

SCIENTISTS ONE, SUPERBUG ZERO

Personal Quest Resurrects Phage Therapy in Infection Fight

BY CARLA GARNETT

At one life-or-death moment, Dr. Tom Patterson was a snake.

In November 2015, he and wife Dr. Steffanie Strathdee were merely two scientists on holiday. The couple had been vacationing on a cruise in Egypt. After a day of pyramid probing and an evening meal aboard ship, Patterson fell ill. Food poisoning, he surmised. A dose of routine antibiotics, they thought, and he'd be ship-shape by morning. Only he wasn't. Sicker and



A now hale and hearty Dr. Tom Patterson visits NIH to describe a hardy superbug.

sicker he grew, as symptom after symptom occurred. Vomiting, abdominal pain, then a back ache. He was diagnosed with gallstone pancreatitis, but that was the least of their problems. That he had some kind of serious infection eventually became clear, but precisely what was wrong—and how to fix it—remained a mystery that would confound

physicians and scientists, and inevitably force Patterson to make medical history.

At Lister Hill Auditorium on Mar. 1 to discuss their harrowing adventure, the erstwhile tourists—she, associate dean of global health sciences at the University of California, San Diego, and he, psychiatry professor in residence there, and both current NIH grantees—are on a mission now, some 3 years after facing down a deadly superbug.

Now completely recovered, Patterson and Strathdee feel compelled to tell how they won—with considerable help from the global village of scientists via social media and PubMed, the online collection of 29 million biomedical literature citations.

“We decided that we needed to tell our story because total strangers stepped up to help us,” said Strathdee, “and we want to pay it forward.”

SEE SUPERBUG, PAGE 6

THE MULTITUDES WITHIN

Ghedin Explores Our Inner Societies

BY RICH MCMANUS

There is bad news for the world's solipsists. Our bodies are crowd scenes—whether you're a hermit or a people person—and the types and number of characters we host can mean the difference between peace in the valley (health) and discordant strife (disease).

In her lecture on microbial networking, Dr. Elodie Ghedin, professor of biology and global public health and director of the Center for Genomics and Systems Biology at New York University, described the neighborhoods where viruses, bacteria and fungi cohabitate in our bodies, in both sickness and health.

“We no longer talk about one pathogen anymore, but about polymicrobial infection,” said Ghedin, who, in addition to having been a fellow in NIAID's Laboratory of Parasitic

SEE GHEDIN, PAGE 8

ON THE BRAIN

Searching for Breakthroughs in Brain Injury Research

BY DANA TALESNIK



Dr. Patrick Kochanek

The field of traumatic brain injury (TBI) has burst onto the public's radar in recent years, bolstered by publicity surrounding sports-related concussions and war-related injuries. The result has been increased funding and research to find new treatments.

“Traumatic brain injury has gone wild in the last few years, with chronic traumatic

SEE KOCHANEK, PAGE 4



What a lab's come to, after 10 years? See p. 12.

ALSO THIS ISSUE

Briefs	2
Workshop Addresses Lack of Diversity in Biomedical Workforce	3
McGowan Named ORS Director	5
Milestones	9
Digest	10
Volunteers	11
Seen	12

'P2P' Program Seeks New Topics

The NIH Office of Disease Prevention (ODP) is seeking new topic proposals for the Pathways to Prevention (P2P) program. P2P addresses complex public health issues that have incomplete or underdeveloped research and for which there is a need for evidence review that assesses the published literature and current state of the science.

Each year, the P2P program conducts workshops that identify research gaps and suggest ways to move the field forward. Seven such workshops have taken place so far.

Workshop proposals may be submitted by any group of two or more institutes, centers or offices and may have multiple co-sponsoring organizations. Other groups, such as other government agencies or trans-agency workgroups, professional societies and advocacy organizations, may also propose topics with an NIH IC as a sponsor.

A workshop on Achieving Health Equity in Preventive Services will take place in June 2019.

ODP is available to discuss the P2P process and workshop ideas. For more information, email NIHP2P@mail.nih.gov.

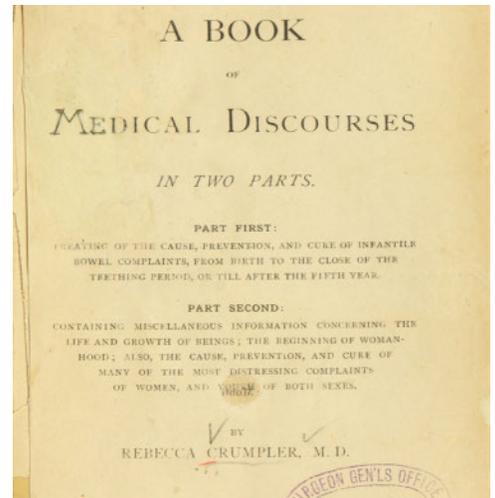


NIH Ranked First Among Top 20 Employers, EOP Poll Finds

NIH took the number 1 spot in the "Top 20 Government Employers Equal Opportunity 2018 Readers Choice" poll, hosted by Equal Opportunity Publications, Inc. (EOP). Readers were asked to name employers that would provide a positive working environment for members of underrepresented groups and places they would most like to work.

Since 1968, EOP has pioneered in diversity recruitment with a portfolio of seven national career magazines, a diversity website, online job board and career expos for women, minority groups and people with disabilities.

In the poll, NIH topped such other government agencies as National Security Agency, IRS and the Departments of Transportation and Labor. Winners also are entitled to post the EOP graphic. To see the emblem and the rest of the top 20, go to <https://bit.ly/2EUMQ2R>. Visit the awards site at <https://www.eop.com/awards-EO.php>.



At left is a portrait of Dr. Elizabeth Blackwell, who in 1849 became the first woman to earn an M.D. degree from an American medical school. At right is Dr. Rebecca Lee Crumpler's *A Book of Medical Discourses*, 1883.

PHOTOS: NATIONAL LIBRARY OF MEDICINE

NLM Observes Women's History Month

During the month of March, NLM is featuring historic medical books written by women as part of its daily tours of the library and the banner exhibition *Rise, Serve, Lead! America's Women Physicians*, which is based on the new website of the same name.

The books include *Medicine as a Profession for Women* (1860) by Elizabeth and Emily Blackwell, who argue that opening medicine to women would benefit both women and men, and *A Book of Medical Discourses* (1883) by Rebecca Lee Crumpler, the first African-American woman to write a medical text. She describes domestic remedies for ailments, how to care for a newborn and general scientific information about anatomy and development. The banner exhibition highlights women breaking barriers, healing communities, advocating, leading and nurturing the future.

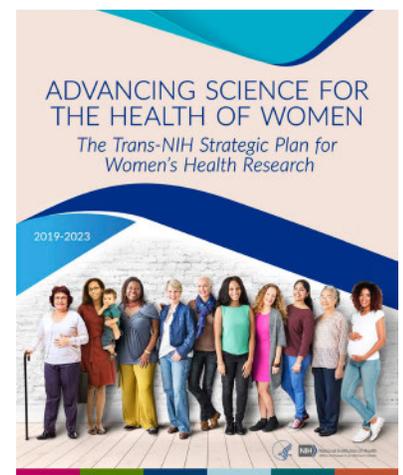
Tours of NLM begin at 1:30 p.m. in the Visitor Center, Bldg. 38A. The banner exhibition on women physicians is on display in the lobby of Bldg. 38. Both are free and open to the public. For viewing more historic texts by women, complete the NLM visitor tour form online at www.nlm.nih.gov/about/vcenter.html.

ORWH Publishes Trans-NIH Strategic Plan

The Office of Research on Women's Health recently published *Advancing Science for the Health of Women: The 2019-2023 Trans-NIH Strategic Plan for Women's Health Research*. The plan provides a framework for coordinating NIH efforts to advance science for the health of women while keeping pace with rapid changes in science and technology, evolving public health needs and legislative mandates.

Developed in consultation with NIH institutes, centers and offices, external stakeholders and the public, the 5-year plan represents a multipronged approach to advance a vision "in which sex and/or gender influences are integrated into the biomedical research enterprise; every woman receives evidence-based disease prevention and treatment tailored to her own needs, circumstances and goals; and women in science careers reach their full potential."

The plan paves the way toward scientific and workforce efforts that ultimately benefit the health and biomedical research careers of women. Population health indicators over the past two decades reveal substantial inequalities between the sexes and demonstrate even greater disparities between women and men in the United States than in peer nations, including a life expectancy for U.S. women lower than that in high-income peer countries. Additionally, maternal mortality rates have risen for some populations of U.S. women, even as these rates decline in other high-income countries. The strategy represents NIH's commitment to address these alarming trends. For details, see orwh.od.nih.gov/sites/orwh/files/docs/ORWH_Strategic_Plan_2019_02_21_19_V2_508C.pdf.



Workshop Addresses Lack of Diversity in Workforce

BY REBECCA NEWTON

In collaboration with the Association of American Medical Colleges, leaders of the National Institute on Minority Health and Health Disparities gathered on campus recently to address barriers contributing to the lack of diversity in the biomedical workforce. This second phase of a 3-phase approach brought together officials from NIH, academia and leading medical associations.

Dr. Ross McKinney Jr., chief scientific officer at AAMC, presented provocative data outlining ways to tackle the issue at hand. Also present were NHLBI director Dr. Gary Gibbons and NIGMS director Dr. Jon Lorsch.

During the first phase, AAMC hosted representatives from participating medical associations at their D.C. headquarters to outline needs and



Above, NIGMS director Dr. Jon Lorsch discusses strategies during the meeting. Below, workshop collaborators gather for a group photo.

PHOTOS: REBECCA NEWTON

define goals for the initiative. Focus groups noted lack of mentorship and funds to support programs and insufficient resources for innovation as key challenges.

The charge for the day was to develop novel approaches, action items and partnering methods. While NIMHD's Scientific Advancement Plan recognizes the institute's commitment to enhancing the diversity of the biomedical workforce by



NIMHD director Dr. Eliseo Pérez-Stable weighs in during a small group discussion.

supporting and promoting training of minority health and health disparities researchers, leaders at the workshop urged a collective effort to help move the needle.

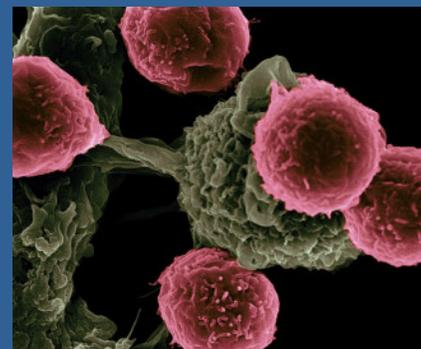
According to the National Science Foundation, Hispanic scientists accounted for only 8.5 percent of health-related occupations in 2015; blacks accounted for only 6.4 percent of this workforce. NIMHD director Dr. Eliseo Pérez-Stable recognizes the benefit of a diverse research workforce. He presented recent estimates from the U.S. Census Bureau indicating that racial and ethnic minority populations in the United States will grow to become half of the population by 2060. "If our workforce is so discordant with the population, then we have a problem," he said.

Making room for the diverse perspectives and cultural sensitivities of the nation's minority racial/ethnic scientists is crucial to improving the health needs of a growing minority population. All doctoral-level scientists—whether laboratory scientists, computation scientists, data scientists, epidemiologists or social scientists—have the opportunity to enrich their science by working on projects within heterogeneous teams. Those that lack diversity miss out on the opportunity to gain a variety of insights from those of varied backgrounds and experiences.

Working with scientists who represent underserved/health disparity populations is not only a good practice but also necessary to sustain public trust and increase minority participation in clinical trials. During breakout sessions, a suggestion was made to engage larger institutions to work with

smaller regional institutions to recruit, mentor and develop diverse talent and train staff with a focus on diversity—a component of NIH's Scientific Workforce Diversity Toolkit. Another idea was to provide mentoring within historically black colleges and universities and science, technology, engineering and mathematics high schools located in areas serving underrepresented students.

The third and final phase of the 3-phase approach will place an emphasis on forming an innovative process to produce deliverables and establishing realistic target dates for their completion. **R**



ON THE COVER: Vaccine-based immunotherapy from novel nanoparticles systems. Researchers at the Texas Center for Cancer Nanomedicine are creating particle-based vaccines for cancer therapy. The particles carry molecules that stimulate immune cells and cancer antigens (proteins) that direct the immune response. This scanning electron microscope image shows dendritic cells (pseudo-colored in green) interacting with T cells (pseudo-colored in pink). The dendritic cells internalize the particles, process the antigens and present peptides to T cells to direct immune responses.

IMAGE: VICTOR SEGURA IBARRA & DR. RITA SERDA, NCI

The NIH Record

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

Editor: Rich McManus
Rich.McManus@nih.gov

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

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

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



The *NIH Record* is recyclable as mixed paper.

NIH National Institutes of Health
Turning Discovery Into Health

Kochanek

CONTINUED FROM PAGE 1

encephalopathy and the recognition that concussion is not a badge of honor but is actually a disease,” said Dr. Patrick Kochanek, director, Safar Center for Resuscitation Research at the University of Pittsburgh School of Medicine. Kochanek, also a professor of critical care medicine, anesthesiology and pediatrics, spoke at a recent CC Grand Rounds Great Teachers lecture in Lipsett Amphitheater.

TBI can cause a range of symptoms, depending on the severity. Long-term effects can include difficulties with cognition, communication and mental health.

“It’s being linked to every chronic neurodegenerative disease under the sun, which has helped spearhead this tremendous interest, so I’ve been calling it the golden age of traumatic brain injury research,” said Kochanek, noting a flurry of collaborative studies now funded by NIH, the Department of Defense, the National Football League and other organizations. “And the trickle into severe traumatic brain injury from all of this has also been spectacular.”

Kochanek attributed current progress to a multi-center consortia approach that honors the vision of the late Dr. Peter Safar, the namesake of the institution he directs. Using this strategy, researchers across multiple sites are converging to identify new biomarkers of brain injury and test therapies in preclinical and clinical studies.

Over the past decade, TBI research has stagnated. Some standard treatments for acute TBI have been archaic and crude, such as intracranial pressure monitoring, which involves inserting a catheter into a drilled hole in the skull. But new drugs tested in clinical trials proved ineffective. Not one neuroprotective therapy made it from bench to bedside, said Kochanek.

The roadblocks have been numerous, from genetic differences in response to injury and treatment to the inability to



Kochanek has high hopes for a U.S. Army-funded preclinical drug and biomarker screening consortium for head injury—Operation Brain Trauma Therapy.

PHOTOS: CHIA-CHI CHARLIE CHANG

replicate study results. Preclinical studies also have uncertainties. Do animal models truly mimic the disease? And what’s the proper dosing between species?

It’s possible that treating the various kinds of TBI—contusion, edema, hematoma, axonal injury among them—may require different precision therapies.



“It’s being linked to every chronic neurodegenerative disease under the sun...so I’ve been calling it the golden age of traumatic brain injury research.”

—DR. PATRICK KOCHANEK



“These diseases, although they’re all TBI, are pretty different and the pathobiology, the treatment for them, and the monitoring and long-term outcome would be expected to be different,” said Kochanek. “So robust therapy that would show benefit across all of them would be necessary.”

One major multi-center initiative is Operation Brain Trauma Therapy (OBT),

a U.S. Army-funded preclinical drug and biomarker screening consortium for head injury. Researchers at multiple centers are testing therapies across multiple models at the same time.

Two biomarkers of interest to DoD are the proteins UCH-L1 and GFAP, which are measured across all the studies. A scoring

matrix rates results for cognitive outcome, motor function, lesion volume and tissue loss. So far, after testing more than 1,500 rats and building a 5,000+ biomarker repository, researchers have made some interesting findings.

“Our first strategy,” said Kochanek, “was to go after low-hanging fruit drugs, FDA-approved for other uses already that could be rapidly translated.”

They began testing 12 promising drugs and became disheartened to learn that the first 4 showed no improved cognitive outcome. There was little literature related to TBI on the fifth drug, levetiracetam,

though they found a study to try to replicate. Success! It was the only drug to produce significant benefit on cognitive outcome.

“Here’s a drug that’s a neuro-developed agent and, of only one preclinical study in TBI, had the most points [in our matrix],” said Kochanek.

The research teams also were encouraged by the sixth drug, glyburide, which reduced necrosis and swelling in the contusion model, the only drug of the 12 to reduce contusion volume 3 weeks after injury.

The biomarkers also proved highly predictive. In the levetiracetam study, the 24-hour GFAP levels predicted a reduction in 21-day lesion volume.

“This was really exciting, that a serum biomarker could [be predictive] in a rigorous, multi-center study,” said Kochanek. “It did not in the other models, which did not show hemispheric tissue loss.”

Last year, the FDA approved the first blood test to evaluate mild concussion in adults based on clinical data generated by OBTT. The test measures levels of UCH-L1 and GFAP released from the brain into blood within hours of a head injury.

“I think the biomarker story like this is really going to catch on,” not only for diagnosing TBI, but also for other uses such as predicting risk of future symptoms and in trauma units.

The remaining 6 drugs in the 12-drug study are still in testing, along with additional biomarkers. Researchers continue looking for personalized therapies that might work for a single TBI type, such as contusion, as well as a magic bullet that might work in all models of TBI.

Preliminary experiments suggest the multi-center strategy can be useful in performing rigorous, reproducible testing, said Kochanek. The OBTT model has received a great deal of press and is generating interest in other fields of acute medicine and neuro-critical care. **R**

McGowan Named ORS Director

Colleen McGowan is the new director of NIH’s Office of Research Services. She comes to ORS from the Clinical Center, where she most recently served as executive officer. In this capacity she oversaw hospital administrative operations for a 2,000-person workforce including human resources and workforce management, patient support services, nutrition, emergency management, social work, spiritual care, medical logistics, housekeeping, facilities infrastructure and space management for the 870,000-square-foot hospital.



McGowan previously served as deputy chief operating officer overseeing acquisition activities and as senior administrative officer for many clinical departments since 2001. She has also served on many trans-NIH groups, including chair of the management intern subcommittee and co-chair of the NIH human resources advisory committee.

Prior to her long history with the CC, McGowan was a Medical Service Corps officer in the U.S. Air Force, working as director of Regional USAF/VA Joint Ventures and director of managed care at David Grant U.S. Air Force Medical Center in California. She directed all managed care activities for a 38,000-patient population, including benefits, marketing, enrollment and claims payments related to health plans.

McGowan was also an administrative fellow with Johns Hopkins Hospital, where she worked for the vice president for administrative services and the director of international services. Earlier in her career, she served as chief financial officer/human resources director at Hill Air Force Base in Utah.

She has a bachelor of science in business administration from the University of North Carolina at Chapel Hill and a master’s degree in health care administration from U.S. Army-Baylor University.

NINDS’s Hallett Receives Brain Stimulation Award

Dr. Mark Hallett, chief of the NINDS Medical Neurology Branch and the human motor control section in the Division of Intramural Research, recently received the 2019 International Brain Stimulation Award from the journal *Brain Stimulation: Basic, Translational and Clinical Research in Neuromodulation*.

The award—which honors outstanding contributions that have profoundly influenced the field of brain stimulation—was presented on Feb. 25 during the 3rd International Brain Stimulation Conference in Vancouver, Canada.



Hallett was recognized for the groundbreaking contributions he has made to enhance understanding of the physiological principles of brain stimulation. His work has included studies of brain reorganization in various disorders and after learning a new motor task, the effects of fatigue on corticospinal excitability and the concept of surround inhibition in the pathophysiological mechanisms of dystonia.

At the conference, Hallett presented the award plenary lecture titled “How to Move an Individual Finger,” which reviewed his laboratory’s work on surround inhibition. “I was very pleased and honored by this award, which actually recognizes the hard work of the many outstanding fellows who have contributed to the human motor control section,” he said.

Hallett earned undergraduate and medical degrees from Harvard University and received his neurology training at Massachusetts General Hospital. He had fellowships in neurophysiology at NIH and in the department of neurology at the Institute of Psychiatry in London.

Before joining NIH in 1984, he was chief of the Clinical Neurophysiology Laboratory at Brigham and Women’s Hospital in Boston and associate professor of neurology at Harvard Medical School. During his career at NINDS, his work has centered on understanding the physiology of normal human voluntary movement and the pathophysiology of different movement disorders.—
Shannon E. Garnett

Wrong Valley

Strathdee and Patterson were supposed to be exploring the Valley of the Kings, the burial grounds of pharaohs, along the Nile in Luxor. Instead, he was skirting the “valley of the shadow of death,” and she was scrambling for answers, courtesy of something no one could seem to pinpoint.

Days turned into weeks; weeks became months. Doctors had exhausted all antibiotic treatment options and Patterson was dying, comatose with organs failing. At hospital bedside, Strathdee knew time was short. He was too weak to take much more. With his life in the balance, she wondered, could she even get through to him for the ultimate decision?

“Honey I know you’re trying very hard to fight this thing,” she said to him. “The doctors don’t have any antibiotics left and I need to know if you want to live. If you want to let go, I’ll understand, but I want to grow old with you. I love you very much. So if you want to live, please squeeze my hand and I will leave no stone unturned.”

Patterson heard her through his addled mind but understood. However, amid all his medical issues, he was also dealing with a practical problem, one of evolution and anatomy.

“I was actually a snake,” he recalled, describing one of several particularly vivid hallucinations

he endured throughout his health crisis. “I mean in my mind, what you need to understand is this isn’t like, ‘I kind of remember being

a snake.’ In my memory there is this place where I was a snake. So when Steff asked me to squeeze her hand if I wanted to live, it was a challenge because snakes don’t have hands. I had to figure out how to wrap my body around her hand and squeeze, and I didn’t know my own strength as a snake, so I squeezed too hard.”

By the Numbers

Six bacterial pathogens make up the so-called “ESKAPE” superbugs that can resist most commonly used antibiotics. Each



Dr. Steffanie Strathdee, with husband Patterson, recounts their ill-fated vacation to Egypt that resulted in the health fight of Patterson’s life and eventually a new research and treatment center dedicated to expand the kind of phage therapy that saved him.

letter in the acronym stands for a deadly organism; Patterson’s foe proved to be a strain of the “A”—*Acinetobacter baumannii*. The hardy bacteria, known to thrive in hospitals, can survive multiple temperatures, conditions and environments.

It had taken two medevacs via Lear jets



“I realized that my husband was becoming somewhat of a poster child for this dystopian future of the superbug crisis.”

-DR. STEFFANIE STRATHDEE



and 7 ambulances over 3 continents and several countries to get Patterson back home to San Diego. Still, familiar surroundings hadn’t presented a cure.

Countless champions—and myriad fortuitous circumstances—factored into Strathdee’s quest to save her husband. That’s partially why the couple documented their story in their new book, *The Perfect Predator*, and why they’re heralding the international scientific community at large.

“If it wasn’t for PubMed, our university hospital at UC San Diego and a global village

of researchers from around the world—like Dr. Chip Schooley and other renowned NIH-funded researchers—he would be dead and I would be holding an urn instead of his hand.”

Strathdee had rejoiced when she felt Patterson’s clasp, which meant he wanted to continue the battle. It also meant she

had to deliver on what seemed an impossibly complex and circuitous search for something to arrest the infection that was by then throughout Patterson’s body.

About a century and 3 decades—respectively,

that’s the period since Western medicine has seriously considered using bacteriophage (“phage” for short) to eat infections like Patterson’s, and the time that has elapsed since Strathdee was a microbiology undergrad familiar with this field of science.

Search Every Sewer?

The rise and success of antibiotics relegated phage therapy research to the back burners of science, particularly in the U.S.

Phages are notoriously finicky and ESKAPE infections are just as fussy. For

this last-ditch therapy to work, bacteria eater would have to be precisely matched to superbug.

Also, speaking of ditches, where does one look for organisms that feast on bacteria? Yep, the sewer is home to both culprit and cure. Fortunately for Patterson, several research labs studying the pathogens have assembled libraries of sample phages. The phage would also have to be purified before being infused to Patterson.

“So now it was up to me,” Strathdee said. “How am I going to find phages that are going to match Tom’s organism? And the reading I did showed that there’s 10 to the power of 31 phages on the planet—that’s 10 million trillion trillion phages. I was so overwhelmed by this. I thought it’s worse than a needle in a haystack.”

She did what anyone else might do in a desperate medical dilemma: She Googled.

She also enlisted all her scientist contacts in the phage hunt. She posted pleas to social media, complete with images of Patterson bedridden in a coma. She called in every favor and was gratified by the response of folks who didn’t know her or her husband. Phage experts from around the globe took up the challenge. The Navy Medical Research Center in Frederick, Md., also joined the hunt along with phage researchers from Texas A&M University.

“I realized that my husband was becoming somewhat of a poster child for this dystopian future of the superbug crisis,” Strathdee quipped.

In March 2016, Patterson became the first person in the U.S. to receive intravenous phage therapy for a systemic



From hundred-year-old bacterial science to global health to the mind amid hallucinations, so many aspects of the superbug story fascinated the audience, which included several institute/center directors, senior investigators and other NIH leaders.

PHOTOS: MARLEEN VAN DEN NESTE



NLM director Dr. Patricia Flatley Brennan (r) introduces the conversation with Strathdee and Patterson.

multidrug-resistant infection. He awoke from the coma 3 days later. In all, he survived 7 cases of septic shock, untold organ system shutdowns and dozens of hallucinations over 9 months. He was lucky, but so many more people are not, Strathdee pointed out.

Opportunities, Moving Forward

In addition to an enormous sense of gratitude toward their large network of colleagues and the wide range of information and other resources made available to them in record time, the couple has a public health message.

“1.5 million people are dying every year

globally due to superbugs,” she noted, “and that’s estimated to grow to 10 million a year, or 1 person every 3 seconds by the year 2050—unless urgent action is taken. And a lot of our governments are actually doing the wrong thing and promoting policies that are misusing and overusing antibiotics, especially in livestock and agriculture.”

The couple’s ordeal also presented opportunities for future scientific research, particularly in the areas of global health, alternative therapies and precision medicine. In fact, Strathdee and one of the scientists who helped battle the bacteria, Schooley, launched and now codirect a Center for Innovative Phage Applications and Therapeutics at UCSD, the first dedicated phage therapy center in North America. They’re hoping to launch two clinical trials in 2019.

“Scientists are often very removed from the public. We see ourselves as NIH-funded researchers who are supported with taxpayer dollars,” Strathdee concluded. “We feel it’s our obligation to share our story with the public so that people can see that scientists are people...We want to make this kind of research accessible...Through our book, we hope that we’ll be able to take this story globally and make a difference in the global superbug crisis.” **R**



Ghedin

CONTINUED FROM PAGE 1

Diseases from 1998 to 2000, was also a MacArthur Foundation awardee in 2011. “What we’d like to know is, does the microbiome contribute to disease severity?”

In a funny way, the behavior of our onboard microbes can be likened to the folks we live among in our neighborhoods, as Ghedin explored such roles as competition, parasitism, mutualism and synergism among our various microbiota. “It’s very difficult to capture” the way they interweave, she said.

Most work in the burgeoning field of microbiome studies has thus far focused on the gut. Ghedin is mainly interested in the genomics of infectious diseases affecting the lungs, respiratory tract and epithelium, and the myriad live-aboards in these sites.

Using postcard images of Kansas City and New York City, she showed that density can determine the number of interactions between microbes, a phenomenon she and her colleagues can map in the laboratory using such concepts as OTUs, or operational taxonomic units, a way of categorizing bacteria based on sequence similarity.

Fungi, a relatively common component of the human airway, add a fresh dimension of complication to investigations of interactions among host bacteria.

★ ★ ★

In a funny way, the behavior of our onboard microbes can be likened to the folks we live among in our neighborhoods, as Ghedin explored such roles as competition, parasitism, mutualism and synergism among our various microbiota.

★ ★ ★

Ghedin calls these interactions “co-occurrence networks,” and they come in two flavors: direct, or physical contact, and indirect, wherein microbes modify their environments. “It’s like your network of Facebook friends,” she said.

One way of snooping on who’s where and doing what with whom is SPIEC-EASI, or sparse inverse covariance estimation for ecological association inference, Ghedin noted. “We can determine the stability of the [microbial] environment and how it relates to disease.”

As in the game of Jenga, wherein players construct a tower of blocks, then try to disassemble the edifice without collapsing the whole thing, scientists can study how the removal of single OTUs affects the stability of an ecosystem.

Ghedin’s team has found that fungi are crucial to the stability of the microbiome.

Lung health is associated with more, rather than fewer, microbial interactions, even inter-kingdom ones, she said.

Scientists have also identified “influencers” and “disruptors.” Influencers tend to restructure microbial interactions, and include HIV, which promotes chronic obstructive pulmonary disease by encouraging *Pneumocystis* colonization. Disruptors, which change network connections, include the flu. “Influenza is a great disruptor,” Ghedin said.

For each disease she has studied, Ghedin has found signature ecologies, which she says are unique to specific conditions.

It will be valuable to be able to predict disease severity by sampling a patient’s microbiome, and mycobiome, she suggested.

“About 25 percent of the population [who come down with flu] develop severe disease,” said Ghedin. “We’re trying to understand why. Is there an age-determinant?”

It turns out that age is a strong determinant of microbial interactions. “The number is very different in neonates, versus adults, versus those who are aged.”

Fusobacterium, too, has emerged as an important hub in networks Ghedin has studied. It tends to lose its “neighbors,” or connections, in disease states.

Ghedin’s team is also studying antibiotic-resistance genes. They are collaborating in household studies of flu transmission among 120 people in Managua, Nicaragua, in an effort to find out if the upper respiratory tract might be the reservoir for antibiotic resistance.

“Our goal is microbiome-directed therapeutics,” she concluded.

Ghedin’s talk was this year’s Rolla Eugene Dyer Lecture, established in 1950 in honor of a former NIH director who was an authority on infectious diseases. **R**



Dr. Elodie Ghedin (c) accepts the plaque for presenting this year’s Rolla Eugene Dyer Lecture from Dr. Julia Segre (l), senior investigator in NHGRI’s Translational and Functional Genomics Branch, and Dr. Alan Sher, NIH distinguished investigator in NIAID’s immunobiology section.

PHOTO: MARIA MASLENNIKOV



NIGMS director Dr. Jon Lorsch (second from l) welcomes the newest members of the NIGMS Council. Shown are (from l) Dr. John Younger, Dr. Enrique De La Cruz, Dr. Celeste Berg, Dr. Squire Booker, Dr. Peter Espenshade and Dr. Darrin Akins.

Six New Members Join NIGMS Advisory Council

Six new members recently joined the National Advisory General Medical Sciences Council:

Dr. Darrin Akins is associate dean for research in the College of Medicine and professor of microbiology and immunology at the University of Oklahoma Health Sciences Center in Oklahoma City. He investigates membrane protein export in cells and how this fundamental process is regulated and altered in bacteria when they encounter changes in their environment or interact with human tissues and cells.

Dr. Celeste Berg is a professor in the department of genome sciences and molecular and cellular biology program at the University of Washington. She uses the fruit fly to investigate cell communication and cell migration, two processes critical for development and human disease progression.

Dr. Squire Booker is a professor in the departments of chemistry and biochemistry and molecular biology and Eberly family distinguished chair in science at Pennsylvania State University and Howard Hughes Medical Institute investigator. His research is focused on deciphering the molecular details by which enzymes containing iron-sulfur clusters catalyze reactions in the cell and using this insight

to manipulate these reactions for use in making biofuels or antibacterial agents.

Dr. Enrique De La Cruz is a professor in the department of molecular biophysics and biochemistry at Yale University. He integrates computer models with biochemical and biophysical experiments to study how actin molecules—essential for cell movement and muscle contraction—form and break.

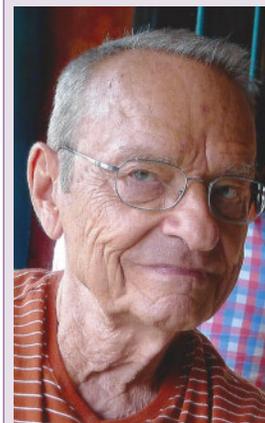
Dr. Peter Espenshade is a professor in the department of cell biology, executive director of the Center for Innovation in graduate biomedical education and associate dean for graduate biomedical education at Johns Hopkins University School of Medicine. He uses a multi-organismal approach to understand mechanisms of nutrient sensing—which are important for cell stability—with particular interest in cholesterol and oxygen.

Dr. John Younger is cofounder and chief technology officer of Akadeum Life Sciences in Ann Arbor, Mich. His research and development efforts focus on cellular interactions with engineered materials and applying those effects to unmet challenges in cell, protein and nucleic acid isolation from clinical material.

NICHD's Corfman Remembered

Dr. Philip A. Corfman died on Feb. 18 in Bowie, Md. He was the first director of NICHD's Center for Population Research (CPR), which was established in 1968 to coordinate and conduct research and training in population health, including research on contraception. Corfman, an obstetrician-gynecologist, spent 20 years at NICHD before leaving for a role at the World Health Organization and later, the Food and Drug Administration.

Corfman received his bachelor's degree from Oberlin College and his medical degree from



Harvard Medical School. He first joined NICHD as a medical officer in the Reproduction Program in 1964 and served in various leadership roles before being named CPR director in 1968. He also was a commissioned officer in the Public Health Service since 1976.

During his time at NICHD, Corfman oversaw large research programs on contraception and behavioral sciences. He stressed the need for the development of family-planning methods for both men and women, as well as for research on the contraceptive needs of teenagers and effects of teen pregnancies. In 1970, he testified before a Senate committee on the health effects and safety of the birth control pill. During the hearings, experts publicly noted the negative side effects of the pill, including a higher cancer risk, which caused interruptions from women protesters in the audience. Corfman is remembered as the only person who paused his testimony to address their concerns.

In 1982, he was named by *Ms.* magazine as 1 of 40 heroes, specifically for "his sensitive response to feminist health activists and his efforts to change the direction of birth control research so that male methods were included and safe methods for women were emphasized."

Corfman received many awards, including the Distinguished Service Award from the American College of Obstetricians and Gynecologists (ACOG). He served on numerous committees for the PHS, FDA, ACOG and the International Planned Parenthood Federation. He also authored papers in journals such as *Nature*, *Science* and the *New England Journal of Medicine*.

He is survived by his 3 sons, Stanley, Timothy and Mark, and by 6 grandchildren.



IMAGE: PETDCAT/ISTOCK

Study of Brain Energy Patterns Provides New Insights into Alcohol Effects

Assessing the patterns of energy use and neuronal activity simultaneously in the human brain improves our understanding of how alcohol affects the brain, according to new research by scientists at NIH. The new approach for characterizing brain energetic patterns could also be useful for studying other neuropsychiatric diseases. A report of the findings is now online in *Nature Communications*.

“The brain uses a lot of energy compared to other body organs and the association between brain activity and energy utilization is an important marker of brain health,” said Dr. George Koob, director of NIAAA, which funded the study. “This study introduces a new way of characterizing how brain activity is related to its consumption of glucose, which could be very useful in understanding how the brain uses energy in health and disease.”

The research was led by Dr. Ehsan Shokri-Kojori and Dr. Nora Volkow of the NIAAA Laboratory of Neuroimaging. Volkow is also director of the National Institute on Drug Abuse. In previous studies they and their colleagues have shown that alcohol significantly affects brain glucose metabolism, a measure of energy use, as well as regional brain activity, which is assessed through changes in blood oxygenation.

“The findings from this study highlight the relevance of energetics for ensuring normal brain function and reveal how it is disrupted by excessive alcohol consumption,” Volkow said.

Results of Trial to Stem Hospital-Acquired Bacterial Infections Published

New findings from a large, randomized clinical trial that compared two infection-control techniques are already being incorporated into practice within the network of U.S. community hospitals where the trial took place. The trial evaluated whether daily bathing with the

antiseptic soap chlorhexidine (CHG)—and in those patients with methicillin-resistant *Staphylococcus aureus* (MRSA), adding the nasal antibiotic mupirocin—more effectively reduced hospital-acquired bacterial infections than bathing with ordinary soap and water. While no statistically significant difference between the two intervention groups was seen within the population overall, the researchers did find that one subset of patients—those with medical devices—experienced a substantial benefit if they received the CHG/mupirocin intervention.

The ABATE (Active Bathing to Eliminate) infection trial was initiated through NIH’s Common Fund program and was managed by NIAID. Results of the study, which involved about 330,000 adult patients in non-intensive care units in the HCA Healthcare system, appeared Mar. 5 in *The Lancet*. Dr. Susan S. Huang of the University of California, Irvine, School of Medicine led the research team.

Previous clinical trials in intensive care units had shown that hospital-acquired infections could be dramatically reduced through such practices as CHG bathing, noted Huang. “Because there was a clear benefit with bacterial decolonization in the ICU setting, we pursued this trial to determine if similar interventions would reduce hospital-acquired infections in non-ICU settings, where the majority of such infections occur,” she said. Decolonization refers to the removal of skin-surface bacteria that are normally harmless, but that may enter the bloodstream following surgery or other procedures and cause infection, including life-threatening sepsis.



IMAGE: DJANGO/GETTY

Rate of Life-Threatening Childbirth Complications Increasing Sharply

Racial and ethnic disparities in severe maternal morbidity—life-threatening maternal complications associated with childbirth—have persisted and increased at high rates among U.S. women, according to an analysis of nearly 20 years of California hospital records funded by NIH. Known risk factors for these complications—such as blood pressure disorders, asthma and Caesarean birth—do not fully explain the increase or why the disparities

remain. The study was led by Dr. Stephanie Leonard of Stanford University School of Medicine and appears in *Annals of Epidemiology*. NICHD and NINR provided funding.

Severe maternal morbidity is a blanket term for 18 indicators of life-threatening maternal conditions associated with childbirth, including kidney failure, fluid in the lungs and heart failure. Study authors analyzed data from more than 8 million live births in California between 1997 and 2014. Severe maternal morbidity was highest among non-Hispanic black women (1.63 percent), followed by non-Hispanic American Indian or Alaska Native women (1.30 percent), non-Hispanic Asian or Pacific Islander women (1.10 percent) and Hispanic women (1.09 percent). Severe maternal morbidity was lowest among non-Hispanic white women at 0.84 percent.

During the study period, severe maternal morbidity increased roughly 170 percent for each group. Future studies might seek information not available from hospital records and health care providers to find reasons for the disparities among racial and ethnic groups, the authors wrote.

Tuberculosis Diagnosis in People with HIV Increases Risk of Death Within 10 Years

Among people with HIV in Latin America, those diagnosed with tuberculosis (TB) at an initial clinic visit were about twice as likely to die within 10 years as people not initially diagnosed with TB, according to findings from a large observational study. This increased risk persisted despite the availability of TB treatment and mirrored patterns seen previously in HIV-negative populations, according to research supported by NIAID. Investigators from the NIAID-supported Caribbean, Central and South America Network for HIV Epidemiology presented the findings Mar. 6 at the Conference on Retroviruses and Opportunistic Infections in Seattle.

People with HIV are at greater risk of TB disease than HIV-negative people due to HIV-related immune system damage as well as geographical and behavioral risk factors shared by both diseases. In 2017, the World Health Organization estimates there were 920,000 new TB cases among individuals with HIV globally, and approximately 300,000 people with HIV died from TB. Due to this large burden of HIV and TB co-infection, NIAID supports research to improve TB prevention, diagnosis and treatment in the context of HIV infection.

“Tuberculosis remains the leading cause of death for people with HIV globally,” said NIAID director Dr. Anthony Fauci. “This new analysis shows how devastating TB can be for people with HIV and underscores the need to do more to prevent and treat this co-infection.”



IMAGE: NIEHS

Vitamin D May Protect Against Pollution-Associated Asthma Symptoms in Obese Children

A new study finds vitamin D may be protective among asthmatic obese children living in urban environments with high indoor air pollution. The study out of John Hopkins University School of Medicine, funded by NIEHS, was published in the *Journal of Allergy and Clinical Immunology: In Practice*.

“The research team has identified many factors that make children susceptible to health problems from air pollution throughout Baltimore’s inner city,” said Dr. Kimberly Gray, administrator for the Children’s Environmental Health Research Centers program at NIEHS.

According to the Centers for Disease Control and Prevention, one in 12 children in the U.S. have asthma, which totals 6.1 million children nationally. Additionally, asthma disproportionately impacts urban minority populations, such as black children. Higher indoor air pollution, from sources such as cigarette smoke, cooking, burning of candles and incense, is linked to greater respiratory problems, including worsening of asthma symptoms and more hospital visits.

“Asthma is an immune-mediated disease,” said Dr. Sonali Bose, lead author of the study and assistant professor of medicine, pulmonary, critical care and sleep medicine at the Icahn School of Medicine at Mount Sinai and adjunct faculty at Johns Hopkins. “From previous scientific studies, we knew that vitamin D was a molecule that may influence asthma by impacting antioxidant or immune-related pathways.”

Bose explained that at the time the study was being conceived, researchers were seeing vitamin D deficiencies across the U.S. “It became very clear that African Americans were at higher risk for vitamin D deficiency, particularly black children,” she said. “We were also noticing a heavy burden of asthma in inner city minority children. It seemed

as though vitamin D deficiency and asthma were coincident and interacting in some way.”

The study tested three factors—air pollution levels in homes, blood vitamin D levels and asthma symptoms—in 120 school-age children with pre-existing asthma in the Baltimore area. One-third of the study participants were also obese. The children were evaluated at the start of the study and 3 times over the next 9 months.

Overall, they found that having low blood vitamin D levels was related to the harmful respiratory effects of indoor air pollution among obese children with asthma. Conversely, in homes that had the highest indoor air pollution, higher blood vitamin D levels were linked to fewer asthma symptoms in obese children.

“What surprised us the most was that the findings of the study showed the effects were most pronounced among obese children,” Bose said. “This highlights a third factor at play here—the obesity epidemic—and helps bring that risk to light when considering individual susceptibility to asthma.”

Study Finds Ebola Survivors in Liberia Face Ongoing Health Issues

Survivors of Ebola virus disease (EVD) in Liberia had a higher prevalence of certain health issues—including uveitis (eye redness and pain), abdominal, chest, neurologic and musculoskeletal abnormalities upon physical exam—when compared to a control group of household and community members who did not have a history of EVD, according to findings from an ongoing study published in the *New England Journal of Medicine*. However, even participants in the control group experienced a relatively high burden of health issues overall.

The study began in 2015 and is following participants for 5 years. It is being conducted by the Partnership for Research on Ebola Virus in Liberia (PREVAIL), a collaboration between the government of Liberia and NIAID. Additional partners in the study include NEI and NINDS, the University of Minnesota in Minneapolis and the Johns Hopkins University Wilmer Eye Institute in Baltimore. The research is led by principal investigators Dr. Mosoka Fallah, deputy director general for technical services at the National Public Health Institute of Liberia, and Dr. Michael Sneller, medical officer at NIAID.

“The PREVAIL study has yielded novel insight regarding the health issues facing some survivors of Ebola virus disease in Liberia and their close contacts,” said NIAID director Dr. Anthony Fauci. “We thank our partners in the Liberian government for their collaboration in the successful implementation of this study and we thank the study volunteers for their selfless participation in this important research.”

VRC Needs Healthy Volunteers

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

Adults with Knee Pain Sought

Clinical Center researchers seek 18-55 year olds with kneecap pain (patellofemoral or anterior knee pain) for a 2-visit outpatient research study. We are studying how muscle weakness around the knee may lead to changes in kneecap motion and pain. Compensation is provided. Learn how to participate by contacting the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010) or prpl@cc.nih.gov. Refer to study 13-CC-0099. Read more at <https://go.usa.gov/x>.

NHLBI Study Recruits Volunteers

NHLBI invites volunteers ages 18-80 of African descent with or without sickle cell trait and patients with sickle cell disease to participate in a one-time-visit research study. Volunteers will provide blood samples that will be used to look for a link between the PKLR gene and pyruvate kinase protein. The PKLR gene is active in the liver and in red blood cells and helps to create protein called pyruvate kinase that is essential in normal functioning of red blood cells. Compensation is provided. For more information about study 18-H-0146, call 1-866-444-2214 (TTY 1-866-411-1010) or visit <https://go.usa.gov/xp8Hx>.

Flu Vaccine Study Seeks Volunteers

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

Post-Transplant Patients Needed

NHLBI researchers are testing whether a mouth rinse containing topical dexamethasone can be used to prevent oral chronic graft vs. host disease in post-transplant patients. If you are 12 years of age or older and have received a stem cell transplant in the last 60 to 90 days, you may be eligible to participate. Study-related tests and procedures are provided at no cost. For more information, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xnhak>. Refer to study 07-H-0005.



McGavern's Lab Marks Milestone

On Mar. 1, Dr. Dorian McGavern's lab in NINDS celebrated its 10th anniversary at NIH, complete with a brain cake to mark the lab's neuroimmunology focus. A fan of the film *Despicable Me*, McGavern, senior investigator in the viral immunology and intravital imaging section, and his minions are shown below at a Halloween celebration last fall.



Dr. Julie Segre

Segre To Give Mider Lecture, Apr. 3

NHGRI's Dr. Julie Segre will present the annual G. Burroughs Mider Lecture as part of the NIH Director's Wednesday Afternoon Lecture Series. Her talk, "Microbiome: Friend and Foe," will be held Apr. 3 at 3 p.m. in Masur Auditorium, Bldg. 10.

Segre's research explores human skin bacterial, fungal and viral communities, enabling studies of alterations associated with pediatric atopic dermatitis, primary immunodeficiency and emerging pathogens. Her work also focuses on integrating whole genome sequencing of hospital pathogens to track possible nosocomial transmissions. These studies integrate DNA sequence technology, algorithm development and clinical studies to explore the diversity of microbes in and on humans in health and disease.

Segre received her undergraduate degree in mathematics (*summa cum laude*) from Amherst College and her Ph.D. in biology from Massachusetts Institute of Technology, where her mentor was Dr. Eric Lander. She completed postdoctoral training at the University of Chicago in the laboratory of Dr. Elaine Fuchs. She began her career at NIH in 2000 and is currently a senior investigator at NHGRI and chief of the Translational and Functional Genomics Branch.

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.