitter @NIHEmplSrvcs; tweet your pictures or posts using #NIHFeedsFamilies. Contact NIH FFF chair Tim Tosten or program coordinator Debra Gale at FedsFeedFamiliesNIH@mail.nih.gov with any questions.

Summer Poster Day, Aug. 8

Summer Poster Day 2019 is scheduled for Thursday, Aug. 8, at the Natcher Conference Center from 9 a.m. to 3 p.m. The event provides an opportunity for summer interns to share the research they have been conducting at NIH and at the same time develop their communication and networking skills.

This year, more than 1,000 summer interns are registered to present posters. Investigators, staff scientists and scientific administrators can make a particularly important contribution to Summer Poster Day by visiting posters and engaging their authors in discussion.

For more information, visit https://www.training.nih.gov/summer_poster_day.



HHS Secretary Alex Azar (r) is greeted by (from l) NIAID director Dr. Anthony Fauci, FDA acting commissioner Dr. Ned Sharpless, NIH director Dr. Francis Collins and CDC director Dr. Robert Redfield.

PHOTOS: CHRIS SMITH, JIN PARK

HHS Secretary, Department Leaders Attend HIV Meeting at NIH

Health and Human Services Secretary Alex Azar visited NIH for the HHS Global-Domestic HIV Meeting: Successes and Challenges Reaching the 95-95-95 Goals. Held June 26 in Bldg. 45’s Kirschstein Auditorium, the day-long meeting gathered department leaders to share ideas about common challenges in the HIV response; exchange lessons learned in HIV policy, program, implementation and research across the global and domestic experiences; and create recommendations for further collaboration across HHS. NIH director Dr. Francis Collins opened the meeting with welcoming remarks. Azar discussed the President’s initiative, Ending the HIV Epidemic: A Plan for America.



Azar discusses the President’s initiative, Ending the HIV Epidemic: A Plan for America.

Later, a panel featuring representatives from HHS agencies offered an opportunity for each to highlight contributions and areas of expertise in ending the HIV epidemic, both domestically and globally.



Shown seated on the panel are (from l) Redfield, Sharpless, Dr. George Sigounas of HRSA, Radm. Michael Toedt of IHS, Fauci and Dr. Elinore McCance-Katz of SAMHSA.

La Spada Plots Progress Leading to Vision-Saving Treatment

BY KATHRYN DEMOTT

A therapy designed to prevent blindness in people with the inherited neurodegenerative disorder spinocerebellar ataxia type 7 (SCA-7) is nearing the launch pad for testing in clinical trials, said Dr. Albert La Spada, director of the Duke University Center for Neurodegeneration & Neurotherapeutics. La Spada, who is spearheading the therapy's development, shared the news at the 11th Sayer Vision Research Lecture held recently.

Development of the therapy has been decades in the making. In 1991, as a graduate student at the University of Pennsylvania, La Spada was the first to show that a genetic mutation known as a CAG-polyglutamine trinucleotide repeat expansion was the root cause of degeneration in X-linked spinal and bulbar muscular atrophy.

Six years later, SCA-7 was found to be caused by this identical type of mutation. The rare autosomal dominant disorder causes degeneration in the cerebellar region of the brain and the retina, the light-sensing tissue in the eye. People with SCA-7 experience difficulty with fine motor activities, speech and walking. As the disease progresses, they often go blind.

Since La Spada's discovery of trinucleotide repeat expansion mutations as the cause of a neurodegenerative disease, more than 35 other neurological disorders have been linked to various repeat expansion mutations, most often trinucleotide repeats.

SCA-7 involves a common pathology shared among neurodegenerative disorders: misfolded proteins that give rise to aggregates in the brain and other nervous system tissues. This commonality highlights the need for therapeutic strategies that prevent or reverse protein misfolding.

Yet despite this shared pathology, neurodegenerative disorders—from Alzheimer's to Huntington's disease—affect patients differently. In each disease, only select types of neurons are vulnerable to the accumulation of misfolded proteins.



On hand at the lecture are (from l) Dr. Albert La Spada; Dr. Jane Sayer, a research scientist at NIDDK who established the lecture series in honor of her parents, Winthrop and Laura Sayer; and Dr. Paul Sieving, NEI director.

La Spada continued studying SCA-7 because the retina is the most accessible part of the central nervous system and therefore is a promising proving ground for studying selective neuronal vulnerability.

Along the way, he and colleagues set their sights on staving off SCA-7-related blindness by preventing protein misfolding in the retina. With NEI funding, they tested an antisense oligonucleotide (ASO) therapy in

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People with SCA-7 experience difficulty with fine motor activities, speech and walking. As the disease progresses, they often go blind.

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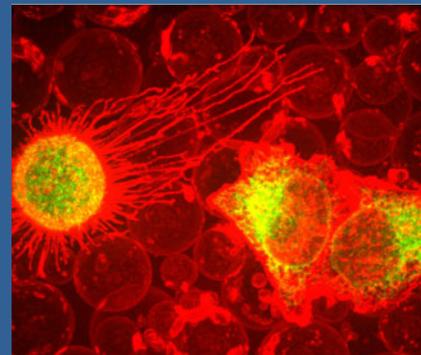
a SCA-7 mouse model. That is, they injected synthetic fragments of DNA into the eyes of mice to bind the RNA responsible for encoding the disease protein. The treatment successfully reduced mutant protein and improved visual function, as reported in their 2018 paper in the journal *Science Translational Medicine*.

In cooperation with Ionis pharmaceuticals, La Spada is producing ASO therapy for patients with SCA-7. If things go as planned, they will begin clinical trials as early as next year.

In anticipation of the trial, NEI is coordinating a trans-NIH natural history study

of SCA-7 to develop methods for tracking disease and measuring treatment effects.

The Sayer Vision Research Lecture Series features prominent scientists conducting vision-related research. It is co-hosted by NEI and the Foundation for the National Institutes of Health. Visit <https://nei.nih.gov/news/special/sayer> for more information about the lecture series and to view the videocast. **R**



ON THE COVER: Cells forming bubbles. On the right, two cells (greenish yellow) are in the process of forming bubbles, or plasma membrane vesicles (PMVs). During the blebbing process, a cell's membrane temporarily disassociates from its underlying cytoskeleton, forming a tiny pouch that, over the course of about 30 minutes, is "inflated" with a mix of proteins and lipids from inside the cell. After the PMVs are fully filled, these bubble-like structures are pinched off and released like those seen in the background.

IMAGE: CHI ZHAO, DAVID BUSCH, CONNOR VERSHEL & JEANNE STACHOWIAK, UNIVERSITY OF TEXAS AT AUSTIN

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Opioids

CONTINUED FROM PAGE 1

“Opium is kind of a magical substance that seems to relieve any kind of pain—physical pain, mental pain, social pain—and produces euphoria,” said Kieffer, who began her lecture, “Opioid Receptors and Brain Function,” by briefly tracing the drug back to its botanical origins thousands of years ago.

A large portion of opium’s mystery was revealed about 200 years ago, Kieffer continued, when a German chemist discovered its active ingredient. Morphine, she said, was shown to produce a “highly efficient analgesia, was a strong painkiller—and is still the strongest painkiller today—but also had strong addictive liability...So the holy grail in the field since then has been to find as good a painkiller as morphine, but one that would be devoid of the addictive liability.”

Kieffer, a long-time NIH grantee and professor in the department of psychiatry at McGill University, was making her second visit to NIH in recent months. She had presented a shorter talk as part of a multi-institute-sponsored symposium, “The Opioid Crisis and the Future of Addiction and Pain Therapeutics: Opportunities, Tools and Technologies” in February.

NIH director Dr. Francis Collins introduced the French molecular neurobiologist as “a giant in the study of the opioid system in the brain, a topic of considerable current interest and importance given the crisis we face in this country of opioid overuse and addiction and opioid overdose deaths.”

The Brain on Opioids

“This is your brain,” declared the speaker, holding an egg up to the camera. “This is your brain on drugs,” he went on, cracking the egg into a sizzling skillet. “Any questions?” he deadpanned.

To people of a certain age, that 1980s-era public service announcement by the Partnership for a Drug-Free America offered a lasting image of the damaging effects of drug use.

To scientists—and perhaps neuroscientists in particular—it could easily have been throwing down a gauntlet: What does the brain really look like on opioids?

Opium has been a societal challenge for decades, Kieffer recounted, describing the Opium Wars in the mid-19th century and today’s opioid crisis. Since 2000, she said,

opioid over-prescription for pain relief has led “many, many people to become addicted to opioids and to transition to heroin or fentanyl use and this alarming increase in overdose.

“During all these years,” Kieffer noted, “neuroscience has dramatically evolved

G-protein-coupled receptor family. They are extremely important as biomedical targets. Half of the drugs used to treat people are agonists or antagonists of G-protein-coupled receptors. We can think of the opioid system as a system that exists in our brain to teach us beneficial behaviors and help us cope with

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“We can think of the opioid system as a system that exists in our brain to teach us beneficial behaviors and help us cope with stress.”

-DR. BRIGITTE KIEFFER

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and we have discovered a fascinating opioid neuronal system.”

Morphine acts by binding on the brain. In 1973, researchers identified opioid binding sites, then known as “opioid receptors.” It took about 40 years, from the identification of binding sites, through the isolation of the first opioid receptor gene, to crystallography of the encoded receptor protein and the resolution of receptor structure.

Kieffer, Collins noted, “was the first to isolate a gene encoding an opioid receptor, research that led to much of what the field now understands about how opioids work at the molecular level...Her work has been transformative.”

Familiar Family

“We know a lot about this protein,” Kieffer said. “We know it atom by atom. These receptors belong to the big

stress. This system is important to regulate reward and aversion processes. It’s also a system that is extremely important to reduce pain and cope with stress.”

Kieffer’s talk covered opioid receptor physiology, in both mood state and drug abuse, homing in on the mu opioid receptor (MOR) in brain circuits. She showed studies identifying MOR as a “single target that mediates both analgesic and adverse [addictive] effects of opioids used in the clinic or abused in the streets.

“MOR is a target to kill pain and many strategies are underway to try to reduce adverse effects mediated by activated mu receptors,” Kieffer said. She recommended more organism-level studies for drug development.

Using knockout mice, “we demonstrated that there is an important role for the mu



In her lecture, “Opioid Receptors and Brain Function,” Kieffer traces the drug back to its botanical origins thousands of years ago.

PHOTOS: LESLIE KOSSOFF



Kieffer covered opioid receptor physiology, in both mood state and drug abuse, homing in on the mu opioid receptor in brain circuits.

opioid receptor—beyond drug abuse—that has to do with natural reward,” such as mother-child bonding, Kieffer said.

MOR Complex

Her group also has learned more about two other opioid receptors, and how the three each “contribute very differently to all facets of addiction” and have “distinct roles in hedonic homeostasis and emotional control.”

In addition, Kieffer suggested more study of opioid peptides produced by our brain, which naturally bind and activate the receptors. “We know much less about the peptides compared to what we know about the receptors,” she said.

Kieffer explained that scientists had hoped to find that receptors had one designated job, but MOR’s role proved to be more complicated.

“MORs facilitate drug-seeking and taking in reward circuits,” she said. “MOR function and adaptation to opioids in aversion centers is key to ‘the problem.’”

Concluding her talk, Kieffer mentioned her group’s new approach, translational neuroimaging, to view receptor function and brain connectivity.

“Gene-to-connectome mapping is feasible in the mouse,” she said. “Brain network analysis is at the crossroads of mechanistic and biomarker research.”

Currently researchers are examining how morphine, fentanyl and buprenorphine affect the brain. In the long term, Kieffer said, “this work will help scientists better understand opioid effects on the brain and predict behavioral effects of a drug.” **R**

Im Explores Health, Culture Ties

TECH-BASED STUDY

“Culture is colorful. Culture is elegant. Culture is in our daily lives. Culture is embedded in our beliefs and attitudes. Culture is...everywhere.”

So began the second NINR Director’s Lecture of 2019 with Dr. Eun-Ok Im describing her research that explores the relationship between culture and health.

Im’s inspiration for her research began when her mother was going through menopause. Im decided to look at Korean culture and women’s health experience after noticing that her mother was suffering from easily manageable menopausal symptoms that she never discussed. Im later transitioned to examining Korean culture as it related to pain management and cancer. Her current research broadly focuses on gender and ethnic health disparities due to cultural influences.

Across her studies, Im uses computer and mobile technology as her method for conducting research. In her first R01 study, she aimed to identify gender and ethnic differences in cancer pain experience among four racial and ethnic groups and develop a decision support system for cancer pain management. This study was one of the first internet-based studies of its kind; Im discussed the challenges she faced as one of the pioneers of this type of technology-based research.

Im has used her research findings to develop technology-based interventions. She advocates for using these interventions because they can reach racial and ethnic minorities across the nation, provide 24-hour access to the intervention and overcome cultural stigma and cultural hesitance by using non-face-to-face interactions.

Im is associate dean for research development and regulatory affairs and Mary T. Champagne professor at Duke University School of Nursing. She has gained national and international recognition as a methodologist, researcher and theorist in international, cross-cultural women’s health.

Im’s lecture is available on NINR’s YouTube channel at <https://youtu.be/xX7iNXVBLJI>.—**Diana Finegold**



NINR acting director Dr. Ann Cashion (l) with Dr. Eun-Ok Im

NIAMS Celebrates Lupus Research Progress at Meeting

Dr. Robert Carter (r), NIAMS acting director, presented alongside speakers from NIAMS, NIDDK and collaborating organizations to celebrate the 25th anniversary of the NIAMS lupus natural history protocol at the annual D.C. Lupus Consortium meeting on May 17. More than 175 researchers, patients, providers and advocates attended the event, which highlighted the evolution and impact of lupus research across NIH.

PHOTO: MARLEEN VAN DEN NESTE



Big Read

CONTINUED FROM PAGE 1

Tommy had a stroke. After meeting him, she learned he'd been a convicted criminal with aggressive tendencies, but he emerged from the stroke with a different personality. The new Tommy was a docile, emotional bloke who took up poetry and painting.

"You would never have known what your brain was capable of if you just read the journal article," Thomson said. As the opportunity arose to meet more patients, she sought to talk with each subject almost as a friend, to learn about their daily lives and how they cope with their extraordinary brain conditions.

"I'm not a doctor so I didn't want to approach these people from a clinical perspective in a hospital environment," she said. "I wanted to specifically go and meet them in their towns, in their homes... Those are the kinds of stories that put brain disorders into context."

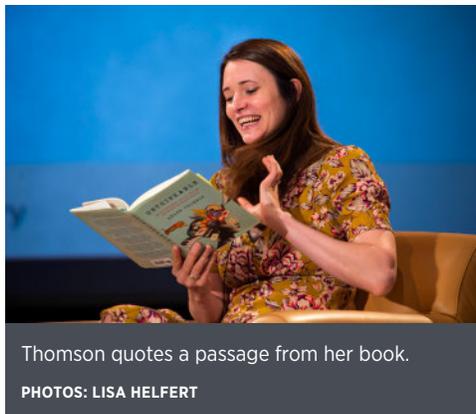
When someone's mental landscape goes awry, the patient usually first fears a brain tumor. "Part of the recovery for some of these people was finding out exactly what part of the brain was [affected]," said Thomson.

One patient, Sharon, gets lost everywhere, even in her own bedroom. She's unable to form a mental map of her surroundings, Thomson writes in her book, because the areas in Sharon's brain involved in navigation don't communicate properly. Sharon discovered if she spins around—what she dubbed the Wonder Woman technique—her brain rights itself for a time, until its disorienting flip hours or days later.

Such stories might touch a nerve, as we see a little of ourselves in these people. "You talk about Sylvia, who has musical hallucinations where there's an orchestra running through her head all the time. That's me!" exclaimed Collins. "Maybe there is not a clear dividing line between the people you wrote about and the rest of us; they just have a more extreme version of something that's part of many human personalities."

Thomson agreed, noting that many people can relate on some level to Sharon's plight of getting lost. "[These people] all had extreme versions of traits that we all possess," she said.

One condition that appears in several people in Thomson's book is synesthesia.



Thomson quotes a passage from her book.

PHOTOS: LISA HELFERT

About 4 percent of people worldwide have a mild form of this generally harmless trait that involves crossed senses. Rubén's colorful auras, for instance, represent an extreme form of color-emotion synesthesia.

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"I'm not a doctor so I didn't want to approach these people from a clinical perspective in a hospital environment. I wanted to specifically go and meet them in their towns, in their homes..."

—HELEN THOMSON

• • •

"What I got out of meeting all these people," Thomson said, "was the importance of talking about our perceptions of the world and understanding that what we see and feel and experience could be completely different to the person sitting next to us."

Most of Thomson's fact-finding missions were amiable, though one interview took an unexpected and frightening turn. When Thomson traveled to Abu Dhabi to meet Matar, his neurologist assured her that he was stable and eager to discuss his condition, called clinical lycanthropy. But unbeknownst to his doctors, Matar had recently stopped taking his

medication. As Thomson sat beside Matar for the interview, he started to snarl and make clawing motions with his hands.

"There was this real internal battle," said Thomson. "You could see he was really struggling to contain this delusion. Part of his mind was in this room with us and part of his mind was turning into a tiger."

It takes talent to communicate science in an interesting, accessible way. When considering whether a science story is newsworthy, Thomson—who holds degrees in neuroscience and science communication—asks whether it meets at least one of these criteria: Is it new, is it relevant and is it something she's excited to share with her friends?

She had intended to use more politically correct words to describe the patients she interviewed. "But it was doing a disservice to the people in the book to call their experiences atypical because that's not how they described them to me," she said. "It's not 'atypical,' they'd say; 'it's really weird.'"

Rubén keeps a copy of the chapter about him to help explain his condition to friends. Sharon, who feared telling anyone of her condition for decades, now tells everyone, proudly displaying a Wonder Woman photo on her fridge. The others also eagerly shared their stories.

"They felt that the more information that was out there on these conditions, other people wouldn't have to hide like they had," Thomson said.

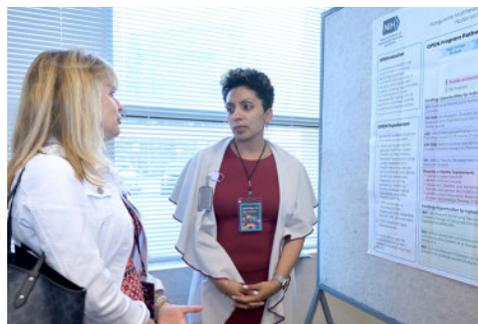


Thomson greets guests and signs copies of her book after the Big Read.



At left, Dr. Cynthia Kubu of the Cleveland Clinic Lerner College of Medicine speaks on neuroethics. At right, Dr. Marguerite Matthews (r) of NINDS presents a poster at the forum.

PHOTOS: MARLEEN VAN DEN NESTE



NINDS, Nonprofits Discuss Cell and Gene Therapies, Big Data

BY SHANNON E. GARNETT

Representatives from more than 50 nonprofit organizations across the country recently joined NINDS at its 13th nonprofit forum “Progress through Partnership.” The 1½-day meeting at the Neuroscience Center gave patient advocacy groups an opportunity to learn about NIH, NINDS and other federal programs, share common interests and interact directly with program staff.

Dr. Lyn Jakeman, director of NINDS’s Division of Neuroscience, introduced the NIH 101 session. “This meeting is really a lot of fun for us to do,” she said. “We get a chance to meet with a lot of you and your organizations one on one in various settings across the country, but this is a chance for you to come to our home base.”

Dr. David Owens of NINDS’s Division of Extramural Activities and Dr. Ernie Lyons of the Scientific Review Branch provided an overview of NIH and NINDS basics. Dr. Jill Morris, a program director in the Neurogenetics Cluster, presented “A Day in the Life of a Program Director.”

“What I really like about my job is that every day is different,” she said. “We are responsible for many different types of activities and we really value the contributions that advocacy groups make in research. [They] are very essential at identifying patient needs and bringing together the patient communities, which is [important] for recruitment in studies and clinical trials and for developing registries. And, they also help us identify gaps in the research, provide funding opportunities and bring together researchers.”

After a welcome by NINDS deputy director Dr. Nina Schor, the meeting featured panel discussions on emerging technologies and topics such as cell therapy, gene therapy and gene editing moderated by forum committee members Dr. Cynthia Rothblum-Oviatt of the A-T Children’s Project and Ronald Bartek of the Friedreich’s Ataxia Research Alliance.

At the end of the day, representatives attended a reception and poster session featuring information on key nonprofit and NINDS initiatives.

Dr. David Adams, NHGRI deputy director of clinical genomics, kicked off day 2 with a presentation on data collection and storage. During this session, big data was defined as data sets that require novel approaches to store and analyze. Adams shared general considerations about privacy, security and data location—especially for international projects.

Dr. Stephanie Devaney, deputy director of the All of Us Research Program, provided the program’s case example of dealing with a large data set. All of Us, a historic effort to gather data from one million or more people living in the United States, is a key element of the Precision Medicine Initiative and will provide data on how individual differences in lifestyle, environment and biological makeup can influence health and disease.

“We are very focused on partnering with our participants and giving information back,” said Devaney. “Ultimately I think our participants are joining the study because they want to see health outcomes change. They want to see us attack health disparities in a different way.” All of Us recently launched an interactive tool—a public data browser—that provides summary statistics from the program’s database.

Nonprofit representatives got an opportunity to meet informally with NINDS program staff and participate in breakout sessions to explore more fully topics on big data and cell and gene therapy.

One highlight of the meeting was the panel “Motivating the Next Generation of Researchers.” Moderated by Geraldine Bliss, a board member of the Phelan-McDermid Syndrome Foundation (PMSF), the panel included three scientists who shared stories of how they began to partner with advocacy groups early in their careers.

As a young investigator after attending a family meeting arranged by PMSF, Dr. Alex Shcheglovitov had an eye-opening experience.

“I got the opportunity to link my research to the problems that people experience in real life and to make the connection that whatever we discover in

the lab can be potentially applied to understand the problems and to help these patients. It was really a transformative experience,” said Shcheglovitov, assistant professor at the University of Utah.

Another forum spotlight was a panel discussion on neuroethics and bioethics co-moderated by Dr. Brandy Fureman of the Epilepsy Foundation and Dr. Khara Ramos, director of the Neuroethics Program in NINDS’s Office of Scientific Liaison. Schor called these topics “absolutely mission-critical issues that every one of us faces in dealing with patients and families and with new developments in science.”

The meeting concluded with a forum favorite—success stories.

“The people in this room and the people who dedicate their lives to building these organizations are just such a motivation for me and I know for so many people out in the world as well as the scientists who work on our diseases,” said panel moderator Susan Dickinson of the Association for Frontotemporal Degeneration. “And it’s especially poignant and really impactful that so many of us in the room are here because of the curveball that fate has thrown us.”

Panelists included Monica Weldon of the Bridge the Gap—SYNGAP Education and Research Foundation; Dr. John Porter, independent consultant for

neuromuscular diseases; and Terri Klein of the National MPS Society. Each presented individual lessons learned. Dickinson then shared the panel’s “recipe for success”—defined as common themes shared across organizations and experience:

- A need to have a critical mass of researchers working on your disease
- The importance of leveraging community data (e.g., registries) and funding from different sources
- The nonprofits’ role as conveners—bringing together families, basic and clinical researchers,

industry and encouraging collaboration and communication across stakeholders.

Schor echoed the significant role of conveners in her closing remarks.

“The role often of an organization like NINDS, like NIH, is really to be a convener—just as you are conveners—to bring people together who come at exactly the same issue with exactly the same mission and vision from very, very different vantage points,” she said. “I think the synergy that you gain by doing that is truly magnificent. And for me, I think the take-home message from this forum is that we, as NINDS and as a committee that includes many of you as well, can assemble a conference that teaches from the back of the room, but the networking that occurs throughout the room and throughout the day is precious.” **R**



NINDS deputy director Dr. Nina Schor gives remarks.

Bacteria

CONTINUED FROM PAGE 1

identify and track the indolent outbreak that was really hard to see,” because it went on for 10 years, said Conlan, associate investigator in NHGRI’s microbial genomics section of the Translational and Functional Genomics Branch. This level of genomic DNA sequencing analysis had never before been applied to tracking a series of infections such as this.

The research is a collaboration between NHGRI and the Clinical Center’s Hospital Epidemiology Service and department of laboratory medicine. Conlan’s former colleague, Dr. Ryan Johnson, conducted most of the analysis. It wouldn’t have been possible without Biowulf, a state-of-the-art supercomputer that enables scientists in the NIH Intramural Research Program to analyze massive datasets and attempt projects whose sheer scale would make them otherwise impossible.

In 2016, the NHGRI branch, led by senior investigator Dr. Julia Segre, began to investigate a small cluster of 4 *Sphingomonas koreensis* infections in the CC over 6 months. Normally, the bacteria “is pretty low on the scale of things you worry about,” Conlan said.

The bacteria, which can be found in water, does not pose a risk to the vast majority of people across the country and even the vast majority of hospital patients. But a large number of patients at the CC are either highly immunocompromised when they arrive, or, as a part of their treatment, their immune system is wiped out in order to give them another chance at life, leaving them susceptible to a wide range of infections.

S. koreensis is a gram-negative, rod-shaped bacteria, Conlan explained. It has features that allow it to live in sterile water. The bacteria forms biofilms that protect them from sanitizers and common antibiotics. *S. koreensis* is intrinsically resistant, meaning it has natural resistance to nearly all antibiotics. That resistance can’t be transmitted to another species.

The NIH Intramural Sequencing Center sequenced six samples from severely immunocompromised patients. While all 6 cases were *Sphingomonas* bacteria, only 4 were the same species—*S. koreensis*. The 4 *S. koreensis* samples taken from the patients were 99.92



Conlan said his team’s work was dependent on whole-genome sequencing, aided by Biowulf.

PHOTOS: MENA BRUNETTE

percent genetically similar, suggesting the samples belonged to the same strain.

To determine the source of the infection, investigators collected samples from several places in the hospital, including from the faucets of sinks in patient rooms. Researchers found genetically diverse, undisturbed bacteria growing in water that came from patient sinks and faucets. All water collected deep within the plumbing system of the hospital and incoming municipal water was negative for *S. koreensis*.

“They have been sitting in there and growing slowly in the nooks and crannies in a number of pipes,” Conlan said. “This improved our understanding of how we should be doing surveillance.”

As a result, in early 2017, the CC made several changes to the plumbing system. They replaced affected pipes and faucets and increased free chlorine levels and increased the temperature of hot water throughout the 3.3-million-square-foot building. The CC has not had a case of *S. koreensis* infection in more than 2½ years.

Conlan then jumped back in time to a separate outbreak in 2011. After the 2011 *K. pneumoniae* outbreak that affected 19 patients, the CC collected samples from the hospital environment to learn how antibiotic-resistant organisms spread. One of the goals of the study, published in 2014, was to learn how bacteria from patient and environmental samples share genetic material. It was the first study of plasmid transfer in a hospital environment.

Conlan said samples were taken from floor drains, housekeeping closets and carts, high-touch surfaces such as doorknobs and manholes on campus. Staff conducted whole-genome clustering to learn how organisms were related to each other and, more specifically, to learn about small, circular DNA molecules called plasmids that are contained in bacterial cells.

The plasmids can move from one bacterial cell to another and confer antibiotic resistance to other bacteria. In mixed populations of bacteria, plasmids can transfer antibiotic-resistance between different strains or species of bacteria—even without having been exposed to antibiotics. Recipient bacteria may go on to form persistent subpopulations or spread.

The study showed the tremendous value of accurate whole-genome sequencing to differentiate bacterial transmissions within the hospital from introductions of multidrug-resistant bacteria in patients who acquired them prior to admission at the Clinical Center.

While drain colonization with antibiotic-resistant bacteria is increasingly recognized as a patient safety risk in hospitals across the nation and around the world, Conlan said, “We found very few examples we could point to of the pipes being dangerous.

“This is a very active, dynamic process going on,” Conlan concluded. “And we hope this research helps us understand it better.” **R**



Two versions of the same photo of a woman—at left, her skin tone is red; at right, it's green. These images illustrate how color plays a key role in how faces are read. Both images are manipulated away from normal, by about the same units in color (green in one direction, red in the other). Both color directions may be deemed meaningful in terms of indicating blushing or sickness.

IMAGE: NEI

Color Plays Robust Role in Reading Faces

Anyone who has ever sensed that a person is sick simply by looking at their face has experienced the wealth of information conveyed by face color. A new study by NEI provides evidence that the human brain's visual system is especially sensitive to the color of faces compared to the colors of other objects or things. Study results were published July 8 in *Nature Communications*.

"The findings underscore the complexity of color perception," said study lead investigator Dr. Bevil Conway, head of NEI's unit on sensation, cognition and action. "Far from operating as a reflex, color perception involves a set of sophisticated brain operations that ultimately assign value and meaning to what we see."

The findings also suggest that social communication cues from faces factored into evolutionary selective pressures that gave rise to trichromatic color vision in our ancestors 23 million years ago.

Elevated Blood Pressure in First Trimester Is Risky in Pregnancy

Elevated blood pressure in the first trimester of pregnancy, or an increase in blood pressure between the first and second trimesters, raises the chances of a high blood pressure disorder of pregnancy, according to a study funded by NICHD.

The study was led by Dr. Alisse Hauspurg of the University of Pittsburgh School of Medicine and appears in the *American Journal of Obstetrics and Gynecology*.

The researchers sought to determine how revisions in guidelines for blood pressure in non-pregnant



Elevated blood pressure in the first trimester of pregnancy raises the chances of a high blood pressure disorder of pregnancy.

IMAGE: WAVEBREAKMEDIA/GETTY

adults might apply to pregnant women. The results suggest that blood pressure readings lower than those traditionally used to identify women as having high blood pressure may indicate a higher risk for a hypertensive disorder of pregnancy, such as gestational high blood pressure, which develops after the 20th week of pregnancy, and preeclampsia, or high blood pressure and protein in the urine. Both conditions increase the risk for stroke in the mother and for stillbirth, preterm birth and low birth weight. Preeclampsia also increases the risk for eclampsia—life-threatening seizures for the mother.

The researchers analyzed data from Monitoring Mothers-to-Be, a study that sought to identify risks for birth and pregnancy complications in first-time mothers. For roughly 8,900 women, researchers compared blood pressure readings in the first and second trimesters of pregnancy to blood pressure status in the remainder of pregnancy. None of the women had stage 2 high blood pressure (140/90 mmHg or higher) at the time they entered the study.

Common Treatment for Hyperthyroidism Increases Cancer Risk

Findings from a study of patients who received radioactive iodine (RAI) treatment for hyperthyroidism show an association between the dose of treatment and long-term risk of death from solid cancers, including breast cancer. The study, led by researchers at NCI, was published July 1 in *JAMA Internal Medicine*.

"We identified a clear dose-response relationship between this widely used treatment and long-term risk of death from solid cancer, including breast cancer, in the largest cohort study to date of patients treated for hyperthyroidism," said lead author of the study Dr. Cari Kitahara of NCI's Division of Cancer Epidemiology and Genetics. "We estimated that for every 1,000 patients treated currently using a standard range of doses, about 20 to 30 additional solid cancer deaths would occur as a result of the radiation exposure."



Findings from a study of patients who received radioactive iodine treatment for hyperthyroidism show an association between the dose of treatment and long-term risk of death from solid cancers.

IMAGE: SHIDLOVSKI/GETTY

RAI, which has been used widely in the United States for the treatment of hyperthyroidism since the 1940s, is one of three commonly used treatments for hyperthyroidism. The other two are anti-thyroid drugs, which have been rising in popularity, and surgical treatment, which is used least often.

The new findings are from a long-term follow-up study of a large cohort of people with hyperthyroidism (mainly Graves' disease) who were treated with radiation between 1946 and 1964, the Cooperative Thyrotoxicosis Therapy Follow-up Study.

In the new analysis—which included nearly 19,000 people from the original cohort, all of whom had received RAI and none of whom had had cancer at study entry—the researchers used a novel, comprehensive method of estimating radiation doses to each organ or tissue.

Most of the radiation is absorbed by the thyroid gland, but other organs like the breast and stomach are also exposed during treatment.



F. Anthony "Tony" Clifford displays award that led to more than 50 years of federal service.

Engineer Clifford Retires After 50+ Years at NIH

NIH is losing a major player in the development of its built environment. F. Anthony "Tony" Clifford has been chief engineer in the Office of Research Facilities since 2003. With more than 50 years of facility leadership experience here, he advanced NIH's mission by working to ensure that its buildings and facilities created a world-class environment for conducting biomedical research.

Clifford has been involved in all aspects of NIH buildings and facilities master planning, design, construction, operation and maintenance since his arrival in 1969. This includes more than 20 million square feet of biomedical research laboratories, a hospital, animal-holding areas, utility plants and related administrative facilities on the NIH campuses.

He joined NIH as engineer-in-charge of NIH's first bio-hazard containment facility. As research programs became more dependent on unique facilities, his professional career also grew as he assumed increasingly responsible leadership positions including chief of the Design Project Management Office, head of the Design and Construction Branch, deputy director and then director of the Division of Engineering Services.

By establishing strong partnerships with NIH leadership and with support from Congress, Clifford's comprehensive NIH Facility Revitalization Program was instrumental in significantly increasing the NIH buildings and facilities appropriation over a 10-year period. This enabled NIH to address aging physical plants and support emerging biomedical technologies and changing research priorities that resulted in a 45 percent increase of the NIH Bethesda real property.

At a retirement ceremony May 20 in Wilson Hall, Clifford was celebrated by NIH

leadership—including Dr. Lawrence Tabak, NIH principal deputy director—ORF staff, family and friends. Throughout his career, he has been an advocate for employee development and enrichment through mentorship and developmental training. In recognition of this, ORF Director Dan Wheeland is restarting the ORF apprenticeship program and renaming it in Clifford's honor.

"For half a century, Tony Clifford has devoted himself to supporting the NIH mission. His professionalism and commitment to the NIH mission have been inspiring. It has been a distinct honor to have served with him," Wheeland said.

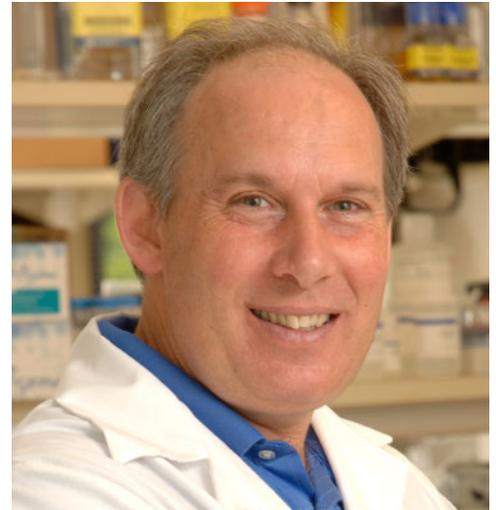
Dr. Alfred Johnson, NIH deputy director for management, conferred on Clifford the title "chief engineer emeritus," the first emeritus title given to an engineer at NIH. Representing Sen. Chris Van Hollen's office, Karen Hendricks presented Clifford with a copy of the *Congressional Record* that includes Van Hollen's tribute to him on the house floor for his 50 years of service to NIH and its surrounding communities. Al Hinton, chief of the NIH Police, presented Clifford with a plaque designating him as an honorary police officer.

"In an effort to capture his 50-plus years of history as an engineer at the NIH, I had the opportunity to share Tony's office with him for his last 3 months as he transitioned to retirement," said Lemuel Canady, ORF's new chief engineer. "Tony has many great stories of the NIH that he willingly shares. I have had the opportunity to hear these stories many times. The more I heard the stories, the more leadership principles emerged, such as humility, integrity, family, compassion, civility, duty and perseverance and honor. I benefited from these stories and learned their lessons and I am honored and prepared to continue the legacy."



At a retirement ceremony in Wilson Hall, Clifford was celebrated by NIH leadership, including Dr. Lawrence Tabak, NIH principal deputy director.

PHOTOS: CHIA-CHI CHARLIE CHANG



Dr. Dennis Drayna

NIDCD's Drayna Retires, Will Serve as Scientist Emeritus

Dr. Dennis Drayna retired in June after 22 years of research, service and mentorship at the National Institute on Deafness and Other Communication Disorders. He was chief of the section on genetics of communication disorders and the Laboratory of Communication Disorders. He continues to serve as a scientist emeritus.

"Dennis is a world-class human geneticist who brought a keen intellect, encyclopedic memory and passion for research and mentoring," said NIDCD scientific director Dr. Andrew Griffith.

Drayna earned a bachelor's degree from the University of Wisconsin in 1975, followed by a Ph.D. from Harvard University in 1981. As a postdoctoral fellow at the University of Utah, he created the first genetic linkage map of a human chromosome. In his work, he developed a map of the human X chromosome, which helped define the genetic locations of many X-linked diseases, such as Duchenne muscular dystrophy. This pioneering work paved the way for the Human Genome Project, which began with a map and went on to produce the sequence of the entire human genome. In 1985, Drayna moved into the biotechnology industry, joining the research department at Genentech. There, he made several important discoveries in human cholesterol metabolism.

In 1992, Drayna transitioned from Genentech to serve as co-founder and director of research at Mercator Genetics in Menlo Park, Calif. In 1996, the Mercator team identified the gene that causes hereditary hemochromatosis, a disorder that causes excessive iron absorption; left untreated, it can lead to organ damage and death. While hemochromatosis is easily treatable, diagnosing patients is difficult. Symptoms vary and can easily be mistaken for other common disorders. Genetic tests for hemochromatosis greatly improved the diagnosis and ability to treat this disorder; these tests are now widely implemented in clinical medicine.

Drayna then moved from private research to the public research arena. He spent a year as a visiting investigator at the National Center for Human Genome Research—now the National Human Genome Research Institute—before joining NIDCD in 1997.

When Drayna first joined NIH, he was hosted in the lab of NHGRI director Dr. Eric Green, where he began developing his own research program. “Having Dennis working in my lab was one of the most intellectually rich experiences of my early career,” noted Green at Drayna’s May 31 retirement symposium.

At NIDCD, Drayna was engaged by the wide range of research within the institute. Fascinated by advances in the molecular understanding of taste perception, he identified the gene that specifies our ability to taste the bitter compound phenylthiocarbamide, or PTC, which had been a well-known variable human trait for almost a century. He went on to find gene variants related to preference for sweet tastes and he worked with industry to better adapt flavoring products for palatability and healthy outcomes in diverse populations. Drayna also held a long-standing interest in auditory pitch perception. He used twin data to show that the inability to recognize musical pitches, also called tune deafness, was highly heritable.

Drayna noted, “The NIDCD may be a small institute, but it has an exceptionally high-quality intramural research program. I’ve found the scientific mission both fascinating and compelling, and the close involvement of clinical experts with basic laboratory scientists has been a real highlight of my research here.”

While many geneticists stop once they have found gene variants associated with a disorder, “Dennis strives to go beyond this, asking what the responsible genes can reveal about pathways involved in that disorder,” said Dr. Simon E. Fisher, director of the department of language and genetics at the Max Planck Institute for Psycholinguistics.

Perhaps the best example of this is Drayna’s work on stuttering. He and his colleagues spent years doggedly pursuing the genetic origins of stuttering, studying families across the world. This work paid off when they serially identified genes that currently account for about 20 percent of persistent stuttering cases. They didn’t stop there, though; by looking at what these genes did, they provided insight into the cellular mechanisms of stuttering, which had been largely unknown.

Drayna’s work is helping to change the perception of stuttering. Rather than the view that stuttering is a psychological manifestation of anxiety or personal shortcoming, people with persistent stuttering can now point to a possible biological cause for their symptoms.

Drayna has always been dedicated to sharing his science and its impacts on human health with mentees, colleagues across NIH, the public and the media. He has been quoted around the world in many of the most prominent media outlets.

His interest in stuttering extends to his charitable activities outside NIH, where he has served as a member of the board of directors of the Stuttering Foundation of America since 2006.

“Dennis cares as much about the community as the science,” concluded Dr. Elyssa Monzack, chief of staff of NIDCD’s Division of Intramural Research.



Dr. Maureen Goodenow, NIH associate director for AIDS research and director of the Office of AIDS Research, at awards ceremony

OAR Director Wins Esperanza/Hope Award

Dr. Maureen Goodenow, NIH associate director for AIDS research and director of the Office of AIDS Research, received the 2019 Esperanza (Hope) Award from the Latino Commission on AIDS on June 7 in New York City.

The commission, a nonprofit organization dedicated to addressing HIV and AIDS in the Latino community, created the Esperanza Award to honor leaders and influencers who make significant contributions to medical research and the fight to stop the HIV epidemic in the United States.

Goodenow joined NIH in 2016 and leads OAR in coordinating the HIV/AIDS research agenda across NIH. Before her tenure here, she was involved in international AIDS efforts as acting director of the Office for Research and Science within the U.S. Department of State, Office of the U.S. Global AIDS Coordinator and Office of Global Health Diplomacy.

As a firm believer in investing in the next generation of scientists, Goodenow has trained more than 50 doctoral and postdoctoral fellows. She also supports the notion that ending the HIV epidemic should be a common goal in partnership with HHS/NIH, community leaders and influencers and other stakeholders and partner organizations such as the Latino Commission on AIDS that reach into their communities and can address their unique challenges in preventing and responding to the HIV epidemic across the nation. **R**

Vaccine Study Needs Volunteers

NIAID researchers seek healthy volunteers, 18 to 70 years old, to participate in an influenza (flu) vaccine study. Scientists are testing an investigational vaccine to determine if it is safe and if there are any side effects. There is no risk of infection since the investigational vaccine product does not contain any virus. Compensation is provided. For more information, call 1-866-833-5433 or email vaccines@nih.gov.

Patients with Liver Disease Needed

NIDDK researchers seek volunteers to participate in a research study. For 30 weeks, participants will receive a medication called semaglutide (typically used for type 2 diabetes), aiming to improve their liver disease and help them lose weight. The study hopes to understand liver damage and its treatment in people with non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH). Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) or email prpl@cc.nih.gov. Read more at <https://go.usa.gov/xmJ8q>. Refer to study 19-DK-0072.

Suffered a Recent Head Injury?

NINR seeks research participants who have experienced a mild to moderate head injury in the last 30 days. The aim of the research is to explore why some people with a head injury go on to develop other conditions such as depression, post-traumatic stress disorder or post-concussion disorder. Compensation is provided. Contact the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010) or prpl@cc.nih.gov. Read more at <https://go.usa.gov/xUaJ4>. Refer to study 14-NR-0032.

Patients with OI Needed for Study

NICHD researchers seek individuals with osteogenesis imperfecta (OI) for study participation. Now enrolling children up to age 12 and people with OI of any age who were previously seen at NIH. For more information, call the Clinical Center Office of Patient Recruitment, 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010). Read more at <https://go.usa.gov/xEYjh>. Refer to study 18-CH-0120.

People with Crohn’s Disease Sought

NIAID is seeking individuals who have Crohn’s disease where current or previous treatments have not worked to control symptoms. Researchers are testing an investigational medication that may control the inflammation and symptoms of Crohn’s disease. Study-related tests, medication and procedures are provided at no cost. Compensation may be provided for certain research-related procedures. Contact the Office of Patient Recruitment, 1-866-444-2214, prpl@cc.nih.gov (TTY for the deaf or hard of hearing: 1-866-411-1010). Read more at <https://go.usa.gov/xNvGp>. Refer to study 17-I-0101.

NIH Follows Own Advice, Takes a Hike

NIH's own research suggests that walking and running regularly may lower your risk of high blood pressure, heart disease and diabetes, strengthen your bones and muscles and help to maintain a healthy weight.

Many NIH'ers followed their agency's exercise recommendations at the 12th annual Take a Hike Day, a non-competitive fun walk/run on June 12.



Several runners approach the end of the 3.25-mile loop around the campus.

The hike is “a great statement that we are the National Institutes of Health, and we care about our health,” said NIH director Dr. Francis

Collins at the starting line in front of Bldg. 1. “We’re always preaching to other people about how to be healthy. Now, we have an opportunity to demonstrate our concern about ourselves.”

A regular exerciser himself, Collins encouraged employees to get at least 30 minutes of exercise per day. “It’s supposed to be really good for your longevity,” he added. “We want all of you to be around a long time because we depend on you to make NIH an amazing enterprise.”

This year, 1,272 NIH'ers registered to walk or jog the 3.25-mile loop around the campus perimeter or a route at one of several off-campus locations, said Chris Gaines, program manager for NIH fitness and wellness services. Participants from NIEHS's Research Triangle Park campus in North Carolina and NIAID's Rocky Mountain Laboratories took part in the hike for the first time.

To learn more about NIH-sponsored events that support your financial, social, career, physical and community well-being, check out <https://wellnessatnih.ors.od.nih.gov>. —Eric Bock



Walkers hike up the final hill before they cross the finish line.



Blowing whistles to start the walk/run are Colleen McGowan, ORS director, and NIH director Dr. Francis Collins.



At left, before the hike, participants warm up on the Bldg. 1 lawn by hula hooping. At right, runners take off at the event's start line. The walkers began their hike shortly afterwards in a second heat.



At left, NIAID employees from 5601 Fishers Lane celebrate upon return from their hike. At right, staffers from the Division of Amenities and Transportation Services and NIH police officers cheer on participants near Bldg. 1.



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