Murthy Discusses Chronic Stress, Solutions

BY ELLEN O’DONNELL

Imagine that you are picking up a set of weights at the gym, an overloaded bag at the grocery store or a small child. As you do this, you’re building muscle mass, “but if you hold that weight for hours and hours, it may do damage to you—and that’s essentially what happens with chronic stress,” according to former surgeon general Dr. Vivek Murthy.

There is “an epidemic of stress in America,” he says, but there are also tools and skills that we can use to counter it and “enhance [our] ability to live a healthier, stronger, more fulfilling life.”

Murthy and NIH director Dr. Francis Collins spoke at this year’s Stephen E. Straus Lecture in the Science of Complementary Therapies about “A Nation Under Pressure: The Public Health Consequences of Stress in America.” They addressed a packed Masur Auditorium and thousands more watching on videocast and Facebook Live. NCCIH’s annual Straus Lecture honors the center’s founding director.

Not all stress is bad, Murthy said. “We have adaptive mechanisms to it, such as the ‘revving up’ of our epinephrine and norepinephrine. This can be helpful in the short term, like if you have to run from a tiger or respond to an acute crisis. But over the long term, it can increase inflammation in the body and increase our risk of cardiovascular disease, cancer, anxiety, depression and a host of other illnesses.”

During his tenure as surgeon general, Murthy took a “listening tour” across America. The recurring theme he heard was that “the stresses in people’s lives were causing them great pain and they didn’t always know how to deal with them...It was so powerful to see how people would react and come together when we talked about stress and emotional well-being.” As a nation, “if we are not addressing stress and emotional well-being, we are missing a major contributor to our health.”

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NIH Veterans Day Celebration, Nov. 9

The entire NIH community is invited to join our military and Public Health Service colleagues to celebrate Veterans Day and to recognize their service and continued contributions to the nation. This year’s celebration will be held on Thursday, Nov. 9 in Masur Auditorium, Bldg. 10, from 10 to 11 a.m.

The event will include a military band, remembrance table ceremony, exhibits from veteran-oriented companies and uniformed services organizations and more. NIH veterans and families of veterans are especially encouraged to attend.

This year's keynote speaker is Army Maj. Gen. (Ret.) James Gilman, who currently serves as chief executive officer of the Clinical Center. Welcoming remarks will be delivered by Navy Commander (Ret.) Jeff McCoy, director of the Division of Design and Construction Management, NIH Office of Research Facilities.

Sign language interpreters will be provided. Individuals who need reasonable accommodation to participate should contact Jayne Lura-Brown at luraj@de45.nidr.nih.gov or (301) 594-5342 and/or the Federal Relay (1-800-877-8339). To find out more about how veterans contribute every day to the NIH mission, visit https://jobs.nih.gov/veterans/vrf.htm.

Lecture on Electronic Health Records, Nov. 1 in Lister Hill Auditorium

The next talk in the National Library of Medicine Biomedical Informatics and Data Science Lectures is titled “Transforming Electronic Health Records from Annoyances to Assistants: A Research Agenda for the Next Decade,” by Dr. James Cimino on Wednesday, Nov. 1 from 2 to 3 p.m. in Lister Hill Center Auditorium, Bldg. 38A.

Cimino is a board-certified internist and clinical informatician, currently a professor of medicine and inaugural director of the Informatics Institute at the University of Alabama-Birmingham School of Medicine. He has been carrying out clinical informatics research, building clinical information systems, teaching medical informatics and medicine and caring for patients for more than 30 years. He was formerly chief of the Laboratory for Informatics Development at the Clinical Center and the National Library of Medicine.

National Symphony Orchestra Performs at CRC

On Sept. 19, the Clinical Center and the Foundation for Advanced Education in the Sciences welcomed the full National Symphony Orchestra to Bldg. 10. The orchestra performed works by Beethoven, Bach and Brahms as well as Duke Ellington, Leroy Anderson, John Williams, Emmanuel Sejourn and Aaron Copland. It featured William Gerlach on trumpet, Eric Shin on vibraphone and Steven Reineke (shown above) as conductor. Their visit marks the NSO’s 18th time performing in the Clinical Center as a part of its Sound Health initiative. NSO ensembles have scheduled performances at the Clinical Center Nov. 9 and Dec. 12. Below at left, NIH director Dr. Francis Collins welcomes the NSO to Bldg. 10. Below at right, patients, families, staff and visitors enjoyed the NSO concert both in the atrium and balconies above.

PHOTOS: MARLEEN VAN DEN NESTE

Heitkemper To Give NINR Director’s Lecture, Nov. 14 in Lipsett

Dr. Margaret Heitkemper will present the fourth 2017 NINR Director’s Lecture on Tuesday, Nov. 14 from 1 to 2 p.m. in Lipsett Amphitheater, Bldg. 10. In her presentation “Symptom Science in Irritable Bowel Syndrome: Biomarkers to Intervention,” she will describe her program of research that addresses the pathophysiology and biobehavioral treatment of irritable bowel syndrome (IBS) and the interaction of stress and symptoms in children and adults. The lecture will be followed by an opportunity for questions and discussion.

Heitkemper is professor and chair, department of biobehavioral nursing and health informatics, adjunct professor, division of gastroenterology, and co-director, Center for Innovations in Sleep Self-Management at the University of Washington. Her current studies are examining blood and fecal metabolite levels, the microbiome and intestinal permeability in men and women with IBS as well as peripheral markers of inflammation.

The NINR Director’s Lecture series is designed to bring the nation’s top nurse scientists to NIH to share their work and interests with a transdisciplinary audience. The event is free and open to the public. For more information and to register, visit www.ninr.nih.gov/directorslecture.
NIH Grantees Win Nobel Prizes

Four NIH grantees were honored with Nobel prizes in early October, three in medicine and physiology and one in chemistry.

The 2017 Nobel Prize in physiology or medicine went to grantees Dr. Jeffrey C. Hall of the University of Maine, Orono; Dr. Michael Rosbash of Brandeis University; and Dr. Michael W. Young of Rockefeller University for their discoveries of molecular mechanisms controlling the circadian rhythm.

The Royal Swedish Academy of Sciences said, “The paradigm-shifting discoveries by the laureates established key mechanistic principles for the biological clock.”

Sharing the chemistry prize with two other scientists was grantee Dr. Joachim Frank of Columbia University. He, along with Dr. Jacques Dubochet of the University of Geneva and University of Basel, Switzerland, and Dr. Richard Henderson of Cambridge University, was honored for the development of cryo-electron microscopy (cryo-EM), which both simplifies and improves the imaging of biomolecules. The Royal Swedish Academy of Sciences said, “This method has moved biochemistry into a new era.”

For many years, scientists have known that living organisms, including humans, have an internal, biological clock that helps them anticipate and adapt to the regular rhythm of the day. Hall, Rosbash and Young aimed to discover how that clock works. They used fruit flies to isolate the gene called period that controls the normal biological rhythm of the day. Clock genes contain instructions for making clock proteins, whose levels rise and fall in a regular cyclic pattern. The researchers went on to discover that PER, the protein encoded by period, accumulated during the night and was degraded during the day. Their discoveries explain how plants, animals and humans adapt their biological rhythm so that it is synchronized with the Earth’s revolutions.

Our clocks influence alertness, hunger, metabolism, fertility, mood and other physiological conditions. For this reason, clock dysfunction is associated with various disorders, including insomnia, diabetes and depression.

“The work of these Nobel laureates to help us understand how our biological clocks work has shone a light on the significance of circadian rhythms on our health and is informing treatments for sleep disorders, obesity, mental health disorders and other health problems,” said NIH director Dr. Francis Collins. “NIH is proud to have supported this groundbreaking research.”

Young and Rosbash have received continuous funding from NIH since 1975 ($17 million and $8 million, respectively) primarily from the National Institute of General Medical Sciences and National Institute of Neurological Disorders and Stroke. Rosbash’s work has also been supported by the National Institute on Aging, National Institute on Drug Abuse and National Heart, Lung, and Blood Institute. NIGMS also supported Hall’s work, providing more than $7 million in funding.

“This work is a great example of how studying fundamental biological processes in model organisms such as fruit flies reveals important principles that translate into a deeper understanding of human biology and disease,” said NIGMS director Dr. Jon Lorsch.

With respect to the chemistry prize, knowing the structure of a molecule reveals important information about how it functions and can provide insight into potential drug targets for fighting disease. Cryo-EM is a method used to image frozen biological molecules without the use of structure-altering dyes or fixatives or the need to coax the molecules into crystalline form, providing a simpler way to generate pictures of the molecules in their normal states and greater understanding of biological function. With cryo-EM, researchers can advance understanding of life’s chemistry and develop pharmaceuticals.

“The work of these [chemistry] Nobel laureates has been game-changing in our understanding of life’s processes and identifying molecular targets for drug development,” said Collins. “NIH is investing heavily in the further development of this technology through the NIH Common Fund’s Transformative High Resolution cryo-EM Program, which aims to improve access for researchers through the creation of national service centers, continued advancement of the technology and developing the skills that researchers need to use this technology.”

Frank has received continuous funding from NIGMS since 1978, having received more than $25 million to date.

“One of the benefits of this prize is that it isn’t just looking backward at what happened in the past, it’s also looking to the future,” said Lorsch. “Recent advances in cryo-EM—made possible by the three winners—are allowing us to make unprecedented advances in areas from our basic understanding of cellular processes to the development of new vaccines.”

NIH National Institutes of Health
Turning Discovery into Health

ON THE COVER: Streptococcus pyrogenese bound to a human neutrophil

IMAGE: NIAID

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.

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Turning Discovery into Health
Woodruff and her husband, Bloomberg View columnist Al Hunt, who were juggling demanding journalism jobs while raising three children, suddenly were thrust into the role of caregivers. They had to do everything for Jeffrey: urinary catheters every few hours, medicines throughout the day, dressing, bathing, assistance with feeding and mobility.

“One once we got over the shock of what happened, we determined ourselves to make Jeffrey’s life as positive as possible,” said Woodruff. They got him the best wheelchair, hired speech, physical and occupational therapists and tried a range of treatments.

“We decided the only way to get through this was to be optimistic, to assume the best, to stay cheerful and to stay busy and I know all of this in the end has made a difference for Jeff,” Woodruff said. “We didn’t dwell on the bad stuff; we were always looking ahead.”

Jeffrey’s condition took a toll on the entire family. While they strove to remain positive, Woodruff said she regrets not taking time to grieve what they had lost. “We just leapt over the grieving process and jumped ahead to how we were going to make the best of it,” she said. “It’s important to acknowledge the sadness and the loss.”

Woodruff said Jeffrey understood what happened to him but never spent much time looking back. Determined to continue his studies, he graduated from high school with the daily help of a hired companion to get him around and assist with his school work. He went on to graduate from community college and then completed a 4-year residential program at a school in North Carolina for students with physical disabilities. “There was not a dry eye anywhere around on that commencement morning in 2010,” said Woodruff.

Jeffrey now lives in a group home in Westminster, Md., where staff provide round-the-clock support. Some are graduate students who have education costs defrayed while gaining invaluable experience working in the health care field.

“I see what they provide,” Woodruff said. “I know the amount of work it takes to take care of Jeffrey and the other individuals, and it is jaw-dropping. It is extraordinary, the work they do...I think it doesn’t get the appreciation it deserves.”

Grateful for access to resources she knows many Americans do not have, Woodruff said she has met and heard the concerns of many parent-caregivers during her advocacy work around the country. “And I think our country needs to do a much better job of recognizing the role of caregivers [who] have to be not only thanked but celebrated.”

Often physically and mentally exhausting, caregiving is a labor of love that plays a vital role in treatment and recovery. It has been receiving increased attention from research and policy communities, but more needs to be done.

More research is needed to improve the health and quality of life for caregiver and patient alike, said NINR director Dr. Patricia Grady, who introduced Woodruff and welcomed attendees to the caregiving summit. There are effective interventions, she said, to improve the informal caregiver’s knowledge and physical health and reduce the burden, anxiety and depression that often afflict caregivers.

Said Woodruff, “[It’s important to make] the American people aware—not that there aren’t many already aware due to personal circumstances...that this is a field that deserves our respect, recognition and indeed our celebration.”
**Stetten Lecturer Amaro Sheds Light on Shape-Shifting Proteins**

Scientists have long sought to visualize the detailed structures and movements of proteins in real time within living cells.

This year's DeWitt Stetten Jr. Lecture will feature one of the leaders in this emerging field: Dr. Rommie Amaro, a professor in the department of chemistry and biochemistry at the University of California, San Diego. Her talk is titled “Computing Cures: Discovery Through the Lens of a Computational Microscope.” The lecture will occur on Wednesday, Oct. 25 at 3 p.m. in Masur Auditorium, Bldg. 10. It is sponsored by NIGMS and is part of the NIH Director’s Wednesday Afternoon Lecture Series.

For decades, scientists have captured the detailed, 3-dimensional images of crystallized proteins. These images have provided invaluable information about thousands of proteins. But they show proteins only in one position—paralyzed unnaturally within a crystal.

State-of-the-art cellular imaging techniques allow researchers to see the movement of individual molecules within a cell. But currently, the tools can only track rather slow movements, not the flip of a protein from one form to another, which occurs in trillions of a second.

Amaro and her colleagues are combining existing techniques and developing new ones to create detailed images of proteins as they move and morph. The scientists then validate the accuracy of their computational predictions using laboratory experiments.

The work promises to deepen our understanding of the ever-active world within cells. It might also point the way to new treatments for countless diseases. For example, the simulations might indicate a way to restore the normal functioning of a protein that, when faulty, causes disease. That’s the goal of one of Amaro’s projects. She focuses on the p53 protein.

A major function of p53 is to prevent cancer. Normal versions of p53 detect damaged DNA—which can cause cancer—and prevent it from being passed on to a new generation of cells.

When p53 isn’t working properly, cells are at high risk for cancer. Defective versions of p53 are associated with more human cancers—about 50 percent of them—than any other malfunctioning protein. As a result, many researchers, including Amaro, seek to reactivate mutant p53 as a way to develop new anti-cancer treatments.

By simulating the movements of p53, Amaro and her team identified a pocket in the protein’s core that only opens when the protein’s shape shifts. Finding this pocket helped to explain how a potential new drug, now in clinical trials, produces its anti-cancer effect. Amaro and her colleagues suspected that the pocket might also provide a foothold for a small molecule that could restore function to mutant p53 proteins.

To see if they could find such a therapeutic small molecule, Amaro and her group computationally tested thousands of small molecules, analyzing the ability of each to fit into p53’s pocket. The scientists then conducted laboratory experiments on 45 of the molecules that, based on computational predictions, appeared most likely to bind in the pocket.

Based on these experiments, one small molecule stood out as having the greatest potential to rehabilitate cancer-causing mutant p53. Building on this discovery, Amaro and her team developed dozens of small molecules that reactivated p53. This work formed the basis for a biotech startup, Actavalon, Inc., to translate these findings into a new anti-cancer drug.

Amaro’s team is beginning to model the movements of ever larger and more flexible structures. Recently, her group simulated how p53 behaves as a tetramer bound to different sequences of DNA. This work showed how p53 can change its “grip” on DNA depending on the DNA sequence. The project also revealed the roles of all portions of the p53 molecule. This information sheds light on how p53 does its job and opens new avenues for drug discovery.

Amaro leads two NIGMS-supported resources at UCSD. She directs the National Biomedical Computation Resource and co-directs the Drug Design Data Resource.

Amaro received her B.S. in chemical engineering in 1999 and her Ph.D. in chemistry in 2005, both from the University of Illinois, Urbana-Champaign.

In 2016, Amaro was named the American Chemical Society Kavli Emerging Leader in Chemistry and also received the Corwin Hansch Award, which is given annually to a scientist under the age of 40 who contributes significantly to the field of computer-aided drug design. Amaro also received a 2010 Presidential Early Career Award for Scientists and Engineers and a 2010 NIH Director’s New Innovator Award.

For more information on the lecture or for reasonable accommodation, contact Jacqueline Roberts at Jacqueline.Roberts@nih.gov or (301) 594-6747.

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**Belshe To Give Chanock Lecture**

Infectious disease and immunology physician and researcher Dr. Robert Belshe will deliver the NIAID Robert M. Chanock Memorial Lecture at 9 a.m. on Tuesday, Oct. 24. His talk, “What Happened to the Superior Efficacy of the Live-Attenuated Influenza Vaccine and Where Do We Go from Here?” will take place in the Bldg. 50 first-floor conference room.

Belshe, who served as an infectious diseases fellow under Chanock, is currently the Dianna and J. Joseph Adorjan endowed chair of infectious diseases and immunology, emeritus, at Saint Louis University Medical Center. He previously designed and led pivotal clinical research—including trials of live-attenuated influenza vaccines—as director of an NIAID vaccine and treatment evaluation unit, first at Marshall University in Huntington, W.Va., and then at Saint Louis University. His laboratory is currently researching live-attenuated respiratory virus vaccines to protect against respiratory syncytial virus, parainfluenza and influenza.

Belshe will discuss why the efficacy of the live-attenuated influenza vaccine has declined over the past two decades. A 1998 study showed the vaccine had significantly improved efficacy in children compared with the inactivated influenza vaccine, but recent studies no longer show the live-attenuated vaccine to be a superior option. Belshe will explore the potential effects of changes in manufacturing methods and the natural evolution of influenza viruses on the reduced efficacy of the vaccine. He also will present an overview of vaccines in development that show promise of improved efficacy against influenza.

Belshe has received numerous honors for his research accomplishments, including the Academy of Science of Saint Louis Outstanding Communicators Award. In 2005, he was also named to the *Scientific American* list of 50 Leaders Shaping the Future of Technology for his work on novel approaches to influenza vaccination.

The lecture honors the late virologist Chanock, who worked at NIAID for more than 50 years, including more than 3 decades serving as chief of the Laboratory of Infectious Diseases. Among other accomplishments, Chanock was the first to identify respiratory syncytial virus in humans as well as several parainfluenza viruses. He also collaborated in developing a rotavirus vaccine, an adenovirus vaccine, a monoclonal antibody to prevent respiratory syncytial virus disease and the first nasal spray influenza vaccine.
the last runner of each team had to run up an incline to the finish line.

“It was tough but fun,” said Dr. Tom Bulea, a biomechanics scientist who ran with team RM Dangerous. “This course was shorter, but it was hard to pace. I wish the finish wasn’t uphill!”

His teammate Rachel Eisenfeld, a pedorthist who works in the CC’s rehabilitation medicine department, agreed. “It would’ve been hard to sprint the whole time,” she said. “You had to plan your speed.”

Each runner traveled 500 meters around the Clinical Center’s south lawn and 10-H parking lot before passing the baton to 1 of 5 teammates. The usual Bldg. 1 course was longer, at 800 meters per runner, but on mostly level ground.

“It was really fun. The ramp going uphill at the end was quite challenging, but we want some challenge in a short run,” said Trinh Pham, a researcher in NCI’s pathology lab and member of team Volleyball JJIRT. His teammates work at different ICs but play volleyball together on campus after work three times a week.

Another team from multiple ICs was Cirque de Sore Leg, a group of contractors who raced together for the first time. “It was great to get outside for a bit,” said Kyle D’Amico, an animal care technician with NEI. “I have not trained for this. I’m just doing this for fun.”

But one team that did train, quite rigorously, showed up ready to win and had the fastest time 2 years running. NIA’s Charm City NeuRUNS finished the relay with a time of 6:56. The second and third place teams, NICHD’s Running Gels and NIDCD’s Hertz So Good, finished just two seconds apart, clocking in at 7:38 and 7:40.

“Beginning in May, we ran together twice each week,” said Dr. Mark Mattson, a senior investigator and lab chief at NIA who ran with and coached the NeuRUNS. Every Wednesday before work, they’d do an early morning high-intensity run at a nearby high school track. On weekends, they did a 90-minute trail run at different state parks in Baltimore.

“Some of the research in my lab is aimed at understanding the cellular and molecular mechanisms by which exercise benefits brain health,” said Mattson. “Such mechanisms are fully engaged in these creative and productive postbac and postdoc fellows on my relay team this year.”

Many relay runners said they hike or bike or hit the gym regularly to stay in shape. Amanda Crinks with NCI’s Hemoglobintrotters said they all run regularly, just not usually together.

And some came purely for fun to jog or walk the course, such as CSR’s Snailin’ Along and Baby Got Track. CSR director Dr. Richard Nakamura also participated with some of his deputy directors on a team called Review Directives.

“We usually walk a lot,” said Nikon Hill-Coston, an extramural support assistant from Snailin’ Along. “We’ve never done this before so we’re excited in a don’t-fall-on-your-face kind of way.”

NIAID’s Pox Jox have been running the relay every year since the relay began, with rotating members. Said Pox Jox’s newest member, postbac Shira Glushakow-Smith, “It was a lot of fun to do non-lab stuff, relax with my section and represent my institute.”

As in years past, the relay was sponsored by the R&W Association and ORS’s Division of Amenities and Transportation Services.

From left, finishing first was NIA’s Charm City NeuRUNS (from l) Keelin Moehl, Yuki Kishimoto, Nate Ghena, Coach Mark Mattson, David Freeman and Aileen Rivell; placing second was NICHD’s Running Gels (from l) Fabio R. Fauz, Laura C. Hernández-Ramírez, Giampaolo Trivellin, Andreas Giannakou and Edra London. In third place was NIDCD’s Hertz So Good (from l) Christian Faaborg-Andersen, Connor Hill, Czarina Ramos, Nora Welsh and Randall Harley.
PHS Commissioned Corps Deploys to Hurricanes

When Hurricanes Harvey and Irma—the only category 4 Atlantic storms to ever hit the U.S. in the same year—made landfall, members of the Public Health Service Commissioned Corps went into action.

In response to Harvey, more than 500 officers from 21 federal agencies made ready. Three of them were from NIH: CDR Angel Garced, an NEI nurse consultant; LCDR Tameka Kastner, a safety and occupational health specialist in the Office of the Director; and LT Neil Barranta, clinical nurse manager at the Clinical Center.

Garced and Barranta were assigned to federal medical stations as direct care providers, while Kastner assumed the role of safety officer in the incident command system. They were among 79 PHS officers initially deployed for 2 weeks in Houston.

The NIH’ers were later mobilized to several locations in west Florida, including Fort Myers and Sarasota County in response to Irma. Some of the PHS officers were also assigned to a Disaster Medical Assistance Team to provide a variety of health care services.

Volkow Confers with President of Iceland

NIDA director Dr. Nora Volkow met with Iceland President Gudni Th Johannesson on Oct. 3 at Bessastadir, the official residence of the president, where the two discussed the science of substance use disorders. Volkow was in Iceland to participate in the Society of Alcoholism and Other Addictions’ (SAA) 40th Anniversary Conference on Drug Addiction Treatment and formal opening of the new SAA treatment center in Reykjavik. Her presentation was titled “Addiction Is a Chronic Brain Disease—What We Know Today.” The SAA is an NGO that is the leading provider of addiction treatment and addiction medicine services in Iceland.

PHS Ceremony Promotes 24 Officers

The 15th annual Public Health Service Commissioned Corps promotion took place recently at Natcher Conference Center. NIH takes time each year to celebrate and acknowledge the accomplishments of corps officers, who continue to carry out the PHS mission to protect, promote and advance the health and safety of our nation. This year, 24 officers were promoted. Additionally, newly retired, new calls to active duty and student training/extern program officers were recognized.

Newly Retired Officers: RADM Deborah Wilson, CAPT Kirk Druey, CAPT Michael Eckhaus, CAPT Thomas Eggerman, CAPT Michele Evans, CAPT John Hsiao, CAPT Chad Koratich, CAPT Francois Lalonde, CAPT Marissa Miller, CAPT Lawrence Nelson, CAPT Michaele Smith, CAPT Pamela Stratton, CAPT Eric Wasserman, CDR Jennifer Pope

New Calls to Active Duty Officers: LT Anahita Agharahimi, LT Lonice Carter, LTJG Ashante Sims

Commissioned Officer Student Training and Extern Program: ENS Kathryn Peterson

Medical Officers—Promoted to Captain: Stephen Hewitt; promoted to Commander: Christopher Ramsden, Mark Roschewski

Engineer Officers—Promoted to Commander: Leo Angelo Gumapas, Andrew Yang; promoted to Lieutenant Commander: Phuong Vo

Scientist Officers—Promoted to Commander: Mark Miller; promoted to Lieutenant Commander: Iman Martin

Environmental Health Officers—Promoted to Lieutenant Commander: Brian Czarnecki

Pharmacy Officers—Promoted to Captain: Jinhee Lee, Elizabeth Yuan; promoted to Commander: Matthew Kirchoff; promoted to Lieutenant Commander: Marleen Tran

Health Services Officers—Promoted to Captain: Tiffany Edmonds, Josef Rivero, Janet Valdez; promoted to Commander: Rafael Torres-Cruz; promoted to Lieutenant Commander: Nicole Pascua

NIH’ers responding to Harvey and Irma included (from l) CDR Angel Garced, LCDR Tameka Kastner and LT Neil Barranta.

NIHers responding to Harvey and Irma included (from l) CDR Angel Garced, LCDR Tameka Kastner and LT Neil Barranta.
The data suggest that stress levels have been increasing, both speakers said, with Collins calling stress “a national affliction” and Murthy citing two major causes—“the shift to a more relentless, 24/7 work culture” and “a change in social engagement and interaction.”

“Our world, and our country in particular, are full of people with thousands of friends on Facebook and Twitter who live in densely populated condo buildings and busy cities, who are profoundly alone,” Murthy said. “In one survey, one-quarter of the respondents said they didn’t have a single person they could confide in about a personal problem.” Social media cannot replace in-person connections, he added, and actually make us feel worse when we compare ourselves to what is really “a fictionalized or partial version of others’ lives.” Money challenges, relationship/family issues and health problems also pile on the stress. Is there a way to lighten the load?

Murthy emphasized social connection, including reaching out in the workplace. However, other tools offer support, too. “Sleep is when our brain regenerates and forms memories and our body tissues heal. When we don’t sleep enough, it impairs our ability to make decisions, learn and heal and hormonal disturbances occur.” Collins added, “You lose your sense of wanting to be creative—you just want to get through the day. For an institution like NIH, where our future depends on our creativity, this [sleep-deprivation situation] is the wrong thing, but it seems to happen too often.”

Meditation “has been shown to be incredibly important and helpful when it comes to stress, [but] sometimes gets subjected to misconceptions and stereotype,” Murthy continued. “I have often said that meditation has a serious branding problem, because people think you’re talking about an Indian yogi sitting cross-legged on the floor for hours and hours.

“Over time, we have learned that meditation can be powerful in inducing a relaxation response.” Murthy added. It’s being used more and more in the Veterans Administration health system, including with post-traumatic stress; a growing number of meditation programs are cropping up across the country, including in schools. The benefits that educators report, he said, include better academic performance, improved behavior, fewer suspensions and lower teacher absenteeism. “Like all things,” Murthy said, “prevention is better than cure if we can get there early enough.

Getting to kids early [with skills to handle chronic stressors] is, to me, the most important form of prevention.”

When discussing research on the biological effects of meditation, Murthy said, “There is not as much research, or high-quality research, on meditation as on other interventions like medications for diabetes or hypertension...but we have what I believe is a significant amount of data and anecdotal experience to tell us that something real here is happening and there’s reason to invest more in this research. What we cannot afford is to allow the typical 7, 10 or more years for a proven intervention to percolate through into clinical practice.” He urged that the entire array of anti-stress tools be viewed with an eye to wherever they could be used. More awareness in the public and among policymakers of the stress problem, and even “a major cultural shift in how we think about and address stress,” may be needed.

Other anti-stress approaches that Murthy and Collins discussed include regular exercise, “which is far more important than we understood and can function as an acute and chronic antidepressant.” They also touched on music, with Collins referring to NIH’s partnership in the Sound Health initiative and Murthy noting music’s “powerful ability to change how we perceive the world and to activate the relaxation response.”

Finally, they urged attendees to pay more attention to self-care. Murthy entreated health care providers specifically: “We’ve all seen those old cartoons of doctors telling their patients not to smoke, while they’re smoking themselves. We’re doing that with stress—we’re telling people to relax and take it easy, get sleep, etc., while we ourselves as clinicians are running ourselves ragged and paying no attention to the profound impact. We need to lead by example and to change the culture in the country, starting with our own culture of medicine.”

Murthy urged listeners to be concerned not only about their own stress, but also that of others. “When someone deals with emotional trauma and stress and it results in acts of violence, it affects all of us. When we have unchecked stress leading to greater levels of addiction in our country, that affects all of us. When stress and emotional discord prevent us from being able to come together and talk about big problems and come to solutions—that, too, affects all of us. We have to think about how we can help to [relieve] stress for people around us...Reaching out to build connections based on compassion and kindness can have a profound effect.”

Disease Resistance Spread Successfully from Modified to Wild Mosquitoes

Using genetically modified (GM) mosquitoes to reduce or prevent the spread of infectious diseases is a new but rapidly expanding field of investigation. Among the challenges researchers face is ensuring that GM mosquitoes can compete and mate with their wild counterparts so the desired modification is preserved and spread in the wild population. Investigators at Johns Hopkins University have engineered GM mosquitoes to have an altered microbiota that suppresses human malaria-causing parasites. These GM mosquitoes preferred to mate with wild mosquitoes and passed along the desired protection to many generations of offspring.

The research was funded by NIAID. The work is reported in *Science*.

The researchers genetically modified *Anopheles* mosquitoes, which in nature spread the malaria-causing parasite *Plasmodium*. The team caged equal numbers of wild and GM mosquitoes and monitored their breeding over 10 generations. Ninety percent of the offspring in each generation passed along the GM trait. Even when combining 10 percent GM with 90 percent wild mosquitoes, the *Plasmodium*-resistance trait dominated after a few generations. Importantly, the GM mosquitoes maintained their resistance to the malaria parasite for 7 years.

The group also showed that the change in the microbiota resulted in a mating preference among the GM and wild mosquitoes. GM males showed a preference for wild females and wild males preferred GM females; these preferences contributed to the spread of the desired protective trait within the mosquito population.

The authors note that work was conducted in a laboratory setting and that more research is needed to determine if what they observed in the laboratory also will occur under natural conditions. Nevertheless, the study suggests that mosquitoes can be genetically modified to compete in nature with wild populations and spread resistance to the malaria-causing parasite. If implemented, this strategy could eventually result in decreased disease transmission to humans.

NIH Researchers Uncover Drain Pipes in Our Brains

By scanning the brains of healthy volunteers, researchers at NIH saw the first, long-sought evidence that our brains may drain some waste out through lymphatic vessels, the body’s sewer system. The results further suggest the vessels could act as a pipeline between the brain and the immune system.

“We literally watched people’s brains drain fluid into these vessels,” said Dr. Daniel Reich, senior investigator at NINDS and senior author of the study published online in *eLife*. “We hope that our results provide new insights to a variety of neurological disorders.”

Reich is a radiologist and neurologist who primarily uses magnetic resonance imaging (MRI) to investigate multiple sclerosis and other neurological disorders thought to involve the immune system. Led by postdoctoral fellows Dr. Martina Absinta and Dr. Seung-Kwon Ha, along with researchers from NCI, the team discovered lymphatic vessels in the dura, the leathery outer coating of the brain.

Lymphatic vessels are part of the body’s circulatory system. In most of the body they run alongside blood vessels. They transport lymph, a colorless fluid containing immune cells and waste, to the lymph nodes. Blood vessels deliver white blood cells to an organ and the lymphatic system removes the cells and recirculates them through the body. The process helps the immune system detect whether an organ is under attack from bacteria or viruses or has been injured.

In 1816, an Italian anatomist reported finding lymphatic vessels on the surface of the brain, but for two centuries, it was forgotten. Until recently, researchers in the modern era found no evidence of a lymphatic system in the brain, leaving some puzzled about how the brain drains waste and others to conclude that the brain is an exceptional organ. Then in 2015, two studies of mice found evidence of the brain’s lymphatic system in the dura. Coincidentally, that year, Reich saw a presentation by Dr. Jonathan Kipnis, a professor at the University of Virginia and an author of one of the mouse studies.

“I was completely surprised,” said Reich. “In medical school, we were taught that the brain has no lymphatic system. After Dr. Kipnis’s talk, I thought, maybe we could find it in human brains?”

To look for the vessels, Reich’s team used MRI to scan the brains of five healthy volunteers who had been injected with gadobutrol, a magnetic dye typically used to visualize brain blood vessels damaged by diseases such as multiple sclerosis or cancer. The dye molecules are small enough to leak out of blood vessels in the dura but too big to pass through the blood-brain barrier and enter other parts of the brain.

At first, when the researchers set the MRI to see blood vessels, the dura lit up brightly and they could not see any signs of the lymphatic system. But, when they tuned the scanner differently, the blood vessels disappeared and the researchers saw that dura also contained smaller but almost equally bright spots and lines that they suspected were lymph vessels. The results suggested that the dye leaked out of the blood vessels, flowed through the dura and into neighboring lymphatic vessels.

“These results could fundamentally change the way we think about how the brain and immune system inter-relate,” said NINDS director Dr. Walter Koroshetz.

Monoclonal Antibodies Against Zika Show Promise in Monkey Study

Using blood samples from an individual previously infected with Zika virus, scientists funded by NIAID have developed an antibody-based Zika virus therapeutic that protected monkeys from infection. Because monoclonal antibodies are generally safe, they believe that this antibody cocktail might be appropriate for uninfected pregnant women; because the antibodies will likely cross the placenta, the researchers hope that administration during pregnancy may protect both the pregnant woman and the fetus from Zika virus. The investigators are hoping to test this concept by pursuing studies in people.

The scientists isolated immune cells from the patient’s blood and used them to make 91 monoclonal antibodies—immune system fighters designed to bind to a specific part of an invading virus or bacterium to stop the infection. They identified three antibodies that bound to Zika virus surface proteins and each neutralized the virus. The researchers then administered a combination of these antibodies to rhesus macaques and exposed the animals to Zika virus one day later. During the 21-day study, all 4 monkeys who received the antibody cocktail showed no virus replication.

Researchers at the University of Miami and the Scripps Research Institute led the project with collaborators in Brazil and the U.S. The work was reported in *Science Translational Medicine*. 
Dr. Amy Poremba has joined NIDCD as a program director.

She completed her neuroscience postdoctoral training at the University of Texas and the National Institute of Mental Health, where she used animal models to explore the neural circuitry of communication. She then joined the department of psychological and brain sciences at the University of Iowa. As a professor there for 16 years, she conducted research on auditory central nervous system processing and communication. Her research focused on the neurobiology of auditory processing, learning, and memory to guide translational efforts aimed at improving care for people with impaired hearing or neurological disorders. While at the University of Iowa, Poremba also served as director of the behavioral and cognitive neuroscience division, where she managed student curricula, graduate program training, faculty and student recruitment and graduate student mentoring.

NHLBI Branch Chief Sorlie Retires After 48 Years

Dr. Paul Sorlie, chief of the Epidemiology Branch in the Division of Cardiovascular Sciences, will retire from the National Heart, Lung, and Blood Institute on Oct. 27 after 48 years of service.

Sorlie received his bachelor’s and master’s degrees from the University of Minnesota, in mathematics and biometry respectively. From 1965 to 1967, he served in Ghana as a Peace Corps volunteer teaching high school mathematics. He came to the then National Heart and Lung Institute in 1969 as a Public Health Service commissioned officer, working as a statistician for the landmark Framingham Heart Study.

In 1971, he took a 2-year break from NIH and lived in Uganda to develop and implement protocols and techniques to evaluate performance of a maternal and child health project in Kampala. He returned to NHLBI in 1973 and has worked tirelessly to advance research in cardiovascular epidemiology ever since. It is also during his tenure at NHLBI that he obtained his doctoral degree in epidemiology at Johns Hopkins School of Public Health.

Sorlie has had a distinguished research and administrative career, leading a wide range of epidemiology research studies, including serving as project officer for the Framingham Heart Study for 11 years and initiating the Hispanic Community Health Study/Study of Latinos, the largest longitudinal health study in the U.S. with a diverse representation of Hispanic/Latino heritage groups. He has had over 150 publications and received numerous awards, including multiple NIH Merit Awards and NIH Director’s Awards.

In addition to his research, Sorlie was a lecturer and course director at the FAES Graduate School at NIH from 1990 to 2010. He has been a mentor to scores of trainees and staff, some here for short visits, others who have continued long and productive careers at NHLBI. He also participated in community volunteer activities during this time.

NINDS Mourns Former Chief of Neurosurgery Oldfield

Dr. John Heiss, SNB chair and residency program director. "Dr. Oldfield was always an inspiration to me,” said Dr. John Heiss, SNB chair and residency program director. "Throughout his life, he successfully balanced neurosurgery, science, professional leadership, social relationships and family life and was a model for aspiring physician-scientists. He aided the research endeavors of scientific colleagues and mentored young neurosurgeons. His motivation to make significant scientific and medical advances never waned. I join his family, friends and colleagues in celebrating his life and mourning his death.”

Born in Mt. Sterling, Ky., Oldfield received his undergraduate education at the University of Kentucky as a physics major and after 3 years entered medical school in 1969. He earned his medical degree from Kentucky in 1973 and completed his general surgical residency training at Vanderbilt University Hospital in 1975. He then spent a year as a visiting registrar in neurology and neurosurgery at the National Hospital for Nervous Disease in Queen Square, London, before beginning neurosurgical residency training at Vanderbilt.

Prior to coming to NIH, he spent a year in private neurosurgical practice in Lexington, Ky.

Oldfield joined NIH in 1981 as a senior staff fellow in the SNB working on the cellular immunology of tumors. He became chief of the clinical neurosurgery section in 1984 and SNB chief in 1986.
From 1987 to 2007, he also was on the faculty at Georgetown University Medical Center, serving as a clinical professor in the department of neurosurgery.

In 2007, Oldfield retired from full-time government service to become the Crutchfield chair in neurosurgery and a professor of neurosurgery and internal medicine at the University of Virginia. There he contributed to the department of neurosurgery research program and led a multidisciplinary effort in the treatment of pituitary tumors.

Even while at UVa., Oldfield continued to visit NIH periodically as a clinical collaborator—training and mentoring NIH neurosurgeons and neurosurgery residents. He fostered the career development of his fellows and other trainees, many of whom achieved tenured positions and chairmanships in neurosurgery departments in the U.S. and internationally.

Among his many research accomplishments, Oldfield developed a new drug-delivery technique—called convection-enhanced delivery—for treatment of central nervous system diseases, including brain tumors, Parkinson’s disease and lysosomal storage diseases. His laboratory developed gene therapy for malignant brain tumors and he directed the first clinical trial of gene therapy within the central nervous system. His research led to new insights into how Chiari I malformation (a structural defect in the base of the skull and cerebellum) caused syringomyelia, a finding that improved treatment of the condition. (Syringomyelia is a disorder in which a fluid-filled cyst forms within the spinal cord.)

Oldfield’s research on cerebral vasospasm (narrowing of the brain’s blood vessels that can cause stroke) after a ruptured brain aneurysm led to clinical trials of novel agents to treat it.

Throughout his career, he received numerous honors including a Public Health Superior Service Award for “successfully managing the SNB, training academic neurosurgeons and advancing the understanding of the biology of brain tumors” and the Grass Medal for Meritorious Research in Neurological Science from the Society of Neurological Surgeons.

Oldfield also received the Farber Award from the American Association of Neurological Surgeons (AANS) for his brain tumor research, the Cushing Award for Technical Excellence and Innovation in Neurosurgery and AANS’s highest honor, named for the father of modern neurosurgery—the Harvey Cushing Medal—for his many years of outstanding leadership, dedication and contributions to neurosurgery.

UK’s Medical Alumni Association recognized Oldfield as “the quintessential clinical scientist” who made “remarkable contributions to the understanding of the nervous system and the practice of neurosurgery.”

Oldfield served on the editorial boards of neurological journals, including co-chair of the Journal of Neurosurgery from 2001 to 2002 and associate editor from 2009. He served as vice-president and president of the Society of Neurological Surgeons. He authored more than 500 scientific and clinical articles and was co-inventor of patents on convection-enhanced drug delivery and genetic therapy.

“Ed’s contributions have advanced neuroscience and medicine in fundamental and critical ways,” said Dr. Russell Lonser, professor and chair of the department of neurological surgery at Ohio State University. "His legacy will endure through his family, the patients’ lives he improved, the important biologic discoveries he made and those fortunate enough to have trained and/or worked with him."

Oldfield is survived by his wife Susan and his daughter Caroline. His family welcomed colleagues and trainees to their home, creating life-long friendships that extended beyond science and medicine.

Below, Dr. Edward Oldfield in one of NIH’s surgical suites; below, a more recent portrait courtesy of the University of Virginia

### Healthy Adults Sought

NIHBI study team seeks healthy adults for a research study. Researchers are studying cells taken from the lungs of healthy individuals to compare to cells taken from individuals with asthma and other lung diseases. Compensation is provided for participation. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at http://go.usa.gov/xKtBk. Refer to study 99-H-0076.

### 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 if 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. Read more at https://go.usa.gov/xNHTJU. Refer to study VRC316.

### Have Hepatitis B?

Do you have chronic hepatitis B? Researchers are testing whether taking an oral antiviral and peg-interferon injection together is safe and better controls the hepatitis B virus as compared to taking only one of the medications. Study-related tests, procedures and medication are at no cost. For more information, contact the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read about the study at http://go.usa.gov/x9nSt. Refer to 15-DK-0082.

### RSV Vaccine Study Needs Healthy Volunteers

NIAID researchers seek healthy volunteers, 18-50 years old, for an investigational vaccine study targeting respiratory syncytial virus (RSV). Compensation is provided. For more information, call 1-866-833-5433 (TTY 1-866-411-1010). Email vaccines@nih.gov or visit http://bit.ly/2nOkOvY. Refer to study VRC316.

### Study of Hereditary Stomach Cancer

NCI researchers need volunteers with hereditary stomach cancer for a clinical study at the Clinical Center. Study-related tests, procedures and medication are at no cost. For more information, call 1-866-833-5433 (TTY 1-866-411-1010). Read about the study at http://go.usa.gov/x9nSt. Refer to 15-DK-0082.

### Study of Hereditary Stomach Cancer

NCI researchers need volunteers with hereditary stomach cancer for a clinical study at the Clinical Center. This study investigates hereditary forms of stomach cancer and the genes that may cause them. All study-related tests and procedures are provided at no cost. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more online: https://go.usa.gov/x78F. Refer to study 17-C-0043.
NIAMS Summer Interns Reflect on Experiences

“Eye-opening,” “influential” and “invaluable” were among the many expressions that the NIAMS 2017 summer interns used when reflecting on their experiences. This past summer, senior investigators in the NIAMS intramural research program spent 2 months mentoring and providing career guidance to 17 students from universities across the United States. From attending lectures and symposia to conducting basic and clinical research, each intern encountered unique opportunities for growth.

“These past two summers have played a pivotal role in my decision to pursue a career in translational research,” explained a returning intern.

“Being a part of the NIAMS enhanced the experience as everyone was invested in making me a better scientist and pushing me to strengthen my laboratory, networking and communication skills,” said another student.

The NIAMS Summer Research Program provides outstanding training opportunities for high school, undergraduate, graduate and medical students. Students can apply online at https://www.training.nih.gov/programs/sip. The application for summer 2018 will be available in mid-November.

Innovative Research Presented at Poster Day

More than 300 research posters representing projects undertaken by NIH Summer Research Program participants filled several display areas within Natcher Conference Center at a poster day on Aug. 10. Among the presenters were Louis Wang (l), a sophomore at Cornell University, and James Xu (second from l), a freshman at Columbia University. Both worked this summer in the infrared imaging and thermometry unit, a trans-NIH intramural resource at NIBIB, on using mobile phones to monitor certain aspects of health. With help from NIBIB mentors Drs. Aleksander Gorbach (third from l) and Alexandr Smirnov (r), NIBIB unit chief, Wang and Xu designed and built a portable video device that enables a mobile phone to monitor the shape of capillaries in a region close to the fingernail—information that can have implications, for example, about rheumatic diseases. The method is wireless and offers continuous monitoring of peripheral microcirculation, even when patients are remote from a clinic or doctor. Working with clinical groups from NIEHS and NHLBI, the team created custom software and specially designed attachments for an iPhone 7 to quantify nail fold capillary density. Hans Prakash, a post-baccalaureate IRTA in the unit who is also a part of the team, is working with the clinical groups to evaluate the device at the Clinical Center.

PHOTO: RAYMOND MACDOUGALL

NIAMS Hosts Ectodermal Dysplasias Workshop

NIAMS recently convened a meeting on ectodermal dysplasias (ED). This group of more than 180 genetic disorders results from defects in the ectoderm—the outer layer of cells—of the embryo. ED affects the development or function of the teeth, hair, skin, nails and sweat glands. Topics discussed included ED classification, cellular defects and early diagnosis. Workshop participants included (bottom row, from l) Drs. Timothy Wright, Rena D’Souza, Isaac Brownell of NIAMS’s Dermatology Branch and Mary Fete; (second row, from l) Drs. Clark Stanford, Birgitta Bergendal, Maranke Koster and Holm Schneider; and (top row, from l) Drs. Clayton Butcher, conference organizer Maria Morasso, chief of the NIAMS Laboratory of Skin Biology, and Timothy J. Fete.

PHOTO: DONYA BERHAN