

## NIH Is Key to Protecting Americans' Well-Being, Azar Says at Town Hall Meeting

BY ERIC BOCK

New Health and Human Services Secretary Alex Azar, who was sworn in on Jan. 29, views himself as a conductor of a symphony orchestra. He says his role isn't to be the best violinist, but to get the best violinist to play his or her best and work in harmony with the rest of the orchestra.

"Whatever crisis comes our way—and there will be crises—my job is not to solve it, but to harness the incredible team we have at this vast, vast organization to conquer that crisis," he said at a Mar. 20 Town Hall meeting in Masur Auditorium.



Alex Azar, new HHS secretary, visits NIH.

"That's a different task than feeling the need to do it yourself."

HHS is "one-fourth of the U.S. government. I calculated the other day that if you stacked us up against [all other] governments, at \$1.2 trillion we are the fifth largest nation on Earth. We are bigger than

the British Empire," he said. "We have been given a lot and to whom much is given, much is expected. And with \$1.2 trillion, we have a lot that we must deliver on."

Azar said that as the premier biomedical research agency in the world, NIH plays an important role in helping HHS meet its mission of enhancing and protecting the well-being of all Americans. The agency has support from people around the country and from its leaders.

While on his first official visit to campus, Azar met with NIH leadership, toured labs and was introduced to patients.

Azar also said it's important "we not get complacent just doing things the way we've always done." He encouraged staff to work within a resource- or choice-constrained environment. Employees should challenge orthodoxies and think of options they'd never considered, he said.

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## SOUL MAN

## Moreland Speaks at First 'Science & Philosophy' Event

BY CARLA GARNETT

Perhaps neuroscientists should focus solely on the brain and leave matters of the mind to philosophers. It's a popular view held by many academic philosophers as well as neuroscientists. After all, both heady disciplines are equally fascinating and multi-faceted, and some investigators of each may only agree that one may never fully understand or explain the other. On the other



Dr. J.P. Moreland

SEE MORELAND, PAGE 6

## KEEP IT SIMPLE

## To Be Productive, Dispense With Complexity, Says Bodell

BY DANA TALESNIK

Life keeps getting busier and more complicated. Are we making things more difficult than they need to be?

"The problem is that complexity is the enemy of meaningful work," said Lisa Bodell, CEO of Futurethink and author of *Why Simple Wins*. "It holds you back from driving growth, from reaching mission, from creating value."



Lisa Bodell

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Celebrating another great CFC season, p. 3.

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**Talent Search Finalists Visit NIH**

On Mar. 12, some 40 finalists (above) in the 2018 Regeneration Science Talent Search spent an afternoon at NIH. Oriented to campus by Dr. Erika Barr, special projects coordinator and director, Community College Programs, Office of Intramural Training & Education, the youngsters visited NIDDK, NHLBI, NIDCD and NINR laboratories and facilities. Last stop was a conversation with NIH principal deputy director Dr. Lawrence Tabak (below, l). The young scientists (below, r) clearly enjoyed the experience.

PHOTOS: CHIA-CHI CHARLIE CHANG



**Celebrate National DNA Day, Apr. 25**

In recognition of National DNA Day, NHGRI will host its annual speaker series with guest Dr. Olivier Noel, CEO of DNAsimple, a startup company that helps accelerate genetic research by connecting DNA donors with research scientists. He has also been featured on ABC's *Shark Tank*. The event will take place on Wednesday, Apr. 25 from 4 to 5:30 p.m. in Lister Hill Auditorium, Bldg. 38A.

Olivier will discuss entrepreneurship and startups in science. For details on the lecture or to register to attend in person, visit <https://www.genome.gov/20519689/celebrate-dna-day-with-nhgri/>.

**Join the Conversation About Alzheimer's Research Participation**

Through Apr. 15

The National Institute on Aging seeks ideas from the wider community—advocates, clinicians, people with dementia, family members, caregivers, researchers and site coordinators—about how to overcome barriers and optimize participation in Alzheimer's research.

Clinical trials and studies are critical to finding a treatment or cure for Alzheimer's disease. Yet efforts in many cases to engage participants in Alzheimer's research have not been able to keep pace with the need. NIA convened this effort, joined by colleagues at the Alzheimer's Association, researchers and others dedicated to trying to solve this problem.

How can you help? Go to NIA's IdeaScale community (<http://bit.ly/ADrecruit>) to contribute your own ideas, browse ideas that have already been submitted, comment and vote for your favorites.

NIA is looking for ideas on how to optimize recruitment by building trusting relationships in local communities, raising national awareness about participation in studies, enhancing the capacity of study sites, tracking progress and cultivating a science of recruitment. The IdeaScale community will be open through Apr. 15.

National DNA Day commemorates the successful completion of the Human Genome Project in 2003 and the discovery of DNA's double helix in 1953. This year marks the 15th anniversary of the project's completion. The goal of the day is to offer students, teachers and the public an opportunity to learn about and celebrate the latest advances in genomic research and explore how those advances might affect their lives.

For more information on National DNA Day, visit <https://www.genome.gov/10506367/national-dna-day/>.



Dr. Olivier Noel

**Share your ideas!**

Visit <http://bit.ly/ADrecruit> to join the conversation with the National Institute on Aging on how to improve Alzheimer's research participation.

[www.nia.nih.gov](http://www.nia.nih.gov)



## NIH 2017 CFC Program a Resounding Success

NIH closed out its 2017 Combined Federal Campaign with a fun-filled appreciation and awards ceremony on Mar. 8 at Lister Hill Auditorium, Bldg. 38A.

“This year’s campaign was a victory for NIH as we exceeded our goal of \$2.2 million toward charities in the U.S. and abroad,” said campaign co-chair and NINDS director Dr. Walter Koroshetz. NINDS served as the lead NIH agency for the 2017 campaign.

The CFC is the federal government’s largest workplace giving campaign, raising millions of dollars for local, national and international charities. This year, some 10,000 charities participated in the National Capital Area CFC.

“I’m proud to say NIH has raised more than \$2 million for the CFC each year for the past 13 years,” said NIH director Dr. Francis Collins, who also served as NIH co-chair and HHS chair. “HHS is one of the lead federal agencies in the CFC and NIH represents about half of all dollars collected by HHS.”

NIH held dozens of events to encourage employee participation. Koroshetz introduced the campaign’s Olympic theme at the kickoff last September, which included remarks by Special Olympics chair Dr. Timothy Shriver and three of NIH’s own Special Olympians. Another campaign highlight was the 3-on-3 Directors’ Basketball Challenge in front of a standing-room only crowd at the Clinical Center outdoor court.

“I don’t think anyone knew how fiercely competitive the institute directors and their teams could be,” said NINDS deputy director

for management Dr. Maureen Gormley, who emceed the awards ceremony. “They played full-contact games and ended with three jammed fingers.”

She had the crowd laughing at several “What would Walter do?” video clips of the games, with multiple choice answers about the NINDS director’s on-court antics. Life-size cutouts of Koroshetz in his game-day T-shirt were posted at various NIH locations during the campaign.

“The results speak for themselves,” said Collins about the NIH response to the campaign theme “Show Some Love.”

During the ceremony, Koroshetz passed the campaign’s Olympic torch to NCATS director Dr. Christopher Austin, who, with NCATS Executive Officer Keith Lamirande, will chair the NIH CFC in 2018. **R**



NIH director Dr. Francis Collins (l) and NINDS director Dr. Walter Koroshetz (r) savor NIH’s achievement with NIH CFC program managers (from l) Debra Gale, Monica Hanson and Christine Brake.



At left, Koroshetz passes this year’s CFC Olympic torch to NCATS director Dr. Christopher Austin, who will chair the NIH CFC 2018 effort. At right, the “What would Walter do?” video tickles the assembled guests.

PHOTOS: CHIA-CHI CHARLIE CHANG



ON THE COVER: Sea lampreys can teach us more about cancer biology, tissue regeneration, evolutionary biology and more. Sea lampreys contain two different genomes and can regrow a severed spinal cord. *NIGMS’s Early-Career Investigator Lecture will feature a researcher who studies the creature; see p. 12.*

IMAGE: JERAMIAH SMITH, UNIVERSITY OF KENTUCKY

### The NIH Record

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Before addressing a town hall (l), Azar attended a briefing with NIH leaders including NIAID director Dr. Anthony Fauci (above, c), who showed the secretary several 3-D print models. At right, NCI Surgery Branch chief Dr. Steven Rosenberg discusses his research with Azar.

**Azar**

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“Every single dollar that we save is a dollar in R01 [an NIH research project grant program] funding that we can put out there,” he said. “Every couple hundred thousand dollars is maybe a young researcher who can get a grant who otherwise wouldn’t be able to get a grant.”

In response to a question from NIH director Dr. Francis Collins about HHS’s ability to respond to a global pandemic, Azar said that while it’s impossible to be fully ready to face infectious disease threats, “we’re better prepared than we were yesterday and we’re better prepared than we were a decade ago.”

Tackling the opioid epidemic will be a key priority for Azar during his time as Secretary. Addiction is a “medical condition, not a

moral failing by those involved,” he said. “We need to use science and evidence-based methods of treating those who have fallen into the trap of addiction.”

One of those methods is medication-assisted treatment, which provides addicts with one of several pharmacologic options, usually combined with social and behavioral interventions.

“We need to be constantly studying what works, disseminating the best information

about what works, the best practices among the states,” he said. “We’re going to be putting a lot of money out there.”

Azar said he spoke recently with the President about the possibility of vaccines for opioid addiction and influenza and immunotherapy for cancer. The President “cares deeply about the mission of NIH and the science that you all are advancing,” he reported.



With Collins (l) and Rosenberg (r), Azar meets patient Dr. Patrick Coughlin and his wife. At right, as a parting gift, Collins presents the Secretary with a set of scrubs. “Just what the world needs,” quipped Azar with a laugh, “a lawyer in the OR!”

PHOTOS: ERNIE BRANSON



## ENGAGEMENT

## Duke's Black Launches NIEHS Diversity Speaker Series

BY KELLY LENOX

Dr. Sherilynn Black of Duke University launched the new NIEHS Diversity Speakers Series recently, sharing compelling results from her previous role as founding director of the Office of Biomedical Graduate Diversity at Duke's School of Medicine. She described new



*“Engaging people from different levels and different areas of the educational experience helps students see that we take this seriously.”*

-DR. SHERILYNN BLACK



approaches that her office pioneered to welcome a more diverse group of students to the school. She is now associate vice provost for faculty advancement at Duke.

“There has been an exponential increase in applications from underrepresented individuals since we started these new recruitment practices [in 2011],” Black said, adding that the number of underrepresented students who ultimately enroll and begin studies in the medical school has nearly doubled.

Efforts to correct disparities in the numbers of men and women in the sciences led to changes that have not yet extended to race, she explained. This is despite research that demonstrates diverse teams have greater success at problem-solving and innovation.

A 2008 book by Dr. Scott Page of the University of Michigan documented the science behind diversity.

“Progress depends as much on our collective differences as it does on our individual IQ scores,” he wrote in *The Difference*. Black pointed out that people too often think of diversity only as a

moral imperative. “They don’t think about it as a scientific concept that is intellectually vital for us to advance as a society,” she said.

“We were so pleased to have someone of Sherilynn’s caliber and achievements to kick off the series,” said Dr. Ericka Reid, who directs NIEHS’s Office of Science Education and Diversity and chairs the series planning committee. “Her insights are

relevant here at NIEHS, as well as in academia.”

Black established a comprehensive program that involved multiple offices and addressed the entire process—from applying,

to success in the program after a student enrolled. “It’s not just going out to conferences and saying, ‘You should apply,’” she said. For example, partnering with other departments across the university is one key to success. “We could not have had the changes that

we’ve had by involving only the School of Medicine,” said Black, listing student groups, administrative offices and others who contributed to the new programs. Her office also partners with academic institutions outside of Duke, numbering 18 so far.



Duke’s Dr. Sherilynn Black launches the new NIEHS series on diversity.



Dr. Ericka Reid welcomes Black to NIEHS.

PHOTOS: STEVE MCCAUF

“Engaging people from different levels and different areas of the educational experience helps students see that we take this seriously,” she said. “And it helps the departments to change the way they’re thinking about admissions.”

Once they arrive on campus, students from backgrounds that are traditionally underrepresented in the sciences continue to face challenges. Using a data-driven approach, Black’s office designed programs to help students overcome those challenges. Examples include social events, workshops on professional development and academic topics, support for qualifying exams and dissertations and an annual retreat for students.

The multifaceted approach is working. “Diversity is now a part of the scientific culture at Duke,” she quoted a faculty member as saying. In her new role focusing on faculty advancement, Black will tackle diversity among faculty, looking at success from the stage of postdoctoral positions all the way through tenure decisions.

## Moreland

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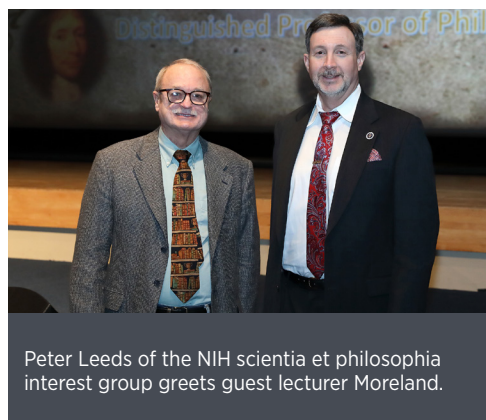
hand, both fields are subject to investigation, testing and the laws of logic. Research in neuroscience can't avoid ultimate implications in the realm of philosophy.

Philosopher Dr. J.P. Moreland explored such dueling perspectives recently in his talk "Philosophical and Empirical-Neuroscience for Determining the Nature and Existence of Consciousness and the Soul," the first lecture in a series hosted by the newly formed NIH *scientia et philosophia* interest group.

The philosopher began by citing a few prominent neuroscientists, including DNA structure co-discoverer Dr. Francis Crick and his colleague Dr. Christof Koch, who co-wrote articles two decades ago on studying consciousness. Moreland said Crick and Koch acknowledged in a 1998 *Cerebral Cortex* article "that the main attitude among neuroscientists is that the nature of consciousness is 'a philosophical problem and best left to philosophers.' Elsewhere they claim that scientists should concentrate on questions that can be experimentally resolved and leave metaphysical reflections to philosophers."

Koch, it should be noted, is world-renowned for his research on the neural bases of consciousness and his articles touting the latest neurobiological tools scientists are using to study it.

Listed by The Best Schools web site as "one of the world's 50 most influential living academic philosophers," Moreland is distinguished professor of philosophy at Talbot School of Theology, Biola University in La Mirada, Calif. He's had considerable time and occasion to contemplate diverse perspectives on consciousness and his conclusion remains constant.



Peter Leeds of the NIH *scientia et philosophia* interest group greets guest lecturer Moreland.

"I think neuroscientific contributions are best when dealing with correlations, causal relations or functional dependencies and discovering more and more details on those," he said. "I think it is philosophical reflection that gets at the very fundamental heart of what exactly is consciousness and what it is that owns or possesses consciousness."

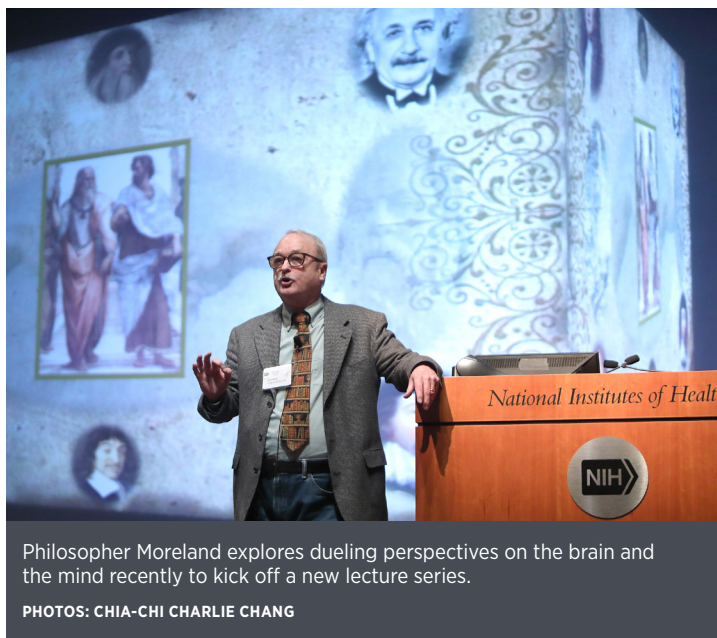
Lest anyone be confused, Moreland defined the brain and brain events and the mind and conscious events as distinctly different. Just because something your brain does—call it a "brain event"—leads your mind to produce something—call it a "mental event"—does not necessarily mean that the two events are the same thing, he explained.

One—the brain—has definable and measurable physical properties that can be shown by electroencephalogram and positron emission tomography scan, for instance. Measurements of the mind's properties, however, are far more elusive and difficult to document "from a third-person perspective, but have a distinct, qualitative texture or a 'what-it-is-like' to them that is made clear to focused, first-person introspection," Moreland said.

Scientists and philosophers have been having mind-body discussions for many years, with all sides endeavoring to clarify and inform their own work as well as its relationship to the others. As a matter of fact, experts from several viewpoints have gathered for hours to debate the topic right here at NIH on at least a couple of occasions within the past 20-odd years.

On Feb. 27 in Masur Auditorium, however, Moreland flew solo and had just 60 minutes that he managed to stretch into 90 and beyond at a post-lecture reception in the FAES bookstore after the formal talk.

In what had all the elements of an advanced grad school course in philosophy—complete with syllabus and bibliography hand-outs upon entry—the professor



Philosopher Moreland explores dueling perspectives on the brain and the mind recently to kick off a new lecture series.

PHOTOS: CHIA-CHI CHARLIE CHANG

talked about ontological questions and "the inadequacy of empirical neuroscientific methodology" to answer them.

Moreland discussed the Law of Identity (also known as Leibniz's Law of the Indiscernibility of Identicals) and why you can't just say the mind is the brain and the brain is the mind.

"Identity is not cause and effect, it's not correlation and it's not functional dependency," Moreland explained. "Just because a mental state functionally depends for its obtaining on a brain state, that is not sufficient to show that the mental state is identical to the brain state."

He went over such basic concepts as "mere property dualism," "physicalism" and "substance dualism" and their differences. To illustrate, he explained how each theory would explain why someone might not be able to experience empathy.

The physicalist, for example, would say the person must have a misfiring neuron somewhere in his brain because otherwise a normal-firing neuron is identical to the feeling of empathy; locate/fix the mechanical problem and his ability to feel empathy should be restored. Not so fast, say the other camps.

Moreland said the two dualists would agree with each other, but for different reasons.

The mere property fan would argue that although empathy is a mind event—"a state of consciousness that can't be reduced to



anything physical”—it happens in the brain and relies on a properly functioning brain in order to occur. “Just like if your eyes get put out, then you can’t have visual sensation, the sense of sight.”

The substance dualist, Moreland noted, would say, “I don’t think the brain is the kind of thing that can have consciousness. The proper nature of the owner of consciousness would have to be a part-less unextended spiritual entity of some kind, but while embodied, there will be an ontological cause-and-effect relationship that goes both ways. If your neurons [in the brain] don’t work then you will not be able to have feelings of empathy in the ego or the self. Occurrences of those feelings still rely on a properly functioning brain, but they are owned by a soul or self.”


Moreland also described the nature of phenomenal consciousness and its five states: sensations, thoughts, beliefs, desires and volitional exercises of active power.

Phenomenal consciousness, he explained, is what people experience as they’re coming to in the recovery room after surgery. Slowly they’re gaining an awareness that only they can experience.

“For any physical object, property or state, we all have equal access to that—including brain measurements—because they’re publicly accessible objects,” he explained. “Consciousness, however, has a way of being known that is not true of any physical state...The person who’s having the state is directly, uniquely aware by way of introspective, private access to the state of consciousness.”

Moreland closed with several arguments for the soul being distinct from the physical body. A person is separate from the gray matter that makes up his or her brain. For one thing, the brain can be divided and even have parts removed, but the individual—the person, the soul—remains the same throughout the diminished capacity of cognitive abilities or loss of brain function.

“The soul is an immaterial substance or thing that contains consciousness and enlivens or animates the body,” Moreland said. “If you don’t like the word ‘soul’ just substitute the word ‘self’ or ‘I’ or ‘ego’ or ‘mind.’”

For details about the new interest group and its upcoming meetings and events, visit <https://oir.nih.gov/sigs/scientia-et-philosophia-interest-group>. 

## ‘CRYO-EM REVOLUTION’

### Subramaniam To Give Mider Lecture, Apr. 11

NCI’s Dr. Sriram Subramaniam will present the annual G. Burroughs Mider Lecture as part of the NIH Director’s Wednesday Afternoon Lecture Series. His talk, “The cryo-EM revolution,” will be held Wednesday, Apr. 11 at 3 p.m. in Masur Auditorium, Bldg. 10.

Subramaniam’s work is focused on the development of advanced technologies for imaging macromolecular assemblies using 3-D electron microscopy and their application to address fundamental problems in infectious disease, cancer and neuroscience.

Research in his lab over the last decade has been guided by the vision that emerging tools in 3-D electron microscopy hold great promise for imaging cells, viruses and protein complexes at high resolution in their native states, thus bridging a major gap in structural biology.

In his talk, he will review examples of recent progress ranging from determination of protein structures at atomic resolution to imaging viruses, cells and tissue at nanometer resolution.

Subramaniam received his undergraduate training in engineering and science at the Indian Institute of Technology in Kanpur, India, a Ph.D. in physical chemistry from Stanford University and completed postdoctoral training in the departments of chemistry and biology at M.I.T. He is currently a senior investigator and founding director of both the Center for Molecular Microscopy and the National Cryo-EM Facility at NCI. He also holds visiting faculty appointments at Johns Hopkins University School of Medicine and the Institute for Advanced Computer Studies at the University of Maryland.

The Mider lecture, established in 1968, recognizes an NIH intramural scientist’s outstanding contributions to biomedical research and honors G. Burroughs Mider, the first director of NIH laboratories and clinics.

For lecture information and reasonable accommodation, contact Jacqueline Roberts, (301) 594-6747 or [robertsjm@mail.nih.gov](mailto:robertsjm@mail.nih.gov).



### Krebs To Speak on Improving Chronic-Pain Management, Apr. 23

On Monday, Apr. 23 at 11 a.m., Dr. Erin Krebs will lecture in Lipsett Amphitheater, Bldg. 10, on “Reframing the Primary Care Management of Chronic Pain.” An internist, Krebs is a health-services researcher and associate professor of medicine at the University of Minnesota Medical School and the Minneapolis Veterans Affairs Health Care System. Her talk is part of NCCIH’s Integrative Medicine Research Lecture Series.

Krebs will discuss the characteristics and clinical needs of patients with chronic pain, including those receiving long-term opioid therapy. She will provide examples of recent and ongoing research and explore opportunities to improve chronic-pain management, including in U.S. military and veteran populations. The lecture will be available at [videocast.nih.gov](http://videocast.nih.gov) and [facebook.com/nih.nccih](http://facebook.com/nih.nccih); more information is at <https://nccih.nih.gov/news/events/IMlectures>.



"Dealing with companies that are complicated makes you not want to work with them," Bodell warned.

PHOTOS: ANDREW PROPP

## Bodell

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Organizations of all sizes can simplify their practices, said Bodell, speaking at a recent Deputy Director for Management seminar in Masur Auditorium. And even small changes can yield big results.

Scripps Health in California, for example, wanted to reduce emergency room wait times, which averaged 8 hours. By simplifying the check-in process, they sped up admissions and increased revenues and patient satisfaction.

Not long ago another large organization, United Parcel Service, rolled out a new policy: no left turns. Bodell said this simple change is saving UPS drivers time and gas on each route while dramatically reducing carbon emissions. And customers are receiving their packages faster.

Simplicity saves time and money and it spares frustration, said Bodell, who related a personal story of trying to buy patio furniture with accumulated credit card points. After an initial runaround, the company mailed her 200 gift cards. Then the web site only let her enter 10 at a time. Many hours and headaches into her supposedly easy online purchase, she was fed up with the company.

"Dealing with companies that are complicated makes you not want to work with them," Bodell said. Successful companies make it simple to get a ride (Uber), share files (Dropbox) or rent a movie (Netflix).

"The startups and groups winning today are operating with speed, because speed is more important than size," Bodell said. "If you're operating with complexity, you can't get there; you can't innovate."

Today's world is increasingly fast-paced and full of distractions, so it's easy to lose focus. "We're conditioned for complexity. We like to multitask...and we create the same level of urgency for everything," said Bodell. "We focus on the daily crap versus the mission-critical."

So much complexity is self-imposed and within our sphere of control, Bodell said. How can we embrace change and simplify so we can get to the meaningful work? It involves shaking things up a bit.

"Change doesn't happen when we're comfortable. It happens when we have productive agitation," said Bodell. "When we're uncomfortable, we question the way things work; we question our assumptions. Right now, we don't question enough and we operate with too much complexity."

It might seem discouraging to try to simplify a large organization, especially a federal one, yet many large organizations are finding ways to ditch complexity in formal and informal ways. Merck, for example, has simplification teams. HBO and Google have bureaucracy-busting sessions.

Simplification can start within a branch or team, or with one person's idea and a willing supervisor. Bodell offered suggestions to help put simplification into practice.

First, identify areas to simplify. Make a detailed list of 20 typical tasks, circle the few you consider most valuable and consider what can be eliminated. Then list desired work that you could finally get around to by eliminating extraneous tasks.

Another suggestion, which requires an open-minded supervisor, is to kill a stupid rule. Choose something that can be changed, said Bodell, something within your sphere of control that can make an impact.

She said an employee at one company asked the CEO to nix the monthly operating report. Much to the employee's chagrin, the CEO disclosed that he created the report, but he also hated it. It was eliminated and nobody missed it.

Employees from every type of workplace identify the same disruptions to their productivity: meetings and emails. "You came [to this job] with a mission and a purpose," said Bodell. "If you can't get to it because of meetings and emails, that's not good."

Another step toward simplification is changing habits. Create a code of conduct unique to your work. Consider eliminating redundancies and prioritizing assignments. Is it possible to shorten meetings, emails and documents? Perhaps resolve to use clearer, jargon-free language.

If you eliminated 1 report or meeting, or whittled down a meeting by 20 minutes, how much more would you get done? Be your own chief simplification officer, said Bodell. Do one thing at a time, see progress and that will inspire you to tackle the next thing. Keep eliminating rules and simplifying.

By killing complexity, the organization builds customer trust, retains staff and shows it can respect individuals' time.

"If you get the work right, you get the culture right, because you can get to the work that matters," she concluded. **R**



## QUEASY QUASISPECIES

**Encapsulated Viruses Are More Infectious Than Single Ones**

BY ERIC BOCK

Once thought to infect cells as a single discrete unit, viruses such as poliovirus, rotavirus and norovirus have now been found to be more infectious when they are wrapped up together in capsules called vesicles than as a single virus, said Dr. Nihal Altan-Bonnet at a Director's Seminar Series in Bldg. 1's Wilson Hall on Feb. 23.

Viruses were thought to enter cells, replicate and exit as single particles that would then go on to infect other cells.

"This is how pretty much everybody—including myself—was thinking of viral transmission," explained Altan-Bonnet, senior investigator and head of the Laboratory of Host-Pathogen Dynamics in NHLBI's Cell Biology and Physiology Center.

Thanks to advances in imaging and spectroscopic technologies, this view is beginning to change as scientists can now observe how viruses transmit themselves between cells.

Another advance in our understanding of viral transmission has come from new genetic sequenc-



Dr. Nihal Altan-Bonnet lectures at a recent Director's Seminar Series in Wilson Hall.

"Having mutations can have profound effects on the next life cycle for each one of these viral progeny," she said, as some mutations can affect a virus's ability to function by preventing replication.

system. So she began imaging cells infected with an RNA virus—poliovirus. A few hours after infection, Altan-Bonnet noticed vesicles containing clusters of polioviruses forming on the cell's surface and budding off.

Before she began her experiments, Altan-Bonnet thought the free poliovirus particles would replicate more efficiently than the same number of poliovirus particles encased in a vesicle. She reasoned that since the particles were independent of one another, they would have opportunity to sample more physical space and infect many more cells.

That was not the case, however. The free poliovirus-infected cell cultures did not yield more virus than the cell cultures infected with vesicles.

She thinks this is because when one or two viruses infect a cell, replication is not that efficient: it takes time for an RNA virus to replicate, and if a virus has a mutation that affects its ability to replicate, the process stops. All the while, the host cell's defenses are trying to stop the virus from replicating.

"A single viral genome, entering a cell, is going to be up against a lot until it gets enough viral proteins made and viral genome replicated to take over the entire cell," she said.

However, when multiple viruses in a vesicle infect a cell, they're "going in with, essentially, an army."



***"A single viral genome, entering a cell, is going to be up against a lot until it gets enough viral proteins made and viral genome replicated to take over the entire cell."***

—DR. NIHAL ALTAN-BONNET



ing methods that have revealed that most viruses don't always copy themselves when they infect a cell—something that's "particularly true for RNA viruses," Altan-Bonnet noted.

This type of virus has its genetic code on strands of RNA. These viruses inject their genetic material into the host cell to replicate themselves.

Whereas previously everyone thought that the progeny viral genomes would be exact copies of the parental viral genome, new sequencing methods have revealed that there is a high level of genetic variation among the replicated RNA genomes.

As a consequence of this finding, these viral progeny genomes are now called "quasispecies."

Altan-Bonnet was curious to know what happened to these viruses as some of them, even with mutations, were still able to transmit infection, go on to another cell and evade detection by the immune

Furthermore, she thinks that different quasispecies carried by the vesicle might work with each other to compensate for each other's weaknesses (i.e. mutations) to become more infectious.

Remarkably, she has found that these vesicles also can transmit infection among organisms. She added that rotavirus, a contagious virus that causes gastroenteritis, and norovirus, an infection that causes sudden vomiting and diarrhea, are traveling as gangs inside vesicles. These vesicles are remarkably stable and stay intact as they pass through the mammalian digestive system.

Altan-Bonnet thinks that the benefits of vesicular transmission, such as generating a high multiplicity of infection, enabling cooperative interactions among quasispecies and suppression of immune responses, are likely exploited by many other viruses including SARS and HIV through other strategies that cluster viruses together so they enter cells in armies. **R**



NIH deputy director for intramural research Dr. Michael Gottesman chats with Altan-Bonnet.

PHOTOS: ANDREW PROPP

## Immune Cells in Retina Can Regenerate

Immune cells called microglia can completely repopulate themselves in the retina after being nearly eliminated, according to a new study in mice from scientists at NEI. The cells also re-establish their normal organization and function.

The findings point to potential therapies for controlling inflammation and slowing progression of rare retinal diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD), the most common cause of blindness among Americans 50 and older. A report on the study was published online Mar. 21 in *Science Advances*.

“Neuroinflammation is an important driver of the death of neurons in retinal diseases,” said the study’s lead investigator Dr. Wai Wong of NEI. “Our study is foundational for understanding ways to control the immune system in the retina.”

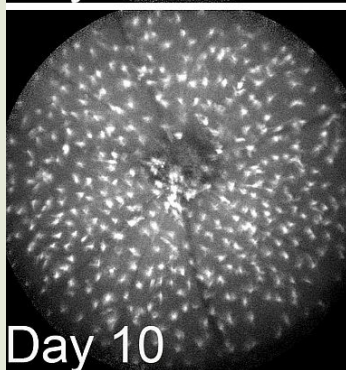
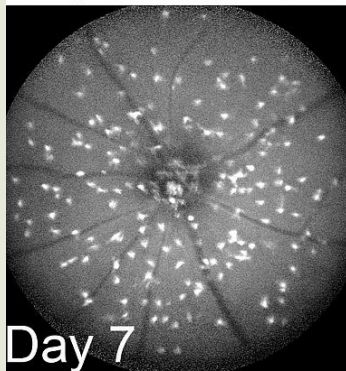
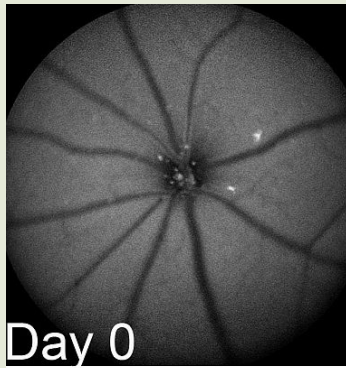
Control of the immune system is important for developing new treatments for a variety of eye conditions, including AMD, RP or for certain types of retinal injury.

The retina is a thin layer of cells in the back of the eye that includes light-sensing photoreceptor cells and other neurons involved in transmitting visual information to the brain. Mixed in with these cells are microglia, specialized immune cells that help maintain the health of the retina and the function of retinal neurons.

Microglia are also present in other parts of the central nervous system, including the brain. In a healthy retina, communication between neurons and microglia is important for maintaining the neuron’s ability to send signals to the brain.

When the retina is injured, however, microglia have an additional role: They migrate quickly to the injury site to remove unhealthy or dying cells. However, they can also remove healthy cells, contributing to vision loss.

Studies show that in degenerative retinal disorders such as AMD and RP, inhibiting or removing microglia can help retain photoreceptors and thus slow vision loss. But return of



Images of mouse retina after being treated with a drug that nearly eliminates immune cells called microglia. On day 0 when the drug was stopped, nearly all microglia are gone; 7 days later, microglia have migrated across the retina, and by day 10 they have increased in number.

IMAGE: WAI T. WONG/NEI

microglia is still important to support the retina’s neurons.

## Islet Transplants Boost Quality of Life for People with Type 1 Diabetes

Quality of life for people with type 1 diabetes who had frequent severe hypoglycemia—a potentially fatal low blood glucose (blood sugar) level—improved consistently and

dramatically following transplantation of insulin-producing pancreatic islets, according to findings published online Mar. 21 in *Diabetes Care*. The results come from a phase 3 clinical trial funded by NIAID and NIDDK.

The greatest improvements were seen in diabetes-related quality of life. Islet recipients also reported better overall health status after transplant, despite the need for lifelong treatment with immune-suppressing drugs to prevent transplant rejection. Researchers observed these improvements even among transplant recipients who still required insulin therapy to manage their diabetes.

The study was conducted by the NIH-funded Clinical Islet Transplantation Consortium.

“Although insulin therapy is life-saving, type 1 diabetes remains an extremely challenging condition to manage,” said NIAID director Dr. Anthony Fauci. “For people unable to safely control type 1 diabetes despite optimal medical management, islet transplantation offers hope for improving not only physical health but also overall quality of life.”

Pancreatic islets release the hormone insulin, which helps control blood glucose levels. In type 1 diabetes, the body’s immune system attacks and destroys the insulin-producing cells in islets.

People with the disease must take insulin to live, but insulin injections or pumps cannot control blood glucose levels as precisely as insulin released naturally from the pancreas. Even with diligent monitoring, blood glucose can often reach levels that are higher or lower than normal.

A low blood glucose level, or hypoglycemia, typically is accompanied by tremors, sweating, nausea and/or heart palpitations. These symptoms prompt the person to eat or drink to raise their blood glucose.

“People with type 1 diabetes who are at high risk for hypoglycemic events have to practice caution every moment, even while sleeping. It is an exhausting endeavor that—like the events themselves—can keep them from living full lives,” said NIDDK director Dr. Griffin Rodgers. “Although islet transplantation

remains experimental, we are very encouraged by these findings, as we are by the rapid improvements in other treatments to help people with type 1 diabetes monitor and manage their blood glucose, including artificial pancreas technology.”

## International Team Confirms New Genetic Mutation Link to ALS

Kinesin family member 5A (KIF5A), a gene previously linked to two rare neurodegenerative disorders, has been definitively connected to amyotrophic lateral sclerosis (ALS) by an international team from several of the world’s top ALS research labs. The findings identify how mutations in KIF5A disrupt transport of key proteins up and down long, thread-like axons that connect nerve cells between the brain and the spine, eventually leading to the neuromuscular symptoms of ALS.

The discovery, published Mar. 21 in *Neuron*, was led by Dr. Bryan Traynor of NIA and Dr. John Landers of the University of Massachusetts Medical School, Worcester, with key funding support from NIA, NINDS and several public and private sector organizations. Genetic data collected by teams of scientists worldwide contributed to the project.

It took a comprehensive, collaborative effort to analyze a massive amount of genetic data to pin down KIF5A as a suspect for ALS, also known as Lou Gehrig’s disease. To zero in on KIF5A, the NIH team performed a large-scale genome-wide association study, while the University of Massachusetts team concentrated on analyzing rare variants in next-generation sequence data. More than 125,000 samples were used in this study, making it by far the largest such study of ALS performed to date.

“The extraordinary teamwork that went into this study underlines the value of global, collaborative science as we seek to better understand devastating diseases like ALS,” said NIA director Dr. Richard Hodes. “These types of collaborative data collection and analysis are important in identifying the pathways underlying disease and in developing approaches to treatment and prevention.”



## Research!America Honors Fogarty's Glass

FIC director Dr. Roger Glass received the 2018 Geoffrey Beene Builders of Science Award for his research and advocacy efforts in global health during Research!America's annual honors dinner on Mar. 14.

Glass was cited for his leadership of NIH efforts to transform African medical education, establish research training programs in West African countries that saw widespread Ebola infection, expand Fogarty's Scholars and Fellows program for early-career scientists and help found the Global Alliance for Chronic Diseases. He was also recognized for his research on rotavirus, norovirus and cholera, and the recent WHO approval of a new low-cost rotavirus vaccine he helped develop over the last three decades.

The award was presented by Mara Hutton, vice president of the Geoffrey Beene Foundation, which was established to honor the late fashion designer and to support research in cancer and Alzheimer's disease. Hutton noted that Fogarty is the most leveraged organization at NIH, with nearly 90 percent of its grants receiving co-funding from other institutes or centers. She thanked Glass for his commitment to improving the health of the world's most vulnerable people.

"He has a conscience for doing the right thing," she said. "He has empathy, tenacity and his leadership reflects the best in the American scientific research community."

Accepting the award, Glass acknowledged NIH director Dr. Francis Collins and other NIH leaders in the audience for their support of Fogarty's cross-cutting global health research and training programs.

"They have all been involved in investments in global health science and this is the most creative, dedicated group of scientists the nation has ever seen," Glass said. "Together they are directing the largest biomedical enterprise in the world that makes discoveries that change our lives and improve the health of people everywhere."

## NIAMS's Katz Receives Dermatologist Academy's Highest Tribute

NIAMS director Dr. Stephen Katz was recently awarded the Gold Medal by the American Academy of Dermatologists (AAD). The medal is the academy's highest tribute and is presented on a "very selective basis to acknowledge outstanding and exceptional service in the field of dermatology."

Katz has been director of NIAMS since August 1995 and was also a senior investigator in NCI's Dermatology Branch from 1974 to 2014. He has focused his research on immunology and the skin.

His work has demonstrated that skin is an important component of the immune system, both in its normal function and as a target in immunologically mediated disease.

Katz and his colleagues have studied Langerhans cells and epidermally derived cytokines, in addition to adding considerable new knowledge about inherited and acquired blistering skin diseases.

NIAMS director Dr. Stephen Katz (r) receives the highest AAD award from the academy's immediate past president Dr. Henry Lim at AAD's 2018 annual meeting.



FIC director Dr. Roger Glass (c) receives the 2018 Geoffrey Beene Builders of Science Award from Beene Foundation executives Tom Hutton and Mara Hutton during the recent Research!America advocacy awards dinner.

PHOTO: RESEARCH!AMERICA

## Flu Vaccine Study Recruits Healthy Volunteers

Vaccine Research Center researchers seek healthy volunteers, 18-70 years old, for an investigational influenza vaccine study. Scientists are testing new vaccines to determine whether they are safe and effective in preventing the flu. Compensation is provided. For more information, call 1-866-833-5433 or email [vaccines@nih.gov](mailto:vaccines@nih.gov). Read more at <https://go.usa.gov/xNH7U>. Refer to study VRC316.

## Healthy Volunteers Needed for Malaria Vaccine Study

NIAID researchers seek healthy volunteers, ages 18-50, for a study testing an investigational malaria vaccine at the Clinical Center. Compensation is provided. To learn how to participate, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xX5t4>. Refer to study 17-I-0067.

## 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/xnYae>. Refer to study 17-H-0118.

## NIDDK Study Seeks Overweight Men

NIDDK researchers are seeking overweight/obese men, 18-50 years old, to participate in a study looking at a potential link between consumption of processed foods and the development of metabolic syndrome. Participants will be required to remain in the hospital for 1 month on 2 separate occasions and eat only the meals provided by NIH during that time. Compensation is provided. To learn more, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xRRE7>.

## NHLBI Study Needs Patients

NHLBI researchers are testing two low doses of danazol on individuals with short telomere disease and bone marrow disease, lung or liver disease. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xnPYm>. Refer to study 18-H-0004.



Dr. Jeremiah Smith (l) studies the sea lamprey (above). As one of the first organisms to have a backbone, the sea lamprey is considered a “living fossil.” It is also considered a delicacy in several European and Asian countries. In the Great Lakes, it is a parasitic pest that has decimated trout populations. The image above is courtesy Wikimedia Commons, U.S. Environmental Protection Agency; see a lamprey image by Smith on the top of page 1.

APR. 17

## Early-Career Investigator To Explain Career Path, Research On Ancient Vertebrate

Pop quiz—which organism:

- Has a backbone but no jawbone
- Contains two different genomes
- Can make a full recovery after its spinal cord is severed

but a predatory parasite that decimates native species elsewhere?

Okay, it’s the sea lamprey.

At the 3<sup>rd</sup> annual NIGMS Director’s Early-Career Investigator Lecture, Dr. Jeremiah Smith, an assistant professor at the University of Kentucky, will describe how his research on this organism is shedding light on cancer biology, tissue regeneration and vertebrate evolution.

Titled “Ancient Bloodsuckers, Disposable Genes and What It All

Means,” the lecture takes place Tuesday, Apr. 17 at 2 p.m. in Natcher Conference Center, Balcony B.

Open to everyone in the scientific community, the lectures are designed to introduce students at the undergraduate level and beyond to cutting-edge science while inspiring them to pursue biomedical research careers. After a 30-minute lecture, Smith will answer questions from students about his research and career path.

NIH trainees are encouraged to attend the lecture and submit questions in advance via [info@nigms.nih.gov](mailto:info@nigms.nih.gov) or #ecilecture on Twitter. For details, see <https://www.nigms.nih.gov/News/meetings/Pages/2018-NIGMS-Directors-Early-Career-Investigator-Lecture.aspx>.

## Postbaccalaureate Poster Day 2018

Postbac Poster Day is scheduled for Wednesday, May 2. It will be held at Natcher Conference Center from 10 a.m. to 3:30 p.m. The Poster Day keynote address will begin at noon followed by presentation of Postbac Distinguished Mentoring Award(s) to NIH investigators selected by the postbacs. Poster session I will take place from 10 a.m. to noon and poster session II is from 1:30 to 3:30 p.m.

Postbac Poster Day provides an opportunity for postbacs to share the research they have been conducting at NIH and at the same time develop their scientific communication and networking skills. Posters will be reviewed by teams composed of graduate students, postdocs and staff scientists/clinicians. The authors of the top 20 percent will receive a letter acknowledging their accomplishments.

Investigators, staff scientists and scientific administrators can make an important contribution to the event by visiting posters and engaging the authors in discussion. For more information, visit [https://www.training.nih.gov/postbac\\_poster\\_day](https://www.training.nih.gov/postbac_poster_day).



Bike to Work Day 2011 featured a novel 2-wheeler.

## Bike to Work Day, May 18

The NIH Bicycle Commuter Club and the Division of Amenities and Transportation Services invite you to celebrate Bike to Work Day on Friday, May 18. Join your friends and colleagues as we celebrate bicycling as an environmentally friendly, fun and healthy alternative to driving.

Register for free at [www.biketoworkmetrodc.org](http://www.biketoworkmetrodc.org). As the event approaches, DATS will send reminders to the NIH community with updates and NIH-affiliated pit stops.

Remember to enter your employer as “National Institutes of Health.” This will help us defend our title as the employer with the most participants.

Also, anyone who registers gets a free 2018 Bike to Work Day T-shirt (available while supplies last).

## 5K Set to Mark National Minority Health Month, Apr. 11

On Wednesday, Apr. 11 from 11:30 a.m. to 1 p.m., join the 2nd Minority Health 5K Walk/Run in recognition of April as National Minority Health Month.

The event will take place on the main campus in front of Bldg. 1. Don’t forget your NIH ID (the course goes outside the perimeter fence) and follow the walk/run at #minorityhealth5K. Register today at <https://nimhd.nih.gov/contactform/registration-form02.html>.

The event is jointly sponsored by the National Institute on Minority Health and Health Disparities, the Office of Research Services and the Recreation and Welfare Association Fitness and Wellbeing Program.