

SCIENCE + INNOVATION + SOCIETY

Farrar Offers 3-Part Prescription for Global Health

BY CARLA GARNETT

The well-being of the world rests atop a three-legged stool, according to Dr. Jeremy Farrar, director of the Wellcome Trust, who also currently chairs the Heads of International Research Organizations. And while two of the legs—science and innovation—are strong and robust, their links to the third critical leg—society—need immediate and constant fortification, or global health could collapse.

“That combination of science, innovation and society is the triangle that Wellcome seeks to put together,” Farrar said recently

in Masur Auditorium at the David E. Barmes Global Health Lecture. “Unless we bring those three things together, emotionally and intellectually, and in everything we do, then I don’t think doing any one of those alone will make the transformational changes that are possible and ensure that science and innovation [are] embraced by and accessible to the greatest number of people, wherever they live.”

Lest there be any doubt, Farrar warned in his lecture “Science in a Changing World,” transformational changes are vital now and in coming years to keep pace with incredible research opportunities and shifting political dynamics.

“The truth is, global health has been an absolutely phenomenal success story,” he pointed out. “Over the last few decades, the transformation in people’s lives around the world has been nothing short of remarkable.”

Consider just one example, he said:

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At NIH for the 2019 Barmes Lecture, Dr. Jeremy Farrar holds a copy of the first *Wellcome Global Monitor*, a report on worldwide health status.

LIFE SAVED HERE

OIT’s Sweeney Comes by Love of NIH Honestly

BY RICH MCMANUS



Kevin Sweeney

Kevin Sweeney, a desktop technician with the Office of Information Technology since last March, has been associated with NIH, man and boy, for much of his life. And he is that rare NIH’er who is grateful not just

for his work at a place that holds high the mission of health, but to be alive at all. Years ago, in a story fraught with serendipity, NIH saved his life.

SEE **SWEENEY**, PAGE 4

AT ROBERTS LECTURE

NIMH’s Berman Discusses Williams Syndrome

BY MOHOR SENGUPTA

In an engaging video, the interaction between two young children is shown. One child is clearly much more social than the other. She continuously tries to interact with the other child, who is seen shying away. Dr. Karen F. Berman, senior investigator and chief of NIMH’s Clinical and Translational Neuroscience Branch, said that the opposite



Dr. Karen Berman

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Poster Day is NIH’s Woodstock. See p. 12.

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Chamber Singers Hold Auditions

The NIH Chamber Singers, a group of 15-20 singers who perform mostly *a cappella* pieces from a wide range of musical styles, will hold auditions at 5:30 p.m. on two Tuesdays—Aug. 27 and Sept. 3—at a private residence off Cedar Lane near the NIH campus. For the upcoming fall season, there is one opening for a baritone/bass.

The season runs through the academic year, from September through May, and each “semester” culminates with a series of three or more performances, one series in December and one in May. Rehearsals take place weekly on Tuesday evenings during the season (5:30-7 p.m.).

Three-part audition consists of singing: in a quartet for evaluation of sight-reading and part-singing ability, scales to help determine appropriate vocal range and a solo of your choice, unaccompanied.

If you are interested, schedule an audition with coordinator Jenn Symonds at symonds.jennm@gmail.com.

Get Trained for Overdose Emergencies

In response to the Surgeon General’s Advisory on Naloxone and Opioid Overdose—knowing how to use naloxone and keeping it within reach can save a life—NIH Public Health Service officers have been trained as trainers under the auspices of the Maryland department of health. Individuals are invited to attend Opioid Overdose Response Training. Sessions are scheduled weekly now through Monday, Dec. 23 at the FAES Terrace classrooms, Bldg. 10. The training is conducted by PHS officers and is under 90 minutes, including hands-on experience with naloxone devices.



Cmdr. Daniel Goldstein and Lt. Cmdr. Raven McGlotten lead a hands-on training session.

PHOTO: PETER KILMARX

Over the past 15 years, communities across the nation have been tragically affected by the opioid epidemic, with the number of overdose deaths from prescription and illicit opioids doubling from 21,089 in 2010 to 47,600 in 2017. Naloxone is an opioid antagonist that is used to temporarily reverse the effects of an opioid overdose. Expanding awareness and availability of this medication is a key part of the public health response to the opioid epidemic. Naloxone is a safe antidote to



NSO Musicians Perform Duets

On July 30, National Symphony Orchestra musicians Jae-Yeon Kim on violin and Ellen Hwangbo on piano performed pieces by Brahms, Kreisler, Gershwin and Ravel for an appreciative audience in the Clinical Research Center atrium. Upcoming concerts in the CRC include the full National Symphony Orchestra on Sept. 26 at 1:30 p.m. and the Washington Chorus on Oct. 10. For a complete listing of future performances in the atrium, visit <https://clinicalcenter.nih.gov/ocmr/music.html>.

PHOTO: DEBBIE ACCAME

a suspected overdose and, when given in time, can save a life.

Sign up to take the training at <https://www.signupgenius.com/go/30e0c4dada72ba2fc1-hands>.

Questions? Contact Cdr. Leo Angelo Gumapas of the Office Research Facilities, leoangelo.gumapas@nih.gov, (301) 832-4320.

‘MedlinePlus’ Magazine Launches New Bilingual Website

The NIH *MedlinePlus* magazine recently launched a new bilingual website that offers content in English and Spanish. Use the English/Español toggle in the magazine header to change the language.

English version, *NIH MedlinePlus Magazine*, is available at <https://magazine.medlineplus.gov/>. Spanish version, *NIH MedlinePlus Revista*, is available at <https://magazine.medlineplus.gov/es/>.



The new magazine contains identical content in both languages. Previously, the separate English and Spanish versions of the magazine had unique content. The *NIH MedlinePlus Salud* magazine was retired and the archived issues are available on the website.

The online version of the magazine uses a continuous publication model that allows immediate publication of an article as soon as it’s ready. It also features additional online-only content that will not appear in the print version.



Volkow, Fauci Present at Conference

NIDA director Dr. Nora Volkow (l, seated) delivered a plenary talk titled “Opioid crisis and its impact on HIV and HCV” at the 10th International AIDS Society Conference on HIV Science in Mexico City in July. Her sister Dr. Patricia Volkow (second from l), an infectious disease specialist at the National Cancer Institute in Mexico City, gave a follow-up talk on “HIV and co-morbidities: Kaposi’s sarcoma. State of the ART and beyond.” The Volkow sisters have never shared a scientific podium until now; they accompanied NIAID director Dr. Anthony Fauci, who opened the session with a presentation on “HIV in 2019: Optimizing the treatment and prevention toolkit.” At right is Dr. Carlos Perez, Catholic University of Chile.

PHOTO: INTERNATIONAL AIDS SOCIETY/JORDI RUIZ CIRERA

Do Microbes, Nervous System Talk to Each Other?

BY ELLEN O'DONNELL

Dr. Isaac Chiu had an idea for a research project that would cross the body and brain and address important biomedical questions related to pain and microbes.

But it wasn't clear where his project would fit among the NIH institutes and centers, and its path wouldn't be entirely known at the start. Could it find a "home" at NIH?

Chiu ended up applying for, and receiving, an NIH Director's New Innovator Award—a small group of elite awards made to early-career investigators for "exceptionally creative, innovative and high-impact" research ideas.

In a recent lecture, Chiu discussed his work under NIH support, including his New Innovator grant co-funded by NCCIH and the NIH Common Fund. His focus has been the nervous system's interactions with bacteria (including those in the gut) and how those interactions could influence pain as well as certain infectious and/or inflammatory diseases.

Chiu is an assistant professor of immunology at Harvard Medical School, where he received his Ph.D. in immunology, and his lecture was part of a microbiome series within NCCIH's Integrative Medicine Research Lectures.

"Pain is something we all experience, and bacterial infections are often painful. Pain is driven by peripheral sensory neurons called nociceptors whose nerve fibers densely innervate barrier tissues [e.g., those of the mouth, gut, skin and respiratory tract] that are exposed to microbes," Chiu said.



Harvard's Dr. Isaac Chiu gives recent NCCIH lecture.

PHOTOS: CHIA-CHI CHARLIE CHANG

"We have found that the nervous system, like the immune system, has developed ways to directly sense bacteria as well as other pathogens [disease-causing organisms]—through receptors on neurons and molecules produced by bacteria. Neurons are not passive, but signal to the immune system in multiple ways. Pain is also a cardinal sign of inflammation. These connections across systems form an exciting area of research," he explained.

His research team's discoveries include that certain distinct bacterial species can activate nociceptors to produce pain and, conversely, that sensory neurons have ways to detect certain bacterial pathogens. An intriguing "flip side" is whether bacteria can not only cause pain, but also silence it.

In one study, his group found that two different bacteria, *Streptococcus pyogenes* and *Staphylococcus aureus*, directly activate nociceptors via "pore-forming" toxins, to produce pain in a rodent model. The team then tried delivering a normally membrane-impermeable pain blocker through those same pores. This basically silenced pain more effectively than ibuprofen or lidocaine. Another discovery was that bacteria are dual-action in that they actively try to cause pain,

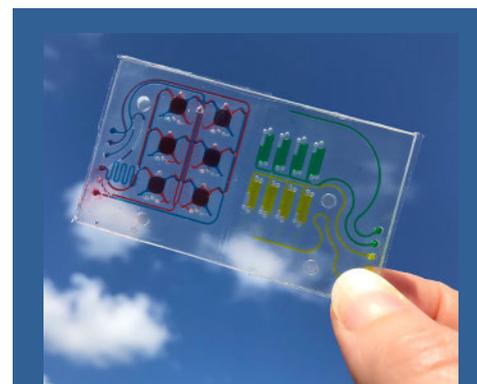
to compromise the immune system and facilitate their own ability to survive.

Chiu has extended this line of inquiry into questions about the gut microbiome, such as: Does the gut microbiota regulate pain? Could gut microbes have a role in the transition from acute to chronic pain? If so, is that action two-way, with the nervous system also altering the microbiota? Do our drug treatments for pain alter the microbiome?

Chiu thinks that there is a connection between the gut microbiome and pain.

"It's still early days," he said, "but there is evidence that nociceptor neurons can respond to different types of gut commensal microbes. The gut microbiome could play an important role in 'tuning' chronic pain. Both the nervous system and opioids regulate the composition of the gut microbiome. Maintenance by neurons of a healthy microbiome could be important in gut physiology and host defense. But, above all, the nervous system talks to the gut and vice versa, and I think that's something we have to think about when treating pain."

The lecture is available at <https://videocast.nih.gov/Summary.asp?Live=31902&bhcp=1>. **R**



ON THE COVER: *Tissue chips in space.* Example of NCATS tissue chip, which contains tiny chambers where human cells live, grow and do their thing. Scientists use tissue chips to study diseases that affect certain parts of the body. Last May, similar chips were launched into space to study the effects of microgravity.

IMAGE: LUCIE LOW, NCATS

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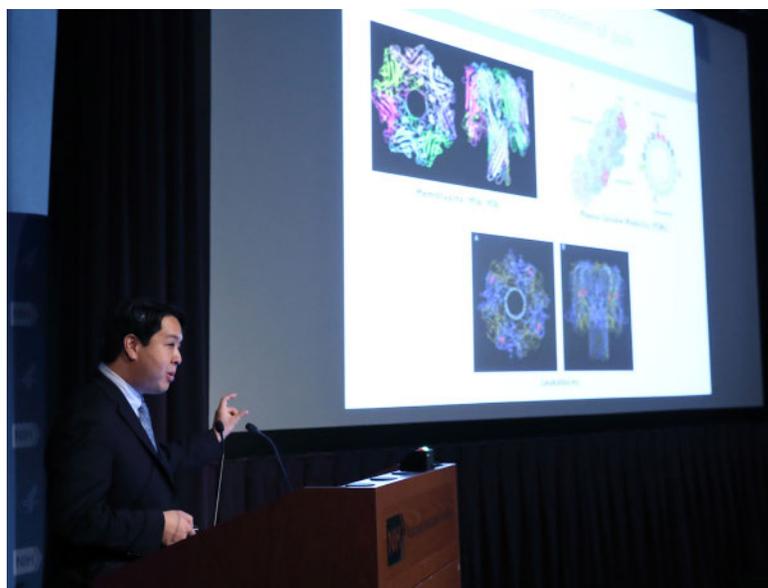
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Sweeney is deeply grateful for NIH's care.

PHOTOS: RICH MCMANUS

Sweeney

CONTINUED FROM PAGE 1

Sweeney, now 63, was an Army brat, born on a base in Heidelberg, Germany. By the time his family moved to Wheaton in 1968, when he was 12, the family had lived—and by Kevin's account, left a rather rambunctious mark—in New York, suburban Chicago, Columbus, Ga., and Atlanta.

"We were horrible children," says Sweeney of his older brother, his twin brother and a younger sister and brother. "What a band of troublemakers my mother had to put up with," he adds, recounting the time his brother pulled him out of a neighbor's pool, to save him from drowning. And the time he dangled by the flesh of his arm from the barbs of a cyclone fence.

"My mother contemplated having a wing of the local hospital named for us, we were there so often."

Not long after the family relocated to Montgomery County, Sweeney and his twin brother—14 minutes older than Kevin—enrolled in a twin study at NIH. He got a patient ID number and spent the summer commuting by bus to NIH for testing and interviews.

"That was my first introduction to NIH."

Sweeney graduated from John F. Kennedy High School in Wheaton, where he had played football and wrestled, then attended Towson State University for a year before realizing that he wasn't ready for college.

For a couple of years he worked odd jobs—sales rep at Hechinger's, which was the Home Depot of its day in suburban D.C.,

★ ★ ★
"I can't express how grateful I am for the treatment I got here."

—KEVIN SWEENEY

★ ★ ★

and dishwasher and busboy at the legendary Capitol Hill watering hole, the Tune Inn, which was owned by a neighbor in Wheaton.

The Tune Inn has birthed many a life lesson over the decades, and Sweeney picked up at least two. There was the night after shift when he decided to ride as a passenger on the back of a customer's Norton 750 Commando racing motorcycle. The driver popped a wheelie at 100 m.p.h. on Independence Ave., as Sweeney hung on for dear life.

Then there was the time Rep. John Anderson, then running for President, decided he would take over the Tune Inn at lunchtime for a staff meeting. The bar's owner told Anderson and his entourage that they could wait in line like everybody else.

"At the Tune Inn, social status doesn't mean a lot," Sweeney observes, drily.

Such experiences convinced Sweeney of the value of an education, so in the next few years, he took courses in information systems management at Montgomery

Sweeney was filling out a questionnaire that inquired about night sweats, or lumps in the throat. Indeed he had a lump near his lower right jaw that soon drew the attention of a series of doctors. A biopsy at Holy Cross Hospital probed a mass under a vein in his neck, and a sample was sent to pathologists at Walter Reed.

It took weeks, but Sweeney, then 29, learned he had synovial cell sarcoma.

The news hit Brenda hard. One day, while delivering mail in Kensington, she was stopped by a customer who noticed that she was not her normal, jovial self. The customer was Dr. Lyndon Lee, a retired NIH scientist. Brenda shared her husband's diagnosis, and soon Lee was trying to enroll him in a protocol at NIH.

"I came to NIH and I met a doctor in Bldg. 10 and told him all I'd been through," said Sweeney. "He said, 'Let me put it in the computer and see what happens.' I turned out to be a good match for his study." His old patient ID number from the twin study was

The Importance of Lightness

Though his experience with body-altering surgery took place 33 years ago, Kevin Sweeney still recalls the episodes of lightheartedness and humor that made his ordeal bearable.

The surgeon who operated on him was a bearded fellow from Baltimore—Sweeney can't remember his name—and he had "a light side to him that really made me relax."

On the day of his procedure, Sweeney, who sported a beard himself in those days, cut it off, assuming that surgeons would need easy access to his jaw.

When his surgeon saw the newly trimmed Sweeney, he exclaimed, "Why'd you cut your beard? I would have done it for you."

Later, during Sweeney's post-op treatment, when all he could handle was soft food, an ice cream party was thrown in his honor. Upon learning the party took place without him, the

surgeon upbraided his patient: "What? You didn't invite me?"

Another time, during radiation treatment at NIH, Sweeney showed up at his appointment and noticed the smell of burning popcorn in the air. Sweeney made it clear that whoever had burned the popcorn better not be manning his radiation treatment.

"The technician started howling with laughter," Sweeney recalls. "She was screaming, 'You're nuts!'"

College while also working full-time in the graphics department at Vitro, a defense contractor in Aspen Hill. It took him 5 years to earn his A.A. degree.

In the summer of 1980, Sweeney married his girlfriend Brenda, whom he had met but not dated in high school. At the time of their wedding, she was a waitress at Bethesda's famed old seafood house, O'Donnell's, but later took a job as a letter carrier, a job that would prove strangely fortuitous.

In the fall of 1985, while participating in a corporate blood drive at Vitro,

still in the system and became part of his inpatient wristband.

Sweeney was given three treatment options, all of which involved surgery. "I said fine—I really had no idea what I was doing."

He underwent surgery—a "modified right neck dissection" that ran from his jaw to his collarbone—in August 1986, with hopes of being well enough to attend a friend's wedding in September.

"They took out muscles and nerves—anything the tumor had grown onto," Sweeney recalls. "It took 7 hours. They

made a movie of the procedure, which is still probably in the archives of NIH.”

Doctors told him his case was of special interest because of the tumor’s location—it normally isn’t found above the shoulders, preferring joints such as shoulders and knees. “That gave them a lot of drive to put me into a protocol,” Sweeney recalled.

Though post-operatively “I had a tremendous loss of ability to hold my head up,” Sweeney soon found himself involved in customary shenanigans: needing to use the bathroom one day in the ICU, he yanked out all his tubes, prompting more than a dozen caregivers to rush his room, thinking he had coded. Then there was the time his twin brother decorated Kevin’s room with toys from Toys R Us, then, toting a plastic bag filled with 1,000 plastic flies, proceeded to leave them all over the Clinical Center.

“He hit all the floors. I thought that was pretty funny.”

Sweeney soon went back to work at Vitro and was able to make that September wedding. His health scare also prompted a new seriousness about school. He enrolled at the University of Maryland University College to get his 4-year degree in computer and information sciences.

There were follow-up radiation treatments at NIH, but he scheduled them for early in the day so he could go to work.

“Everyone at NIH was very kind and very nice and very helpful,” he said. “I couldn’t have had a better experience, going through that part of it.”

His ordeal left him with limited ability to enjoy food for several months.

“Beer tasted like crap,” he remembers. “When that happens, you know you’re in trouble.”

Because of nerve removal, he was left with Horner’s syndrome, a drooping of the right eyelid.

Halfway through his course of radiation, he suffered a breakdown.

“It finally hit me one day,” he said. “Why me? Why am I going through this? I started crying while I was sitting in my car. I guess it was the release of all that pent-up pressure and tension.”

Soon, however, he snapped out of his funk when he remembered that his dad—a career military man and West Point graduate who had died of a heart attack just 5 years earlier—would want him to “stand up and

march through it. From that point on, I just decided to go on.”

He had lost so much weight that an NIH doctor threatened to have him re-hospitalized and force-fed, but once radiation treatment ended, Sweeney began to mend.

“The farther away I got from radiation, it all started to come back to me—even beer.”

NIH kept him on a post-treatment plan for the next decade. Sweeney had to check in every 3 months. Thyroid medication, which he is still on, took care of an organ burned up in therapy.

He also needed speech therapy, to correct surgery-related changes in the timbre of his voice.

Thirty-three years after his operation, Sweeney considers himself well and truly cured, though he still has problems with his neck and shoulders related to muscles removed during surgery.

“My experience at NIH was tremendous,” he concludes. “The most heart-breaking thing in all those 10 years of follow-up was the trip I had to make from EKG on the first floor. I’d pass young children on their way to cancer treatment. That broke my heart, to see them go through what I did at such a young age. I’d pray for them.

“Some people get dealt a bad hand pretty early,” he continued. “Other people have to wait for it. I’m just blessed that nothing went wrong. I personally consider my wife [who recently retired after 38 years with the Postal Service] to have saved my life. She’s my hero when it comes to this.”

A believer in paying it forward, Sweeney now donates blood and plasma at the Red Cross “as payback. You’ve got to be willing to pay back society, if they did something for you.”

He even coached 8-year-old girls in softball, as part of his restitution.

“That was some tough payback,” he laughs.

“I can’t express how grateful I am for the treatment I got here,” he said. “And the cost would have been crushing. I had only been married for 5 years when it happened. Every little thing I needed, every pain, was taken care of.”

Though he owes his life to what went on there, Sweeney still finds Bldg. 10 baffling.

“I got lost in it the other day for half an hour!” **R**

21st Salzman Award in Virology Calls for Abstracts

The Foundation for the National Institutes of Health and the NIH virology interest group announce the 21st Annual Norman P. Salzman Memorial Award in Virology to recognize outstanding research accomplishments by a postdoctoral fellow or research trainee working in the field of virology here. The award honors the 40-year NIH career of Salzman in virology research and his accomplishments mentoring young scientists. The winning fellow or trainee will receive a plaque and \$2,500 stipend. The awardee’s mentor will also receive a plaque.

Applications for the award are due by Monday, Sept. 30. Find forms and information at <https://fnih.org/what-we-do/programs/salzman-memorial-award-and-symposium>. Applications must be submitted by email to SalzmanSymposium@mail.nih.gov.

The award will be presented at the annual Norman P. Salzman Virology Symposium on Monday, Nov. 18 in Lipsett Amphitheater, Bldg. 10.

The symposium will feature four speakers prominent in virology. A lunch reception follows.

This year’s keynote will be delivered by Dr. Barton Haynes, Frederic M. Hanes professor of medicine and immunology, director of the Human Vaccine Institute in the department of medicine at Duke University School of Medicine. His topic is “Development of a Broadly Protective HIV Vaccine: How and When Will We Get There?”

The 2019 tribute speaker will be Dr. Malcolm A. Martin, chief of the Laboratory of Molecular Microbiology and chief of the viral pathogenesis and vaccine section, National Institute of Allergy and Infectious Diseases.

For more information, contact organizing chair Dr. Arifa Khan at Arifa.Khan@fda.hhs.gov or Janelle Lewis of FNIH at jlewis@fnih.org, (301) 594-3919. Individuals with disabilities who need sign language interpreters and/or reasonable accommodation to participate in this event should contact Lewis and/or the Federal Relay (1-800-877-8339).



The symposium honoring Dr. Norman P. Salzman (above) features keynote speaker Dr. Barton Haynes (below).



Global Health

CONTINUED FROM PAGE 1

Between the turn of the century and 2012, 700 million people did not contract malaria, and 3.5 million lives were saved from the disease because biomedical research advances were developed with and for the communities affected.

“Science—bed nets and artemisinin combo therapy—were brought together with communication, with the embrace of society and with true leadership,” Farrar explained.

Citing several other conditions for which prevention or treatment strategies have worked, he said the scientific community nevertheless cannot rest on its laurels but must be more vigilant to see that gains are not lost.

“As these diseases are disappearing from many parts of the world through vaccination and as people lose that personal experience or connection to these diseases, things like the anti-vaccine movement become more powerful,” Farrar said.

His organization recently released its first *Wellcome Global Monitor*, a survey of 149,000 people in 140 countries about their views on health and science. Findings in the report offer a framework for global health policy-making, Farrar said, but also forecast trouble ahead for cultural thinking.

“At the very moment when scientific advances are perhaps at their most exciting in decades,” he said, “we are facing a society and a political environment that is questioning the very advances that have been made... The movement questioning the benefits of



NIH director Dr. Francis Collins (l) and FIC director Dr. Roger Glass greet Farrar.



Farrar delivers the Barmes Lecture, which is jointly sponsored annually by the Fogarty International Center and the National Institute of Dental and Craniofacial Research.

PHOTOS: MARLEEN VAN DEN NESTE, MENA BRUNETTE

vaccination is a harbinger of more challenging questions coming from parts of society. As a scientific community, we have been complacent that people would just accept scientific advances and would thank us for them. We’ve got to engage much better than we have in the past.”

He acknowledged anti-vax trends in France, the United Kingdom and the United States, predicting that the “public health impact would be devastating” if vaccination skepticism spread from western nations to countries such as Bangladesh and Rwanda. “We have to see this as one of our great challenges.”

As an example of the damage societal factors can add to a public health crisis, Farrar described the ever-worsening Ebola outbreak in the Democratic Republic of Congo, where science—attributed to NIH and a unique global partnership—has provided a viable vaccine, but the society seems “unwilling to embrace the technological advance...Ebola in an urban setting, with its dense mobile population and complex community interactions and trust in authorities, is a completely different epidemic than in the rural setting of 1976 [when first identified], and that change is what is driving Ebola in the DRC at the moment.”

Farrar sees other concerns—climate change and the environment, urbanization, migration—challenging what he called the “new global health.” Obesity, cancer and non-transmissible diseases and delivery of treatments for chronic diseases and the rapid rise of drug-resistant infections/anti-microbial resistance all weigh heavily on world health care systems. Such issues, he suggested, demand completely different economic models, political mindsets and training of the next-generation medical staff.

There will be “unbelievable changes in society in the next 20 to 30 years in ways we cannot yet predict but will be very disruptive,” he said.

Farrar noted that the travel route between Asia and sub-Saharan Africa is one of the fastest growing in the world currently; a few decades ago, it was nearly non-existent. Increased connectivity opens new routes for potential pandemics, dengue spreading to Africa or yellow fever causing epidemics in Asia for the first time in history.

“At the moment, the double whammy of infectious and non-communicable diseases is putting an enormous strain on many countries’ health systems...Advances in many areas of medicine, immunotherapies for cancers, for instance, have to be made

affordable and accessible to the maximum number of people around the world. Otherwise we will face an ever-increasing inequitable world with all the ramifications of that—a huge challenge.”

Wellcome is uniquely untethered, Farrar admitted, describing the organization’s “incredibly privileged” position of having its own endowment, an independent governing board and no shareholders to keep happy. “It comes with a tremendous responsibility to be accountable for what we do and to be as transparent as we can be...[But] in order to achieve the real change we seek, we have to work in partnership with others.”

Farrar reminded the audience that many around the world view NIH as the world’s greatest science institution.

“Coming to work every day at NIH, you might take for granted that your research centers and your clinical care are within the same compound,” he said. “Your clinicians and your scientists go between the two without impediments and intellectually are friends, you share your coffee breaks, lunch, work...That is not normal everywhere.”

He said he worries about the growing separation between research scientists and clinicians. “For the future development of all our health, medicines, drugs, vaccines and devices, we absolutely need that clinical acumen and clinical insight, partnering with great discovery science,” he declared. “How can we ensure that clinical scientists of the future retain a clinical capacity and are comfortable in the laboratory, and respect the great strengths of both of those?”

In addition to structure and function, Farrar said other qualities of NIH also draw global admiration.

“What you do in the world and what you stand for and the values that you epitomize are the things that the rest of us look up to... It’s a question we must all ask ourselves: If we don’t stand up now for the values we hold dear at this time of real change politically around the world, then when? And if not us, who?”

“Don’t forget the leadership role you play, the generosity with which you do that and the huge respect that the world has for this institution and for the American people. Thank you for that leadership, that generosity and respected partnership and never, never step back from it.” **R**

SEPT. 11

Research Festival Events Set

The 2019 Research Festival will be held all day on Wednesday, Sept. 11. The format this year includes 3 plenary sessions, a “lightning round” of 3-minute talks and a midday poster session featuring posters from selected FARE award winners and tenure-track investigators. A 2-day Technical Sales Association (TSA) Exhibit Tent Show follows, Sept. 12-13.

Festival schedule includes:

- **9/11 Anniversary Observance and Moment of Silence**, Masur Auditorium, Bldg. 10, 8:46 a.m.—the time on Sept. 11, 2001, when hijackers deliberately crashed American Airlines Flight 11 into floors 93 through 99 of the North Tower, 1 World Trade Center.

- **Plenary Session I. Celebrating NIH IRP Contributions to Curing Metabolic Diseases**, Masur Auditorium, 9–10:50 a.m. (4 20-minute talks): Dr. Ferid Murad, George Washington University; Dr. Marston Linehan, NCI Urologic Oncology Branch chief; Dr. Josephine Egan, NIA clinical director; Dr. Kevin Hall, NIDDK integrative physiology section chief.

- **Data Blitz: Lightning Round**, Masur Auditorium, 11 a.m.–12:20 p.m. (about 20 3-minute talks). Postdoctoral FARE award winners provide 3-minute summaries of their research.

- **Poster Session**. FAES Terrace, Bldg. 10, 12:30–1:30 p.m. More than 100 scientific posters including some by select postdoctoral FARE award winners and tenure-track investigators representing each NIH institute and center with an intramural program. Also, several scientific directors compete in a bakeoff/cookoff; other light refreshments will be served.

- **NIH Green Labs Fair**. South Lobby, Bldg. 10, Noon–2 p.m. Exhibits and information on environmentally friendly products, practices and initiatives. Learn about products directly from their vendors, discover practices by lab staff who actually use them and inquire about NIH initiatives with folks who run them. All employees, contractors and visitors are invited.

- **Special Exhibits on Intramural Resources**, Central Corridor, Bldg. 10, noon–2 p.m. Tables staffed by CIT, the NIH Collaborative Research Exchange (CREx), the National Library of Medicine, the Office of NIH History and Stetten Museum and more. Virtual reality demos will take place in the NIH Library.

- **Lunch**. Noon–2 p.m. Visit the food trucks in parking lot 10H (near the South Lobby) for set meals for sale.

- **Plenary Session II. Celebrating NIH Efforts to Combat Physical and Emotional Pain**, Masur Auditorium, 2–3 p.m. (4 12-minute talks). Dr. Carlos Zarate Jr., NIMH Experimental Therapeutics & Pathophysiology Branch chief; Dr. Lauren Atlas, NCCIH section on affective neuroscience and pain investigator; Dr. George Koob, NIAAA director and NIDA neurobiology of addiction section chief; Dr. Andrew Mannes, Clinical Center department of perioperative medicine chief.

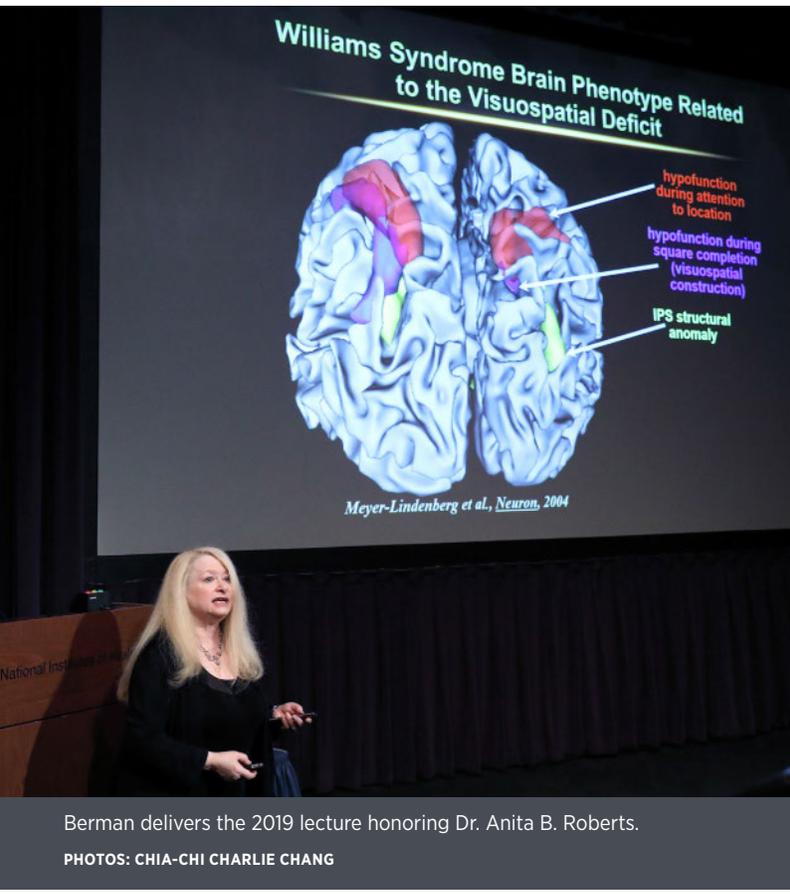
- **Plenary Session III. Celebrating Cutting-Edge Technologies at the IRP**, Masur Auditorium, 3–4 p.m. (4 12-minute talks). Dr. Adam Phillippy, NHGRI genome informatics section head; Dr. Elizabeth Kang, hematotherapeutics unit head, genetic immunotherapy section, NIAID Laboratory of Clinical Immunology and Microbiology; Dr. Hari Shroff, NIBIB section on high-resolution optical imaging senior investigator; Dr. Hannah Valentine, NHLBI Laboratory of Transplantation Genomics senior investigator.

- **Award Ceremony & Reception**, South Lobby, Bldg. 10, 4–5 p.m. Informal award ceremony and reception featuring food and music. Recognition of FARE awardees and winner of the cooking/baking competition. NIH Director’s band, aka “ARRA” (Affordable Rock’n’ Roll Act), in concert under the canopy of the South Lobby.

- **Sept. 12-13 TSA Tent Show**. Morning and early afternoon, parking lot 10H. Exhibitors will display state-of-the-art equipment and services by biomedical research suppliers. Vendors wishing to participate can register at <http://www.gtpmgt.com>. To view list of confirmed exhibits, visit <http://www.gtpmgt.com/attendees.php?id=4>.



In a 2016 image, NIH deputy director for intramural research Dr. Michael Gottesman cheers the annual celebration of homegrown science.



Berman delivers the 2019 lecture honoring Dr. Anita B. Roberts.

PHOTOS: CHIA-CHI CHARLIE CHANG

Berman

CONTINUED FROM PAGE 1

behavior pattern was the work of gene dosage.

Berman was the guest speaker at the annual Distinguished Women Scientists at NIH lecture series, held recently in memory of NIH scientist and mentor Dr. Anita B. Roberts.

Berman and her colleagues used functional MRI to take pictures of brain regions in individuals with Williams syndrome (WS), caused by deletion of the 7q11.23 locus in one of the two chromosome 7s (hemi-deletion). In people with WS, “the behavioral features that are distinctive are good language and face recognition but severe problems with visual-spatial construction,” Berman said, describing the cognitive profile of individuals with WS. Berman’s group identified the intra-parietal sulcus region of the brain in WS as associated with these cognitive traits.

“Since we published this, it has probably been one of the most well-replicated and reliable brain phenotypes that has been reported in Williams syndrome,” Berman said. “For us, that means that it is a great brain phenotype for mapping gene effects,” she added, discussing how her group identified genes responsible for WS-specific cognitive traits.

The gene for lim kinase 1 (LIMK1) appears to be associated with cognitive phenotypes in WS. “We found that people with this gene hemi-deleted had visual-spatial construction impairments and reduced intra-parietal sulcus gray matter and neuro-activation, similar to those findings in WS,” Berman said, stressing that they were particularly interested in LIMK1 because it is important in neuron maturation and migration.

Her group subsequently saw, in a large cohort of healthy individuals, that variations in the LIMK1 gene sequence were associated with grey matter volume changes in the same regions of the brain as those affected in WS. Furthermore, neural communication between dorsal and ventral visual streams in

score as highly gregarious, people-oriented, tense, sensitive and visible on a well-validated personality questionnaire,” Berman said. Her group found that the insula region of the brain is associated with personality traits in WS.

The gene GTF2I, which is located toward the end of the 7q11.23 genetic locus, was found to be specifically associated with insula volume in studies by Berman’s group. Therefore, the GTF2I gene and the insula region are responsible for behavioral aspects of WS, analogous to the LIMK1 gene and the intra-parietal sulcus region, which are responsible for the cognitive aspects.

“GTF2I, like LIMK1, is a very interesting protein and gene...It binds to promoter regions of various genes and could influence a variety of genetic pathways,” Berman said. Mouse pups with an extra copy of the GTF2I gene showed increased separation anxiety in a study by extramural colleagues. Conversely, deletion of one copy of this gene caused decreased separation anxiety, reflecting human behavior in WS. Additionally, “Variation in this very same gene is important not only in the transition of wolves to domestic dogs, it is also related to how friendly current dog species are,” Berman noted, describing the findings of a study by an NHGRI team.



“Since we published this, it has probably been one of the most well-replicated and reliable brain phenotypes that has been reported in Williams syndrome.”

—DR. KAREN F. BERMAN



the brain also varied as a function of LIMK1 sequence differences in the gene. “What’s remarkable here is that both the structural and functional differences occur in the same direction, according to LIMK1 haplotype,” Berman concluded.

In addition to their distinctive cognitive profile, individuals with WS have high sociability. They are socially fearless from infancy but have anxiety in non-social environments. In a short video, a child with WS shows no separation anxiety (on being away from her mom) when she interacts with a boy she doesn’t know. “People with WS

Individuals with a duplicated 7q11.23 locus have a number of cognitive and behavior traits that contrast with those seen in people with WS. The former suffer from social and separation anxiety, but they are adept at visual-spatial construction.

Closing her talk, Berman described how copy number variation at the 7q11.23 locus is a great example of gene dosage directing stepwise phenotypic changes. This and similar work can help in our understanding of how genes work through the brain to influence complex human behaviors and disorders, she concluded. **R**

Mattson, Expert on Brain Aging, Science of Fasting, Retires

BY ELIZABETH HUTMAN

Dr. Mark Mattson, renowned for his research on brain aging, Alzheimer's disease and the health benefits of calorie restriction and intermittent fasting, retired from the National Institute on Aging recently. During his distinguished career, Mattson inspired peers and lab teammates with his diligent work ethic and research productivity. He remains recognized as one of the world's most highly cited neuroscientists, with a long track record of achievements and numerous awards.

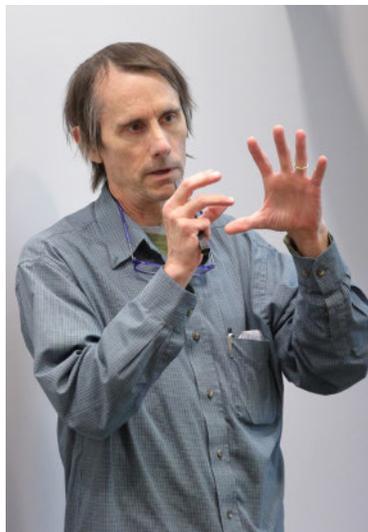
In June, an international symposium drew dozens of Mattson's current and past colleagues and mentees to Johns Hopkins' Mountcastle Auditorium to celebrate his contributions to science. Throughout the day-long symposium, speakers recalled Mattson as a mentor who led by example.

"I do not have enough words to express

and an example to all, and I am certain that his next journey will be adventurous and successful."

During his almost 20 years at NIA, Mattson led the Neuroscience Research Laboratory, which focused on understanding what goes wrong in the brain in Alzheimer's and Parkinson's diseases and stroke. His team made numerous discoveries that revealed the cellular and molecular mechanisms by which intermittent metabolic challenges—exercise and intermittent fasting—enhance cognition and protect the brain against age-related dysfunction and degeneration.

Using mouse models, Mattson and his team found that both dietary energy



Dr. Mark Mattson recently retired from NIH after almost 20 years.

PHOTO: ERNIE BRANSON

restriction and fasting diets in humans.

A native of Minnesota, Mattson received his Ph.D. in biology from the University of Iowa and then began his career at the Sanders-Brown Research Center on Aging at the University of Kentucky Medical Center. In 2000, he became chief of NIA's Laboratory of Neurosciences with a joint appointment at Johns Hopkins University School of Medicine.

Dr. Jonathan Geiger, Chester Fritz distinguished professor at the University of North Dakota School of

Medicine and Health Sciences, recalled being impressed with Mattson's productivity while they were colleagues at Kentucky. "Once I made the mistake of asking Mark what his secret to success was," Geiger said. "He made it clear to me that there is no secret, no trick, to being successful—it takes dedication and hard work!"

Mattson is looking forward to continuing his teaching at Johns Hopkins School of Medicine's graduate neuroscience program. His future projects also include writing books based on his research and helping plan future studies on intermittent fasting in patients with chronic diseases.

"I deeply appreciated the opportunity to visit with former lab members and collaborators who enriched my life during the past four decades," Mattson said. "It was wonderful to reminisce about our collective

"I do not have enough words to express my gratitude to Mark for his excellent contribution to the science, for his collaborative and generous spirit toward other scientists, and for being such a good colleague, friend and mentor."

—DR. LUIGI FERRUCCI

my gratitude to Mark for his excellent contribution to the science, for his collaborative and generous spirit toward other scientists, and for being such a good colleague, friend and mentor," said Dr. Luigi Ferrucci, NIA scientific director. "His life is an inspiration

restriction and intermittent fasting play a significant role in delaying and slowing the progression of neurodegenerative diseases. These findings resulted in several novel therapeutic approaches and, more recently, early-stage clinical trials testing calorie



Past colleagues and mentees honored Mattson (front row, 7th from left) at a symposium in his honor on June 3.

PHOTO: CHIP ROSE

contributions to the fields of neuroscience and aging, and to contemplate our future directions in life and science. This was a highly fulfilling segment of my life and I will always have fond memories of my experiences with the many colleagues and friends that I had the great fortune of working with at NIA." 



A recently published study shows that repetitive sequences—'hotspots' of DNA evolution—emerge early in tumor evolution but fade away in later phases.

IMAGE: KIRSTYPARGETER/GETTY

NIH Researchers Uncover Role of Repetitive DNA, Protein Sequences in Tumor Evolution

A team of researchers from the National Library of Medicine and collaborating academic research institutions developed a method to measure a type of gene mutation involved in the evolution of cancer. This type of mutation, called "repeat instability," may be useful in early cancer diagnosis. Findings were published in the *Proceedings of the National Academy of Sciences*.

Cancer is primarily caused by mutations in certain genes. The most thoroughly studied cancer-associated mutations involve the substitution of one nucleotide of DNA for another in genes known as oncogenes and tumor suppressors.

In this study, the researchers identified a different type of mutation active in cancer, one that increases and/or decreases repetitive segments of DNA and protein sequences in various genes. These changes are collectively called "repeat instability."

Researchers developed a computational methodology to quantify variations in the repeat content of gene and protein sequences. They analyzed sequence data from 325 patients with a variety of cancers, including breast, prostate, bladder and lung, as well as individual patients with metastases. Using computational biology techniques, the researchers compared the sequences from the cancer tissue with those from healthy tissue adjacent to the cancer site and to blood, which served as the control.

"This study shows that repetitive sequences, which are 'hotspots' of DNA evolution, emerge early in tumor evolution but fade away in later phases, particularly during the transition to metastatic states, though they leave clear marks in the genome," said Dr. Eugene Koonin, a co-author of the study and head of NLM's evolutionary genomics research group.

"The study found that non-cancerous tissue adjacent to tumors had patterns of repetitive sequences

that were similar to those detected in tumors," said NLM's Dr. Erez Persi, lead author on the paper. "This fact, and the reduction in repeat sequences seen once the cancers metastasized, suggests the potential for using repeat sequences in the early diagnosis of cancer."

Experimental Treatment Slows Prion Disease, Extends Life of Mice

Scientists using an experimental treatment have slowed the progression of scrapie, a degenerative central nervous disease caused by prions, in laboratory mice and greatly extended the rodents' lives, according to a new report in *JCI Insight*. The scientists used antisense oligonucleotides (ASOs), synthetic compounds that inhibit the formation of specific proteins.

Prion diseases occur when normally harmless prion protein molecules become abnormal and gather in clusters and filaments in the body, including the brain. The diseases are thought to be always fatal. Scrapie, which affects sheep and goats and can be adapted to rodents, is closely related to human prion diseases such as Creutzfeldt-Jakob disease, which is currently untreatable. Thus, scrapie is a valuable experimental model for the development of human prion disease therapies.

In the studies, NIH scientists and their colleagues injected ASOs into the spinal fluid of mice already infected with scrapie or that were challenged with scrapie proteins within weeks of the injection. Ionis Pharmaceuticals specifically designed ASO1 and ASO2 to reduce the rodents' supply of normal prion protein. Rodent studies using different dosages of ASO1 and ASO2 were conducted at NIAID's Rocky Mountain Laboratories and at the Broad Institute.

RML scientists injected either ASO1 or ASO2 into mice 14 days prior to infecting them with scrapie, and then 7 or 15 weeks after infection. Mice treated with ASO1 did not show clinical signs of disease for a median 250 days, or 82 percent longer than untreated mice (137 days), and they lived 81 percent longer than untreated mice (259 days versus 143 days). Mice treated with ASO2 did not show clinical signs of disease for a median 272 days, or 99



Scientists using an experimental treatment have slowed the progression of scrapie in laboratory mice and greatly extended the rodents' lives.

IMAGE: ROGER ASBURY/ISTOCK

percent longer than untreated mice (137 days), and they lived 98 percent longer than untreated mice (283 days versus 143 days). In the Broad Institute experiments, mice received either ASO1 or ASO2 2 weeks before infection with scrapie and then 7 weeks after infection. Both ASOs delayed rodent weight loss. Mice treated with ASO1 and ASO2 both lived longer than untreated mice.

The RML group also tested the ASOs against established prion disease, treating mice 17 weeks after they were infected with scrapie—near the onset of clinical signs. Mice treated with ASO1 did not show signs of clinical disease for a median 189 days, or 33 percent longer than untreated mice (142 days). They also showed slower disease progression and lived 55 percent longer than untreated mice (244 days versus 157 days). ASO2 had no beneficial effect.

The researchers plan to expand their scrapie ASO studies to human prion diseases. Other researchers have seen promising initial results in humans with ASOs directed against Alzheimer's disease, amyotrophic lateral sclerosis (Lou Gehrig's disease) and Huntington's disease.

'Wildling' Mice Could Help Translate Results in Animal Models to Results in Humans

Researchers at NIH have developed a new mouse model that could improve the translation of research in mice into advances in human health. The mouse model, which the scientists called "wildling," acquired the microbes and pathogens of wild mice, while maintaining the laboratory mice's genetics that make them more useful for research. In two preclinical studies, wildlings mirrored human immune responses, where lab mice failed to do so. Led by scientists at NIDDK, the study was published online in *Science*.

"We wanted to create a mouse model that better resembles a mouse you'd find in the wild," said Dr. Barbara Rehermann, chief of the immunology section in NIDDK's Liver Diseases Branch and senior author on the study. "Our rationale was that the immune responses and microbiota of wild mice and humans are likely shaped in a similar way—through contact with diverse microbes out in the real world."

Microbiota refers to the trillions of tiny microbes, such as bacteria, fungi and viruses, that live in and on the bodies of people and animals and play a critical role in keeping immune systems healthy. Unlike squeaky clean lab mice raised in artificial settings, wild mice have developed symbiotic relationships with microbes they have encountered in the outside world—just as people have done.

Rehermann and Dr. Stephan Rosshart, the study's lead author and NIDDK postdoctoral fellow, have long sought to improve animal models of complex diseases in humans. In 2017, they led research showing that transferring wild mice gut microbiota into lab mice helped the mice survive an otherwise lethal flu virus infection and fight colorectal cancer.



Researchers transferred microbiota from the natural world to the laboratory world.

IMAGE: NIH MEDICAL ARTS/NIDDK

In the current study, they transplanted embryos of the most commonly used strain of laboratory mice for immune system research into female wild mice, who then gave birth to and raised wildlings. The researchers and their collaborators compared the microbiota of the wildlings, wild mice and lab mice. They found that the wildlings acquired the microbes and pathogens of wild mice and closely resembled wild mice in their bacterial microbes present at the gut, skin and vagina, as well as in the number and kinds of fungi and viruses present.

“A healthy microbiome is important not only for the immune system, but also for digestion, metabolism, even the brain,” said Rosshart, who recently completed his fellowship in NIDDK and will open a new lab in Germany. “The wildling model could help us better understand what causes diseases and what can protect us from them, thus benefitting many areas of biomedical research.”

The researchers also tested the stability and resilience of the wildlings’ microbiota and found the microbiota was stable across five generations and resilient to environmental challenges. For example, when the mice were given antibiotics for 7 days, the lab mice’s gut microbiota changed

and did not recover, while the wildlings’ microbiota fully recovered. Further, when the mice were fed a 10-week high-fat diet, the microbiota of the lab mice changed significantly and never returned to baseline. The wildlings’ microbiota changed only mildly and recovered shortly after the diet ended. The authors suggest that the stability and resilience of wildlings, if the model is used widely, could improve the validity and reproducibility of biomedical studies.

Finally, the researchers tested how well the wildlings could predict human immune responses. To do so, they drew from two studies where drugs used to target immune responses were successful in treating lab mice in preclinical trials but consequently failed to have therapeutic effects in humans. In the current study, the researchers treated wildlings and lab mice with the same drugs. The wildlings, but not the lab mice, mimicked the human responses seen in clinical trials.

“We always strive for effective ways to shorten the gap between early lab findings and health advances in people, and the wildling model has the potential to do just that,” said NIDDK director Dr. Griffin Rodgers. “By helping to predict immune responses of humans, the wildling model

could lead to important discoveries to help treat and prevent disease, and ultimately, improve human health.”

Study To Test Seasonal Flu Vaccines with Two Adjuvants

An early-stage clinical trial is evaluating two licensed seasonal influenza vaccines, administered with or without novel adjuvants, for their safety and ability to generate an immune response. Adjuvants are compounds added to vaccines to induce stronger and longer-lasting immune responses.

The phase 1 study is enrolling healthy adult volunteers at eight sites across the United States. The trial is funded by NIAID.

According to the Centers for Disease Control and Prevention, influenza vaccination can greatly reduce the risk of infection or severe influenza-related illness that may require hospitalization. Although seasonal influenza vaccines have been widely available for decades, their effectiveness varies from year to year, depending on how well the vaccine matches the disease-causing influenza virus strains that

are circulating at that time. When people receive a vaccine containing an adjuvant, they are more likely to produce a stronger immune response to the vaccine, which may better protect them from the disease.

“As part of a comprehensive research effort to develop more effective and durable influenza vaccines, NIAID not only supports the development of new vaccines, but also efforts to improve seasonal vaccines that are already available,” said NIAID director Dr. Anthony Fauci. “We hope this trial will increase our understanding of how adjuvants could help confer better protection from seasonal influenza.”

The trial will enroll 240 healthy volunteers ages 18 to 45 years at 8 vaccine and treatment evaluation units—a network of clinical trial sites funded by NIAID. Dr. Patricia Winokur of the University of Iowa Carver College of Medicine is principal investigator of the trial, which is expected to last approximately 18 months.

Volunteers will be randomly assigned to receive one dose of either the Fluzone quadrivalent influenza vaccine or Flublok quadrivalent influenza vaccine. The vaccine will be given alone or in combination with either the AF03 or the Advax-CpG55.2 adjuvant.

Fluzone and Flublok are manufactured by Sanofi Pasteur, the vaccines global business unit of Sanofi, and are reformulated each year to best match the anticipated seasonal influenza strains selected by the World Health Organization.

The two novel adjuvants being tested have shown promise in animal models at enhancing the immune response to influenza vaccines. In additional animal studies, both were shown to be well-tolerated when given in conjunction with either Flublok or Fluzone. **R**



A person receives the seasonal influenza vaccine (flu shot).

PHOTO: NIAID

VOLUNTEERS

HIV Vaccine Study Needs Subjects

Vaccine Research Center researchers seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-444-1132 (TTY 1-866-411-1010) or email vaccines@nih.gov. Se habla español.



Gathering of healthy minds. Annual Summer Research Program Poster Day, an NIH rite of the season, brings hundreds of young scientists together, sharing their experiences.

Poster Day 2019 Draws Crowd to Natcher

PHOTOS: CHIA-CHI CHARLIE CHANG, RICH MCMANUS

There is only one day of the year at NIH when battalions of young people can be found toting their posters along the sidewalk in the vicinity of Natcher Bldg. (see photo below).

That day was Aug. 8, when the annual NIH Summer Research Program Poster Day was held, featuring some 1,000 posters exhibited by youngsters showing off their summer's effort.

It was Woodstock for science, but instead of 3 days, it was only 1 day of peace, love and scholarship, broken into four sessions from 9 a.m. to 4 p.m.

One session was devoted to HiSTEP, the High School Scientific Training and Enrichment Program, which provides opportunities for students from schools with a large population of financially disadvantaged kids.

Attendance and spirits were high at the event, which drew many seasoned NIH investigators who support the effort. The day was organized by the Office of Intramural Training and Education.



Alexis O'Keiffe (l) of Howard University College of Medicine shares her research.



Virtual reality was part of exhibit above, while below, NCI Center for Cancer Research director Dr. Tom Misteli (c) chats with author Francesca Bonetta-Misteli (r).



Poster Day was in part a celebration of the diversity of talent NIH attracts to summer science experiences.



Megan Trick, a post-baccalaureate fellow in the hematology service of the Clinical Center's department of laboratory medicine, explains her work to a visitor.



Above, Vatsal Agarwal (r) discusses his poster with a visitor to the event. Below, Eve Crompton of NCI's Genetics Branch explains her work to a neighboring exhibitor.

