

SUPERBUGS & DRUGS

Pamer Lab Studies How Antibiotics Can Disrupt GI Tract

BY DANA TALESNIK

Patients may, at times, have a gut feeling that antibiotics are making them ill. That's because some of the antibiotics they're taking to treat or prevent bacterial infections are also changing their intestinal microbiota, making them particularly susceptible to dangerous antibiotic-resistant infections.

The growing epidemic of antibiotic-resistant infections such as *Clostridium difficile* (*C. diff*), *Klebsiella pneumoniae* and vancomycin-resistant enterococcus (VRE), is usually attributed to the overuse and misuse



Dr. Eric Pamer discusses the importance of robust microbiota in managing infections.

of antibiotics. Recent evidence shows that even the proper use of antibiotics may be putting people at risk for these potentially lethal superbugs.

One patient who needed antibiotics for a bacterial infection associated with cancer treatment subsequently developed recurrent *C. diff* infections, recounted Dr. Eric Pamer, director of the Center for Microbes,

Inflammation and Cancer at Memorial Sloan Kettering Cancer Center, during his Jan. 10 Wednesday Afternoon Lecture Series presentation in Masur Auditorium.

"*C. difficile* infection represents an amazing example of how the normal microbiome provides resistance against infection," said Pamer, "and how the antibiotic treatment that's commonplace in hospitals renders patients highly susceptible."

The goal, then, is to re-establish the GI tract's natural resistance against these antibiotic-resistant bacteria by restoring the healthy, diverse microbes that comprise the microbiota. One treatment option is fecal transplant, a procedure that makes some people squeamish.

"Many people recoil from the process of having feces from another individual administered to them—whether you're a physician doing it or a patient receiving it,"

SEE ANTIBIOTICS, PAGE 8

WINDOW ON BRAIN

Südhof Explores Molecular Logic of Neural Circuits

BY RICH MCMANUS

When a Nobel laureate comes to speak in Masur Auditorium, there is a flurry of pre- and post-synaptic activity, much of it having to do with audience members snapping cellphone pictures of the speaker.

Such was the case Jan. 31 when Dr.



Dr. Thomas Südhof

Thomas Südhof, who shared the 2013 Nobel Prize in physiology or medicine, discussed the molecular logic of synapse formation. There is growing evidence that impairments in the logic

SEE SYNAPSES, PAGE 4



Dr. Daniel Levy talks about Framingham study.

FROM RISK FACTORS TO GENETICS

NHLBI Marks Year 70 of Iconic Framingham Heart Study

BY MARK SAMPSON

Some 50 years ago, NIH researchers introduced two words into the American lexicon that flipped the public's thinking about heart disease on its head—"risk factors."

Those words emerged from the landmark

SEE FRAMINGHAM, PAGE 6



Challenges issued on Wear Red Day, p. 12.

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NRC Commissioner Baran Tours NIH

In early February, NIH hosted a visit by Commissioner Jeff Baran (third from l) of the U.S. Nuclear Regulatory Commission (NRC), which is the lead regulatory agency licensing the use of radioactive material for the NIH Intramural Research Program. The visit was not an inspection, but a brief tour of NIH programs, showcasing the variety of applications using radioactive materials. The tour included a visit to: the Clinical Center's cyclotron and PET department; NIBIB's Current Good Manufacturing Practice Laboratory, where radiopharmaceuticals are custom-made; the CC nuclear medicine and transfusion medicine departments; and the NCI Laboratory of Tumor Immunology and Biology. Seeing operations first-hand and hearing NIH researchers discuss the challenges involved in radiation safety regulations will allow Baran to better understand the impact of regulatory rulemaking in a biomedical research environment. Joining Baran on the tour are (from l) Dr. Ron Neumann, chief, CC nuclear medicine department; Dr. Elizabeth Jones, director, CC radiology and imaging sciences department; Tim Tosten, acting director, Office of Research Services; Dr. Brad Wood, chair, NIH radiation safety committee; and Cathy Ribaudo, director, Office of Research Services' Division of Radiation Safety. For more information on radiation safety at NIH, visit <https://drs.ors.od.nih.gov>.

Webinar on Using Networks to Link Genotype to Phenotype, Mar. 5

The next Mind the Gap webinar from the NIH Office of Disease Prevention will explore using networks to link genotype and phenotype, drawing on examples from cancer, chronic obstructive pulmonary disease and the analysis of data from 38 tissues provided by the Genotype-Tissue Expression (GTEx) project.

The webinar will be held Monday, Mar. 5 from 11 a.m. to noon. The speaker is Dr.



Dr. John Quackenbush

John Quackenbush, a professor of biostatistics and computational biology at the Dana-Farber Cancer Institute and a professor of computational biology and bioinformatics at the Harvard T.H. Chan School of Public Health.

Quackenbush's research uses massive data from DNA sequencing and other assays to model functional networks in human cells. By comparing

networks between groups of individuals, he has found new drug targets, explored chemotherapy resistance and investigated differences between the sexes. He has made pioneering discoveries about how the genetic variants work together to determine our traits.

Quackenbush will accept questions during the webinar via WebEx and Twitter. Use the hashtag #NIHMTG.

Registration is required. Register at <https://nih.webex.com/nih/onstage/g.php?MTID=e9f735e4e21f26513661ad1f7f04bd814>.

Chesler Opens NCCIH Lecture Series

Mar. 12

The first speaker in the spring 2018 Integrative Medicine Research Lecture Series sponsored by NCCIH will be Dr. Alexander Chesler, a Stadtman investigator in NCCIH's section on sensory cells and circuits. He will discuss "Under Your Skin: Molecules and Cells for Touch and Pain" on Monday, Mar. 12 from 11 a.m. to 12:15 p.m. in Lipsett Amphitheater, Bldg. 10.

The somatosensory system provides us with the ability to detect touch, temperature and painful stimuli. Chesler will describe how studying patients with a rare and inherited disease helped reveal a key molecule for detecting touch and proprioception,

the so-called "sixth sense" that enables the awareness of one's body in space. He will also discuss how recent advances in genetics and functional imaging in model systems are being leveraged to uncover mechanisms involved in acute and chronic pain.



Dr. Alexander Chesler

Chesler received his B.A. in biology from Bard College and his Ph.D. from Columbia University, where he studied the olfactory system. He did his postdoctoral studies at the University of California, San Francisco, using natural products and molecular genetics to probe the sensory pathways that detect painful stimuli.

Chesler joined NIH in 2013 as an Earl Stadtman investigator. His work at NCCIH focuses on determining the molecular and cellular mechanisms underlying the sensations of touch, temperature and pain.

Regeneron Finalists To Share Research

Regeneron Science Talent Search 2018 finalists will share their research with the public on Sunday, Mar. 11 from 2 to 5 p.m. at the National Museum of Women in the Arts, 1250 New York Ave. NW, Washington, D.C. The event is free and open to the public. In January, STS sponsors Regeneron Pharmaceuticals, Inc., and Society for Science and the Public named 40 finalists (from a pool of 300 select scholars) in the nation's oldest and most prestigious science and math competition for high school seniors. The competition, known as the Westinghouse Science Talent Search from 1942 to 1997 and the Intel Science Talent Search from 1998 to 2016, is designed to engage and inspire the next generation of scientific leaders. Traditionally, the finalists visit NIH; see coverage from 2017, https://nihrecord.nih.gov/newsletters/2017/04_07_2017/story5.htm. For details on this year's event and a list of the 40 finalists, visit <https://student.societyforscience.org/>.

Help with NIH Training Needs Assessment

The NIH Training Center will soon administer the biennial 2018 NIH Training Needs Assessment (TNA). Take this opportunity to let the NIHTC know the training you are seeking for success. The last TNA occurred in 2016. Don't let another 2 years slip away without making your training needs known. The more responses to the TNA, the better training options the NIHTC can offer. New this year: shorter assessment, targeted questions, IC reports available this summer. Questions? Send an email to NIHTrainingCenter@nih.gov.

Schor Named NINDS Deputy Director

BY SHANNON E. GARNETT

Pediatric neurologist Dr. Nina Schor was recently appointed as deputy director of the National Institute of Neurological Disorders and Stroke. She officially joined the institute in January.

Before coming to NINDS, Schor served as chair of the department of pediatrics and pediatrician-in-chief at Golisano Children's Hospital at the University of Rochester in New York.

"Dr. Schor's experience running a large university department and children's hospital, along with her extensive basic research background and clinical work, make her an ideal candidate for this position," said NINDS director Dr. Walter Koroshetz. "We are delighted to welcome her and look forward to working with her to advance the NINDS mission as it relates to neuroscience and neurological disease research."

As deputy director, Schor will work with Koroshetz in program planning, budgeting and guiding the institute's scientific and administrative functions.

"It is truly an honor and a pleasure to assume the position of NINDS deputy



director," said Schor. "NINDS is uniquely poised to ensure that the best of biomedical science is applied to make tomorrow's state-of-the-art better than anything of which we dare to dream today. What a privilege it will be to work to improve the lives of people with neurological disorders across a national stage."

Born in Bayside, N.Y., Schor earned her undergraduate degree from Yale University,

her Ph.D. in medical biochemistry from Rockefeller University and her medical degree from Weill Cornell Medicine. She completed residency programs in neurology and pediatrics at Children's Hospital and Harvard Medical School in Boston. Following her residencies, she was a professor, chief of child neurology and associate dean for medical student research at the University of Pittsburgh.

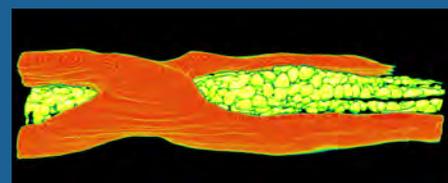
Schor was the principal investigator on numerous NIH-funded grants. Her research focused on neuroblastoma—a type of pediatric cancer—and neuronal death caused by oxidative stress, which occurs when harmful forms of oxygen molecules damage cells.

Throughout her career, she has mentored more than 80 postdoctoral fellows and graduate, medical and undergraduate

students. While at the University of Rochester, she was the first director of the Translational Biomedical Science Ph.D. Program and played an integral role in developing the program and recruiting graduate students.

Schor has earned numerous awards and honors including the American Neurological Association Distinguished Neurology Teacher Award, being named a fellow of the American Academy of Neurology and serving on the board of directors for neurology at the American Board of Psychiatry and Neurology. She has been an active member of many professional societies including the Society for Pediatric Research, American Society of Pediatric Department Chairs and the American Neurological Association.

In addition to her research, Schor is a poet whose work has been published in the *Neurology* journal and in a poetry chapbook. **R**



ON THE COVER: Blood vessel (red) in a mouse heart and mitochondria (green) in an adjacent heart muscle cell as viewed under an electron microscope. February is American Heart Month.

IMAGE: BRIAN GLANCY, NHLBI

NLM Hosts Lecture on 'Deep Learning,' Mar. 7

The NLM Informatics and Data Science Lecture Series will feature the talk "Translating from Chemistry to Clinic with Deep Learning," to be given by Dr. S. Joshua Swamidass on Wednesday, Mar. 7 from 2 to 3 p.m. in Natcher Conference Center, Rm. E1/E2.

Swamidass is an assistant professor of laboratory and genomic medicine at Washington University School of Medicine. His group studies information with new computational methods at the intersection of biology, medicine and chemistry. He is funded by the National Library of Medicine to model bioactivation pathways and how bioactivation pathways change in children.

Sign language interpreters will be provided. Individuals who need reasonable accommodation to participate should contact Ebony Hughes, (301) 451-8038, Ebony.Hughes@nih.gov or the Federal Relay (1-800-877-8339).

The talk will be broadcast live and archived at <http://videocast.nih.gov/>.



'CHEMISTRY TO CLINIC'

The NIH Record

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Synapses

CONTINUED FROM PAGE 1

of neural circuits is associated with the development of autism, schizophrenia, Tourette's syndrome and intellectual disability, he reported.

Now at Stanford, where he is a Howard Hughes Medical Institute investigator in the department of molecular and cellular physiology, Südhof focused on neurexins, cell-adhesion molecules crucial to the proper function of synapses.

Neurexins "come in two flavors, alpha and beta," Südhof explained, "and there is a third form—gamma." They are arguably the best-understood signaling molecules among a raft of them present when synapses form and do their jobs.

Especially interesting to Südhof is NRXN1, a large neurexin gene that, when mutated, is associated with more than 90 percent of common neuropsychiatric disorders. "But it is associated in a manner that we do not understand," he said.

Südhof and his colleagues study how nerve cells are connected into networks via synapses. "We are looking for initial insights into how it works.

"It always amazes me to consider how large the human brain is, with its vast,

★ ★ ★

"It always amazes me to consider how large the human brain is, with its vast, overlapping, interdigitated networks of trillions of synapses and billions of neurons."

-DR. THOMAS SÜDHOF

★ ★ ★

overlapping, interdigitated networks of trillions of synapses and billions of neurons," he said. "Compared to the human genome, it is actually amazing how much bigger it is than the genome [the brain has 10^{12} neurons and 10^{15} to 10^{16} synapses compared with the genome's 4×10^9 base pairs of DNA and 22,000 genes]. It will be very difficult to find out how it works. This is arguably the most challenging goal we have now in biomedical research."

Despite a wide variety in approaches to understanding the brain, Südhof said there is convergence on the importance of understanding neural circuits.

At their core are synapses, "specialized



Nobelist Südhof and his colleagues study how nerve cells are connected into networks via synapses. Below, he chats at a reception after his lecture.

PHOTOS: CHIA-CHI CHARLIE CHANG

intercellular junctions...that form the fundamental computational unit of the brain. Not all of them are the same. Much depends on their location and history of connection. These differences are essential to understand how they are formed and specified. Synapse formation is a lifelong process with multiple components."

mouse models with conditional mutations to characterize how mutations impair normal synaptic function. They are learning that the same mutation in different individuals causes different symptoms.

Among the threads to pull on: the most frequent single-gene mutation in schizophrenia involves NRXN1.

Südhof's final slide put the role of neurexins as a tool for learning how the brain functions into sharp relief. It featured a Swiss Army knife, labeled Neurexin, with its multiple tools ("ligands") extended.

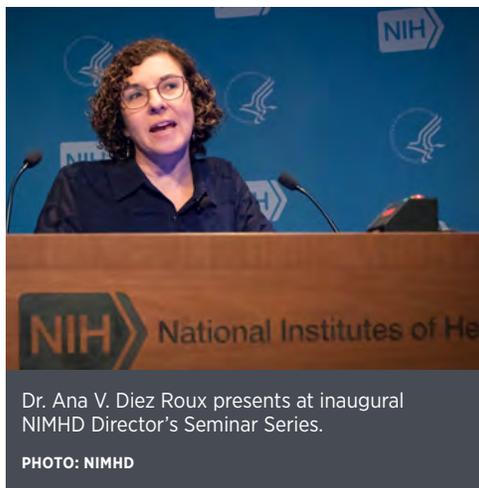
"Neurexins contribute to the molecular logic that determines synapse properties," he said. "They are central control switches. We can use them to dissect the molecular signals responsible for the activity and organization of synapses."

A small red knife versus a 1,200-gram organ with trillions of synapses: ya gotta start somewhere. **R**

Sailing Association Open House, Mar. 8

The NIH Sailing Association invites everyone to its open house on Thursday, Mar. 8 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln. Explore your interest in learning to sail and discover opportunities for sailing with NIHSA. There will be information about 6-week basic training classes, the club's racing program and social activities offered by NIHSA. A fee of \$5 at the door includes pizza, drinks and snacks. For more information, visit www.nihsail.org/.





Dr. Ana V. Diez Roux presents at inaugural NIMHD Director's Seminar Series.

PHOTO: NIMHD

NIMHD Launches Inaugural Director's Seminar Series

The National Institute on Minority Health and Health Disparities recently launched a new series to stimulate dialogue on scientific issues affecting minority health and health disparities. More than 150 employees and guests attended the inaugural NIMHD Director's Seminar Series. Dr. Ana V. Diez Roux, dean and distinguished university professor of epidemiology in the Dornsife School of Public Health at Drexel University, presented "Challenges and Opportunities for Health Disparities Research."

Diez Roux is internationally known for her research on the social determinants of population health and the effects of neighborhoods on health. "For more than 20 years, Dr. Diez Roux's work has impacted public health research, policy and practice," said NIMHD director Dr. Eliseo Pérez-Stable. "She was an excellent choice to start our new seminar series and I know her years of research will help shape new questions for us at NIH."

Prior to her presentation, Diez Roux met with NIMHD staff to discuss her research and share thoughts on current trends.

"She provided a great foundation for the new series and I look forward to the additional speakers we will be able to bring to NIH," said Dr. Regina Smith James, NIMHD director of clinical and health services research.

Dates and details about the next lecture will be announced soon.

NIH Pavilion Needs Volunteers for USA Science and Engineering Festival

Consider volunteering to support the NIH pavilion at the USA Science and Engineering Festival (<https://usasciencefestival.org/>). NIH will host family-friendly activities for the anticipated 350,000-plus festival attendees on Saturday, Apr. 7 (10 a.m.–6 p.m.) and Sunday, Apr. 8 (10 a.m.–4 p.m.) at the Walter E. Washington Convention Center, Washington, D.C. You can help with hands-on activities or as a general volunteer and sign-up for a shift of your choice. View the selection of NIH volunteer opportunities and learn more at <https://dpcpsi.nih.gov/SciFest/index>. The festival is a national grassroots effort to advance STEM education and inspire the next generation of scientists and engineers. Festival exhibitors and other participants come from major academic centers, leading research institutions, government agencies, cutting-edge high-tech companies, museums and community organizations. Stop by and see the fun activities that NIH offers to festival visitors.



Children listen while a volunteer explains the mock lab activity in the NIH pavilion at the 2016 USASEF.

New Child Care Center Open for Play (and Now Hiring!)

In the culmination of a 17-year project, NIH's newest child care center on campus, the Northwest Child Care Center (NWCCC), Bldg. 23, opened to NIH children and families in June 2017.

The new facility, located across from the Clinical Center, includes 14 classrooms, 3 well-equipped play yards, a commercial kitchen, lactation room and multi-purpose room.

The approximately 21,000-square-foot facility has numerous unique aspects including increased child safety and security; exceptional indoor and outdoor early-childhood learning environments; and attainment of Leadership in Energy and Environmental Design (LEED) silver certification. NWCCC is licensed to provide care for children ages 6 weeks to 6 years old.

The Office of Research Services also introduced Rockville Day Care Association (RDCA), Inc., as the organization providing child care services in the new center. RDCA has a decades-long history of providing a quality, play-based curriculum for young children in Montgomery County. NWCCC teachers and administrators are already building a loving, supportive community for NIH families. Learn more about RDCA at <https://rockvilledaycare.org/>.

Being able to access quality, affordable child care is critical to families with young children. While NWCCC won't fulfill the entire NIH demand for child care, it's an important step to make sure more NIH families receive the services they need. The NIH child care board and the Child and Family Programs team work collaboratively to explore avenues to ensure quality child care and other work-life services for the NIH workforce.

Ultimately, the new center will welcome 170 children for full-time care, once all staff positions have been filled. The shortage of qualified early childhood educators is a well-known challenge in the D.C. metropolitan area, as well as across the country. RDCA is working to fill the open positions with educators who have experience with developmentally appropriate and play-based early education.

Share the position descriptions at the link below with early childhood educators in your life and help achieve NWCCC's full enrollment with future researchers, teachers, public servants, explorers and adventurers. Find a list of open positions at <https://rockvilledaycare.org/careers/>.

HELP WANTED

Framingham

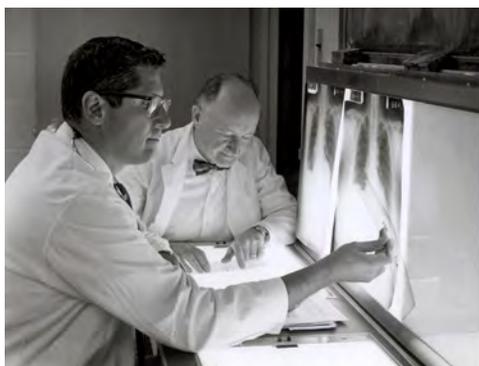
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Framingham Heart Study to characterize conditions that researchers discovered can increase a person's likelihood of developing heart disease—high blood pressure and high blood cholesterol, then later, smoking, obesity, diabetes and physical inactivity. Before Framingham, researchers knew little about the causes of heart disease; the study's early discoveries spurred development of new treatments and public health practices that have helped people get healthier and reduced deaths from heart disease.

That was the message delivered Feb. 1 by Framingham director Dr. Daniel Levy in a special lecture to mark the 70th anniversary of the long-term, multigenerational study, now a joint project of the National Heart, Lung, and Blood Institute and Boston University. The talk, held in Natcher Conference Center, was the first in a yearlong series of science lectures organized by NHLBI, which is also celebrating its 70th anniversary this year.

During his lecture, “Unraveling the Mysteries of Cardiovascular Disease: Lessons from NHLBI’s Framingham Heart Study,” Levy described the history of the study and its many contributions to heart health. He also highlighted new research developments, including the study’s more recent focus on genetic risk factors and their use to advance precision medicine.

“Framingham has been an exceptional contribution to medical science,” said Levy, who is also chief of NHLBI’s Population Sciences Branch and professor of medicine at Boston University School of Medicine.



Early images from the Framingham Heart Study: Associate director Dr. William Kannel (l) measures heart size, alongside tech J. William Claffey. At right are pathologist Dr. Cesare Tedeschi (l) and Dr. Thomas Dawber, first director of the study.

IMAGES COURTESY HECHT COLLECTION, OFFICE OF NIH HISTORY



Discussing 70 years of the Framingham Heart Study are Dr. David Goff (l), director of the NHLBI Division of Cardiovascular Sciences, and study director Levy.

“It has provided an immeasurable return on investment for NHLBI, both on the extramural side and the intramural side.”

Levy noted that around 1900, most people thought of heart disease as an inevitable part of aging. At the time, the leading causes

But by the mid-1940s, nearly half the deaths in the United States could be traced to a new culprit—heart disease.

Levy pointed out that public attention to heart disease grew after the death of President Franklin D. Roosevelt in April 1945.

• • •

“Framingham has been an exceptional contribution to medical science. It has provided an immeasurable return on investment for NHLBI, both on the extramural side and the intramural side.”

-DR. DANIEL LEVY

• • •

of death were infectious diseases—namely, pneumonia, tuberculosis and infectious diarrhea. These infections, he added, contributed to the relatively short life expectancy of Americans—about 50 years.

Records show that during his presidency, Roosevelt’s blood pressure had increased steadily until it reached what now are recognized as highly dangerous levels shortly before his sudden death from a stroke.

“Did he die out of the blue, with no warning signs whatsoever?” Levy asked the audience. “I think the evidence suggests that there were plenty of warning signs.” Yet because little was understood about high blood pressure (hypertension) as a risk factor for heart disease and because there were few anti-hypertensive treatments at that time, Roosevelt did not receive the care available today, Levy said.

It was against this backdrop that federal health officials in 1948 decided to establish NHLBI (then called the National Heart Institute) and also launch the Framingham Heart Study. Designed initially as a prevention program, the study included 5,200

adult men and women with no signs of heart disease, living in Framingham, Mass.

With the aid of extensive health data collection (including physical activity records and food intake surveys) and early computing technology, clues began to emerge about the underlying causes of heart disease in the study participants.

Then in 1961, a major turning point came with the publication of an article in the *Annals of Internal Medicine*.

Titled “Factors of Risk in the Development of Coronary Heart Disease—6-Year Follow-up Experience,” the study introduced the phrase “factors of risk,” which was inverted to create the now-common term “risk factors” for heart disease; the authors have since been credited for its origin.

In that seminal publication, the study identified high blood pressure and high cholesterol as risk factors for developing heart disease. The finding “opened up the field of preventive cardiology,” Levy said. In subsequent years, researchers identified many additional risk factors for heart disease, including cigarette smoking and diabetes.

Levy noted that Framingham was almost de-funded in 1969, as reported in the *New York Times*. However, influential politicians weighed in, citing its impact on understanding heart disease and its potential to save lives.

Not only was the program saved, but by 1971, Framingham began to recruit a second generation of participants, called the Offspring cohort. The newly evolved study focused on the familial basis of heart disease. It also introduced new screening tools, including echocardiograms and treadmill stress testing.

By 1999, the *Washington Post* declared the study number 4 on a list of the most important medical advances of the 20th century.

“That was rather flattering, but Framingham has never rested on its laurels,” Levy said. “New opportunities in science have led to new scientific research in Framingham.”

The completion of the Human Genome Project almost two decades ago, led by physician-geneticist (and now NIH director) Dr. Francis Collins, helped create



Also marking the 70th anniversary of establishment of NIH's National Heart Institute are (from l) Goff; Dr. Paul Sorlie, retired former chief of the Epidemiology Branch in the Division of Cardiovascular Sciences; Levy; and NHLBI director Dr. Gary Gibbons.

PHOTOS: ANDREW PROPP

a new direction for the study. By 2002, Framingham had recruited a third-generation cohort with a focus on genetic underpinnings of heart disease.

Since then, with advances in technology, the study has continued to expand and deepen its focus on genetics. NHLBI's TOPMed (Trans-Omics for Precision Medicine) program, which includes whole-genome sequencing to uncover genetic mechanisms of disease, contains research data from 4,200 participants in

Framingham. Many other groups worldwide have formed partnerships with investigators to further explore underlying factors of heart disease.

More recently, these studies have begun to reveal the genes that contribute to high blood pressure. Others are exploring biomarkers for atherosclerosis (cholesterol deposits in the arteries) and trying to identify new molecular targets to treat and prevent heart disease.

Seventy years after the study began, heart disease remains the leading cause of death in the U.S. But thanks largely to the Framingham study and our improved understanding of heart disease risks, deaths from heart disease have declined significantly. Levy noted that compared to 1968, when the rate of coronary heart disease deaths in the U.S. reached its peak, 1.4 million such deaths were averted in 2014 alone.

“We are reaching our stride and hope we will be able to continue those studies into the future,” Levy said.

The lecture is archived at <https://videocast.nih.gov/summary.asp?Live=26979&bhcp=1>. 

Teens Educated on Drugs, Alcohol

National Drug & Alcohol Facts Week, an annual health observance for teens to shatter the myths about drug and alcohol use, took place Jan. 22-28. Every year, the number of events increases, with activities being held in all 50 states and around the country.

This year, the observance saw 2,320 total events, some held in international sites including Pakistan, Afghanistan, Myanmar, Mexico, Northern Mariana Islands, South Africa, the U.K., Ireland, Zimbabwe, Ghana, Nigeria, Micronesia, Ukraine and Zambia.

Launched in 2010 by NIDA, and in partnership with NIAAA since 2016, National Drug & Alcohol Facts Week links students with scientists and other experts to counteract the myths about drugs and alcohol that teens get from the internet, social media and movies. Online resources included several new drug-specific toolkits for event holders to use, a pledge card and the popular National Drug IQ Challenge, an interactive quiz accessible on mobile devices for teens to test their knowledge about drugs and alcohol.

Visit <http://teens.drugabuse.gov/national-drug-facts-week> for more information. To see pictures of NDAFW events across the nation, visit <https://www.flickr.com/photos/nida-nih/collections/>.



Students at Agha Khan Higher Secondary School in Karachi, Pakistan

Antibiotics

CONTINUED FROM PAGE 1

said Pamer. “[There are efforts] to try to get beyond transplantation of feces and potentially identify the specific organisms that are in the microbiota that confer resistance to these various pathogens.”

At MSKCC, Pamer and his colleagues study the microbiota of patients undergoing cancer treatment. Chemotherapy and radiation take a severe toll on the immune system; the highest rates of infection are seen in patients undergoing hematopoietic stem cell transplant. Many cancer patients receive broad-spectrum antibiotics as prophylaxis or to fight infections they developed during treatment.

“I think we increasingly recognize that the broad-spectrum antibiotics that we recommend profoundly affect the commensal microbiota, in essence leaving the patient with an open wound,” said Pamer. This enables such pathogens as VRE to thrive in the gut. Closing the “wound” would require re-establishing a microbiome that confers resistance to infection.

Pamer’s research could have a profound impact on preventing hospital-acquired superbugs, a leading cause of bloodstream infection. The ability to identify patients at high risk for these infections could dramatically reduce transmission of these organisms in health-care settings.

Curiously, many of Pamer’s patients who became colonized with vancomycin-resistant enterococcus had been given an antibiotic other than vancomycin.

“We now know the emergence of many of these hospital pathogens that we’re combating in our immune-compromised patients and our post-surgical patients actually result from the destruction of anaerobic bacteria in the colon,” he said, “which enables these bacteria to expand and become dominating species in these individuals. The loss of anaerobic species almost always correlates with the administration of antibiotics.”

Pamer and his colleagues Dr. Ying Taur and Dr. Joao Xavier recently received



“I think we increasingly recognize that the broad-spectrum antibiotics that we recommend profoundly affect the commensal microbiota, in essence leaving the patient with an open wound,” said Pamer. Below, he greets lecture attendees in the NIH Library.

PHOTOS: CHIA-CHI CHARLIE CHANG

an NIAID grant to study how changes in the microbiota’s composition stimulate the emergence of antibiotic-resistant organisms. We were a good fit for this study, said Pamer, because “from a medical perspective, we have the most intensely characterized humans on the planet.” The MSKCC group has retrieved vast, detailed data from



patients’ electronic medical records during their multi-week hospital stays and has obtained and sequenced daily fecal samples that show how bacteria expand in the gut during and after antibiotic regimens.

But Pamer and his colleagues wanted to move beyond feces, so they’ve been culturing and sequencing gut bacteria that confer resistance or susceptibility to different pathogens. Now, instead of using fecal samples, he said, “we’re able to assemble a handful of organisms that provide resistance to VRE.”

Clostridium scindens, an obligate anaerobe that converts primary to secondary bile salts, provides a high level of protection against *C. diff*. On the other hand, certain strains of *Blautia producta* highly inhibit growth of VRE and other gram-positive organisms but have no effect on *C. diff* or gram-negative bacteria such as *Klebsiella*.

Pamer’s lab currently is studying organisms that might resist these gram-negative rods. Recent studies identified four bacterial species that, upon addition to cecal contents of an ampicillin-treated mouse in an ex-vivo culture, completely inhibit growth of *Klebsiella*.

Ongoing studies suggest that a low pH and the presence of short-chain fatty acids can inhibit *Klebsiella* growth.

“If we know someone’s GI tract doesn’t have secondary bile salts or short-chain fatty acids, we know the patient is extremely vulnerable to hospital-acquired infection,” said Pamer.

In a recent cohort of 94 bone marrow transplant patients, Pamer said, there was 8 percent transplant-related mortality (generally attributed to infection or graft-versus-host disease) over 3 years in patients with a highly diverse intestinal microbiota. In contrast, patients who lost diversity and anaerobic bacteria in the gut had 52 percent transplant-related mortality.

“We’re hopefully moving into an era where more and more of us will be identifying specific microbial combinations that can be re-administered to patients after they undergo extreme medical therapies, such as stem cell transplantation, but perhaps others as well,” said Pamer.

Prescribing antibiotics may need to be followed by implantation, in one form or another, of a microbiota that can protect vulnerable patients from these pathogens. **B**

Eye Could Provide ‘Window to the Brain’ After Stroke

Research into curious bright spots in the eyes on stroke patients’ brain images could one day alter the way these individuals are assessed and treated. A team of NIH scientists found that a chemical routinely given to stroke patients undergoing brain scans can leak into their eyes, highlighting those areas and potentially providing insight into their strokes. The study was published in *Neurology*.

“We were kind of astounded by this—it’s a very unrecognized phenomenon,” said Dr. Richard Leigh, an assistant clinical investigator at NINDS and the paper’s senior author. “It raises the question of whether there is something we can observe in the eye that would help clinicians evaluate the severity of a stroke and guide us on how best to help patients.”



A chemical given to stroke patients undergoing brain scans can leak into the eyes, perhaps providing insight into strokes, study says.

IMAGE: DUNCAN1890/ISTOCK

The eyes glowed so brightly on those images due to gadolinium, a harmless, transparent chemical often given to patients during magnetic resonance imaging scans to highlight abnormalities in the brain. In healthy individuals, gadolinium remains in the blood stream and is filtered out by the kidneys. However, when someone has experienced damage to the blood-brain barrier, which controls whether substances in the blood can enter the brain, gadolinium leaks into the brain, creating bright spots that mark the location of brain damage.

Previous research had shown that certain eye diseases could cause a similar disruption to the blood-ocular barrier, which does for the eye what the blood-brain barrier does for the brain. Leigh’s team discovered that a stroke can also compromise the blood-ocular barrier and that the gadolinium that leaked into a patient’s eyes could provide information about his or her stroke.

“It looks like the stroke is influencing the eye, and so the eye is reflective of what is going on in the brain,” Leigh said. “Clearly these results are preliminary, so future studies will have to be attuned to this to fully understand its impact.”

Compound Prevents Neurological Damage, Shows Cognitive Benefits in Mouse Model of Alzheimer’s Disease

The supplement nicotinamide riboside (NR)—a form of vitamin B3—prevented neurological damage and improved cognitive and physical function in a new mouse model of Alzheimer’s disease. The results of the study, conducted by researchers at NIA, suggest a potential new target for treating Alzheimer’s disease. The findings appeared in the Feb. 5 issue of *Proceedings of the National Academy of Sciences*.

NR acts on the brain by normalizing levels of nicotinamide adenine dinucleotide (NAD⁺), a metabolite vital to cellular energy, stem cell self-renewal, resistance to neuronal stress and DNA repair. In Alzheimer’s disease, the brain’s usual DNA repair activity is impaired, leading to mitochondrial dysfunction, lower neuron production and increased neuronal dysfunction and inflammation.

“The pursuit of interventions to prevent or delay Alzheimer’s and related dementias is an important national priority,” said NIA director Dr. Richard

Hodes. “We are encouraging the testing of a variety of new approaches and this study’s positive results suggest one avenue to pursue further.”

The international team of scientists was led by Dr. Vilhelm Bohr, senior investigator and chief of NIA’s Laboratory of Molecular Gerontology, with Dr. Yujun Hou, a postdoctoral investigator in the laboratory.

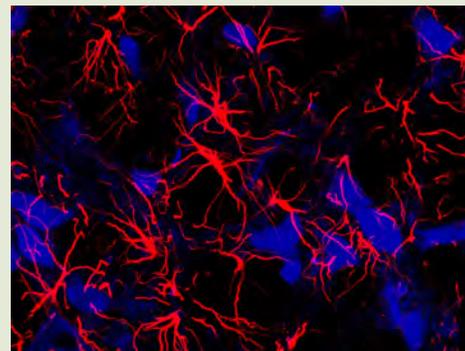
Based on their studies in human postmortem brain, they developed a new strain of mice mimicking major features of human Alzheimer’s such as tau pathology, failing synapses, neuronal death and cognitive impairment. Using this animal model, the researchers tested the effects of an NR supplement by adding it to the drinking water of the mice.

Over a 3-month period, researchers found that mice who received NR showed reduced tau in their brains, but no change in amyloid-beta.

Star-Like Cells May Help Brain Tune Breathing Rhythms

Traditionally, scientists thought that star-shaped brain cells called astrocytes were steady, quiet supporters of their talkative, wire-like neighbors, called neurons. Now, an NIH study suggests that astrocytes may also have their say. It showed that silencing astrocytes in the brain’s breathing center caused rats to breathe at a lower rate and tire out on a treadmill earlier than normal. These were just two examples of changes in breathing caused by manipulating the way astrocytes communicate with neighboring cells.

“For decades we thought that breathing was exclusively controlled by neurons in the brain,” said Dr. Jeffrey C. Smith, NINDS senior investigator and a senior author of the study published in *Nature Communications*. “Our results suggest that astrocytes actively help control the rhythm of breathing. These results add to the growing body of evidence that is changing the way we think about astrocytes and how the brain works.”



A fresh look at the brain and breathing: NIH study in rats shows that star-shaped brain cells called astrocytes (red) may play an active role in breathing.

IMAGE: JEFFREY C. SMITH LAB, NINDS

Smith’s lab investigates how breathing is controlled by the rhythmic

firing of neurons in the pre-Bötzinger complex, the brain’s breathing center that his lab helped discover. For this study, his team worked with Dr. Alexander Gourine of University College London whose lab found that astrocytes in neighboring parts of the brain may regulate breathing by sensing changes in blood carbon dioxide levels.

At least half of the brain is composed of cells called glia and most of them are astrocytes. Recently, scientists have shown that astrocytes may communicate like neurons by shooting off, or releasing, chemical messages, called transmitters, to neighboring cells.

In this study, the scientists tested the role of astrocytes in breathing by genetically modifying the ability of astrocytes in the pre-Bötzinger complex to release transmitters. When they hushed the astrocytes in rats by reducing transmitter release, the rats breathed and sighed at a lower rate than normal. In contrast, if they made the astrocytes chattier by increasing transmission, the rats breathed at higher resting rates and sighed more often.



Dr. Sang-A Park

NIH Mourns Loss of Postdoctoral Fellow Park

Dr. Sang-A Park, 27, a postdoctoral fellow at the National Institute of Dental and Craniofacial Research, was hit by a car at about 5:30 p.m. on Monday, Jan. 22. She was taken to Suburban Hospital, where she died about 4 hours later.

“Clearly, like so many of our researchers, [Park] was a talented scientist with much to

In January 2017, she was accepted into a fellowship program supported by the Korean Research Institute of Bioscience and Biotechnology.

At Park’s funeral, Dr. Bob Angerer, NIDCR scientific director, said, “I did not know Sang-A well, but I wish I had...She had a passion for science and for understanding how the world works. One of my colleagues remarked that she was often in the building at night—she told her parents that she didn’t want to go home at night because she was having so much fun in the lab.”

He continued, “Sang-A proved to be the kind of young researcher all mentors look for—a ‘self-starter’ who took the lead in her project and delighted in discussions about interpretation of results and plans for the next experiment. It usually takes several years to produce a significant paper, but after only a little over a year, Sang-A had finished almost all the work for her first first-author paper. That paper, and others to follow from projects to which she contributed, will be a permanent record for this outstanding young scientist.”

Added Angerer, “Everyone I have heard from speaks of her cheerfulness, her positive approach to life and to science and her willingness to help and support others. We offer our deepest sympathy to her family for

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“Sang-A proved to be the kind of young researcher all mentors look for—a ‘self-starter’ who took the lead in her project and delighted in discussions about interpretation of results and plans for the next experiment.”

-DR. BOB ANGERER

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contribute,” said NIH director Dr. Francis Collins, in an email to employees on Jan. 23. “I am deeply saddened by this tragedy. Our heartfelt thoughts and prayers go out to Dr. Park’s family, friends and colleagues.”

Park, a native of South Korea, had come to NIH in October 2016 as a visiting fellow in NIDCR’s mucosal immunology section. She had earned a B.S. (2007), M.S. (2011) and Ph.D. (2013) at Ewha Womans University’s College of Pharmacy in Seoul, South Korea. Her field of study was TGF-beta signaling and its crosstalk with other pathways in breast cancer stem cells post-chemotherapy.

the loss of their remarkable daughter and thank them for sharing her with us.”

Park’s lab chief, Dr. Wanjun Chen, noted, “Dr. Sang-A Park worked on an important project of understanding how a group of immune cells named Th9 cells are generated. Th9 cells have been recently demonstrated to have anti-tumor activity. Her work will help us understand and potentially develop therapy for human patients with cancer...She was a truly outstanding scientist and one of the best fellows I have trained so far.”

With the help of the NIH Korean Scientists Association, the Foundation

for Advanced Education in the Sciences has established a memorial fund in Park’s name. To make a voluntary contribution, visit <https://faes.org/content/donate-faes> and choose Park Memorial Fund in the donation form.



An internationally acclaimed statistical expert on radiation risk assessment, Dr. Charles E. Land passed away on Jan. 25.

NCI Statistician Land Dies

Dr. Charles E. Land, an internationally acclaimed statistical expert on radiation risk assessment, died Jan. 25 at his home in Portugal. He retired in August 2009 from his position as principal investigator in the Radiation Epidemiology Branch (REB) in NCI’s Division of Cancer Epidemiology and Genetics after a 34-year career.

Land will be remembered not only for his pioneering work in modern radiation dose-response analysis and modeling of low-dose cancer risk, but also as a delightful, humble man who loved his family, Japan, music and his work. He was a generous mentor and beloved friend to his colleagues and many others.

Land earned a Ph.D. in statistics from the University of Chicago and began his career studying radiation at the Atomic Bomb Casualty Commission (ABCC) in Hiroshima, where he conducted the first dose-response analysis of cancer risk in the Life Span Study cohort of atomic bomb survivors.

In 1975, he joined NCI as a founding

member of REB. He continued collaborating with the ABCC and its successor, the Radiation Effects Research Foundation, and led numerous other studies. In a series of seminal investigations, he and colleagues clarified the pattern of breast cancer risk associated with radiation exposure. These studies provided new mechanistic insights into breast carcinogenesis, while serving as the prototype for epidemiologic studies of other radiogenic cancers.

His work on the probability of causation was critical for the U.S. workers radiation compensation program. The statistical models that he developed formed the basis for the online Interactive RadioEpidemiological Program, which is still in use today. Land was also instrumental in elucidating the cancer risk following radioactive fallout from the U.S. nuclear weapons testing program. In addition, he analyzed data for studies of global and other radioactive fallout scenarios and initiated a study of thyroid nodules among residents in radiation-contaminated Kazakhstan.

REB chief Dr. Amy Berrington said, “Charles was a deep thinker and great character who made important contributions to many areas of radiation research. I still refer frequently to his classic 1980 *Science* paper, where he elegantly explained the statistical and practical difficulties in low-dose radiation epidemiology.”

Land served on many radiation protection committees, including the Three Mile Island follow-up research subcommittee. His numerous honors included the NIH Director’s Award and NIH Merit Award and the NCI Charles Harkin Award for Research in Thyroid Cancer.

He is survived by his wife Vera and sons David and Graham.

NIDDK Mourns Chemist Glaudemans

NIDDK alumnus Dr. Cornelis P.J. “Neil” Glaudemans, 85, died on Feb. 1 following a series of respiratory and cardiac complications.

An NIDDK scientist for more than 30 years and past chief of its Laboratory of Chemistry, he was a well-known carbohydrates expert. Among his many career highlights was work leading to a single-shot shigella vaccine. He retired in 1998 and



Dr. Cornelis “Neil” Glaudemans

served for 2 more years as scientist emeritus. Glaudemans was born in 1932 in the Dutch East Indies, where his father worked with a shipping company. His early education was interrupted during WWII by 3 years he spent in Japanese concentration camps. After the war, his family returned to Holland where he went to secondary school and college, obtaining his B.Sc. degree in chemistry from the University of Utrecht in 1954. He went to Canada for graduate education at McGill University, receiving his Ph.D. in 1958.

He came to NIH in 1962 as a postdoctoral associate. Three years later he joined the faculty of Yale University Medical School and simultaneously served as visiting scientist at New York University Medical Center. After returning to NIH, he collaborated with Dr. Michael Potter of the National Cancer Institute in work on the molecular interaction of myeloma monoclonal antibodies with bacterial antigens.

Over the years, he received the assistance of some 40 postdoctoral associates in the Visiting Program.

Glaudemans’ family owned several sailboats, ending with a 34-foot vessel—the Wilhelmina—in which they often cruised the Chesapeake Bay. With friends, and often with one of his six sons, Glaudemans sailed from Annapolis to Maine, Puerto Rico, Tortola in the British Virgin Islands and Charleston, S.C.

For about a decade, Glaudemans taught celestial navigation for yachtsmen in the Montgomery County Adult Education Program and wrote a monograph on the subject. His two greatest passions were ensemble playing (violin) baroque and classical music and painting watercolors and oils.

Glaudemans authored and co-authored some 190 scientific publications. He became a citizen of the U.S. in 1964.

He was predeceased by his wife Marlene in 2005. **R**

served for 2 more years as scientist emeritus.

Glaudemans was born in 1932 in the Dutch East Indies, where his father worked with a shipping company. His early education was interrupted during WWII by 3 years he spent in Japanese concentration camps. After the

NHLBI Study Needs Patients

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

Flu Vaccine Study Recruits Healthy Volunteers

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

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.

Study Needs Overweight Men

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

Healthy Volunteers Needed

NIAID researchers are seeking healthy volunteers, 18-50, to participate in a respiratory syncytial virus (RSV) challenge study at the Clinical Center. RSV is the most common cause of respiratory and lung infection in infants and older adults. Researchers will use what they learn to test new antivirals and vaccines in the future. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xnpZD>.



At left, on Feb. 2—Wear Red Day—NHLBI director Dr. Gary Gibbons (front, c) joins in a Move with Heart line dance in the Clinical Research Center atrium. Above, pledge station volunteers stand by, happy to accept vows and distribute information. Below, campaign stickers make pledges official.

'MOVE WITH HEART' 'Wear Red Day' Launches Heart Month

Led by NHLBI director Dr. Gary Gibbons and staff, NIH got in the mood to move on National Wear Red Day, Feb. 2. Spreading the message to "Move with Heart" for at least 150 minutes a week, a crowd enthusiastically joined in a grand line-dancing effort in the Clinical Research Center's atrium as part of NHLBI's campaign for American Heart Month.

During February and throughout the year, NHLBI encourages all Americans to increase their physical activity. Research shows that being physically active can help lower the risk of heart disease and stroke. The institute sent out a call on social media for others to share in the day, "Sporting red for National #WearRedDay?...Submit your video pledge to move more for your heart health today! <http://www.movewithheartpledge.com/>."

On Twitter, Gibbons was shown pedaling a stationary bike, vowing, "My pledge is to move more for a healthier heart by having more meetings on the move!" He challenged NIH director Dr. Francis

Collins, "Now it's your turn to take the pledge...@NIHDirector!"

Rising to the occasion, Collins tweeted a video of himself and his wife Diane Baker moving a monster tire, "I accept your challenge, Gary, and pledge to move more for my heart health. I challenge @Surgeon_General to do the same..."

The nation's doctor, Surgeon General Jerome Adams, responded by posting a video of himself going for a layup on the basketball court. "...I pass the ball to @SGottliebFDA...The ball is in your court!"

Off the main campus, at an annual NHLBI Division of Cardiovascular Sciences Wear Red Day potluck lunch, staff shared red-colored foods to highlight the day. The luncheon took place at the Rockledge II Bldg.



Clinical research nurse Karyn Hawkins supports Move with Heart campaign.



At left, at the Rockledge II Bldg., NHLBI Division of Cardiovascular Sciences staff share red-colored foods at their annual Wear Red Day potluck lunch. At right, NIH director Dr. Francis Collins issues his Move with Heart challenge after rolling a monster tire in the gym.



Above, campus eateries offered healthy food samples and tastings. Below, Bldg. 1 is decked out in red for the month.



PHOTOS: CHIA-CHI CHARLIE CHANG, JENNIFER STROHM, KIM SEIGFREID