NIH RECORD

February 16, 2024
Vol. LXXVI, No. 4

SPEAK, TWEET AND REPEAT?

Songbirds Begin to Reveal Mysteries of Spoken Language

BY ERIC BOCK

Humans, parrots, songbirds and hummingbirds share an unusual ability: they are capable of vocal production learning. That is, they can hear and repeat new sounds even if they weren't born making them, said Dr. Erich Jarvis during the recent Marshall W. Nirenberg Lecture in Lipsett Amphitheater.

Such learning is rare, said Jarvis, professor in the Laboratory of Neurogenetics of Language at Rockefeller University and investigator at Howard Hughes Medical Institute. Parrots, songbirds, hummingbirds and humans, dolphins, whales, bats, elephants and seals are the only vocal learners in nature. When one of these species hears something new, they can imitate, produce and "pass on those vocal repertoires culturally, from one generation to the next," he noted.

Recent Nirenberg lecturer Dr. Erich Jarvis accepts a certificate from NIH Deputy Director for Intramural Research Dr. Nina Schor.

PHOTO: PAULE JOSEPH

Vocal learning is just one component of spoken language. Some other components, like auditory learning, are more common in the animal kingdom. A pet dog, for instance, can understand human commands like sit, stay or roll over, but cannot vocally reply in kind.

"A dog can understand those human words, but can't respond, 'ok, you got it,'" Jarvis explained. In response, a dog might bark, an innate behavior. They can learn to bark in different contexts, such as wanting food or attention. This is called vocal usage learning.

Humans and parrots are the most advanced vocal production learners. A pet parrot can learn to produce over 400 words and combine them into unique sentences. In comparison, one of our closest

SEE **JARVIS**, PAGE 8

Young Turns the Phage Toward New Therapies

BY DANA TALESNIK

Dr. Ryland Young

Germs can be exceedingly stubborn. As bacteria and fungi devise new ways to evade antibiotics, there's an urgent need for alternative approaches to overcome these resistant germs. Researchers are moving ever closer to a viable alternative.

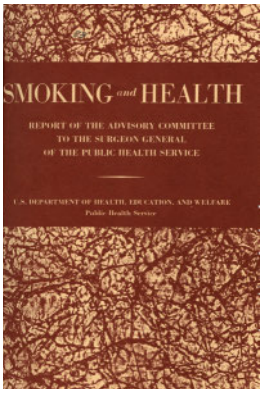
Phage therapy is emerging as an important tool against multi-drug-resistant bacterial infections. Much of what's known about bacteriophages—viruses that target and kill bacteria—comes from research led

SEE **YOUNG**, PAGE 4

Historic Public Health Report Marks 60th Anniversary

BY KRIS HEITMAN

Smoking and Health: Report of the Advisory Committee to the Surgeon General, published 60 years ago in January 1964, reshaped the way Americans viewed smoking. As the scientific foundation of a highly effective public health campaign, it provided a new model for changing individual behavior.



Smoking had become wildly popular in the first half of the 20th century, even as epidemiologists and pathologists demonstrated its connections with lung

SEE **REPORT ANNIVERSARY**, PAGE 6

NIH, Gates Foundation leaders meet. See p. 3.

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Shultz-Cherry To Deliver Annual Dyer Lecture, Feb. 28

Dr. Stacey Shultz-Cherry of St. Jude Children's Research Hospital, will deliver the Rolla E. Dyer Lecture, part of the Wednesday Afternoon Lecture Series (WALS), on Feb. 28 from 2 to 3 p.m. ET. The title of the lecture is "Influenza Pathogenesis and Therapeutics in Vulnerable Populations." The presentation will be held in Lipsett Amphitheater, Bldg. 10 and videocast at https://videocast.nih.gov/watch=51122.

Dr. Stacey Shultz-Cherry

Recognized internationally for her studies on the pathogenesis of influenza and intestinal viruses, Schultz-Cherry leads a research laboratory in St. Jude's department of infectious diseases. She also is deputy director of the WHO Collaborating Centre for Studies on the Ecology of Influenza in Animals and Birds, co-director of both the NIAID-funded Center for Excellence in Influenza Research and Surveillance and the Collaborative Influenza Vaccine Innovation Center.

The annual Dyer Lecture, established in 1950, is one of the oldest NIH lecture series and honors the former NIH director who was a noted authority on infectious diseases. The lectureship features internationally renowned researchers who have contributed substantially to medical as well as biological knowledge of infectious diseases.

More information about WALS is posted at https://oir.nih.gov/wals.

DEIA Competition Announces Awardees

The Chief Officer for Scientific Workforce Diversity (COSWD) recently announced the 10 awardees of the NIH Institutional Excellence in Diversity, Equity, Inclusion and Accessibility (DEIA) in Biomedical and Behavioral Research Prize Competition.

Each of the following institutions will receive a $100,000 prize for demonstrating exceptional dedication and innovation in fostering DEIA within research environments. NIH awarded three prizes to limited-resource institutions (LRIs*).

California State University, San Marcos*
Duke University
Rochester Institute of Technology*
University at Buffalo, State University of New York
University of California, Davis
University of California, San Francisco
University of Florida
University of Illinois Chicago
University of Puerto Rico, Rio Piedras*
Vanderbilt University

Prize recipients designed a broad range of innovative DEIA policies and evidence-informed programs, tools and activities that promote equity and eliminate structural barriers to success among students, postdoctoral scholars and faculty in the research enterprise.

COSWD administers the competition, which is cosponsored by UNITE and 24 institutes and centers. The COSWD team will host a virtual symposium this summer for representatives from the prize-winning institutions to share their DEIA interventions that resulted in sustained, measurable change.

Watch for information about the symposium in the coming months and visit the competition website https://www.nihdeiaprize.org/ to learn more about the prize recipients.

'AMPLIFYING VOICES, BUILDING BRIDGES'

Register for NIMH 75th Anniversary Symposium

In March 2024, the National Institute of Mental Health (NIMH) will continue its year-long 75th anniversary celebration with its second symposium, "Amplifying Voices and Building Bridges: Toward a More Inclusive Future."

The event will focus on NIMH's role in society and feature presentations from health equity, sociology, psychiatry and public health experts. It will bring together people living with mental illness, clinicians and communities to reflect on past and present challenges in mental health research and chart a more inclusive path forward.

Key themes include:
Inclusion in research
Disparities in health and access to care
Diversity in the mental health workforce

The event will be held on Monday, Mar. 18 from 8:30 a.m. to 5 p.m. ET at the National Archives Building in Washington, D.C., and virtually. The event will also be recorded and archived on the NIMH website.

Register for the symposium at https://go.nih.gov/fwUYMAL. Registration is required for both in-person and virtual participation.

This symposium is one of several NIMH anniversary events planned. For more information on the celebration, visit nimh.nih.gov/75years.

NIAAA Promotes Facts About Teen Drinking

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) recently posted Facts About Teen Drinking, a web resource for young people that features research-based information on underage drinking. It includes info on how alcohol adversely affects the body, how to identify signs of an alcohol-related problem and where to get help when needed. Check it out at https://go.nih.gov/bFiCKPv.

VOLUNTEERS

Eczema Study Seeks Participants

Eczema, a stubborn skin problem that shows up as redness and intense itching, can affect people of all ages. It's more common in infants and young children. Various triggers, such as irritants, allergens and stress, can worsen eczema symptoms, increasing discomfort and flare-ups that affect health and sleep. NIH researchers are looking for volunteers ages 3-21 for an eczema study. Contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #15-I-0162. Online: https://bit.ly/3BGyFLD.

Study in Search of Pregnant Women with SCD

A research study at NHLBI is looking for pregnant women with sickle cell disease (SCD) between ages 18 and 45 who are at risk of having an infant with SCD to donate their baby's cord blood. Tests and procedures provided at no cost. Contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users call 711) or ccopr@nih.gov. Refer to study #01-H-0122. Online https://go.nih.gov/6KDclKd.

At left, NIH Director Dr. Monica Bertagnolli, technologist-philanthropist Bill Gates (c) and Dr. Trevor Mundel of the Gates Foundation participate in a discussion about the role of artificial intelligence in biomedical research and clinical studies at the recent 10th annual NIH-Gates Foundation Leadership Workshop on Global Health. At right, Gates underscores the importance of developing and supporting infrastructure for public health programs in international settings during the welcome session of the workshop.

PHOTOS: CHIA-CHI CHARLIE CHANG

NIH Hosts Annual Global Health Workshop with Gates Foundation

Leaders of NIH and the Bill & Melinda Gates Foundation gathered Jan. 29 at the Porter Neuroscience Research Center for the 10th annual NIH-Gates Foundation Leadership Workshop on Global Health. The all-day agenda included a welcome session with Bill Gates and NIH Director Dr. Monica Bertagnolli, who gave a presentation, "Accelerating Innovative Clinical Trials," during the opening scientific session.

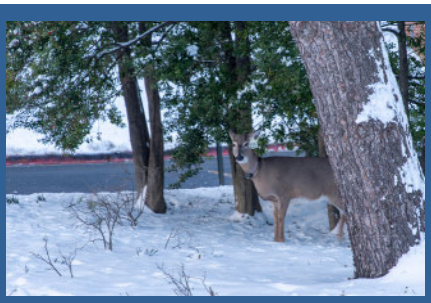
NHLBI Director Dr. Gary Gibbons and Dr. Anita Zaidi, president of Gates's gender equality division

In his remarks, Gates underscored the importance of developing and supporting infrastructure for public health programs in international settings. Bertagnolli discussed the critical need to expand evidence to guide clinical care—connecting new knowledge to clinical practice and everyday life so that all people live healthier lives.

NIH and the Gates Foundation began working in partnership in 2003, when the foundation created its Grand Challenges in Global Health Initiative. The initiative invited scientists to collaborate on 14 specific goals that could lead to breakthrough advances in medicine.

In addition to Bertagnolli and Gates, other leaders in the biomedical research community who attended this year included NIH Principal Deputy Director Dr. Lawrence Tabak; John Burklow, NIH chief of staff; Dr. Jeanne Marrazzo, director of the National Institute of Allergy and Infectious Diseases; Dr. Gary Gibbons, director of the National Heart, Lung and Blood Institute; Dr. Diana Bianchi, director of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development; former NIH Director Dr. Francis Collins; Dr. Robert Califf, commissioner of the Food and Drug Administration; Dr. Julie Gerberding, CEO of the Foundation for NIH; and from the Gates Foundation, Dr. Trevor Mundel, president of global health; Dr. Chris Karp, director of discovery and translational sciences; and Dr. Anita Zaidi, president of the gender equality division.

Leaders at the workshop include (from l) Bertagnolli; Gates; Mundel; Dr. Chris Karp, Gates Foundation director of discovery and translational sciences; Dr. Robert Califf, commissioner of the Food and Drug Administration; NIAID Director Dr. Jeanne Marrazzo; and Zaidi.



ON THE COVER: *A deer outside Bldg. 15 on the NIH campus in Bethesda*

IMAGE: DUSTIN HAYS/NEI

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email nihrecord@nih.gov.

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NIH National Institutes of Health
Turning Discovery Into Health

Young

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by Dr. Ryland Young, featured speaker at NIH's annual DeWitt Stetten Jr. Lecture.

"Even when others turned away from the field, [Young] saw the potential to use phages with their facile genetics, molecular biology and biochemistry to ask specific and important biological questions," said Dr. Jon Lorsch, director of the National Institute of General Medical Sciences, who introduced the lecture.

Young, founding director of the Center for Phage Technology at Texas A&M University, has called phages "bacteria with brains." Bacteriophages have tails allowing them to carry and insert their DNA into the targeted bacteria in seconds. These DNA tail phages are diverse and abundant in nature—found in soil, in the ocean—and in the human body.

Understanding phage lysis—how phages destroy the bacterial cell and wall—is integral to developing new antibacterial therapies.

Lysis was once believed to be a passive process. But back in medical school in 1977, Young discovered phage lysis might be a timed event.

While conducting phage infection experiments, he realized he had forgotten to infect one culture, so he started that infection three minutes later. Amazingly, all the cultures underwent lysis (the destruction of the bacterial cells) at the same time, except for the one late culture, which lysed exactly three minutes later. Further experiments would confirm phage lysis is highly controlled over time.

"This is a biological event that can keep time on the order of minutes to seconds," Young said. "I have children who couldn't keep track of time at the level of days."

Young's continuing research then revealed what's regulating lysis timing, a single protein of 105 amino acids. He named that protein a "holin."

Produced by bacteriophages, holins activate and control degradation of the host's cell wall. There are more than 200,000 different holins among thousands of unrelated gene families, noted Young. A holin has two functions—to cause lysis and to cause it at the right time.

Lysis genes are often found on cassettes. Young focused on the lambda lysis cassette, which contains genes from one transcript that turns on eight minutes after infection.

"This makes it easy to study in terms of the kinetics," he explained.

The lambda lysis cassette has four genes arranged in the order of the assaulted bacterial envelope. Each of these genes work to break through the cell's wall and target the outer and inner membranes.

Holins, he said, accumulate in the cell membrane, where they reach critical concentration. The proteins aggregate and get converted into giant holes, which have the rather unfortunate name S-holes. These S-holes allow lysozymes to escape and attack the cell wall. By forming holes in the inner membrane, holins are causing instant cell death.

"After we started this crusade to understand the lambda holin, which I view as the most important protein and organism in the world, [we discovered] there are two functional types of holins," said Young.

The new type of holin made tiny holes, or pinholes, about 100 times smaller than the canonical S-holes. These new "pinholins" are not as well timed as canonical holins, said Young. He showed a movie slide of pinholins lysing several genes, then eventually exploding. "If you did lambda S protein with this, they'd all be lysing in a minute or two, so it's not quite as well controlled."

Another critical type of protein in phage lysis is the spanin, which mediates the last step during lysis. In a nutshell, he said, there are two types of holins, two types of endolysins that target peptidoglycan (chains of peptides that form the bacteria's cell wall) and two types of spanins.

NIGMS Director Dr. Jon Lorsch (l) presents the Stetten lecturer plaque to Young.

"There are all these different possibilities and we've either found them in nature or constructed in a laboratory almost every combination of these three components," said Young. "As far as we can tell, all double-stranded DNA phages use holin systems and I suspect there must be powerful evolutionary forces to make that happen."

Bacteria are tricky, complex structures that aren't easily overcome. Destroying them at the right time is key, and that's where phage lysis comes in. After phages infect a bacterial cell and replicate, they can initiate lysis, which kills the bacteria while leaving the phages time to escape.

This process remains under study and holds vast potential as an alternative way to treat resistant bacterial infections.

Young's decades-long research on bacteriophages is paving the way toward alternative treatments for resistant bacterial infections.

PHOTOS: LESLIE KOSSOFF

Lecture on Disparities in Diabetes Prevention Set for Feb. 29

The National Institute on Minority Health and Health Disparities (NIMHD) Director's Seminar Series will host a virtual lecture featuring Dr. O. Kenrik Duru, professor at the David Geffen School of Medicine at the University of California, Los Angeles.

Dr. O. Kenrik Duru

The presentation, "Disparities in Diabetes Screening and Prevention by Race and Ethnicity," will be given on Thursday, Feb. 29 from 2 to 3:30 p.m. ET and available online at https://videocast.nih.gov/watch=54227 (no registration required).

Duru's research interests include enhancing physical activity among minority seniors and designing interventions to reduce disparities in medication adherence and clinical outcomes among people with diabetes. He also has a strong career/research focus on diabetes care and prevention and working with populations experiencing health disparities.

After the lecture, NIMHD Director Dr. Eliseo J. Pérez-Stable will facilitate a Q&A. Virtual audience members will be able to submit questions and comments at NIMHDDSS@mail.nih.gov.

The event is open to all NIH staff, trainees and external groups. For details, visit https://go.nih.gov/CrDZTiW.

Returned Peace Corps Volunteers Sponsor Blood Drive

The Returned Peace Corps Volunteers at NIH will sponsor a blood drive in conjunction with the NIH Blood Bank during National Peace Corps Week, Feb. 26-Mar. 1. Show your support by donating blood at the Clinical Center Blood Bank (Bldg. 10, Rm. 1C713) or platelets at the Fishers Lane Donor Center (5625 Fishers Lane, Rockville, MD 20852). Both types of donations benefit up to three CC patients. To learn more about donating, including whether you are eligible, call (301) 496-1048 and mention the Returned Peace Corps Volunteers drive. For details about the drive, contact Joan Romaine (RPCV, Gabon, 1995-1997) at joan.romaine@nih.gov.

Wood Receives Outstanding Researcher Award

The Radiological Society of North America (RSNA) has honored Dr. Bradford J. Wood, founding director of the NIH Center for Interventional Oncology, with the 2023 Outstanding Researcher Award. Recipients of this award have made significant contributions to radiology research over the last 15 years that have fundamentally changed the future of the field.

A trailblazer of interventional approaches to deliver lifesaving treatments to people with cancer, Wood exemplifies the character of a translational scientist who applies investigative techniques to real-world clinical practice.


Dr. Bradford J. Wood

"Brad Wood is the tip of the spear when it comes to innovative research in the field of interventional radiology," said RSNA President Dr. Matthew Mauro. "I have admired him and his work for many years, as he dedicated himself to the advancement of this growing specialty."

Wood leads a diverse multidisciplinary team that develops and translates devices, software and navigation approaches via public-private-academic partnerships to address unmet clinical needs. These technologies and techniques have improved outcomes for patients with cancer and other conditions.

He also serves as chief of interventional radiology at the Clinical Center and holds appointments at the National Cancer Institute, National Institute of Biomedical Imaging and Bioengineering, as well as the University of Maryland as adjunct professor of biomedical engineering.

Wood earned his medical degree in 1991 from the University of Virginia. He then completed fellowships in vascular and interventional radiology and in abdominal and interventional radiology at Massachusetts General Hospital (MGH) and Harvard Medical School.

He held clinical and teaching positions at MGH/Harvard and Georgetown University before he was recruited to NIH. From 2006 to 2008, he served as acting co-chief of radiology.

A mentor to hundreds of trainees, scientists, physician-scientists and engineers at the Clinical Center, Wood has overseen the authorship of several books and more than 600 peer-reviewed manuscripts. His papers have been cited over 40,000 times. He holds more than 50 patents for advanced systems and techniques that target disease.

NIAAA Launches Middle School Resource

NIAAA launched a new web resource, NIAAA for Middle School. The site contains information and interactive activities to help parents, caregivers and teachers of middle school students introduce and reinforce key messages about peer pressure, resistance skills and other important topics related to underage drinking.

NIAAA for Middle School replaces and continues the objectives of the long-standing Cool Spot website, remaining grounded in the Alcohol Misuse Prevention Study from the University of Michigan.

Visit the new site at https://go.nih.gov/Ry9GSoH.

CONTINUED FROM PAGE 1

cancer and other deadly diseases. The scientific results were taken up by nonprofit advocates such as the American Cancer Society, American Heart Association and the National Tuberculosis Association, precursor to the American Lung Association. But tobacco companies publicly dismissed the then-novel research as inconclusive and, as more American households bought televisions, the industry stepped up its pro-smoking advertising campaigns.

In 1956, Surgeon General (SG) Leroy Burney convened a year-long study group to review the available research. That review confirmed the causal relationship between smoking and lung cancer, which Burney then announced as the official opinion of the U.S. Public Health Service (PHS).

The tobacco industry aggressively questioned PHS's interpretation of the data, and Burney issued a still-stronger statement in 1959.

Yet U.S. smoking rates continued to rise: By 1960, more than 40% of adult Americans reported actively smoking. The public health challenge was thus to convince Americans to make decisions about whether to smoke—or quit—in light of sound scientific evidence.

U.S. Surgeon General Dr. Luther Terry (l) addresses a press conference at release of the 1964 *Report on Smoking and Health*. Advisory committee members who compiled the report sit behind the podium.

PHOTO: NLM

Burney's successor, SG Luther Terry, convened a second study group in November 1962. This time, members were asked to prepare a formal report for publication.

Terry's committee worked for just over a year, without fanfare, meeting mostly in offices in the basement of NIH's brand-new National Library of Medicine (NLM) building (see sidebar below).

NLM staff helped compile more than 7,000 publications, including many studies conducted at or funded by NIH.

In the five years since Burney's press conference, new research had directly linked smoking tobacco with several other deadly diseases that were already rising health concerns.

Taken together, the effects of smoking produced a 70% increase in mortality over nonsmokers, and smokers had been found to face a 10- to 20-fold increase in the risk of death from lung cancer—although quitting was shown to substantially improve the odds. Scientists had also determined that women who smoked while pregnant had babies with significantly lower birth weights.

Terry presented the report's highlights in a press conference on Jan. 11, 1964, prompting shocked stories in newspapers and TV programs across the U.S. and abroad. Catchy public service announcements soon followed.

LOCATION, LOCATION, LOCATION

NIH Site of Committee Deliberations Humble

For all of its momentous responsibility and undertaking, the 10-member group tasked with advising the U.S. surgeon general on the health effects of smoking held forth in somewhat humble surroundings—a super-subbasement of the National Library of Medicine (NLM) building newly constructed on NIH's Bethesda campus.

"The staff was housed on C level in NLM, far away from the madding crowd," said Donald Shopland, who was still a teenager when he was assigned a job supporting the committee. "C level back then only contained journals published prior to 1946 that were in significantly less demand than the more current journals on A level. As a result, few people were on the floor, except for the occasional library tech who retrieved journals from that era. C level is three floors below ground."

Immediately after the committee was formed, the Public Health Service constructed short-term offices for the staff, Shopland recalled. In addition, a temporary enclosure was erected next to the offices.

"The staff affectionately called it the 'bullpen,'" Shopland said, "and that is where the full committee met to discuss the evidence and put their final report together."

The 10-member surgeon general advisory committee meets in its "bullpen," a temporary structure built on the C Level of the National Library of Medicine. The two individuals sitting at the head of the table to the right are Assistant Surgeon General Dr. James Hundley and Staff Director Dr. Eugene Guthrie.

Accommodations were far from lavish. The enclosure stood less than 6 feet tall, was completely open at top and bottom and had no doors. And, being cast far from the public eye perhaps offered the group more freedom of expression.

"It wasn't unusual to hear a few ugly words being

The full committee staff gathers with Surgeon General Dr. Luther Terry at an awards ceremony he hosted in August 1964. Indicative of the times, ashtrays were prominent fixtures in the room.

In 1965, Congress stepped in with the Federal Cigarette Labeling and Advertising Act, compelling U.S. tobacco companies to print health warnings directly on cigarette packets and requiring the SG's office to produce annual reports on smoking and health, thereby ensuring attention to emerging questions such as health consequences for women (1980), nicotine addiction (1988), effects by race and ethnicity (1998), effects of secondhand smoke (1986, 2006, 2010) and risks of e-cigarettes (2018). In 1969, legislators passed the Public Health Cigarette Smoking Act to prohibit cigarette advertising via television and radio.

The 1964 Report on Smoking and Health thus left an admirable legacy. While smoking is still a leading cause of preventable death, U.S. rates now hover at an all-time low of about 11%. Youth smoking, which peaked at 36.4% in the late 1990s, is currently less than 2%.

Read more about the historic report online at https://go.nih.gov/QZJbehf.

Surgeon General Dr. Luther Terry, shown in uniform with a group of staffers. Donald Shopland (r), age 18 at the time, is one of the last survivors who staffed the committee.

PHOTOS COURTESY DON SHOPLAND

said as the committee 'debated' the evidence," Shopland remembered. "More than a few shouting matches occurred too."

Since committee members maintained their full-time academic positions back home, they always met on weekends—usually beginning on Friday and going through Saturday. Later, meetings extended into Sunday and even Monday.

"Obviously that meant the staff worked weekends too," Shopland lamented. "In fact, certain members of the staff worked most weekends. It wasn't unusual for some of the core staff to turn in timecards with as many hours of overtime as regular time."

Now set to become an octogenarian this fall, Shopland, who eventually served as coordinator of the National Cancer Institute's Smoking and Tobacco Control Program, may be the sole surviving person to have worked on the groundbreaking report.

A book, *Clearing the Air. The Untold Story of the 1964 Report on Smoking and Health*, which he and two fellow staffers wrote with two committee members gives the inside scoop on "just what went into putting that landmark report together." It will be published soon.

New Web-Based Health, Safety Applications To Debut

NIH's Office of Research Services' Division of Occupational Health and Safety (DOHS) will soon launch two new web-based applications to improve and personalize individual safety at NIH.

On Monday, Feb. 26, all NIH staff will use the myCority application to submit safety suggestions, request lab clearances, report indoor air quality concerns, complete ergonomic adjustment guides for computer workstations or laboratory environments and more.

This summer, staff will begin using the app to access personal occupational health information and related programs (for instance, animal exposure program, tuberculosis screening, etc). Until then, staff will continue to use HealthRx.

Beginning Monday, Mar. 25, the Electronic Registration System (ERS) will become the new place to submit, track, update and renew research involving recombinant/synthetic nucleic acids and/or potentially infectious biological materials studied in the Intramural Research Program.

All submissions to the current system—PI Dashboard—must be completed by Wednesday, Feb. 21 to ensure review and data integration to ERS.

A new Health and Safety Application Resources SharePoint site will be available soon via a link on the DOHS homepage: https://ors.od.nih.gov/sr/dohs/Pages/default.aspx. The site will contain information about applications, workflows, PDF user guides and step-by-step videos to walk you through each process.

2023 CFC Officially Ends

NIH has exceeded its goal of $1 million for the 2023 Combined Federal Campaign (CFC), raising more than $2.16 million for charities.

"This is an incredible achievement and I am proud to be part of such a caring community," said NIH Director Dr. Monica Bertagnolli in a recent email to staff. "This year's success is a testament to YOUR generosity. On behalf of the 5,000 charities that participated in the 2023 CFC, thank you for your support."

CFC is the annual workplace fundraising drive among federal employees. The National Institute of Nursing Research (NINR) was lead institute for NIH's 2023 campaign.

Bertagnolli thanked NINR Director Dr. Shannon Zenk for heading the effort and Dr. Jonathan Horsford, senior policy advisor in NIH's Office of the Director, for serving as HHS CFC national campaign manager.

Jarvis is greeted by Dr. Paule Joseph of NIAAA (c) and Dr. Neil Hanchard of NHGRI.

Jarvis

CONTINUED FROM PAGE 1

relatives, a gorilla, can't even get out one word, even though some gorillas have a vocabulary of understanding 7,000 words.

"That raises the question: why can't we get our closest relatives to say something as simple as 'apple,' when parrots can tell you the variety of an apple, like golden delicious or Macintosh," he said.

Following up on the 1970s work of his former Ph.D. adviser Dr. Fernando Nottebohm, Jarvis completed the identification of the brain pathways for vocal learning in canaries in the 1990s. Experiments showed that when a bird sings a learned song, it activates increased expression of genes in parts of the brain associated with vocal learning. The longer the bird sings, the stronger the gene expression becomes.

Further research revealed every species capable of vocal learning showed similar brain pathways—one for learning and one for production.

What's remarkable is that songbirds, parrots and hummingbirds seem to have independently evolved, Jarvis observed. Each species has similar—but not identical—brain circuitry in seven brain regions.

In 2014, Jarvis co-led a consortium that sequenced the genomes of 48 bird species representing nearly all bird orders. The new evolutionary tree revealed that parrots, songbirds and hummingbirds are distantly related, suggesting that each species independently gained the vocal learning ability.

"If you would argue a common origin of these vocal learning circuits in birds, you have to go back to the time of mass extinction of dinosaurs," he said.

The size of an animal's brain does not determine whether it is capable of vocal learning. The brains of 3,000 zebra finches can fit inside one human brain. Yet, these birds can imitate sounds, while dogs cannot.

During experiments where birds not only sang, but moved around in a coordinated way, he noticed that regions responsible for song learning were next to regions responsible for movement.

"It seems like vocal learning circuits are embedded within this motor learning circuit," he explained.

Around the same time, Jarvis's colleagues studied what happened inside a person's brain when they were taught a new dancing sequence. MRI scans revealed that the most active brain regions were adjacent to the parts of the brain that controlled speech. Another study showed that only vocal learning species can also dance to the beat in music.

Jarvis proposed that the brain areas targeted for vocal learning evolved as a specialization of a pre-existing motor pathway that controls movement. He calls it the motor theory of vocal learning origin.

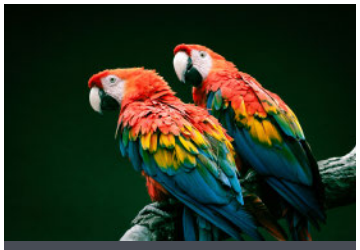
All vertebrates have regions in the brain that are responsible for processing complex sounds, he said. It's why a dog can understand spoken human commands. Additionally, they all have motor learning circuits for learning how to move, such as flying or walking, and another pathway for producing that movement. To explain these findings, he proposed that these circuits are replicated multiple times "to get hooked up to different muscle groups to control different body parts."

In vocal learning species, "it's replicated one more time through some genetic mutation," Jarvis suggested. "This new replicated circuit takes over the brain stem circuit for vocal behavior to get an emergent vocal learning circuit."

This circuit makes fine motor control in the larynx, also known as the voice box, possible. It allows for the production of imitated speech. "I call this brain evolution by brain pathway duplication," he said.

More recently, a postdoctoral researcher in Jarvis's lab found that songbirds that displayed more complex vocal learning had larger brains and were better at solving problems.

"There seems to be a correlation between vocal-learning ability, problem solving and the ability to learn how to dance," he said. More research must be conducted to determine why this is the case.



Macaw parrots

TAGIR FASKHUTDINOV/SHUTTERSTOCK

His lab is also studying the genes associated with song and spoken language. There are hundreds of genes in speech and song-learning circuits that have evolved similar specialized expression levels in birds and humans.

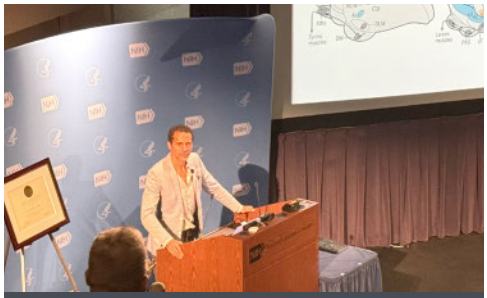
Since 2017, Jarvis has been chair of the Vertebrate Genomes Project, an ambitious effort to sequence the genomes of 70,000 vertebrate species. Understanding the DNA sequence between all vertebrates will enable study of how genes have contributed to their evolution and survival.

The project first evaluated multiple genome sequencing and assembly approaches extensively of a hummingbird species. Having higher-quality genomes will allow the lab to make important observations about what genes are associated with speech deficits or disorders.

Even though humans and songbirds developed these circuits independently, the brain pathways for speech in species 300 million years removed from humans can reveal insights about what genes are involved in certain brain regions.

"Just because it's convergent doesn't mean it's not relevant," he concluded.

Established in 2011, the Nirenberg lecture honors its namesake for his work to decipher the genetic code, which resulted in his receiving the 1968 Nobel Prize in Physiology or Medicine.

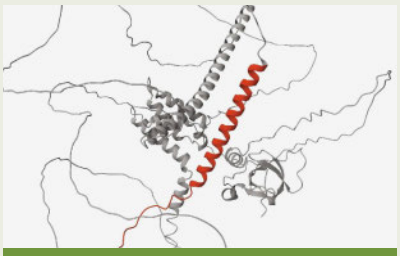


LECTURE PHOTOS COURTESY PAULE JOSEPH

Abnormal Proteins Found in Spinal Fluid of People with ALS and Dementia

NIH researchers detected abnormal proteins in the spinal fluid of people with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), which could help improve diagnosis of these diseases. The findings were published in *Science Translational Medicine*.

The proteins in question are built from "cryptic" exons—abnormal portions of RNA, the cell's instructions for how to build proteins. Cryptic exons occur when TDP-43, a protein that regulates how RNA is processed, stops functioning normally. TDP-43 dysfunction is linked to ALS, FTD, Alzheimer's disease and Limbic Associated TDP-43 Encephalopathy (LATE).



Protein containing a cryptic peptide (red) that results from a lack of functional TDP-43, as in ALS and FTD

IMAGE: NINDS

The findings advance our understanding of how cryptic exons may be involved in the dementia disease process and could help identify diseases involving TDP-43 dysfunction before symptoms appear.

"We show that TDP-43 pathology causes brain cells to mis-splice hundreds of RNAs and that some of these RNAs are translated into new proteins that are not normally found in healthy cells," said NINDS senior investigator Dr. Michael Ward, co-director of the iPSC neurodegenerative disease initiative at NIH's Center for Alzheimer's and Related Dementias (CARD) and senior co-author. "This conceptual discovery may enable future development of sensitive diagnostic tests to detect TDP-43 pathology in living patients."

There is currently no single test that can definitively diagnose ALS or FTD, and the symptoms can resemble those of other disorders. To help diagnose the disorders, doctors perform a physical exam, assess symptoms, conduct brain imaging and use tests to rule out other conditions.

Until now, scientists had not explored the possibility that some cryptic exon transcripts are not degraded, but instead generate new proteins. The authors speculate these new proteins might be seen as foreign by our immune system, thereby triggering inflammation that could contribute to neurodegeneration.

This study was funded in part by the NINDS Intramural Research Program, NIA and CARD.

Switching to Vegan or 'Keto' Diets Rapidly Affects Immune System

NIH researchers observed rapid and distinct immune system changes in a small study of people who switched to a vegan or a ketogenic (keto) diet.

Scientists closely monitored various biological responses of people sequentially eating vegan and keto diets for two weeks, in random order. They found the vegan diet prompted responses linked to innate immunity—the body's non-specific first line of defense against pathogens—while the keto diet prompted responses associated with adaptive immunity—pathogen-specific immunity built through exposures in daily life and vaccination. Metabolic changes and shifts in the participants' microbiomes—communities of bacteria living in the gut—were also observed.

PHOTO: ANTONINA VLASOVA/SHUTTERSTOCK

More research is needed to determine if these changes are beneficial or detrimental and what effect they could have on nutritional interventions for diseases such as cancer or inflammatory conditions.

The keto diet is a low-carbohydrate diet that is generally high in fat. The vegan diet eliminates animal products and is high in fiber and low in fat.

The study was conducted by researchers from NIAID and NIDDK's metabolic clinical research unit in the Clinical Center. The 20 participants were diverse with respect to ethnicity, race, gender, body mass index and age.

Each person ate as much as desired of one diet (vegan or keto) for two weeks, followed by as much as desired of the other diet for two weeks. Throughout the study period, blood, urine and stool were collected for analysis. Participants remained on site for the entire month-long study, allowing for careful control of the dietary interventions. Switching exclusively to the study diets caused notable immune system and metabolic changes in all participants.

The results of this study demonstrate that the immune system responds surprisingly rapidly to nutritional interventions, suggesting it may be possible to tailor diets to prevent disease or complement disease treatments.

Cognitive Behavioral Therapy Alters Brain Activity in Children with Anxiety

NIH researchers have found that children with anxiety disorders have overactivity in several brain regions, including the frontal and parietal lobes—important for cognitive and regulatory functions, such as attention and emotion regulation—and deeper limbic areas like the amygdala, which are essential for generating strong emotions, such as anxiety and fear.

IMAGE: ISEEU2/SHUTTERSTOCK

They also showed that treatment with cognitive behavioral therapy (CBT) led to improvements in clinical symptoms and brain functioning. The findings illuminate the brain mechanisms underlying the acute effects of CBT to treat one of the most common mental disorders. The study, published in the *American Journal of Psychiatry*, was led by researchers at NIMH.

In the study, 69 unmedicated children diagnosed with an anxiety disorder underwent 12 weeks of CBT following an established protocol. CBT involves changing dysfunctional thoughts and behaviors through gradual exposure to anxiety-provoking stimuli.

The researchers used clinician-rated measures to examine the change in children's anxiety symptoms and clinical functioning from pre- to post-treatment. They also used task-based fMRI to look at whole-brain changes before and after treatment and compare those to brain activity in 62 similarly aged children without anxiety.

Following three months of CBT treatment, children with anxiety showed a clinically significant decrease in anxiety symptoms and improved functioning. Increased activation seen before treatment in many frontal and parietal brain regions also improved after CBT.

However, eight brain regions continued to show higher activity in anxious compared to non-anxious children after treatment. Changing activity in these regions may require a longer duration of CBT, additional forms of treatment or directly targeting subcortical brain areas.

Anxiety disorders are common in children and can cause them significant distress in social and academic situations. They are also chronic, with a strong link into adulthood, when they become harder to treat.

ARTIFACT WHISPERER DEPARTS

NIH History Office's Founding Curator Lyons Retires

BY CARLA GARNETT

Call her the Dr. Doolittle for historical objects. If the legendary veterinarian's chats with animals offer invaluable insight into their world, then Michele Lyons's talks with scientific artifacts provide a similar glimpse into NIH's rich origins and enterprise.

Associate director and founding curator of the Office of NIH History and Stetten Museum (ONHM), Lyons—who converses with inanimate items and translates their language for the rest of us—wrapped up her NIH career at the end of 2023.

A palm-size piece of polyurethane that became an artificial heart valve. A metallic watch fob, circa 1908, identifying Green River Whiskey as "the official whiskey of the U.S. Marine Hospital Service." Artifacts of all sorts come to life in Lyons's voice.

"Michele is blessed with a calling," observed Dr. Kim Pelis, ONHM director, at the Dec. 11 lecture on important moments and themes in NIH history that Lyons presented as a parting gift to attendees. "Quite literally, objects call to her—and she listens," Pelis continued. "Over a 30-year career of collecting objects on NIH history, of telling their stories and of following those objects and stories wherever they have led, she has transformed the History Office and NIH's historical record alike."

In 1988—when the museum was still just a gleam in its creators' eyes—Lyons, a grad student in the museum studies program at George Washington University, came to NIH as a summer intern. ONHM Founding Director Dr. Victoria Harden immediately recognized a kindred soul. She hired Lyons as a contract curator in 1990 on an exhibit to commemorate the career of Dr. Scotty Pratt, "Computers in Medical Research."

Lyons was called upon again in 1992, to curate an exhibit describing the work to find a non-addicting opiate by Dr. Kenner Rice's lab. Harden recalled finally securing Lyons on an ongoing half-time contract in 1995, "essentially to do everything associated with the museum collection. She has overseen multiple moves of the instruments. She has catalogued most of the more than 4,000 objects."

Before then, Lyons spent four years as a program coordinator at the U.S. Information Agency and two years before that as a visual information specialist in the exhibits service of the agency.

Michele Lyons (r), associate director and founding curator of the Office of NIH History and Stetten Museum, with ONHM Founding Director Dr. Victoria Harden

Over the succeeding years, Lyons would be courted and tempted by other history-related entities dangling bigger budgets and better salaries, but Harden was always able to coax the curator to stay, evoking the unique bond forged between story and storyteller.

"The Stetten Museum is your baby," Harden reminded her every once in a while, appealing to Lyons's deep connection to the thousands of photographs, manuals, documents, devices, instruments and exhibits she has collected, catalogued and curated in order to record, preserve and share the NIH narrative.

Inevitably, Lyons would decide to stay put—there were always new artifacts to unearth and vital conversations to chronicle.

"Sometimes the stories that the objects in our collection tell are pretty technical, scientific and medical discoveries," Lyons explained during her lecture, "but they always have a human element. Because fundamentally, NIH history is the story of how people have worked together toward one end."

Artifact whisperer at work, "conversing" with historic objects

At the end of the talk, Chris Wanjek, communications director for the NIH Office of Intramural Research, ONHM's administrative home, turned the tables on Lyons. Employing a series of slides, he walked the audience through several objects that told the curator's own story at NIH, including the hardhat in her office and her personal vehicle—both things she used over her career to collect and often manually move and transport donations to the museum.

"Unfortunately, we lose 30-some years of institutional memory when Michele retires, but we're grateful to have had her," he concluded. "Thank you, Michele."

"I'll miss meeting all of the people," Lyons said. "I always wanted to be the president of the Royal Society, because you could learn all the cool new stuff about all the fields of study from all the people who were doing it. That's pretty much what I ended up being—president of the Royal Society of NIH, at least. I will miss meeting all the different people and learning about all their work and their lives, because so much of it is so fascinating."

Watch Lyons's recent lecture, part of History & Context: The ONHM Seminar Series, at https://videocast.nih.gov/watch=53816.

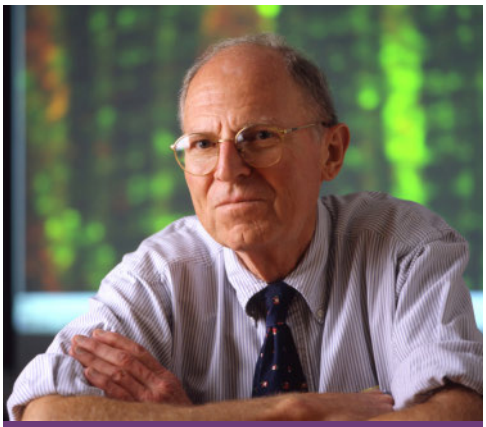
Musa Named NIH Engineer of the Year

Joseph Musa has been chosen as engineer of the year for NIH. As an agency winner, he will be honored at the National Society of Professional Engineers (NSPE) 2024 Federal Engineer of the Year Awards ceremony to be held at the National Press Club in Washington, D.C. on Feb. 23.

NIH Engineer of the Year Joseph Musa

Presented by NSPE, and now in its 45th year, the award is the only one of its kind to solely recognize outstanding engineers employed in the federal government.

Founded in 1934, NSPE supports more than 500,000 professional engineers and the public by fostering licensed professional engineers in service to society, promoting confidence that engineering decisions affecting people's lives are made by qualified and ethically accountable professionals.



Scientist Emeritus Dr. Paul Plotz

PHOTO: RHODA BAER

NIAMS Remembers Scientist Emeritus Plotz

Dr. Paul Plotz, who dedicated nearly four decades of service to science at NIH, passed away on Jan. 13 at age 86 after a long illness. He was a world-renowned rheumatologist, immunologist and researcher known internationally as an expert in myositis, an inflammatory muscle disease and rare autoimmune condition.

After serving in a variety of leadership roles, including as chief of the Arthritis and Rheumatism Branch at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), and NIAMS acting scientific director and acting deputy director, Plotz retired from NIH in 2011. He also was senior advisor to then-NIH Deputy Director for Intramural Research Dr. Michael Gottesman.

As a scientist emeritus at NIAMS, Plotz was awarded the 2013 Presidential Gold Medal from the American College of Rheumatology (ACR), which recognizes outstanding achievements in rheumatology over an entire career and is the highest award ACR bestows.

A fourth-generation physician, Plotz conducted groundbreaking immunology and muscle disease research and was instrumental in advancing understanding of autoantibodies, autoimmune disease and inflammatory muscle diseases. Among the many advances he accomplished, Plotz helped redefine how physicians think about and manage myositis, which helped lead to the first clinical trials in the field for people with the disorder.

Early in his career, he worked to advance understanding of systemic lupus erythematosus, an autoimmune condition, as well as autoantibodies and other components of the immune system, greatly contributing to what is known about disease mechanisms in autoimmune disorders. He later investigated clinical, immunologic and genetic aspects of several muscle diseases. Read more about his work at https://irp.nih.gov/catalyst/19/5/symposium-honors-niams-paul-plotz.

Plotz earned his undergraduate and medical degrees from Harvard University and completed a residency at Beth Israel Deaconess Medical Center in Boston. He joined NIH in 1965 as a clinical associate in the Arthritis and Rheumatism Branch at the National Institute of Arthritis and Metabolic Diseases (now NIAMS).

He will be remembered as a loving husband, father, mentor and friend, as well as an accomplished scientist with a lifelong commitment to and passion for human rights and volunteerism.

Survivors include his wife of 60 years, Judith; sons John and David; and his extended family.

Scientist Emeritus Dr. Harish Pant had worked at NIMH and NINDS.

Scientist Emeritus Pant Is Mourned

Scientist Emeritus Dr. Harish Pant died peacefully Dec. 22 at his home in Lake Forest, Ill., following a chronic illness. He was 85.

"Described as a deep, thoughtful and kind person, Pant was committed to furthering the field of neuroscience and the fundamental understanding of neuronal physiology, translating his work to better the lives of those affected by neurological disorders, and helping those around him," said Dr. Walter Koroshetz, director of the National Institute of Neurological Disorders and Stroke (NINDS). "He changed our understanding of neuroscience and neurodegenerative diseases and supported and inspired those who were fortunate to know him. His commitment to mentorship extended beyond borders, influencing hundreds of scientists globally."

Pant was born on Jan. 1, 1938, in the remote farming village of Jakhera in Uttarakhand, India. He earned his Ph.D. in physics, with a specialty in molecular spectroscopy, from Agra University in India, and pursued postdoctoral studies at Michigan State University with a focus on electron and ion transport in model membrane systems.

After his graduate training, Pant joined Dr. Ichiji Tasaki in the Laboratory of Neurobiology at the National Institute of Mental Health in 1974.

While working in Tasaki's lab, Pant was introduced to the Marine Biological Laboratories (MBL) in Woods Hole, Mass., and the giant squid axon model system—which was critical to many of Tasaki's discoveries, such as saltatory conduction, and to Pant's contributions to neuroscience.

In his time at NIH and MBL, Pant worked closely with Dr. Harold Gainer, chief of NINDS's Laboratory of Neurochemistry.

In 1987, Gainer appointed Pant as chief of the section of neuronal cytoskeletal protein regulation. Pant made many critical contributions to the understanding of neuronal cell biology and the pathophysiology of neurodegenerative disorders.

His lab focused on understanding the mechanisms of topographic regulation of neuronal cytoskeleton proteins through post-translational modification, particularly the role of kinase cascades in normal brain function and contributing to neurodegeneration.

"Pant's legacy will live on through his family, his seminal contributions to the field of neuroscience and those who trained and worked with him," said Koroshetz.

Pant is survived by his wife of 50 years, Kamala, and children—Alok (Melissa) Pant, Manish (Kaylan) Pant and Garima Pant.

NIH Staff Member Dies in Tragic Accident

NIH mourns the loss of Akwasi Addae, age 45, who died on Jan. 10 after falling into an air-handling intake shaft while conducting repair work on the exterior of the Clinical Research Center. Addae—on staff in the Division of Facilities Operations and Maintenance within the Office of Research Facilities (ORF)—was an electrician in the Clinical Center Facilities Management Branch.

Akwasi Addae

Addae had joined NIH in 2015 and was well-loved and respected by his colleagues. He had recently been promoted, a major career milestone.

"As an electrician, he literally brought power and light to the clinical spaces that he was assigned to, but he also figuratively brought power and light to his colleagues through his contagious energy and passion," said ORF Director Dan Wheeland. "He was a consummate professional and dedicated employee."

The Occupational Safety and Health Administration is investigating the accident to help determine the cause and confirm proper safety measures are in place and followed.

Addae is survived by his wife, Rita, and four children.

Snow Days on Campus

PHOTOS: DUSTIN HAYS

Two snowstorms in the same week blanketed the Washington region in mid-January, the first significant snowfall in the area in two years. By week's end, up to 6 inches of snow had fallen on the Bethesda campus.

While many NIH'ers were permitted to work from home during that week, many essential personnel and crews commuted in, from researchers and clinicians to security and other emergency staffers.

NIH owes a debt of gratitude to the Division of Facilities Operations and Maintenance within the Office of Research Facilities (OD/OM/ORF/DFOM) for swiftly clearing streets, sidewalks, pathways and parking lots, providing safe access for all who trudged in.

ABOVE: a view of the Centennial Anchor with Bldg. 3 in the background; at left, a south view of Bldg. 16, the Lawton Chiles International House, also known as Stone House.

BELOW: At left, snow blankets areas around the Clinical Center, seen on the horizon, and, at right, the lawn of the Natcher Bldg.