NIH RECORD

August 1, 2025
Vol. LXXVII, No. 16

Freeman Reflects on Caring for Patients with Rare Immune Syndromes

BY DANA TALESNIK

When Dr. Alexandra Freeman arrived at NIH 20 years ago, little was known about the rare disease she would come to focus on—Job's syndrome. Drawn to NIH by the opportunity to help people with immune disorders and study their condition over time, she now shares lessons learned along the way and new reasons for hope.

Dr. Alexandra Freeman in the Clinical Center

Freeman primarily sees patients with Job's syndrome, which afflicts less than 900 people worldwide and is the more common in a group of hyperimmunoglobulin E syndromes (HIES). These genetic diseases cause chronic problems throughout the body including severe lung, skin, bacterial and fungal infections as well as joint, bone and dental issues.

"It's a tricky disease," said Freeman, a senior clinician at NIH and director of NIH's primary immune deficiency clinic.

SEE **FREEMAN**, PAGE 5

'CASCADE OF CARE'

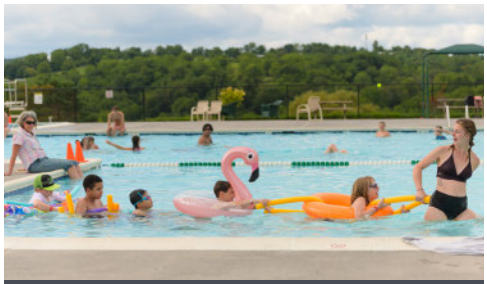
Bhattacharya Interviews Volkow in New Podcast

BY DANA TALESNIK

"I love data. I love being in the laboratory," said Dr. Nora Volkow, director of NIH's National Institute on Drug Abuse, in her discussion with NIH Director Dr. Jay Bhattacharya. The two colleagues chatted for 45 minutes in June on Bhattacharya's new bi-weekly podcast, the Director's Desk. The series is publicly available on YouTube.

Dr. Jay Bhattacharya hosts "The Director's Desk."

SEE **PODCAST**, PAGE 3



The annual Camp Fantastic brings joy to pediatric cancer patients. See p. 8.

ALSO THIS ISSUE

A CRISIS OF CONNECTION

Engineers, Building Team Come to the Rescue During Boiler Outage

BY AMBER SNYDER

It was the eve of an important cell harvesting event when things went awry.

Room temperatures began to decrease and relative humidity rose, disrupting the delicate balance required for the NIH's National Cancer Institute's (NCI) Cell processing Modular facility's function—to produce tumor infiltrating lymphocytes (TIL), specialized immune cells that recognize and kill cancer cells.

Engineer Derrick Lam gives a thumbs up to a properly functioning control panel.

PHOTO: AMBER SNYDER

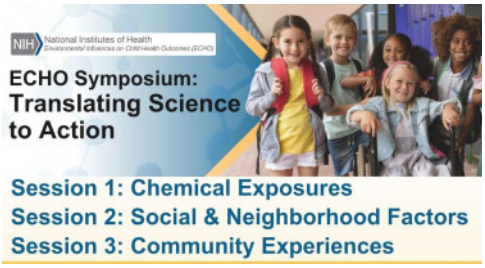
Patients with difficult-to-treat cancer may not produce enough TILs on their own. A therapy developed by NCI researchers lets doctors extract TILs from the patient, grow and expand them in Bldg. T30, and then reinfuse the modified TILs into the patient at a much higher concentration to treat certain types of cancer. Environmental conditions in the building such as pressure and temperature need to be tightly controlled to support this work.

But on the evening of Sept. 18, 2024, one day before a patient in the Clinical Center was due to undergo this process, the humidity was climbing in

SEE **BOILER**, PAGE 4

ECHO To Host Symposium on How Environment Influences Child Health

Sept. 15



The NIH Environmental Influences on Child Health Outcomes (ECHO) Program office will host the inaugural ECHO symposium: Translating Science to Action on Sept. 15 in Bldg. 45 and online.

The day-long event will bring together researchers, clinicians, policymakers, advocates, community leaders and more to explore how early environmental factors influence child health—and how we can translate science into meaningful action.

Supported by NIH, the ECHO program aims to understand the effects of a broad range of early environmental influences on child health and development. ECHO is dedicated to both learning what factors affect child health and to finding ways to enhance it. The program's research has the potential to enhance the health of children for generations to come.

Register at https://cvent.me/8229Py.

CCDI to Host Fall Symposium

The Childhood Cancer Data Initiative (CCDI) will host an in-person symposium in Bethesda on Oct. 6 and 7 with an option to attend online. This event is open to the public, though registration is required.

Online registration will close on August 7. On-site registration will not be available.

This National Cancer Institute symposium brings together the childhood cancer community to learn about CCDI programs and resources intended to advance research and clinical care—with the aim of fostering collaboration and innovation.

Attendees can expect to:

- Hear the latest on CCDI, its user-friendly platforms and tools, the Molecular Characterization Initiative (MCI) and its impact on new therapeutic target discovery, and NCI childhood cancer research programs.
- Understand how big data and real-world evidence in childhood cancer can support research and improve treatment outcomes.
- Learn about CCDI-funded data use projects, including updates on Clinical Laboratory Improvement Amendments (CLIA) certification of solid tumor methylation classifiers.
- Join industry pioneers and network with researchers, clinicians and advocates.
- Meet principal investigators and young investigators and hear about their research in an informal and easy-to-understand format.

Those interested in presenting a poster can submit an abstract (https://events.cancer.gov/nci/ccdi-symposium/abstract) by August 7, 2025 at 5:00 p.m. E.T. To register, visit: https://events.cancer.gov/nci/ccdisymposium/registration.

Clinical Center Renovates Pediatric Clinic

The NIH Clinical Center (CC) renovated the entrance and waiting areas of the 1H outpatient pediatric clinic, located on the CC's first floor.

The clinic offers preventive and acute care—including checkups, immunizations and treatment for illnesses and minor injuries—for children and teens.

Check out the clinic's bright new look!

PHOTOS: MARIA MASLENNIKOV

NCATS Awards Quantum Biomedical Technology Innovations

NIH's National Center for Advancing Translational Sciences (NCATS) announced the winners of the first stage of its Quantum Computing Challenge.

These teams designed solutions to identify and propose novel applications of quantum computing and quantum algorithmic approaches to apply toward cases within clinical, translational and biomedical problem areas.

The 10 winning teams comprise multidisciplinary experts from universities, clinics and the private sector. They will receive an award for their quantum algorithm and computing proposals in speeding drug discovery, improving clinical risk predictions, diagnosis and therapeutics, and enhancing biomedical imaging and genomic data analysis. And, they're invited to participate in stage 2 of the challenge. The total prize purse is up to $1.3 million across the two stages of the challenge.

Learn more about the teams and their proposals: go.nih.gov/X1OTx3w.

Recent progress in quantum information sciences (QIS) has led to a new generation of quantum technologies that harness the power of quantum physics and engineered quantum states in the fields of sensing, computing, networking and communications. Such technologies can provide promising novel capabilities in early disease detection that can lead to improved diagnostic approaches and treatment, as well as enable new computational approaches.

NCATS established the Quantum Biomedical Innovations and Technology (Qu-BIT) program to support development of biomedical and translational use cases for the new generation of quantum technologies. Under this program, NCATS launched two challenge competitions to spur development in the fields of quantum sensing and quantum computing for biomedical applications.

Podcast

CONTINUED FROM PAGE 1

The Director's Desk podcast series explores groundbreaking work in conversations with people driving innovation in biomedical research and public health.

In their discussion, Volkow expounded on the root causes of drug addiction, the opioid crisis and NIDA research that's shaping drug prevention and treatment efforts.

Volkow is a psychiatrist who began studying addiction while finishing her medical residency, during which she used imaging to see how drugs affect different areas of the brain. People who become addicted, she said, lose their ability to self-regulate.

"Drugs hijack the main motivational circuit that we have in our brains...that drives our actions," she explained. Research combats the myth that using drugs when you are addicted is a choice. Rather, addiction is a brain disease linked with specific functional and neurochemical changes in the brain. Like other diseases, addiction is a product of biology and our environment.

Volkow candidly shared that there's a history of alcohol use disorder in her family. "But I have always had multiple alternative reinforcers and a very supportive social environment," she said, "that gave me resilience to counteract my genetic risk."

The conversation also focused on responding to the opioid crisis. Bhattacharya recounted hearing in the early days, in the 1990s while he was still in medical school, about new opioids to treat pain that were touted as nonaddictive.

"I was struck by this," he said. "You enter medicine because you want to help people who are in pain, and help people with disease. There was goodwill around this. But it turned out the drugs were quite addictive."

Volkow concurred. "This is a perfect example of the negative consequences of the health care system having neglected addiction as a disease," she said. Doctors and medical students were not trained on their management, she added, and could not recognize when their patients were becoming addicted.

It also illustrates how clinical practice can be influenced by limited scientific evidence—in this case a small study published in the *New England Journal of Medicine*—incorrectly concluding that opioids were not addictive when given to pain patients. Bhattacharya said this underscores the need for verification and replication in research.

Bhattacharya discusses strategies to address drug addiction with NIDA Director Dr. Nora Volkow (r) in June.

Opioids play a role in treating severe acute pain, noted Volkow, but this article made clinicians overconfident and they started to prescribe them for moderate, lesser pain while alternative pain medications went underutilized. "We in the scientific field need to provide data that is robust and, as scientists, we should be able to question models and assumptions," she said.

Volkow said a "cascade of care" is needed to help prevent addiction and facilitate its treatment and recovery. One of NIDA's main efforts to combat drug overdose fatalities has been to determine how to increase the distribution and access to naloxone and to develop more user-friendly versions of this life-saving drug.

Volkow went on to explain how naloxone works. Opioids bind to receptors in brain centers that control respiration. When a person overdoses on opioids, they typically stop breathing, lose consciousness and, if not treated, they die.

"Naloxone gets in the brain immediately," she said. "It removes the opioid from the receptor, breathing returns and [naloxone] saves a life. It's almost magical, if you give it in time at the correct dose."

Volkow also discussed the NIH-wide HEAL (Helping to End Addiction Long-term®) initiative, through which NIH has greatly expanded research on addiction and pain. Under HEAL, NIH has made a major investment in research to facilitate implementation of evidence-based addiction screening, prevention and treatment interventions in health care, justice and community settings and to accelerate the development of new therapeutics.

Addiction is a condition of the brain, summarized Bhattacharya. How the brain reacts to drugs and how the social context in which a person lives are interconnected and critical to preventing and overcoming addiction.

Family and other community support bolsters resilience, Volkow underscored. In combatting addiction, she said: "What we need to address as a society is what we can do to strengthen those social networks that are so necessary to prevent it."

To watch this and other episodes of the podcast, see: https://bit.ly/40GpHuE.

ON THE COVER: *Wisterias in bloom behind Bldg. 50 on the Bethesda campus*

IMAGE: MARLEEN VAN DEN NESTE

The NIH Record

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

Editor:
Dana Talesnik • *Dana.Talesnik@nih.gov*

Assistant Editors:
Eric Bock • *Eric.Bock@nih.gov*
Amber Snyder • *Amber.Snyder@nih.gov*

Subscribe via email:
https://go.usa.gov/x6mgQ

Follow: **nihrecord.nih.gov/**

National Institutes of Health
Turning Discovery Into Health

The reheat boilers in Bldg. T30

Boiler

CONTINUED FROM PAGE 1

Bldg. T30, home to one of NCI's TIL labs. The building's reheat boilers —which heat water to warm the air and provide precise temperature and humidity control via an automated control system—had shut down.

The loss of temperature and humidity control is critically important in T30 because it is an Aseptic Processing Facility (APF), a cleanroom which processes or supports the processing of drugs and/or biologic products in accordance with current good manufacturing practices (cGMP) for human use. Precise environmental control is vital to the functioning of T30 and the other APFs on main campus.

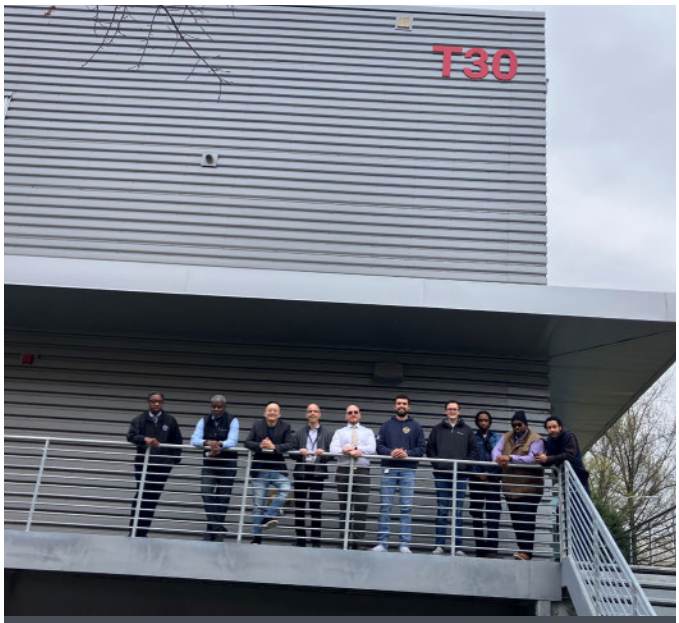
NCI needed the facility to be fully functioning as soon as possible so the scientists could complete the critical cell processing for their patient. But without the boilers, the scientists couldn't accurately control the temperature in the building.

Who could reconnect the boilers?

The APF team within the Division of Facilities Operations and Maintenance (DFOM) immediately got to work.

"If the facilities are doing their job, people may not think about us—which is a good thing," said Derrick Lam, a supervisory general engineer on the APF team. "But we are constantly working in the background to maintain facilities and provide physical spaces to do science."

For Lam and his colleagues, that means monitoring and performing upkeep on the automated systems that control the environment of each APF on main campus. It takes a village: the DFOM APF team is split into an engineering team and a building team, which work together to plan, coordinate, troubleshoot and document events with the APF end users and quality assurance teams. In this case, that was the NCI Surgery Branch (SB) Cell Production Facility (CPF) unit management (UM) and quality assurance (QA).



From l to r, Donald Edwards, Courtney Morgan, Derrick Lam, Paul Sanzone, Ryan Jones, Matt Dmuchowski, Matthew Spielman, Omar Campbell, Reggie Floyd and Marcus Farrell

Within minutes of the initial incident on Sept. 18, the APF team started troubleshooting. Lam and his APF colleagues immediately got to work, some even staying onsite through the night as they worked to troubleshoot and keep the NCI CPF UM and QA teams abreast of the situation.

"DFOM APF continued to follow up and provide information on the timeline of events, allowing NCI SB and the Division of Technical Resources' Facilities Compliance and Inspection Branch to capture the incident in their respective reporting systems," explained Jack Fisher, a QA manager with the NCI SB.

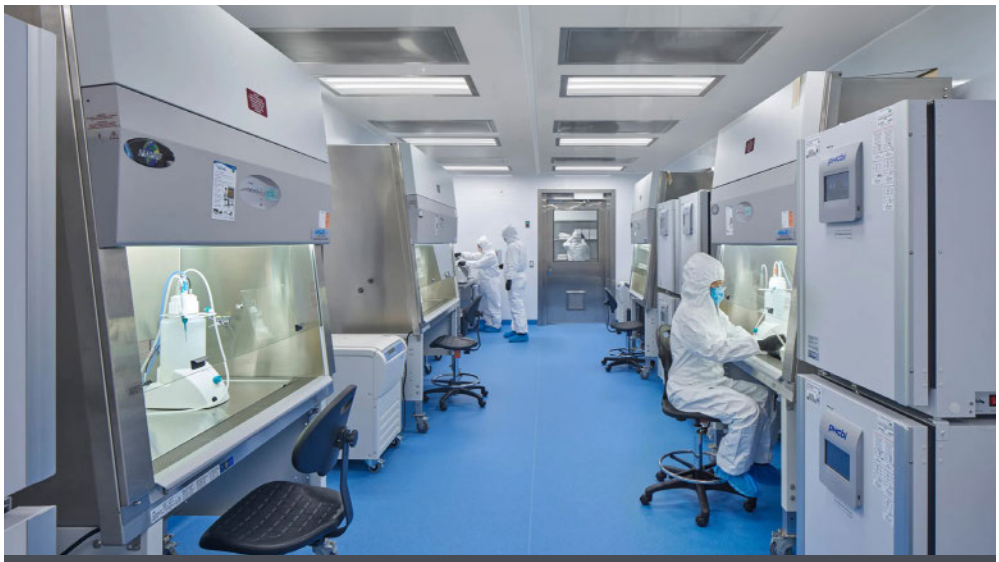
The temperature and humidity controls in T30 were restored mid-morning on the 19th, in time for the patient's cell harvesting event.

"The timely and ongoing communication between DFOM APF, CPF UM and SB QA enabled a successful harvest of cell product for patient treatment without risk to the safety of the product, and only a slight delay," reported Fisher.

For Lam, the experience helped drive home his team's role in the greater NIH mission.

Although the circumstances were stressful, the experience demonstrated the importance of understanding the urgency of each other's work, and the value of interdisciplinary teams at NIH.

"The DFOM APF building team, engineers and NCI scientists worked really well together by understanding and appreciating the criticality of each other's work," Lam concluded.



The CPF requires a delicately maintained environment to produce TILs for immunocompromised patients.

Freeman

CONTINUED FROM PAGE 1

"One thing that makes it really challenging is that people often look way better than they are."

Over the years, Freeman has met with nearly 200 children and adults with Job's syndrome who are part of a natural history study. The systemic problems usually change with age, she noted. Children tend to have recurring eczema, skin infections and pneumonia. The adults, as they age, have more difficulty with arthritis, spine disease, cardiovascular disease and intestinal issues.

"We try to give them a lot of medical education and talk about how hard it is having a disease that, if doctors have heard of it, they don't know much about it," Freeman said. "We try to empower them and help them to ask the right questions."

Freeman also promotes collaborations across and beyond NIH toward better understanding specific aspects of the disease.

Thanks to one collaboration with a group at the University of North Carolina, "We now think the lung disease in part is from problems in the immune system but also from problems in the lung epithelium," she said. This progress is important toward better treating adult patients who frequently are hospitalized with lung disease.

Freeman also is collaborating with a radiologist at NIH to analyze brain and heart imaging as well as NIH investigators who study wound healing. These and other collaborations are paving the way for new therapies.

One hopeful sign is that her patients are living longer. "Things have gotten a lot better over the years in terms of survival," Freeman noted. When she first came to NIH, few Job's patients lived past 50. Now, her oldest patient recently turned 74. She attributed the longer lifespan to earlier diagnosis, better understanding of the disease and better treatments, such as improved antifungal medications to tackle fungal pneumonia.

Another newer treatment, an eczema injection, has also been lifechanging for many of her patients, so much so that it might help explain the sudden baby boom in her young adult patients. As their skin and quality of life improve, she said, more of her patients are having children.

Although many of the chronic medications her patients regularly take are unsafe during pregnancy, Freeman is increasingly discussing family planning options with her patients. "Now, our patients are living longer, feeling better and more men and women are having children," she said.

Freeman started her career as a pediatric infectious disease physician. She studied biology at a small college in Minnesota, then attended medical school at Georgetown University. After completing her residency at Yale New Haven Children's Hospital and a fellowship at Northwestern University, Freeman began caring for children who were immune compromised due to cancer, bone marrow transplants, HIV or other immune deficiency disorders.

Freeman (r) poses with Harper Spero (l), an NIH partner in research for Job's syndrome who hosts a podcast featuring people with 'invisible illness.'

Freeman and her family then moved back to the Washington area as she had landed a job at NIH's National Institute of Allergy and Infectious Diseases (NIAID). There, she auspiciously met Dr. Steven Holland, an NIH immunology expert, who suggested she study Job's syndrome.

In 2005, Freeman began caring for Job's patients. Two years later, the genetic cause was discovered and she began writing review papers and giving talks while working with her growing patient cohorts. It was a stimulating time to be working in this specialty.

"It was this explosion of new diseases that were being described that I got to be the clinician for," Freeman said.

"NIH is so special," she noted. "You could not do what I do anywhere else." A big city hospital might see a few of these patients over time but NIH can fly them in and give them free care. "We can see so many more patients—no matter their background—and level the playing field, provide medication and care for them. It's the perfect setup."

Freeman is heartened by the support network created among patients who have come to NIH.

"Because we can bring them here, they can form their own community, which is important for their health care and advocacy," she said.

The outlook is hopeful. There have been huge advances in the last 15 years and there are new therapies on the horizon. Freeman said, "Every generation is doing so much better than the generation before and we expect things to keep improving."

Freeman (r) poses with NIH's Dr. Steven Holland (c) and trainee Bianca Chan at the Clinical Immunology Society's summer program in 2023.

NCI's Pommier Retires

Dr. Yves Pommier

Dr. Yves Pommier, a molecular pharmacologist who has conducted pioneering work on the mechanisms of topoisomerase and PARP inhibition as well as on the discovery of novel biomarkers for anti-cancer drug responses, is retiring after 45 years at NIH's National Cancer Institute (NCI).

Pommier grew up in Caen, France, near the famed World War II beaches of Normandy. He attended medical school there before moving to Paris for his residency in hematology/oncology.

"It was very fortunate that the chair of my school in France was a good friend of Bruce Chabner, who was director of what was then called the Division of Cancer Treatment at [the National Cancer Institute] NCI. My Parisian chair and Bruce started a little program where they selected two or three students a year to come to the U.S. who they thought would be the future of academia in France. My chair got me involved, got me connected to come, and Bruce was my first mentor," said Pommier.

Early in his NCI career, with Dr. Kurt Kohn and others, Pommier helped discover how topoisomerase (TOP1) inhibitors work and expanded the understanding of how bioregulatory networks operate. "It was such an exciting time, and I was so happy at NIH that I just couldn't go back to Europe. They wanted me to come back to Paris, but I had too much pleasure doing what I was doing here."

For the past four decades, Pommier has been a leader in the field of DNA topoisomerase biology, biochemistry, molecular pharmacology and its cancer relevance. As chief of the Developmental Therapeutics Branch, he has overseen the branch's clinical/translational research program, which emphasizes new approaches to cancer treatments targeting DNA and connected biomarkers.

Pommier is internationally recognized for the discovery and development of TOP1 inhibitors. Three of his TOP1 inhibitors are in phase 1/2 clinical development and all show potent activity in clinical studies and in patient-derived xenograft models of triple-negative breast cancers.

To help advance finding the best treatments for each patient, he developed a tool called CellMiner to perform genomic analyses in patient-derived cancer cell lines. While developing these tools, Pommier discovered the broad relevance of an interferon-inducible gene, *Schlafen 11* (*SLFN11*), which has become one of his latest contributions. He recently showed its inactivation in approximately half of patient-derived cell lines and tumors and how the gene irreversibly arrests the replication of cells with replicative DNA damage while stabilizing proteins.

Pommier received an NIH Merit Award in 1992 as well as three NIH Director's Awards since 2011. Over the course of his career, he has authored more than 800 publications, holds more than 30 patents and has mentored dozens of fellows and trainees who went into medical and scientific careers.

NCATS to Receive FNIH Sanders Partnership Award

The Foundation for the National Institutes of Health (FNIH) will award the 2025 Charles A. Sanders, MD, Partnership Award to three groups or organizations. Within NIH, the recipient is the National Center for Advancing Translational Sciences (NCATS). The Partnership Award recognizes people or organizations that have made significant contributions to the FNIH's work in support of NIH's mission.

NCATS is the NIH lead for the Accelerating Medicines Partnership® (AMP) Bespoke Gene Therapy Consortium, which aims to streamline manufacturing and preclinical testing for gene therapies for rare diseases. It played a critical role in the 2020 launch and execution of the Accelerating COVID-19 Therapeutic Interventions and Vaccines program, which helped identify treatments.

NCATS participates in several AMP programs as well as the Biomarkers Consortium and design phase projects focusing on development of regulatory approval for pediatric medical devices, new approach methodologies (NAMs) and drugs for ultra-rare cancers.

A 2024 NCATS summer intern in the lab

The award is named for the founding chairman of FNIH's board of directors. The recipients will be awarded at a ceremony in October in Washington.

FNIH President and CEO Dr. Julie Gerberding said, "We are deeply grateful for their generous commitment to team science and investment in the future of biomedical research."

NIH Mourns the Passing of Biochemist Matthaei

Dr. Johann Heinrich Matthaei, an esteemed German biochemist and former NIH postdoctoral researcher, passed away on July 7 in Göttingen, Germany at age 96.

Dr. Johann Heinrich Matthaei

From 1960 to 1962, Matthaei was a fellow at NIH where he conceived and executed the seminal "polyU" experiment alongside Dr. Marshall Nirenberg. Beginning on May 15, 1961, Matthaei showed that polyuracil directs the synthesis of polyphenylalanine, proving that UUU is the codon for phenylalanine—cracking the first element of the genetic code. Published in the *Proceedings of the National Academy of Sciences* (*PNAS*) later that year, these results propelled the decoding of the remaining codons by 1966.

Matthaei at NIH

This foundational work, led by Nirenberg, paved the way for decoding the language of DNA and ultimately led to Nirenberg's 1968 Nobel Prize. Matthaei acknowledged it "pained" him not to be included in that Nobel Prize, yet he remained undeterred.

Returning to his native Germany in 1963, he became director of molecular genetics at the Max Planck Institute for Experimental Medicine in Göttingen, mentored numerous doctoral students, completed his habilitation in 1966 and, until late in life, lectured for the Studienstiftung des Deutschen Volkes (German Academic Scholarship Foundation). In a message to the *NIH Record*, his son Albrecht wrote, "My father's time at NIH meant a great deal to him. Until his death, he enjoyed talking about his research stay in Maryland."

NIH Study Links Particulate Air Pollution to Cancer Mutations among Nonsmokers

PHOTO: LANAELCOVA/SHUTTERSTOCK

NIH scientists and their colleagues at the University of California, San Diego, have found that fine-particulate air pollution, which includes pollution from vehicles and industry, was strongly associated with increased genomic changes in lung cancer tumors among people who have never smoked.

By assembling the largest-ever whole-genome analysis of lung cancer in individuals who have never smoked, researchers were able to link air pollution exposure to increased cancer-driving and cancer-promoting genetic mutations. This could potentially lead to more prevention strategies for never-smokers. Results were published in *Nature*.

Researchers analyzed lung tumors from 871 never-smoker patients across 28 geographic locations worldwide as part of the Sherlock-Lung study. They found associations between air pollution exposure and changes in the *TP53* gene, and other genetic mutational signatures previously associated with tobacco smoking.

They also observed a relationship between air pollution and telomeres, which are sections of DNA found at the end of chromosomes that are related to the cells' inability to replicate. Telomeres shorten naturally with age. However, scientists found fine particulate air pollution was linked to premature shortening of telomeres.

By beginning to uncover the mechanisms through which tissues acquire cancer-causing or cancer-promoting mutations following environmental exposures, this study helps scientists better understand the primary drivers of lung cancer in never-smokers—who represent up to 25% of all lung cancer cases globally.

Interestingly, the researchers found that exposure to secondhand smoke may have a lower overall ability to cause genetic mutations, known as mutagenicity, compared to air pollution.

Breast Cancer Risk in Younger Women May be Influenced by Hormone Therapy

NIH scientists have found that two common types of hormone therapy may alter breast cancer risk in women under age 55.

PHOTO: AFRICA STUDIO/SHUTTERSTOCK

Researchers discovered that women treated with unopposed estrogen hormone therapy (E-HT) were less likely to develop the disease than those who did not use hormone therapy. They also found that women treated with estrogen plus progestin hormone therapy (EP-HT) were more likely to develop breast cancer than women who did not use any hormone therapy. Together, these results could help guide clinical recommendations for hormone therapy use among younger women.

The two hormone therapies analyzed in the study are often used to manage menopause symptoms or following hysterectomy (removal of uterus) or oophorectomy (removal of one or both ovaries). E-HT is recommended only for women who have had a hysterectomy because of its known association with uterine cancer risk.

The researchers conducted a large-scale analysis that included data from more than 459,000 women under 55 years old across North America, Europe, Asia and Australia. Women who used E-HT had a 14% reduction in breast cancer incidence compared to those who never used hormone therapy. This protective effect was more pronounced in women who started E-HT at younger ages or who used it longer. In contrast, women using EP-HT experienced a 10% higher rate of breast cancer compared to non-users, with an 18% higher rate seen among women using EP-HT for more than two years relative to those who never used the therapy.

The association between EP-HT and breast cancer was particularly elevated among women who had not undergone hysterectomy or oophorectomy. Doctors may consider gynecological surgery status when evaluating the risks of starting hormone therapy.

The results align with previous large studies that documented similar associations between hormone therapy and breast cancer risk among older and postmenopausal women and extends these findings to younger women experiencing menopause.

How Exercise Can Protect Against Alzheimer's

PHOTO: MONKEY BUSINESS IMAGES/SHUTTERSTOCK

Exercise has well-known protective effects in Alzheimer's disease (AD).

In a study that appeared in *Nature Neuroscience*, a research team looked for exercise-induced changes in gene activity in a mouse model of AD. They focused on a region of the hippocampus called the dentate gyrus. The hippocampus is essential for memory and learning, and the dentate gyrus is where new hippocampal neurons form. This region is also susceptible to changes during both exercise and AD.

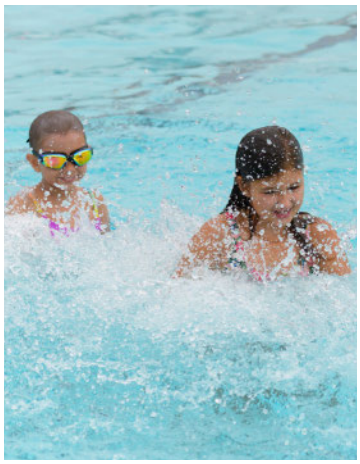
For exercise, mice were allowed to run freely on a wheel over a 60-day period. The AD mice who exercised had better cognitive function than the sedentary AD group. Exercise led to changes in gene activity in both healthy mice and AD mice, but the affected genes differed between the groups.

Certain gene activity changes were specific to AD mice across various cell types. Exercise restored some of these genes' activities to healthy levels. Many of these recovered genes occurred in immature neurons, suggesting exercise has an impact on new neuron formation in the hippocampus. One exercise-recovered gene, *Atpif1*, was particularly important for neuron development and survival.

Exercise also had positive effects on gene activity in several types of brain support cells: Oligodendrocyte progenitor cells, which produce the cells that make the insulating myelin sheath on neurons; a subset of immune microglia that activate in response to AD and can reduce the damage it causes; and astrocytes, which help maintain the brain-blood barrier.

Finally, the team compared their mouse data with human AD and control brain tissue data. Many of the genes with abnormal activity in the mouse AD model were similarly affected in people with a hereditary form of AD. This suggests the findings in the mouse model may be applicable to AD in humans.

More exercise is associated with lower risk of AD, better cognitive function and less cognitive decline in people with AD. The cellular level effects of exercise remain unclear but could reveal novel ways to treat AD and other neurodegenerative diseases. —**Brian Doctrow,** *NIH Research Matters*



Kids Have Fun at Camp Fantastic

PHOTOS BY MARLEEN VAN DEN NESTE

In a few days, the annual Camp Fantastic will be underway in Front Royal, VA.

Founded by the non-profit Special Love, Inc. in 1983, this week-long summer camp hosts children undergoing treatment for cancer or who are in recovery. NIH's Pediatric Oncology Branch coordinates all aspects of care at the camp, with an onsite medical facility staffed by NIH physicians, nurses and volunteers.

These photos from last year's camp show some of the fun activities that week, which included swimming, pickleball, climbing, horseback riding, arts and crafts and science experiments.

The hope is always for abundant sunshine. Last summer, though, the weather didn't cooperate. During the last few days of camp, tornadoes in the vicinity caused flooding and the facility lost power.

The situation presented major challenges for camp counselors, volunteers and medical staff on site who had to make sure the campers had food and access to operational medical equipment. Organizers almost canceled the rest of the week due to the significant health and safety concerns but then, that Friday morning, the power returned and the kids continued their fun activities through the weekend.

In these photos from last summer, the kids pack in a load of fun activities during their time at Camp Fantastic. The nearby storms had knocked out power for a couple of days but the campers, counselors, medical team and volunteers would not be deterred in their quest for a memorable week.