

GERM THEORY

Yong Discusses Wonderful World of Microbes

BY DANA TALESNIK

The topic is quite infectious, though most kinds of microbes are not. We're colonized by trillions of bacteria and other microbes, the bulk of them beneficial or harmless. Fewer than 100 species of bacteria can even cause infectious diseases in people, writes author Ed Yong in his bestselling book *I Contain Multitudes: The Microbes Within Us and a Grander View of Life*.

Yong, a British science writer living in Washington who writes regularly for *The Atlantic*, recently sat down with NIH director Dr. Francis Collins to discuss his



Author Ed Yong on stage with NIH director Dr. Francis Collins at the Big Read event

book at the second annual Big Read. This giant book club event in Masur Auditorium followed weeks of informal book discussions at the NIH Library among interested staff.

In writing *I Contain Multitudes*, a title borrowed from a line in the Walt Whitman poem *Song of Myself*, Yong said he wanted to convey that microbes aren't just bugs that

make us sick. They're the dominant form of life on the planet, he said. They're everywhere and they do interesting things.

"Microbes are fascinating to me; they're sort of natural underdogs," said Yong. "They've been feared and reviled for a very long time and we're starting just now to understand how important they are...It's fodder for a lot of good narrative."

A story he recently covered for *The Atlantic* highlights the tenuous relationship among microbes, hosts and the environment. The mystery involved saigas, Central Asian antelope, whose globular noses Yong likened to a Dr. Seuss character. In 2015, two-thirds of the entire population died within a couple of weeks in a land area the size of Florida. The culprit turned out to be a normally harmless bacterium that lives in the saiga's nasal cavities but became lethal when it seeped into their bloodstream. The microbes

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Kids enjoy live music at camp BBQ; see p. 12.

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ANIMAL INSTINCTS

Biologist Studies How Species Reconcile, Cooperate

BY DANA TALESNIK

In the minutes before the inaugural talk in the Gadlin Lecture Series, dozens of people entered Lipsett Amphitheater in search of empty seats. When reserved seats were opened to the first takers, the seatless scurried over to claim chairs, in what almost seemed like a behavioral experiment set up by the guest speaker.

The lecture honored Dr. Howard Gadlin,



Dr. Frans de Waal

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NIH Cannot Forget Patients With Chronic Pain

BY ERIC BOCK

There's a joint crisis of pain and addiction in America, said NIH director Dr. Francis Collins. On one hand, 25 million Americans report chronic pain daily. On the other hand, an estimated 2 million Americans are addicted to opioid pain relievers.

"If there's good news, it's that research has been moving along—particularly research in neuroscience—to revolutionize our understanding of what's happening in the brain



Dr. Jerome Adams

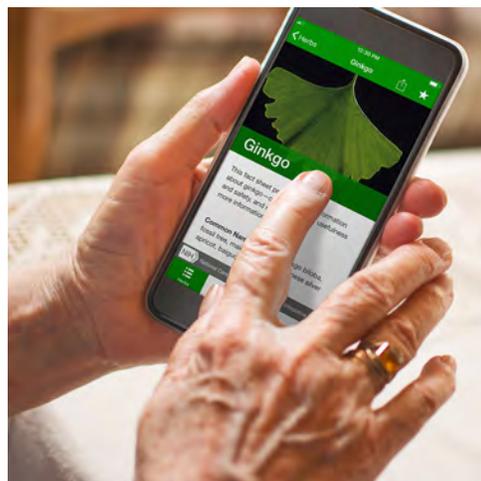
SEE **CHRONIC PAIN**, PAGE 8

Aug. 9

Summer Poster Day at Natcher

Summer Poster Day 2018 is scheduled for Thursday, Aug. 9, at 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 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.



New App Puts Herbal Information at Your Fingertips

NCCIH has released its first mobile app, HerbList, a free resource of research-based information on the safety and effectiveness of dozens of popular herbs and herbal products. Curious about echinacea, acai, ginkgo or turmeric? Reliable information is available on them and on more than 50 other herbs marketed for health purposes. Don't have an internet connection? No problem—HerbList works offline.

“HerbList is part of NCCIH’s effort to inform consumers and health care providers within the complementary and integrative health space,” said NCCIH acting director Dr. David Shurtleff. “People are considering herbs and herbal supplements for self-care and other reasons. It’s important that they are aware of what the science says about safety and effectiveness.”

The app’s source information is NCCIH’s *Herbs At a Glance* series of fact sheets.

HerbList is available free for both iOS and Android devices through links at <https://nccih.nih.gov/Health/HerbListApp>.



Music Plays On at CRC Atrium

Musicians hit high notes this summer as part of the Clinical Center’s music in the atrium series. Recent performances have included the University of Maryland Jazz Quintet (above); local pianist, composer and singer Chris Urquiaga (lower left); and a string quartet from the National Symphony Orchestra (lower right). The concerts, held in the Clinical Research Center’s atrium, support an environment of care and healing. Patients, their families and visitors as well as NIH staff are invited to attend. Mark your calendars for upcoming concerts, including the full NSO orchestra Sept. 18: <https://clinicalcenter.nih.gov/ocmr/music.html>.



Stratakis Honored by Alma Mater

NICHD scientific director Dr. Constantine Stratakis (r) was recently honored at the University of Athens, where he got his start. He received an honorary doctorate from the university, presented by Prof. George Zografos, vice-rector of the National and Kapodistrian University of Athens. Also receiving an honorary doctorate was Dr. Owen Rennert, NICHD’s former scientific director.



NIDA’s Etz Receives Award

NIDA health scientist administrator Dr. Kathy Etz (l) was presented with the 2018 Advances in Culture and Diversity in Prevention Science Award in Washington, D.C., at the recent 26th annual meeting of the Society for Prevention Research. Etz was nominated for her outstanding contributions to advancing the field of prevention science. She was recognized for her work to enhance the understanding of culture in prevention science and the development and adaptation of effective prevention strategies for traditionally underserved and/or underrepresented populations, including racial and ethnic minorities. Presenting the award is SPR president Dr. Leslie Leve.

NCI Team Discusses Transplantation Advances

BY RICH MCMANUS

There's something about cyclophosphamide. Administered to patients who have undergone hematopoietic stem cell transplantation, the drug is highly effective in preventing one of the most common, and deadly, post-transplant complications—severe graft vs. host disease (GVHD).

Over the last 50 years, there has been what Dr. Ronald Gress calls a dramatic evolution in hematopoietic transplant therapy. Chief of NCI's Experimental Transplantation and Immunology Branch and deputy director of the Center for Cancer Research, he has been on the frontier of transplantation biology since his arrival at NIH.

At Clinical Center Grand Rounds recently, Gress and colleague Dr. Christopher Kanakry, assistant clinical investigator in the same branch, outlined advances in what is not only replacement therapy for a patient's immune system but also the first form of effective immunotherapy.

The infused stem cell product, used mainly in cancer patients, "carries an immune system with it," Gress noted.

It is no longer as important as it once was to find matched donors for transplant. So-called allogeneic transplant—meaning genetically similar, but not identical—has long required that the donor and recipient are genetically matched at what is called the human leukocyte antigen (HLA) region. Based on recent advances, using donors not fully matched at this region is now possible. "Almost everyone now has a donor," Gress noted.

Historically, there have been four major obstacles to allogeneic stem cell transplant, he explained: Graft rejection, GVHD (either acute or chronic), relapse (which represents a failure of the immunotherapeutic graft vs. leukemia or graft vs. tumor effect of transplant) and immune incompetence, which endures years after transplantation in adults.

"The mission of our branch is to overcome these four," said Gress, "with a goal of curative hematopoietic stem cell transplantation."

All four obstacles arise, one way or another, from T cells—"They are tied together in a knot, so to speak," said Gress.

Twenty years ago, in hematopoietic stem cell transplantation, the recipient underwent myeloablation, or complete elimination, via chemicals or radiation, of his or her bone marrow. Today, immune-ablation, or targeted removal of host T cells, is a new standard. Both processes deplete a patient's T cells (the T is for thymus, where these immune cells are educated).



Dr. Ronald Gress (l) and Dr. Christopher Kanakry, both of NCI's Experimental Transplantation and Immunology Branch, recently discussed advances in the field.

PHOTO: CHIA-CHI CHARLIE CHANG

There are two paths to T-cell reconstitution in transplant patients: the thymic-dependent T-cell pathway and the peripheral expansion pathway.

• • •

"In 3 years, this talk will be very different. The field is very fast-moving."

-DR. RONALD GRESS

• • •

If a patient is young enough and the amount of prior chemotherapy or radiation exposure is not extreme, the thymus produces the crucial T cells. Adults depend on the peripheral path. Gress and his team are trying to correct flaws in both sources of T cells.

In order to increase the peripheral pool of T cells, NCI scientists have had some success with IL-7, a homeostatic cytokine. A new trial using IL-7 is currently being designed, said Gress.

"In 3 years, this talk will be very different," he said. "The field is very fast-moving."

Kanakry, who trained at Johns Hopkins—one of the pioneering centers, along with Fred Hutchinson Cancer Research Center, of the hematopoietic cell transplantation field—noted that only 30 percent of transplant patients have an HLA-matched related donor. Thanks to cyclophosphamide, which is effective not only against GVHD but also in preventing rejection of the new immune system, it is no longer necessary to strive for identical HLA-matching.

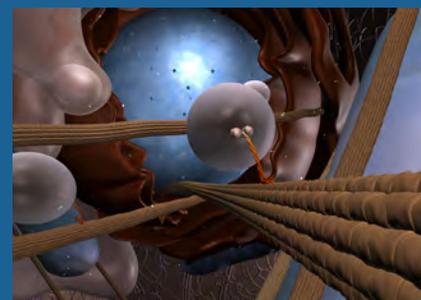
"There is less burden of immunosuppression therapy, too," he said. "It is fast becoming the standard treatment around the world for patients without a matched donor. And it's inexpensive and easy to administer."

As effective as cyclophosphamide is, Kanakry said very little is known about how it actually works. He has spent the past few years trying to understand that. Cyclophosphamide, one of the oldest anti-cancer drugs in the arsenal, is now being repurposed for GVHD prevention.

The dose of cyclophosphamide is crucial, Kanakry pointed out; both too little and too much are unhelpful to patients. It is also effective even if the patient lacks a thymus.

Relapse is the leading reason allogeneic hematopoietic stem cell transplants fail, Kanakry said. He hopes that a complete understanding of how cyclophosphamide works will allow him to rationally integrate other therapies to decrease this major remaining barrier to successful transplants.

The full talk is available at <https://videocast.nih.gov/summary.asp?Live=27681&bhcp=1>. **R**



ON THE COVER: RNA molecules. Scientists have harnessed the power of RNA interference to study the function of many individual genes by reducing their activity or silencing them. This process allows researchers to identify genes and molecules that are linked to particular diseases.

IMAGE: NCATS

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Big Read

CONTINUED FROM PAGE 1

went haywire, it's believed, in response to extreme climate fluctuations.

"Relationships between hosts and microbes are often on this knife's edge between disease and health, between parasitism and commensalism [peaceful coexistence], and that can tip easily," said Yong. It's a reminder, he added, that the microbe-host relationship may evolve as the world around us changes.

Most of Yong's book focuses on how the microbiome works, develops and can be manipulated in humans and animals. The last chapter is devoted to microbes in the environment. Do our choices, from building design to sterilizing surfaces, contribute to the spread of pathogens? It's an area of ongoing debate.

Regardless, Collins interjected affably, nothing said during the conversation absolves NIH clinicians from handwashing.

Throughout the Big Read, Yong and Collins discussed the art of making science writing dynamic and comprehensible.

"A lot of people think of science as a set of discoveries or papers, but it's so much more than that," said Yong. "It's stories of successes and failures; it's the motivations that got people into this in the first place; it's tales of feeling out of place or curious about something and these human universals that make science so compelling."

One microbial procedure with mixed results is fecal transplant. Transferring the microbiome contained within poop from a healthy donor to a patient has proven

effective in fighting *Clostridium difficile*, a bacterial infection often resistant to antibiotics. So far, though, said Yong, fecal transplant has much less success against other types of infection.

"Altering someone's microbiome is as complicated as changing a rain forest or a coral reef," he said.

A major drawback of fecal transplant, apart from the ick factor, is that the donor's stool can transfer all kinds of diseases. The therapy might solve one condition but impart others, said Yong, so it's critical to explore regulatory issues and long-term risks.

Another promising area is disease control. Many insects, and some mosquito breeds, carry bacteria called *Wolbachia*. While scientists were studying the organism's reproductive properties, they discovered that the kinds of mosquitoes that don't carry *Wolbachia* are the ones that carry and spread dengue, yellow fever and Zika virus.

In clinical trials in tropical areas worldwide, scientists are injecting small groups of pathogenic mosquito breeds with *Wolbachia* and releasing them into the wild. Potentially, after a few generations, these mosquitoes will naturally carry the bacteria and no

longer be vectors for human disease.

"I think it's an interesting example of basic research having these unexpected and wonderful applications," said Yong.

The investigators have had to tread carefully, though, since conducting such experiments in nature is bound to create public concern. "You're basically saying to people: we want to release mosquitoes on your property," said Yong. "They've been loaded up with bacteria they don't normally have...Those insects will probably bite you. Are you cool with that?"

Uncertainties abound in science, said Yong, and can make for illuminating stories.

"I don't think you need to tell people you're going to change their lives or change the world to get them excited about science," he said. One of his most widely read articles, he noted, concerned hippo dung.

Writing a book is a lonely endeavor and there's the underlying fear it won't sell, said Yong.

"I wrote the book because I thought it would be an intellectually satisfying exercise and I was going to be proud of the product regardless of how well it did. Everything on top of that is a bonus."

★ ★ ★
"Altering someone's microbiome is as complicated as changing a rain forest or a coral reef."

-ED YONG

★ ★ ★



At upper left, Yong enjoys the book-signing that followed his chat with Collins (above).

PHOTOS: CHIA-CHI CHARLIE CHANG

Alzheimer's Summit Features Research Advances, Recommendations

More than 3,000 participants from government, academia, industry, nonprofit organizations and the public recently convened on campus and online to discuss how much has been accomplished and what is needed to enable precision medicine research for Alzheimer's and meet the research goal of the National Plan to Address Alzheimer's Disease—to treat and prevent it by 2025.

The NIH Alzheimer's Disease Research Summit 2018: Path to Treatment and Prevention led to a series of recommendations designed to guide



"This should be a meeting you will tell our grandkids about 10 years from now," NIH director Dr. Francis Collins told attendees. "That you were here, in a critical step towards the cure for Alzheimer's disease, which ultimately emerged."

efforts to build a collaborative, multi-stakeholder research environment capable of delivering urgently needed cures for people at all stages of the disease.

As many as 5.5 million older Americans live with AD, and the number is expected to climb to nearly 14 million by 2050 unless ways to delay, treat or prevent it are discovered. Millions more have other types of dementia or serve as caregivers.

"Alzheimer's disease is a worthy and complex foe," said NIH director Dr. Francis Collins, who welcomed summit participants. "Yet science's armament is growing daily, and we know so much more."

NIA director Dr. Richard Hodes noted advances in recent years, including increased federal funding for Alzheimer's research that has enabled more opportunities for a wide range of study.

Since the last summits held in 2012 and 2015, NIH has helped launch public-private partnerships that have advanced and integrated discoveries in basic, translational and clinical research using open-science platforms for data sharing. Hodes mentioned, for example, the Accelerating Medicines Partnership-Alzheimer's Disease, which has identified more than 100 novel candidate targets for drug discovery.



Panelists respond to audience questions at a session on understanding the impact of the environment to advance disease prevention. They are (from l) Martha Clare Morris, Rush University; Andrew J. Saykin, Indiana University; Mariana G. Figueiro, Rensselaer Polytechnic Institute; Jennifer Manly, Columbia University; Laura Baker, Wake Forest School of Medicine; and Chirag Patel, Harvard Medical School.

Scientists are learning more about how many different proteins, metabolites and other molecular players act and interact—with each other and with certain genetic variants—to influence the onset and progression of Alzheimer's.

Several speakers reiterated support for the "multiple shots on goal approach" and continued expansion of data-driven approaches from target discovery all the way to late-stage clinical development. The hope is to be able to treat people at risk of Alzheimer's long before memory loss and other dementia symptoms appear and to arrest disease progression as well as deliver treatments for cognitive and behavioral symptoms.

Recent discoveries in Alzheimer's have been aided in part by big data, said Dr. Eliezer Masliah, director of NIA's Division of Neuroscience. For example, researchers using a "systems biology" approach have modeled various brain networks to look for biological drivers of Alzheimer's disease. These studies have also helped identify new brain regions to study. Similarly, big data has enabled large-scale genomic studies that have identified many more risk factor genes associated with Alzheimer's.

Speakers at the summit emphasized the importance of public datasets and partnerships that facilitate data sharing and collaboration.

"We are trying to make the open science and open source ethos the norm in Alzheimer's research," said Dr. Suzana Petanceska, a program officer for NIA's Division of Neuroscience and one of the lead organizers of the event. "The good news is that funding organizations and publishers are beginning to come together and align incentives to maximize the sharing of data and research resources."



More than 3,000 people attended the AD summit.

For instance, the Model Organism Development and Evaluation for Late-onset Alzheimer's Disease consortium, formed in 2016, is designed to deliver up to 50 new rodent models for late onset Alzheimer's and enable their rapid distribution for use in basic research and therapy development without intellectual property barriers; in addition, the consortium will make the data rapidly available to researchers at-large and establish rigorous methods for testing new candidate therapeutics.

With so many possible influences on AD, from genetic variants to cardiovascular risks, researchers at the summit called for a more individualized understanding of people with or at risk for Alzheimer's. What causes Alzheimer's in one person—and what treatments work—may be different than in another person. Progress will require a better understanding of individual differences in biology, lifestyle and environment.

"This is a critical time in Alzheimer's research, with new opportunities to build upon what we have learned," said Hodes. "We must continue to foster creative approaches that leverage emerging scientific and technological advances, establish robust translational infrastructure for rapid and broad sharing of data and research tools and work with funding partners and other stakeholders to cultivate and sustain an open science research ecosystem." **R**

De Waal

CONTINUED FROM PAGE 1

director emeritus of NIH's Office of the Ombudsman, Center for Cooperative Resolution, who attended the talk. The overflow crowd was a testament to the lecture that was to follow by Dr. Frans de Waal, director, Living Links Center and psychology professor at Emory University. A renowned biologist and primatologist, de Waal studies animal social behavior and repeatedly demonstrates that animals are emotional, empathetic beings.

In biology, "Emotions prime you for action," said de Waal. "Being fearful doesn't do you any good unless the fear makes you escape or fight." It is unclear if, like people, animals are conscious of their emotions and have the sort of feelings that we often express in language.

"Emotions are expressed in the body and that's something we can see and measure," he said.

A kiss, for example, is not always just a kiss. Chimpanzees kiss when they greet each

competitive, aggressive or even jealous, said de Waal, but most are inclined toward cooperation. Primates, for example, are generally playful, peaceful creatures that sometimes fight. Afterward, they reconcile and even comfort each other.

Macaques are known to be conciliatory, said de Waal, but other monkey species are less appeasing. Another animal that rarely reconciles is the domestic cat. But from observing animal infidels in the wild and in captivity, de Waal said, elephants, wolves, dolphins and even some birds are among the many species that make peace after fighting.

"I'm from a family of six boys, which maybe primed me to study these phenomena," he said.

De Waal primarily works with chimps and bonobos, which tend to be cooperative by nature. In one experiment, several chimps had to simultaneously pull a lever to get food. Despite some mild competition and a few freeloaders, the chimps learned they had to work together to get their reward, which they ultimately shared with each other.

Great apes are also known for their empathy. When a bonobo cries, another rushes to hug and console him. Elephants do this too. They wrap their trunks around each other when one is upset.

Apes and elephants both go a step further, helping friends in need, such as an elephant helping another out of a ditch or a chimp choosing the right tool for a task and handing it to another chimp.

"Targeted helping requires a cognitive understanding of what the problem is and what the solution is, and I think certain large-brained species are capable of that," said de Waal. "Animals who also [can recognize themselves in the mirror] may have more complex forms of empathy than those who don't."

Rowena, a chimp with a hole on her head from a scuffle, looked in the mirror, inspecting her injury. Pepsi, the elephant, looked in the mirror, taking his trunk up to touch a mark above his eye. "Your dog doesn't do this," said de Waal. "If your dog does this, I want you to call me."

Many animals prove time and again that they're caring, sharing creatures, particularly among their own kind. A bonobo will share his food with another bonobo, even though it means less food for him. In the wild, when threatened by a leopard or other predator, chimps will selflessly endanger themselves to rescue a fellow chimp.

"We were the first ones to demonstrate that chimpanzees do care about the

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"I look at my monkeys as capitalists. They're comparing their income, after all."

-DR. FRANS DE WAAL

• • •

other or to make up after fighting, similar to humans, said de Waal. When bonobos, close relatives to chimps, are physically attracted, they tongue kiss, much like humans. The kissing gourami, however, is a fish that locks lips not with affection, but out of aggression.

Anyone who strenuously objects to anthropomorphism—attributing human-like behavior to animals—is in what de Waal has termed "anthropo-denial."

When a baby gorilla gets tickled, the noises he makes may not sound to us like laughter, but it's his version of the giggles. People are not different from other primates, de Waal underscored. "You need to respect in your language the homologies [shared characteristics among species] that exist."

Different animals at times get



Enjoying the lecture are (from l) NICHD scientific director Dr. Constantine Stratakis, Brenda Hanning and her husband Dr. Howard Gadlin, and NIH director Dr. Francis Collins.

NCI Accelerates Rural Cancer Control Research

Why are death rates from cancer decreasing much more slowly in rural areas compared to urban areas—and the rates are already nearly 10 percent higher in rural areas? Put another way: Why is this cancer disparity getting worse and what can be done to address this divide?

More than 250 researchers, clinicians and community partners from a wide range of backgrounds and expertise gathered at NIH recently to address these and other questions regarding cancer disparities in rural populations. The objectives of the meeting, Accelerating Rural Cancer Control Research, were threefold: to identify gaps in research and practice; to build partnerships across the country with various health-related entities (federal, national and local) to address challenges and disseminate solutions; and to highlight and identify methods to address competing and common agendas of clinics/providers, researchers and community/patients.

Dr. Shobha Srinivasan, health disparities research coordinator in NCI's Division of Cancer Control and Population Sciences, opened the meeting. She said that as she worked to prepare for launch of the Accelerating Rural Cancer Control Research program, it was humbling “to see and to understand what is really happening in our rural communities across America and the challenges they face—and the resilience that they show in the face of all those challenges.”

NCI director Dr. Ned Sharpless noted that rural cancer control is not a new area of research for NCI, given that institute programs have focused on rural health for more than 20 years. So why have this meeting now? “We have better data,” said Sharpless. “Better sources of data, better aggregation of data and we're involving researchers who can use this data with different expertise.

“No one approach or no one idea is going

to solve this disparity,” added Sharpless. “Just as the biologic heterogeneity of cancer means that no single treatment can extinguish all tumors, no single intervention or even suite of interventions can address the cancer disparities we see in rural America.”

Presentations and discussions provided attendees with a glimpse of health disparities in Delta, Appalachia, Alaska, Hawaii, Southwest, Colonias, Reservation and Frontier communities, illuminating circumstances and variations in rural regions throughout the country.

Meeting presenters emphasized how

small investments can lead to big gains, and the power of partnership and collaboration. As Dr. Robert Croyle, director of NCI's Division of Cancer Control and Populations Sciences, said: “We want to build stronger bridges amongst those who do work in rural health, and facilitate interdisciplinary cross-sectional collaboration...whether it's in a clinical or research setting, or a local or federally funded center, such as those supported by HRSA's [the Health

Resources and Services Administration] Federal Office of Rural Health Policy, which has played a long-standing role in this area.”

Speakers also stressed the importance of strong infrastructure and of intervening simultaneously at multiple levels—at the individual/patient level, at the doctor/health care provider level, at the facility level, at the network level and at the health department level. The need to work with communities to provide services that they're interested in and from which they'll benefit was highlighted repeatedly, with numerous examples given of programs that brought sustained health improvements.

Throughout the conference, images were shared of the rural areas on which the meeting focused. The hope is that the conference, the resulting discussions and collaborations and the RFA (request for applications) to incentivize more research in this domain will propel advances in addressing rural health disparities, so that living in these rural communities does not mean living with poorer health. **R**



“If two related species [like apes and people] show very similar reactions to very similar situations,” said de Waal, “you have to assume shared psychology behind it.”

PHOTOS: MARLEEN VAN DEN NESTE

well-being of others,” said de Waal. In fact, chimps will even refuse a reward until the other chimp gets one.

Monkeys, on the other hand, aren't so altruistic and get especially flustered at unequal rewards. When doing the same simple task rewards one monkey with a cucumber and the other with a more coveted grape, the first monkey screeches in protest.

“I look at my monkeys as capitalists,” said de Waal. “They're comparing their income, after all.”

Chimpanzees, like people, sometimes equalize the outcome to preserve the relationship. “Chimpanzees and humans both have the capacity of thinking forward,” said de Waal. They realize if they take everything, their partner might get upset.

“If two related species [like apes and people] show very similar reactions to very similar situations,” said de Waal, “you have to assume shared psychology behind it.”

With his research, de Waal offers insights into human emotion and behavior. Perhaps most importantly, his work also reminds us to appreciate and respect all animals for the complex emotional beings that they are. **R**

RURAL
CANCER
CONTROL
RESEARCH



NCI director Dr. Ned Sharpless

Chronic Pain

CONTINUED FROM PAGE 1

and the peripheral nervous system, both in addiction and in pain,” said Collins during the 2018 NIH Pain Consortium Symposium’s keynote address held recently.

However, scientists must translate those promising basic research findings into non-addictive treatments for pain, he said. Potential alternative treatments might include drugs, devices or even behavioral interventions.

“We need safe and more effective strategies beyond what we have right now, particularly for those individuals for whom opioids are a poor choice,” he said.

In April, NIH announced the launch of the HEAL (Helping to End Addiction Long-term) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. The initiative was made possible by a funding boost from Congress.

“We’re going from basic to behavioral and everything in between. We’re promoting innovative partnerships, including with other government agencies—particularly SAMHSA—and also with advocates and industry,” Collins said.

Ultimately, the initiative will gather more information about what happens when acute pain turns into chronic pain in at-risk patients, identify better targets for pain management, create pre-clinical screening platforms and establish a clinical pain research network.

“We would very much like to have better means of assessing pain, going beyond the unfortunate 1-10 scale, which we all realize is flawed in multiple ways and affects many of the decisions about whether something is working or not,” Collins said.

After the keynote address, U.S. surgeon general Dr. Jerome Adams joined Collins on stage for a fireside chat. As the nation’s doctor, Adams conveys complex scientific information in plain language to the public so people can improve their health and reduce their risk for illness and injury.

Responding to the opioid epidemic is a key priority for Adams. Recently, he wrote a surgeon general’s advisory urging the public to carry the overdose-reversing drug naloxone with them. An overdose can happen anywhere, anytime. Both Adams and Collins carry the drug.

“If we’re going to turn this opioid epidemic around, we need naloxone to be as ubiquitous as CPR,” he said. “Someone

could bust down the door right now and say, ‘Someone’s in the bathroom and they’ve overdosed.’”

He believes “stigma is the biggest killer we have out there.” It affects the nation’s ability to respond to the opioid crisis by preventing people from coming forward and admitting they have a problem.

“We’ve got this belief in our country...that pain is just something you’ve got to suck up and have to deal with,” he added.

Lack of access to health care services is another barrier that prevents people from receiving the care they need. When Adams was growing up, he was diagnosed with asthma. To get treatment for their son, his parents drove him to Washington, D.C., a 2-hour drive from his home in rural southern Maryland. If his parents weren’t able to take time off from work, they had to cancel the appointment.

He thinks mental health consults should be a part of routine health care. Instead of asking “What’s wrong?” doctors must ask “What happened?” Many Americans have experienced trauma in their childhood, which leads to increased risk for drinking, smoking, criminal behavior and chronic pain.

Adams would like to work with NIH to write the first surgeon general’s report on trauma and resilience. Collins said the agency would embrace that opportunity.

“We want to minimize the trauma people face, but, at some point, we aren’t going to be able to avoid all of it,” noted Adams. “The question is ‘How do we build resilience?’”

Minorities have been disproportionately undertreated for chronic pain, said Adams. Many patients with sickle cell disease, for instance, don’t receive the treatment they deserve because they’re labeled as drug seekers, he explained.

Adams challenged the audience to think beyond research papers. Scientists’ voices can be just as powerful when they write newspaper opinion pieces or participate in radio show interviews.

“Your voices can be just as powerful and reach more people sometimes in an op-ed in the local paper,” he concluded. “We need to figure out how better to get the message out to the public so there’s a hunger for what you’re working on.” **R**



NIH director Dr. Francis Collins (l) and Adams discuss chronic pain at fireside chat.

PHOTOS: ANDREW PROPP

Teen Crash Risk Highest During First 3 Months After Getting Driver's License

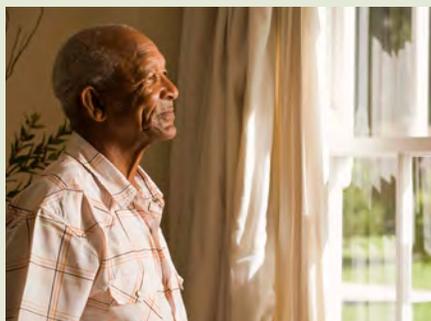
Teenage drivers are 8 times more likely to be involved in a collision or near miss during the first 3 months after getting a driver's license, compared to the previous 3 months on a learner's permit, suggests a study led by NICHHD. Teens are also 4 times more likely to engage in risky behaviors such as rapid acceleration, sudden braking and hard turns during this period. In contrast, teens on a learner's permit drove more safely, with their crash/near crash and risky driving rates similar to those of adults. The study appears in the *Journal of Adolescent Health*.

"Given the abrupt increase in driving risks when teenagers start to drive independently, our findings suggest that they may benefit from a more gradual decrease in adult supervision during the first few months of driving alone," said NICHHD senior investigator Dr. Bruce Simons-Morton, one of the authors of the study.

The study is one of the first to follow the same individuals over time, from the beginning of the learner period through the first year of independent driving, while continuously collecting information using software and cameras installed in the participants' vehicles.

The study also evaluated parents' driving in the same vehicles, over the same time, on similar roads and under similar driving conditions as their children. Near-crash events were those requiring a last-moment maneuver to avoid a crash, while crashes were physical contact between the driver's vehicle and another object.

The study enrolled 90 teenagers and 131 parents in Virginia and the data collection system was developed by the Virginia Tech Transportation Institute, Blacksburg.



Viral species may have a role in Alzheimer's disease biology.

IMAGE: JUPITER IMAGES/THINKSTOCK

New Evidence That Viruses May Play a Role in Alzheimer's

Analysis of large data sets from post-mortem brain samples of people with and without Alzheimer's disease has revealed new evidence that viral species, particularly herpesviruses, may have a role in Alzheimer's disease biology.

Researchers funded by NIA made the discovery by harnessing data from brain banks and cohort studies participating in the Accelerating Medicines Partnership-Alzheimer's Disease consortium. Reporting in the June 21 issue of *Neuron*, the authors emphasize that their findings do not prove that the viruses cause the onset or progression of Alzheimer's. Rather, the findings show viral DNA sequences and activation of biological networks—the interrelated systems of DNA, RNA, proteins and metabolites—may interact with molecular, genetic and clinical aspects of Alzheimer's.

"The hypothesis that viruses play a part in brain disease is not new, but this is the first study to provide strong evidence based on unbiased approaches and large data sets that lends support to this line of inquiry," said NIA director Dr. Richard Hodes. "This research reinforces the complexity of Alzheimer's disease, creates opportunities to explore Alzheimer's more thoroughly and highlights the importance of sharing data freely and widely with the research community."

Novel Drug Therapy Partially Restores Hearing in Mice

A small-molecule drug is one of the first to preserve hearing in a mouse model of an inherited form of progressive human deafness, report investigators at the University of Iowa, Iowa City, and NIDCD. The study, which appears online in *Cell*, sheds light on the molecular mechanism that underlies a form of deafness (DFNA27) and suggests a new treatment strategy.

"We were able to partially restore hearing, especially at lower frequencies, and save some sensory hair cells," said Dr. Thomas B. Friedman, chief of NIDCD's Laboratory of Human Molecular Genetics and a coauthor of the study. "If additional studies show that small-molecule-based drugs are effective in treating DFNA27 deafness in people, it's possible that using similar approaches might work for other inherited forms of progressive hearing loss."

The seed for the advance was planted a decade ago, when NIDCD researchers led by Friedman and Dr. Robert J. Morell, another coauthor of the current study, analyzed the genomes of members of an extended family, dubbed LMG2. Deafness is genetically dominant in the LMG2 family, meaning that a child needs to inherit only one copy of the defective gene from a parent to have progressive hearing loss.

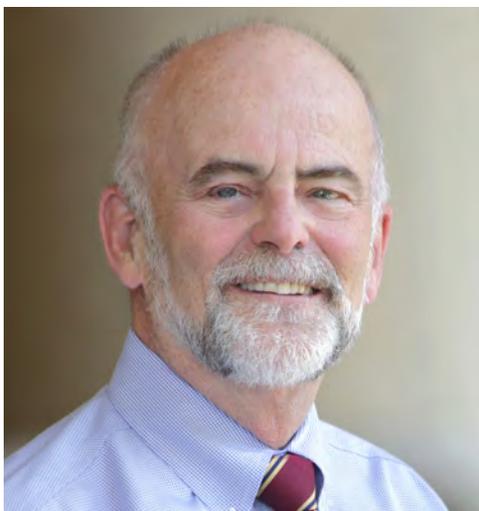
The investigators localized the deafness-causing mutation to a region on chromosome 4 called DFNA27, which includes a dozen or so genes. The precise location of the mutation eluded the NIDCD team, however.

A crucial clue to explain the DFNA27 form of progressive deafness arose from later studies of the mouse RE1 silencing transcription factor, or *Rest*, gene conducted by researchers at the University of Iowa. Dr. Botond Banfi and Dr. Yoko Nakano, lead authors of the current study, discovered that mouse *Rest* is regulated through an unusual mechanism in the sensory cells of the inner ear and this regulation is critical for hearing in mice. Because the human counterpart of the mouse *Rest* gene is located in the DFNA27 region, the Iowa and NIDCD researchers teamed up to reexamine the mystery of DFNA27 progressive deafness.



A new treatment strategy for deafness offers hope.

IMAGE: EMIR MEMEDOVSKI/ISTOCK



Dr. Paul Coates, director of ODP

ODS Director Coates Retires

Dr. Paul Coates, director of the Office of Dietary Supplements, has retired. He came to ODS as director 19 years ago after a 20-year academic career as a human geneticist and 6 years at NIH, where he was introduced to the field of nutrition and the translation of research into policy.

Under Coates' leadership, ODS has become known around the world as a place where the scientific investigation of dietary supplements is encouraged and supported and where trustworthy advice about these ingredients and products can be obtained.

Reflecting on his time at ODS, Coates said, "ODS has grown substantially in size, in budget and in impact over the years and it's been a privilege to be part of that growth. I've had the pleasure of working with truly talented and dedicated people; I hope they have enjoyed it as much as I have."

"Many people can retire with a sense of accomplishment and a job well-done. But far fewer can retire with the knowledge that they were pioneers in a field," said Dr. Barry Kramer, director of the NCI Division of Cancer Prevention and former director of the Office of Disease Prevention (ODP). "Paul has been a pioneer, building the field of dietary supplement science. He has literally written the rulebooks on judging evidence in dietary supplements and has brought a large measure of order to the field."

Coates served as acting director of ODP from December 2010 through September 2012. He also served from 1996 to 1999 as

deputy director of NIDDK's Division of Nutrition Research Coordination (DNRC). In that role, Coates helped to coordinate human nutrition research efforts, both at NIH and between NIH and other government agencies.

"Paul has been my go-to expert on many nutrition topics and on everything related to dietary supplements," said Dr. David Murray, ODP director. "He leaves ODS acting director Dr. Joseph Betz with a full complement of federal staff and contractors, a balanced budget and a new strategic plan for the office."

Dr. Joan McGowan, recently retired director of NIAMS's Division of Musculoskeletal Diseases, commented, "One of the most significant leadership footprints in Paul's tenure at ODS is in the area of vitamin D research. Paul and his staff took the leadership to identify some addressable gaps, not only in research but also in research tools like standards—working across not only NIH but other federal agencies like NIST and

faculty of the University of Pennsylvania School of Medicine and the Children's Hospital of Philadelphia (1975-1993), where he was research professor in the departments of pediatrics and biochemistry/biophysics. His Ph.D. degree in human genetics was from Queen's University in Canada (1972) and his postdoctoral training took place in the department of human genetics and biometry at University College London (1972-1974).

His major research interests for many years focused on inborn errors of human lipid metabolism.

Coates conducted some of the early studies of fatty acid oxidation disorders in infants and children. With an international team of collaborators, he was responsible for defining many of the genetic defects of human mitochondrial fatty acid oxidation. He also has studied the metabolism of intestinal and hepatic lipoproteins in people, to identify the metabolic defects in inherited hyperlipidemias. These studies

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"Many people can retire with a sense of accomplishment and a job well-done. But far fewer can retire with the knowledge that they were pioneers in a field."

-DR. BARRY KRAMER

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FDA, and internationally with a number of national health and nutrition surveys."

Coates was co-chair of the joint DHHS/USDA steering committee overseeing plans for the National Nutrition Summit that was held in Washington in May 2000. He was also a member of the federal steering committee that oversees development of the Dietary Reference Intakes.

Prior to joining DNRC, Coates was NIDDK's program director for the Type 2 Diabetes Research Program (1993-1996) and project officer for the multi-center clinical study called Epidemiology of Diabetes Interventions and Complications (1994-1996). From 1994 until his departure from NIDDK, he maintained an active role in career development and fellowship training in the Division of Diabetes, Endocrinology and Metabolic Diseases.

Before coming to NIH, Coates was on the

have led to a new understanding of the role of environmental factors, such as diet, in the manifestation of genetic disease.

In 2011, Coates received the Conrad A. Elvehjem Award from the American Society for Nutrition for public service in nutrition. In 2013, he was made a fellow of the American Society for Nutrition and was elected to serve a 2-year term as its at-large director. He is lead editor of the *Encyclopedia of Dietary Supplements*, now in its second edition, and associate editor of the *American Journal of Clinical Nutrition*. He has published 140 original papers in the peer-reviewed literature, along with 46 editorials, reviews and chapters and 4 books.

Dr. James Anderson, director of DPCPSI, commented, "I am grateful for Paul's leadership and dedication to ODS. The division and NIH wish him and his wife, Vivian, the very best in their retirement."



Sandi Franklin

Franklin Retires from CSR

BY PAULA WHITACRE

When Sandi Franklin first joined the Center for Scientific Review (then Division of Research Grants) as a messenger in 1988, paper-based communication ruled. The amount of paper-based mail, including grant applications and intra-NIH correspondence, was voluminous.

By the time she retired in May, paper-based delivery made up a smaller part of her responsibilities, but communications remained as important as ever. In different ways, she still facilitated communication between people—such as emailing the management company of Rockledge II to report maintenance issues and ensuring colleagues received their mail and packages correctly, sometimes trouble-shooting during office moves and renovations.

Filing grant applications also used to occupy a large part of her time. “It was drudgery filing all the grants,” Franklin recalled at a CSR party in her honor. “They used to say that—one day—the applications would all come in online. I really thought it would not be in my working career.” In fact, CSR started receiving applications online in 2004 and accepted its last paper application in 2014.

Throughout her career, Franklin listened to audiobooks when she delivered mail—389 in total, both fiction and nonfiction. Among the most memorable, she said, were essays by physician Oliver Sacks and Rabbi Harold Kushner and novels by Stephen King.

Franklin was born in Washington, D.C., and grew up in Silver Spring. She worked for a year at NOAA and for 5 years in the private sector before coming to NIH. “Every day, I would hear about sicknesses, and I felt so proud to be part of an organization that is working to heal people,” she said.

Marilyn Cuzzolina, acting deputy chief of CSR’s Division of Management Services, worked with Franklin for the past three decades and they often rode the shuttle to the NIH campus together. “Sandi was congenial, and was always asking great questions that no one else thought of,” Cuzzolina said, remembering some of her on-point concerns during office renovations.

Franklin also delivers her own messages to the larger world. In addition to reading and listening to books, she enjoys sharing her own expertise and opinions. She wrote a publication with advice on losing weight, based on her own experience losing (and keeping off) a significant amount of weight. A self-described penny-pincher, she also shares tips about saving money. She submits letters to the editor and other pieces to many publications and has had the satisfaction of seeing her name in print numerous times.

Franklin and her husband live in Rockville, with his retirement scheduled for later in 2018. They hope to travel, especially on short trips to smaller towns in the region. She admitted to still getting adjusted to retirement as a new way of life. But just as she adapted in her role as an NIH messenger as technology changed, she expects to embrace this new chapter in life.



NIDA’s Compton Receives West Award for Addiction Research

NIDA deputy director Dr. Wilson Compton recently received the James W. West M.D. Quality Improvement award at the National Association of Addiction Treatment Providers awards ceremony in Denver. He was honored for dedicating the past 25 years of his life to research on addiction. The West Award was established in 2000 to recognize new, innovative and successful addiction treatment advancements, both clinical and operational, that improve the quality and quantity of addiction treatment. The award is named in honor of West, a longtime quality-improvement advocate and medical director emeritus at the Betty Ford Center.

Healthy Volunteers Needed

Vaccine Research Center researchers seek healthy volunteers, 18-60 years old, for a study evaluating the dosage of two investigational products that target HIV. Compensation is provided. There is no risk of infection. For more information, call 1-866-833-5433, email vaccines@nih.gov or visit niaid.nih.gov/about/vrc.

Are You at Risk for Breast Cancer?

NCI is seeking women who are at risk for developing breast cancer. Researchers want to learn more about how certain cells progress to breast cancer. There is one screening visit and one study visit to the Clinical Center to collect cells within the breast ducts. Compensation is provided. More information: Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read about the study at <http://go.usa.gov/chSFC>. Refer to study 02-C-0077.

Patients with ME/CFS Needed

NINDS researchers are seeking individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) where persistent fatigue started after recovery from an infection. Study participation includes an initial inpatient visit of 5-10 days with up to 8 hours of testing each day. Some participants will be eligible for a second exercise stress study inpatient visit of 5-10 days with up to 8 hours of testing each day and overnight measurement at the Clinical Center. No cost for study-related tests and procedures and you may receive compensation for your participation. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) and refer to study 16-N-0058. Read more at <https://go.usa.gov/xQmWj>.

NCCIH Seeks Healthy Volunteers

NCCIH is seeking healthy volunteers 12 and older to participate in a pain perception research study. Compensation is provided. To learn how to participate, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010) or email cc-prpl@cc.nih.gov. Refer to study 16-AT-0077. Read more online at <https://go.usa.gov/xQZkr>.

Volunteers with Leukemia Needed

NHLBI researchers need volunteers with CLL (chronic lymphocytic leukemia) or small lymphocytic lymphoma (SLL) for a new investigational treatment study. Researchers are adding pembrolizumab (an immunotherapy agent) to standard treatment. If you have received treatment for CLL and progressed or have high-risk genetic changes, such as deletion 17p, TP53 mutation, NOTCH1 mutation or complex cytogenetics, you may be interested in participating. To learn more, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more online at <https://go.usa.gov/xQ7RY>. Refer to study 17-H-0118.

'The Directors' Entertain at Camp Fantastic BBQ

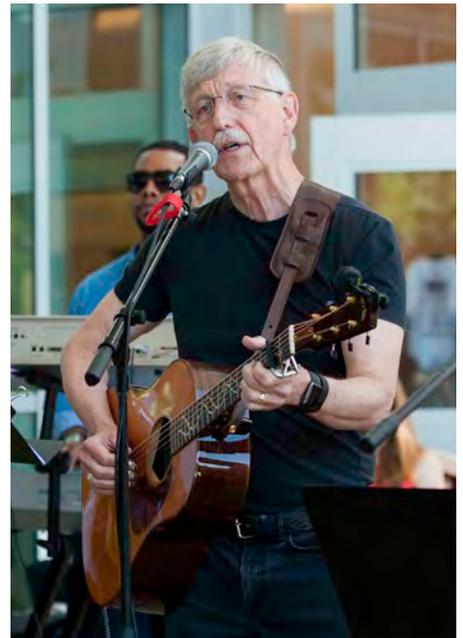
Fronted by NIH director Dr. Francis Collins, The Directors, also known as the Affordable Rock and Roll Act, entertained for 2 hours on June 12 on the south side of the Clinical Center at the annual Camp Fantastic BBQ. "Who said scientists don't know how to rock?" quipped bandleader Collins.

The summer staple raises funds for a camp in Front Royal, Va., that offers a week of freedom and fun each August for pediatric patients at the Clinical Center and other area hospitals.

Food was available from a variety of vendors, free funnel cakes (courtesy of the NIH Federal Credit Union) were distributed and the R&W community market included cupcakes and other baked goods, pickles, candy, fruit, tea and jewelry, among other items.

There was also a silent auction, a variety of games including cornhole and Jenga and a photo booth for quick snapshots.

PHOTOS: MARLEEN VAN DEN NESTE



ABOVE: The Directors rock out, at top, for a group of young fans, below. From top right: NIH director Dr. Francis Collins delivers a tune. Dave Smith of Special Love, Inc., which sponsors Camp Fantastic, tells guests about the camp. The final two photos show some of the market activities that were part of the event.