

National Institutes of Health

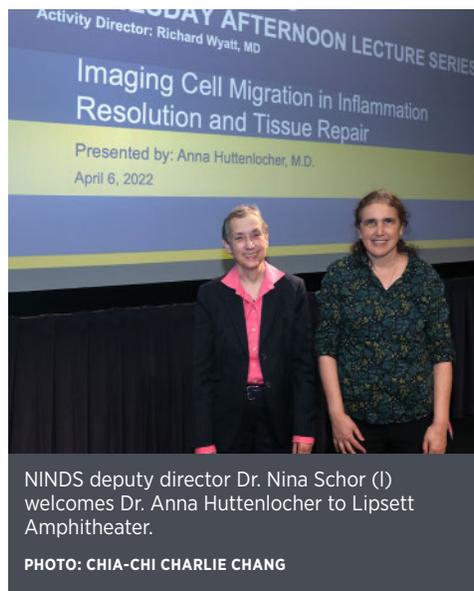
REVERSE MIGRATION

Insight Into Neutrophil Behavior Yields Clues About Inflammation

BY ERIC BOCK

Understanding how a type of white blood cell called a neutrophil behaves at the site of a tissue injury might one day lead to advances in wound repair and inflammation, said Dr. Anna Huttenlocher, at the first in-person NIH Director’s Wednesday Afternoon Lecture in Lipsett Amphitheater since March 2020.

Known as the immune system’s first responders, neutrophils move quickly to sites of tissue damage or infection, said Huttenlocher, a professor of pediatrics and



NINDS deputy director Dr. Nina Schor (l) welcomes Dr. Anna Huttenlocher to Lipsett Amphitheater.

PHOTO: CHIA-CHI CHARLIE CHANG

medical microbiology and immunology at the University of Wisconsin-Madison.

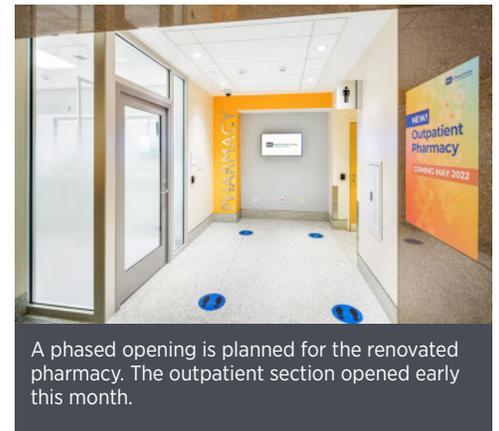
Her lab uses zebrafish as a genetic model

SEE **NEUTROPHIL**, PAGE 4

CC Cuts Ribbon on Renovated Pharmacy

NIH acting director Dr. Lawrence Tabak joined Clinical Center CEO Dr. James Gilman at a ribbon-cutting event on May 18 for the newly constructed pharmacy.

Read about the space’s new features, procedures and technology on p. 5.



A phased opening is planned for the renovated pharmacy. The outpatient section opened early this month.



NIH designers garner accolades. See story, p. 11.

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TWEETS, QUACKS & CHIRPS

Tabin Explores How Birds Develop Voices

BY CARLA GARNETT

“All the little birds on Jaybird Street | Love to hear the robin go tweet tweet tweet”

Notwithstanding Bobby Day’s 1958 chart-topping *Rockin’ Robin*, scientists have been pondering bird song since the 1700s. In fact, longtime NIH grantee Dr. Cliff Tabin and his laboratory have collaborated with paleontologist colleagues to delve back even farther for clues—into the Cretaceous Age of dinosaurs.

Over the course of more than 30 years,

SEE **BIRD SONG**, PAGE 6



American robin
PHOTO: MICHAEL BENDER

Rogers Studies Factors that Optimize Infant Brain Development

BY DANA TALESNIK

Social and economic disadvantages can affect the developing brain, impeding opportunities for children to thrive. Research shows these adverse exposures also can have an impact in infancy and even earlier.

Dr. Cynthia Rogers uses magnetic resonance imaging (MRI) to study how social determinants of health affect early brain development. Socioeconomic imbalances, she said, “set off exposure, both prenatally

SEE **ROGERS**, PAGE 6



Dr. Cynthia Rogers

Epel To Speak on Emotional Well-Being and Eating Behaviors, June 23

Dr. Elissa Epel, professor and vice chair in the department of psychiatry at the University of California, San Francisco (UCSF), will present

“Advancing Research on Emotional Well-Being and Regulation of Eating” on Thursday, June 23 from noon to 1 p.m. ET. The event is part of NCCIH’s Integrative Medicine Research Lecture Series. Registration is not required and NIH staff and the public are welcome.



Dr. Elissa Epel

Given the rising levels of global stress, including from the Covid-19 pandemic, loneliness and mental health problems are on the rise, adding to the burden of chronic diseases. Most health-oriented research takes a harm-reduction approach, i.e., identifying and mitigating problems to reduce disease burden. Understanding and promoting emotional well-being (EWB) may yield another important strategy to accomplish this and significantly improve people’s health.

Epel is principal investigator of a new, NIH-funded research network to develop resources and a multidisciplinary community of scholars focused on researching EWB. She will discuss this work and, in addition, how stress and compulsive eating are interrelated (a longtime research focus for her). Her team has developed interventions in this area such as mindfulness-based training modules.

At UCSF, Epel is also director of the Aging, Metabolism and Emotions Center and the Consortium for Obesity Assessment, Study and Treatment. She holds a Ph.D. in clinical and health psychology from Yale University. Epel has coauthored a bestselling book, *The Telomere Effect*, with Dr. Elizabeth Blackburn.

The lecture will be streamed live and archived on NIH Videocast and NCCIH Facebook. More information is at <https://bit.ly/IMLSEpel>.

NIH Library Reopens

The NIH Library in Bldg. 10 has reopened. The reading room now is open Monday through Friday from 8:30 a.m. to 4 p.m.

Library staff are prioritizing safety. In addition to cleaning and disinfecting the area, they have implemented new safety protocols and rearranged the layout to ensure NIH safety guidance is followed.

For details, visit www.nihlibrary.nih.gov/. Contact the library by phone (301) 496-1080 or email nihlibrary@nih.gov.

NIMHD Staff Member Donates Hair to Charity for Kids

BY SHELEKA TURNBULL

Dr. Maryline Laude-Sharp, scientific review officer at NIMHD, usually sports a short-cut hairdo, but that all changed during the pandemic. Like many people, she didn’t want to visit the salon and risk exposure to Covid-19. And so, her mane grew longer than it had in a very long time. By March 2022, her usual ear-length hair was cascading down her back.

Laude-Sharp decided it was time to cut her hair and finally visited a salon. But the strands didn’t just fall to the floor to be swept up and discarded. Instead, she walked out with 11 inches of her hair clasped in a ponytail and neatly tucked into a Ziploc bag.

A few months ago, encouraged by her children, Laude-Sharp decided to donate her hair to charity. Her two girls had been donating their hair since elementary school, inspired by their school counselor, who was also a regular donor.

Laude-Sharp’s two-toned hair is mainly white, with much darker tresses in the back, so she had to find an organization that accepted gray hair. After researching the different organizations, she packaged and mailed her hair to Maggie’s Wish 4 Kids of Michigan. Wish 4 Kids is a nonprofit that provides wigs and support services to children ages 3 to 18 who experience hair loss due to cancer treatment, alopecia, trichotillomania, burns and other disorders.

“I’m very happy that my children encouraged me to donate my hair, because I’m sure this will have a huge impact on a child who really needs it,” said Laude-Sharp. This is my first time donating, but I’m glad I had the opportunity to do so and would like to encourage others.”

She sees hair donation as an act of love that can help people who are struggling with medical complications resulting in hair loss. Laude-Sharp’s advice to anyone who wishes to donate is, “Do your research on organizations that specialize in this mission so you can make an informed decision. Each organization has detailed requirements such as length and the type of hair they accept.”



NIMHD’s Dr. Maryline Laude-Sharp, with her donation and newly cropped hairdo

Virtual Workshop on Nutritional Interventions for People with Cancer

The NIH Office of Disease Prevention will host the Pathways to Prevention Workshop: Nutrition as Prevention for Improved Cancer Health Outcomes on July 26–28. This virtual workshop is free and open to the public.

As many as 80 percent of people with cancer experience malnutrition, but nutritional screening and interventions are not standard parts of outpatient cancer care in the U.S. More research is needed to inform development of guidelines and services for the prevention and treatment of cancer-associated malnutrition.

Workshop speakers will discuss the current scientific evidence on how nutritional interventions affect cancer health outcomes. After the workshop, an independent panel will draft a report on evidence gaps and identify priorities for future research.

The workshop is cosponsored by NCI, NIA, NICHD and NIH Office of Nutrition Research. Learn more or register for the workshop at prevention.nih.gov/P2P-NutritionCancerHealth.



NINR Releases Strategic Plan

The National Institute of Nursing Research has released its 2022–2026 Strategic Plan, which outlines its vision for supporting science that advances nursing research to solve pressing health challenges and inform practice and policy. Learn more at www.ninr.nih.gov/aboutninr/ninr-mission-and-strategic-plan.

Two NIH'ers Are Sammies Finalists

Two NIH employees are among 2022 finalists for the Samuel J. Heyman Service to America Medals (Sammies), the nonpartisan, nonprofit Partnership for Public Service recently announced during Public Service Recognition Week. Considered the “Oscars of federal service,” the Sammies are the premier awards program recognizing America’s best in government.

Named for the partnership’s “late founder who was inspired by President Kennedy’s call to serve in 1963, the awards align with his vision of a dynamic and innovative federal workforce that meets the needs of the American people,” according to the Sammies website.



NICHHD director Dr. Diana Bianchi and NIAID clinical director Dr. Cliff Lane are finalists for 2022 Sammies.

This year’s NIH nominees are:

NIAID clinical director Dr. Cliff Lane—finalist for the Paul A. Volcker Career Achievement Award. The partnership cited Lane for conducting “pioneering work to combat HIV/AIDS that has saved countless lives, organized breakthrough clinical trials

NIH'ers Among National Academy of Sciences Electees

The National Academy of Sciences announced on May 3 the election of 120 members in recognition of their distinguished and continuing achievements in original research. These elections bring the total number of active members to 2,512. The new electees at NIH are:

- Dr. Barney Graham, former investigator and chief, Viral Pathogenesis Laboratory; and former deputy director and consultant, Vaccine Research Center, NIAID

- Dr. Michael Lichten, research microbiologist and senior investigator; head, microbial genetics and biochemistry section; and deputy chief, Laboratory of Biochemistry and Molecular Biology, Center for Cancer Research, NCI

- Dr. Deborah Morrison, senior investigator; head, cellular growth mechanisms section, Center for Cancer Research; and chief, Laboratory of Cellular and Developmental Signaling, NCI Frederick Cancer Research and Development Center

- Dr. Julie Segre, senior investigator, microbial genomics section, NHGRI

NAS is a private, nonprofit institution established under a congressional charter signed by President Abraham Lincoln in 1863. It recognizes achievement in science by election to membership and—with the National Academy of Engineering and the National Academy of Medicine—provides science, engineering and health policy advice to the federal government and other organizations.



New NAS electees are (above) Dr. Barney Graham (l), Dr. Michael Lichten; below, Dr. Deborah Morrison (l), Dr. Julie Segre.

SEGRE PHOTO: ERNESTO DEL AGUILA, NHGRI



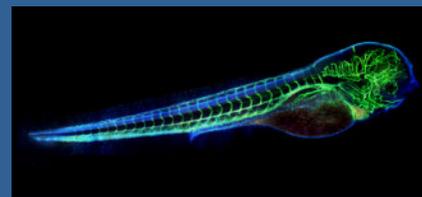
for Ebola in Africa and helped establish medical guidelines to treat Covid-19 during the pandemic.”

NICHHD director Dr. Diana Bianchi—a Covid-19 Response finalist for “initiating critical clinical research to understand the medical implications of Covid-19 on underserved populations, including pregnant women, children and people with disabilities.”

In addition, both NIH’ers are eligible to win the People’s Choice Award, which is based on online voting results.

To learn more about the Sammies, visit <https://servicetoamericamedals.org/>.

To vote for the People’s Choice, go to <https://servicetoamericamedals.org/people-choice-award/> through July 1. **R**



ON THE COVER: *Zebrafish embryo. The blue areas are cell bodies, the green lines are blood vessels and the red glow is blood. The image was created by stitching together five individual images captured by a hyperspectral multipoint confocal fluorescence microscope that was developed at the Eliceiri Laboratory.*

IMAGE: ANDREAS VELTEN, ELICEIRI LABORATORY, UNIVERSITY OF WISCONSIN-MADISON

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National Institutes of Health
Turning Discovery Into Health



Huttenlocher delivers the first in-person WALIS lecture since the start of the pandemic.

Neutrophil

CONTINUED FROM PAGE 1

system to study because they are transparent. Advances in live imaging allow the lab to watch the non-invasive, real-time movement of neutrophils in response to injury or infection. In zebrafish, neutrophils are found in the head and in the caudal hematopoietic tissue, a region near the tail.

“We’re interested in what distinguishes neutrophil response to tissue damage and microbial signals,” she said. “And in particular what signals promote the resolution of neutrophil inflammation.”

Huttenlocher’s lab discovered that neutrophils leave sites of tissue damage, a process called “reverse migration.” At the time of the finding, “the dogma was that neutrophils go into sites of tissue damage, die and then get cleared by macrophages,” another type of white blood cell that surrounds and kills microorganisms, removes dead cells and stimulates the action of other immune system cells.

New data suggest reverse migration might be involved in systemic inflammation, she said. These findings would have implications for several diseases, including pancreatitis, acute respiratory distress syndrome and cancer.

Understanding what regulates reverse migration is important because there is a balance that must be maintained, Huttenlocher said. Too many neutrophils can cause hyper inflammation while too few cause an immune deficiency, which leads to chronic infection and impaired healing.

A signaling protein called myeloid-derived growth factor (MYDGF) regulates the movement of neutrophils to wounded, but not infected, tissue in zebrafish larvae.

In one study, the tail of a zebrafish with a MYDGF-deficiency was burned. After the injury, scientists observed increased neutrophil activity at the site of the wound.

These results suggest the protein limits neutrophil inflammation and promotes reverse migration. The exact mechanism is yet to be completely understood.

Going forward, Huttenlocher hopes to learn more about how neutrophils interact with macrophages at wound sites. In addition, her group is studying how MYDGF affects macrophages.

Studying neutrophil reverse migration and how inflammation resolves might one day answer key questions about the immune system’s response to infection and sterile injury, she said.

Huttenlocher’s full talk can be viewed at <https://videocast.nih.gov/watch=44239>. 

NIAMS Coalition Gathers Virtually for Eighth Biennial Meeting

A group of more than 90 professional and voluntary organizations concerned with diseases in the NIAMS portfolio gathered virtually last fall for the Coalition Outreach and Education Meeting: Creating Connections for Science. The biennial event brings together NIH staff and coalition members to discuss what’s happening at NIH and NIAMS, network with colleagues and exchange ideas about how to best collaborate.

The meeting started with a brief history and overview of the coalition, presented by the meeting co-chairs.

NIAMS director Dr. Lindsey A.

Criswell followed with her first state-of-the-institute address to the coalition. She highlighted her goals as NIAMS director and described key NIH and institute activities, including the Advanced Research Projects Agency for Health and the Accelerating Medicines Partnership program.

Event sessions covered several topics—NIH initiatives to reduce Covid-19 health disparities and address structural racism, best practices for engaging underserved populations and how to share data networks to build a more inclusive research enterprise. The meeting also included an update on the NIH Helping to End Addiction Long-term initiative.

To read the full meeting summary, visit: <https://go.usa.gov/xukCw>.—

Stephanie A. Mathews



NIAMS director Dr. Lindsey A. Criswell



After the lecture, an attendee greets Huttenlocher while Schor talks with NIH deputy director for intramural research Dr. Michael Gottesman.

PHOTOS: CHIA-CHI CHARLIE CHANG



On hand for the renovated pharmacy's May 18 ribbon cutting are (from l) acting pharmacy chief Capt. Richard DeCederfelt; Clinical Center CEO Dr. James Gilman; NIH acting director Dr. Lawrence Tabak; Dr. Alfred Johnson, NIH deputy director for management; Dr. Tara Schwetz, NIH acting principal deputy director; Dr. Michael Gottesman, NIH deputy director for intramural research; and Dr. Marilyn Farinre, pharmacy operations chief.

PHOTO: CLINICAL CENTER OFFICE OF COMMUNICATIONS AND MEDIA RELATIONS

'OUTDATED TO OUTSTANDING' Renovated CC Pharmacy Begins Phased Opening

Who says you can't come home again? After years of construction and operating out of temporary locations, the Clinical Center Pharmacy recently reopened in a renovated space.

The 10,000-square-foot facility incorporates the pharmacy's outpatient, unit-dose and intravenous admixture unit (IVAU) operations into a single site.

The outpatient section opened in early May. The unit-dose section opens at the end of May. The IVAU will come online this fall.

"NIH invested extensive thought and resources into planning and building a pharmacy that supports our three pillars of patient safety, clinical quality and world-class research," said CC CEO Dr. James Gilman.

The pharmacy's development was guided by four key principles:

- Safety of patients and staff
- Efficiency to save time, money and eliminate errors
- Positive staff impact by creating a workplace with high morale, excitement and engagement
- Regulatory compliance to ensure that the pharmacy meets or exceeds any regulations governing it

Cross-departmental teams worked to ensure that the project provided uninterrupted, safe pharmaceutical care for Clinical Center patients. Medication preparation and dispensing services are supported by state-of-the-art automation to protect patient safety and streamline operations.

"Our goal was to move from outdated to outstanding and I think we've hit the mark," said Capt. Rick DeCederfelt, acting chief of the pharmacy department.

While many things changed behind the scenes, the impact on the patient experience was minimal. Patients meet with a facilitator during the check-in process, continue to check in at a kiosk and the waiting area in front of the travel office remains the same.

A new outpatient medication pick-up area features three transaction windows with several features to help with patient privacy: frosted glass dividers, acoustic wall coverings and sound-absorbing ceiling panels.

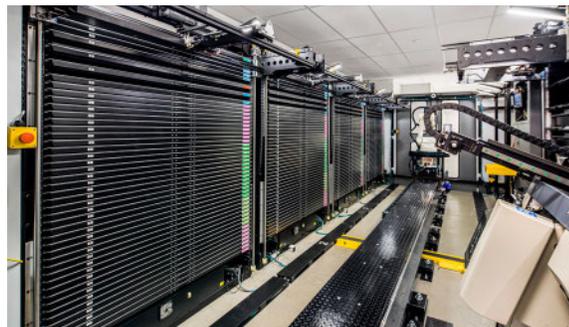
Behind the scenes, new procedures will improve both patient experience and safety. A new system will automate storage and retrieval of prescriptions, making pick-up faster, more accurate and more efficient.

At the core of the pharmacy is the XR-2 automated central pharmacy system, a robotic management mechanism that stores and dispenses medications. The robot weighs more than 20,000 pounds and is so massive that it had to arrive in 2 separate deliveries. Simply unloading the crates of materials from the delivery truck took over 4 hours.

The pharmacy has 44 cold units to accommodate medications that need to be stored at different temperatures. There are 36 refrigerators, 6 -20° Celsius freezers and 2 freezers that can store medication at -80° Celsius.

To support prescription mail services, there is a separate area for packing medication shipments and special secure package doors for efficient pick-up by mail carriers.

When the IVAU comes online, it will be protected

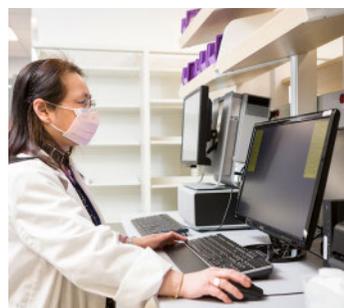


XR-2, the robotic medication management system that stores and dispenses medications

by high-efficiency particulate air (HEPA) filters placed throughout the facility to filter the air supply. Differential pressure, temperature and humidity will be continuously watched through the pharmacy's environmental monitoring system and the CC's building automation system.

The renovated IVAU follows a single hood, single room concept that makes it easier to isolate a compounding area where customized medications are made and to continue operations if problems arise.

"We've invested in long-term sustainability of the sterile environment and focused on excellence by creating in-house standards exceeding regulations and industry best practices to support and conduct clinical research by providing safe, high-quality care—one patient, and one medication, at a time," DeCederfelt said.—Donovan Kuehn (with contributors Esther Jeon, Christina Martin, Nadia Guirguis, Falguni Kanthan and Marilyn Farinre) **B**



At left, pharmacy technician Kyfia Clarke acts as a patient receiving medication from pharmacist Hon Lam, at a transaction window of the new pharmacy. At right, staff pharmacist Nga Pham verifies prescriptions.

and postnatally, of the developing brain to a lot of factors that we think lead to impaired development and then ultimately to poor outcomes for the child.”

These social determinants—economic stability, education, access to quality health care, food security, neighborhood environment—are all interconnected and account for as much as 75 percent of population health outcomes, Rogers noted. Disparities, amplified by racial biases, often are rooted in poverty.

Children who grow up impoverished are more likely to have developmental challenges. “Now we’re increasingly showing [via] science that this is potentially [due to] changes we are seeing in the brain,” said Rogers, a child psychiatrist and professor of psychiatry and pediatrics at Washington University. She discussed her research at a NIMH Director’s Innovation lecture earlier this year.

A baby’s brain develops rapidly in utero, growing in size and complexity particularly in the third trimester, and in the first couple years of life.

“The immature brain, because of this rapid brain growth, is more vulnerable to the environment and to the social determinants that these children can be exposed to both in utero and ex utero,” Rogers said.

Studies have linked the volume of cortical brain matter (related to attention and memory) and the hippocampus (involved in learning and memory) to socioeconomic status. Both prenatally and postnatally, psychosocial stress related to poverty, not to mention such related factors as poor nutrition and environmental toxins, can have adverse effects on the developing brain.

Rogers focused her presentation on two NIMH-funded studies conducted by her lab. One of them, the preterm birth study, examines changes in brain structure and function in premature babies, who are at greater risk for developmental issues and psychiatric disorders, particularly anxiety, attention deficit-hyperactivity disorder and autism spectrum disorder.

The babies in the study are fed and swaddled, then take a nap as they enter the MRI scanner. Researchers look at colors and signals of brain networks related to cognition

and psychiatric symptoms. When they scanned babies born at 27 weeks gestation, then conducted developmental follow-up at ages 2 and 5, they found activity in multiple brain regions in the neonatal scans that predicted symptoms related to social skill and attention deficits at ages 2 and 5.

This finding is important for disparities research. In the U.S., Black women have the highest rates of preterm birth. Rogers’s lab is finding growing evidence that prematurity has profound effects on the newborn brain and that preterm birth correlates with poverty.

“If you think about social determinants, a lot of it has to do with where you live, where your school is and access to resources,” said Rogers.

Using the area deprivation index developed by the University of Wisconsin, Rogers’s lab found strong links between neighborhood poverty and striatal connectivity to the prefrontal cortex. In other words, neighborhood poverty during the prenatal and perinatal period is related to brain connectivity at birth.

A larger study, e-LABE (Early Life Adversity and Biological Embedding), sheds additional light on how socioeconomic disadvantage affects the neonatal brain. In a sample of 400 babies scanned at birth, those from more socioeconomically disadvantaged

homes had less cortical gray matter and white matter volumes. Researchers also observed effects across different brain regions among infants whose mothers experienced psychosocial stress while pregnant.

Kids, however, can be resilient. But can they overcome poverty-related brain changes?

“I think a lot of folks are concerned about stigmatizing children by saying if you’re in poverty, your brain changes,” Rogers said. The good news is some studies are showing “there are ways in which your brain is developing optimally for the environment that you’re in and there might be ways your brain develops that can still make you successful.”

One way to mitigate disparities and improve cognitive and behavioral outcomes

is through anti-poverty programs and other assistance to improve economic stability. Another is to improve health care equality, including better routine and preventive care for mothers and babies.

Rogers continues doing her part to help. She founded and co-directs the



Measuring Brain Functional Connectivity

- Resting state Functional MRI (rs-fMRI)

BOLD Signal

Seed Region

Correlations

Functional Brain Networks

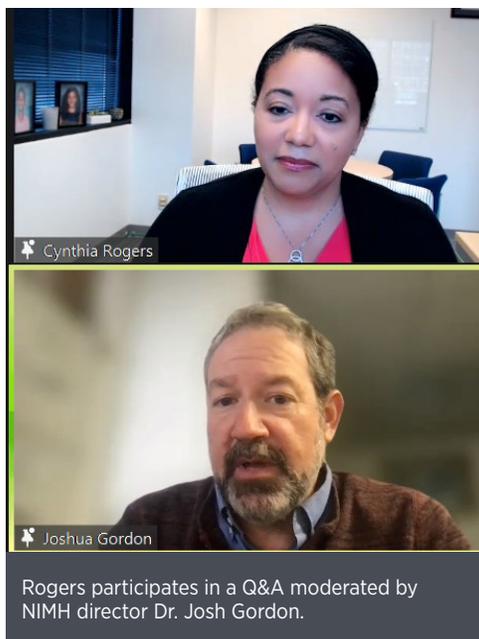
- Somatomotor-Hand
- Somatomotor-Mouth
- Auditory
- Rostralsplenial
- Visual

- Fronto-parietal
- Dorsal Attention
- Cingulo-opercular
- Parietal Memory
- Salience
- Ventral Attention
- Default Mode

Resting State Functional Connectivity

Fox 2005

Researchers look at colors and signals of brain networks related to cognition and psychiatric symptoms.



Perinatal Behavioral Health Service (PBHS) in St. Louis, where social workers, therapists and psychiatric clinicians provide mental health and substance use care in pregnancy and postpartum, as well as education, screening, care coordination and mental health treatments.

PBHS operates inpatient and outpatient care throughout the Washington University Medical Center. More than half of the patients have an income of less than \$20,000 and most are on Medicaid. About half are Black perinatal patients, the demographic least likely to have access to mental health care, noted Rogers.

“We really are passionate about the fact that this should be done in an equitable way,” she said, “and increasing access to care for those who typically don’t receive it.”

Recently, the service also began addressing basic needs. PBHS added a food pantry, offers referrals to a range of community resources and is piloting a housing assistance program.

“If we’re interested in improving health, either through research or through clinical care, how can we do that if we’re not addressing [the social determinants] responsible for three-quarters of the outcome?” asked Rogers. “It’s really important that we embrace this as health systems, as practitioners.”

For more information about the monthly NIMH Director’s Innovation Speaker Series, see: <https://go.usa.gov/xuza7>. 

Quiroz To Present Mahoney Lecture on Aging

‘PATH FOR ALZHEIMER’S PREVENTION’

Dr. Yakeel T. Quiroz, a clinical neuroscientist whose research is focused on the study of cognitive and brain changes that predispose individuals to develop dementia later in life, will deliver the next Florence Mahoney Lecture on Aging, June 8 at 3 p.m. ET.

Quiroz’s presentation, “Charting the path for Alzheimer’s prevention with the Colombian kindred with autosomal dominant Alzheimer’s disease,” will take place virtually via <https://videocast.nih.gov/44272>. She will discuss how longitudinal studies conducted with Colombian families with autosomal dominant Alzheimer’s disease (AD) have informed biomarker research, disease prevention and treatment development.

A limited number of audience members will be welcome to attend in Lipsett Amphitheater, Bldg. 10. If you are interested in attending in person, email WALSoffice@od.nih.gov.

An associate professor in the departments of psychiatry and neurology at Massachusetts General Hospital and Harvard Medical School, Quiroz currently serves as director of the MGH Multicultural Assessment and Research Center and the Multicultural Alzheimer’s Prevention Program. In her research, she uses multimodal neuroimaging methods, including PET and fMRI, and integrates genetics, biofluids and neuropsychological data to examine some of the earliest changes associated with the risk or protection for AD.

Quiroz is principal investigator on the NIH-funded COLBOS (COLombia-BOSton) biomarker study that follows individuals from the world’s largest extended family with a single, Alzheimer’s-causing mutation (E280A in Presenilin1). This was the first study to show that tau pathology was evident in the brains of cognitively unimpaired individuals with autosomal dominant AD, several years before onset of symptoms. It demonstrated for the first time that brain amyloidosis was necessary for the initiation of tau pathology in these individuals.

Under the auspices of her COLBOS study, Quiroz assessed a mutation carrier from the Colombian kindred who remained resistant to Alzheimer’s dementia for nearly 30 years after her estimated age at clinical onset. She had two copies of a rare APOE variant (i.e., APOE3 Christchurch mutation), the highest amyloid plaque deposition in the kindred, and relative sparing of downstream biomarker effects.

In related experimental studies, Quiroz’s group demonstrated that the Christchurch mutation may protect against AD by limiting tau pathology and neurodegeneration in the face of high amyloid pathology, which has opened new avenues for Alzheimer’s research and treatment.

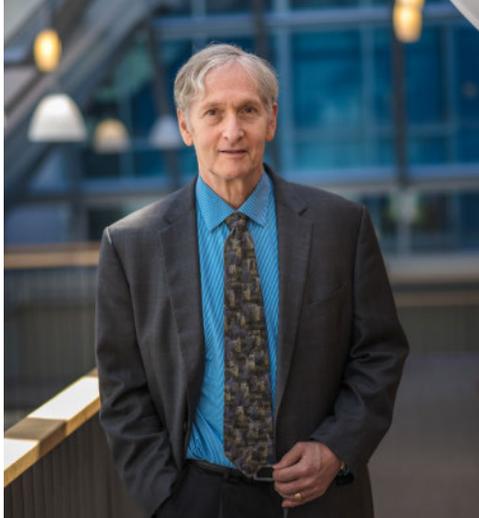
Her findings have helped researchers re-conceptualize Alzheimer’s as a sequence of changes that begins decades before cognitive decline, and which may be targeted by promising disease-slowing treatments and prevention strategies at a time in which they might have their most profound effect.

A native of Colombia, South America, Quiroz earned her bachelor’s from the University of Antioquia, Medellin, Colombia in 2000; master’s in cognitive neuroscience in 2006 and her Ph.D. in clinical psychology in 2013, both from Boston University. Her postdoctoral training was in clinical neuropsychology at MGH. She joined the faculty of Harvard Medical School/Massachusetts General Hospital in 2015.

Quiroz has been recognized broadly for her research, including with the NIH Director’s Early Independence Award, an MGH Research Scholar Award and the Alzheimer’s Association’s Inge Grundke-Iqbal Award for Alzheimer’s Research.

Mahoney lectures are sponsored by NIA and named in honor of Florence Stephenson Mahoney (1899–2002), who devoted much of her life to successfully advocating for the creation of NIA and increased support for NIH.





At Harvard Medical School, longtime NIH grantee Dr. Cliff Tabin studies structural and functional development in birds and other animals.

lab examined the genetic pathways that lead to formation of the syrinx in order to understand its morphogenesis and how the adaptation arose.

He said most tetrapods (four-limbed animals) such as amphibians, mammals and reptiles use their larynx—voice box with pulsating vocal chords in the throat—to speak. Birds are the exception, though. While they also have a larynx, theirs doesn't come with the vibrating “flaps” that produce sound. A separate organ, the syrinx, located in a bird's chest, enables our feathered friends to make sounds.

Syringes, Tabin noted, are shaped dramatically different in individual bird species, which accounts for their unique “songs.” The wood thrush, for example, can harmonize with itself, producing a complex song using two sets of vocal chords.

Unique to Physique

Why does the wood pigeon sound different than the white-throated sparrow?

“The syrinx is a beautiful, diverse organ,” said Tabin, playing recorded “songs” of both birds. His lab now is studying the structure's diversifications.

Both larynges and syringes are composed of cartilage. The variety of shapes in which the cartilage grows regulates muscles differently and locates a bird's vocal folds in different areas. Think of the intricacies in the design of horn instruments, for example. Chambers and airways built into a clarinet's body allow it to produce sounds different from those of a tuba or oboe. In this analogy, the vocal folds of vibratory tissue would be the equivalent of the reed for the oboe.

Somewhere on the evolutionary spectrum, birds lost the ability to use their larynx to make sound and developed the

syrinx for that function instead. Tabin's group and paleontologists at the University of Texas-Austin wanted to learn how and why that happened.

Premise for Peeps

Researchers analyzed the airway RNA sequences of alligators (which form larynges) alongside those of chickens (which develop syringes in addition to larynges). Turns out that something called the hedgehog signaling pathway (Shh) acts as a directional guide for forming parallel cartilage rings in the airway of tetrapods.

In birds, Shh has taken on a second important role as a timing mechanism, allowing the syringeal cartilage to form in a distinct shape prior to the formation of other airway cartilages, which would otherwise interfere with them.

Tabin's group has also been able to draw strong parallels between birds' genetic development of the vibratory tissue of the syrinx and genetic formation of the vocal cords in the larynx of other animals.

“We argue that the syrinx developed from the larynx by co-opting some of the regulatory networks that were already in place,” he said.

Thinking back farther in time, Tabin considered where the laryngeal gene networks may have come from. Scientists know that the larynx evolved in early air-breathing tetrapods to protect the airway. It's thought that laryngeal valves—the vibrating flap-like vocal folds that produce sound—then formed, enabling animals to vocalize.

The larynx networks, Tabin speculated, which emerged prior to the syrinx, may be related to a body's other “floppy, movable tissues,” similar to those found in heart valves, which developed even earlier in evolution.

“Birds built a new vocal organ from scratch,” Tabin concluded.

Its formation depended on altering the timing of the formation of the novel voice box relative to the development of the rest of the airway. And, although the larynx doesn't function the same in fowl, he said, birds were able to mimic some of the organ's structural features and create a novel instrument—the syrinx—that makes birds' music uniquely their own.

Watch Tabin's archived lecture in full at <https://videocast.nih.gov/watch=44216>.

Bird song

CONTINUED FROM PAGE 1

Tabin's work in bone, limb and organ formation has been funded by several institutes including NIAMS, NHLBI, NIDDK, NHGRI and NICHD. In a Wednesday Afternoon Lecture Series talk titled “How did birds evolve the capacity to vocalize?,” he shared some of his group's research. Their effort to document and explain the whens, hows and whys of birds gaining voice opens fascinating potential investigations regarding not only voice but also other functional and structural developments in human health and in the animal kingdom at large.

The George Jacob and Jacqueline Hazel Leder professor of genetics and chair of the department of genetics at Harvard Medical School, Tabin studies the genetic basis of structure and form during embryo development and over evolutionary time.

Flock Formations

Birds “sing” using a unique vocal organ called the syrinx—an example of the evolution of a novel structure. Tabin's

Now Hear This

To sample the incredible variety and diversity of bird vocalization, visit www.birds.cornell.edu/home/. “Cornell Lab of



Different birds with distinctive voices (from l) Northern mockingbird, Carolina wren and Northern cardinal

PHOTOS: MICHAEL BENDER

Ornithology is a great resource for audio of the songs,” suggests Dr. Michael Bender, program director, NIGMS Division of Genetics and Molecular, Cellular and Developmental Biology (and *Record* bird photographer). “Just search by species name and click on the audio button on the species account.”

2022 NIEHS Spirit Lecture Recognizes Bernard

BY JOHN YEWELL

“Great minds think differently,” said Dr. Marie Bernard, NIH chief officer for scientific workforce diversity, during her recent virtual NIEHS Spirit Lecture. “That is the catchphrase that motivates everything I do and that we do on my team.”

The Spirit Lecture began in 2002 as an annual event to recognize highly respected, outstanding women of notable achievement. Bernard received the honor this year. Part of the institute’s Diversity Speaker Series, the talk is held each year during Women’s History Month.

“Dr. Bernard embodies everything the NIEHS Spirit Lecture Award recognizes,” said NIEHS and National Toxicology Program director Dr. Rick Woychik. “I can’t think of a more highly deserving recipient.”

Bernard leads NIH efforts to recruit, cultivate and promote a diverse array of scientific talent, with the goal of advancing research innovation. She also co-leads the agency’s UNITE initiative, which aims to end structural racism in biomedical research.

She previously served as deputy director of the National Institute on Aging from 2008 to 2021. Her research focuses on nutrition and function in older adults, particularly minority populations, and she is a thought leader on the science behind scientific workforce diversity.

According to Bernard, several studies reveal the need for diverse scientific perspectives. For example, a 2015 paper revealed that articles published by researchers of the same ethnicity were more often associated with lower-impact journals and fewer citations.

“Diversity makes a difference,” Bernard said.

Lack of attention to diversity can constrain scientific advancement, she noted, citing research published in the *Proceedings of the National Academy of Sciences*.

Analyzing more than 5 million scholarly articles, authors found a link between greater diversity among researchers and greater production of new scientific knowledge.

Compared with men of the same races, Latina, Black and White women tended to have fewer publication credits in engineering, technology, mathematics and physics, but more in health, psychology and the arts. Asian men and women were roughly equal.

“The authors’ conclusion was that a different body of knowledge would be produced in the absence of these inequities,” said Bernard.

She said the results also reflect the reality of academic advancement.

“When you look at the professoriate, there’s a fair



Dr. Marie Bernard, NIH chief officer for scientific workforce diversity, delivered this year’s NIEHS Spirit Lecture.

amount of diversity at the instructor level, but as you approach the department chair level, there’s much less,” she said.

So, what can be done to enhance diversity in biomedical research?

“Be transparent and accountable in hiring and promotion,” said Bernard.

“Make diversity metrics public by posting data on research funding,” she added.

“My office has taken the lead in enhancing recruitment and retention by creating a search protocol to identify candidates for scientific positions. We’ve provided curated lists of individuals for consideration and trained search specialists across NIH. We’re not virtue posturing.”

Bernard also emphasized the importance of support programs, such as childcare and virtual work opportunities.

“All the wonderful diversity statements in the world are not going to make for institutional change,” she said. “We are aligning our values with our award system, with new performance expectations for diversity, equity, inclusion and accessibility.”

UNITE is one example. It requires each NIH institute and center to develop a racial and ethnic equity plan.

“NIEHS is fully immersed in this and my hat is off to you,” said Bernard, who also wants to build on NIH’s Distinguished Scholars Program (DSP) that is open to tenure-track researchers who have demonstrated a strong commitment to promoting diversity and inclusion.

To that end, her office recently launched the 21st Century Scholars Program, which replicates principles of the DSP for extramural program staff. **R**

NIGMS Receives Certificate of Excellence in Citizen-Centric Reporting

BY BRITTANY MERTH

The Association of Government Accountants (AGA) recently awarded NIGMS with a Certificate of Excellence in Citizen-Centric Reporting for fiscal year 2020.

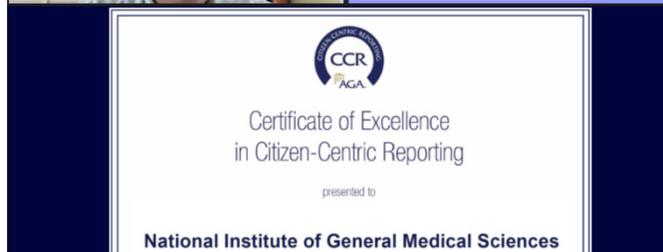
The certificate is part of the AGA’s citizen-centric reporting initiative, which aims to help simplify communication and transparency between government and its citizens.

As part of the initiative, AGA encourages government organizations to prepare and distribute an

annual citizen-centric report (CCR) that is written with the American public and taxpayer in mind.

Since the initiative’s inception in 2007, more than 400 federal, state and local governments as well as public sector organizations have produced CCRs giving constituents a better understanding of how their tax dollars are spent.

NIGMS director Dr. Jon Lorsch accepted the award from Ann M. Ebberts, AGA chief executive officer, during a virtual ceremony in April.



NIGMS director Dr. Jon Lorsch accepts a communication award from Ann M. Ebberts, AGA chief executive officer, at a virtual ceremony.

“NIGMS is committed to providing the best possible return on investment to American citizens and we’re honored to be recognized as a leader in government transparency,” Lorsch said.

You can review the NIGMS CCR at: www.nigms.nih.gov/about/dima/Documents/nigms-ccr.pdf.

NIH Starts Clinical Trial of Epstein-Barr Vaccine

NIAID launched an early-stage clinical trial to evaluate an investigational preventative vaccine for Epstein-Barr virus (EBV). EBV is the primary cause of infectious mononucleosis and is associated with certain cancers and autoimmune diseases. The phase 1 study, which will be conducted at the Clinical Center, is 1 of only 2 studies to test an investigational EBV vaccine in more than a decade.

EBV is a member of the herpes virus family and one of the most common human viruses. It is spread through bodily fluids, primarily saliva. Of those who contract infectious mononucleosis, roughly 10 percent develop fatigue lasting 6 months or longer.

Approximately 1 percent of all EBV-infected individuals develop serious complications, including hepatitis, neurologic problems or severe blood abnormalities. EBV also is associated with several malignancies, including stomach and nasopharyngeal cancers and Hodgkin and Burkitt lymphomas, as well as autoimmune diseases, such as systemic lupus erythematosus and multiple sclerosis.

The study will evaluate the safety and immune response of an experimental vaccine developed by NIAID's Laboratory of Infectious Diseases in collaboration with its Vaccine Research Center. The adjuvant—intended to enhance the immune response induced by the investigational vaccine—was developed by the biotechnology company Novavax, based in Gaithersburg, Md.

The vaccine works by targeting EBV glycoprotein gp350, which is found on the surface of the virus and virus-infected cells. EBV gp350 is also the primary target for neutralizing antibodies found in the blood of people naturally infected with EBV.

The study will enroll 40 healthy volunteers ages 18 to 29, half of whom have evidence of prior EBV infection. More information about the study is available at: www.clinicaltrials.gov/. Use the identifier NCT04645147.

Hypertension During Pregnancy Linked to Future Cardiac Events

An NIH-funded study explains factors related to increased risk for heart attack or stroke among women who had hypertension, or high blood pressure, while pregnant. Women who experienced such complications during pregnancy had a 63 percent increased risk for developing cardiovascular disease later in life.

While hypertensive pregnancy complications previously have been linked to increased cardiovascular risks, the current study controlled for pre-pregnancy shared risk factors including obesity before pregnancy and family history of heart attack or stroke. Researchers also found that high blood pressure, high cholesterol, type 2 diabetes or being overweight or obese after pregnancy accounted for most of the increased risk between pregnancy complications and future cardiovascular events.

The findings, published in the *Journal of the American College of Cardiology*, could support health care providers in developing personalized heart disease prevention and monitoring strategies for women who had hypertension during pregnancy. The information could also help bridge the gap that often occurs after a woman ends obstetric care and resumes or starts care with another provider.

Using health data shared by more than 60,000 participants in the Nurses' Health Study II, the research represents one of the most comprehensive reviews evaluating links between future cardiovascular events in women who have had preeclampsia or gestational hypertension—or increased blood pressure during pregnancy. Preeclampsia, a more severe complication marked by a sudden rise in blood pressure, can affect the organs and be dangerous for both mother and baby. Both conditions are often diagnosed after 20 weeks of pregnancy.

"Women with a history of gestational hypertension or preeclampsia should be informed that they have an increased risk for cardiovascular disease," said Dr. Jennifer J. Stuart, a study author and associate epidemiologist at Brigham and Women's Hospital and Harvard Medical School. "Women and their providers have lacked clear direction on what to do in the intervening years between delivery of a hypertensive pregnancy and the onset of cardiovascular disease."

The research was supported by grants from NHLBI, NCI and NICHD.



An NIH-funded study explains factors related to increased risk for heart attack or stroke among women who had hypertension while pregnant.

PHOTO: ADRIATICFOTO/SHUTTERSTOCK

Retinal Cell Map Could Advance Therapies for Blinding Diseases

An NIH discovery is shedding light on tissue targeted by age-related macular degeneration and other eye diseases. Researchers have identified distinct differences among the cells comprising a tissue in the retina that is vital to human visual perception. NEI scientists discovered five subpopulations of retinal pigment epithelium (RPE)—a layer of tissue that nourishes and supports the retina's light-sensing photoreceptors.

Using artificial intelligence (AI), the researchers analyzed images of RPE at single-cell resolution to create a reference map that locates each subpopulation within the eye. A report on this research is published in *Proceedings of the National Academy of Sciences*.

"These results provide a first-of-its-kind framework for understanding different RPE cell subpopulations and their vulnerability to retinal diseases, and for developing targeted therapies to treat them," said NEI director Dr. Michael Chiang.

"The findings will help us develop more precise cell and gene therapies for specific degenerative eye diseases," said the study's lead investigator, Dr. Kapil Bharti, who directs the NEI ocular and stem cell translational research section.

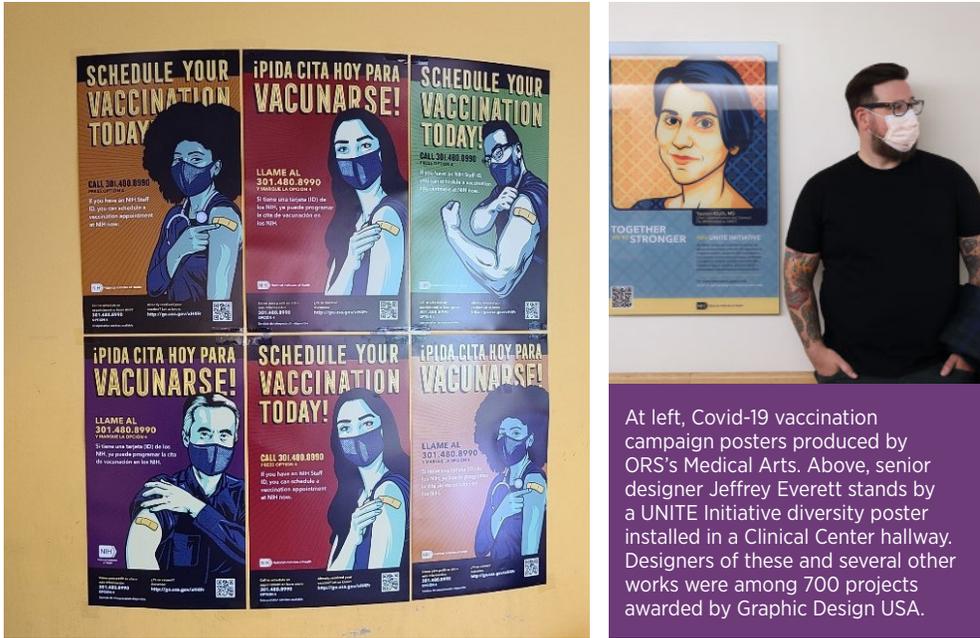
Vision begins when light hits the rod and cone photoreceptors that line the retina in the back of the eye. Once activated, photoreceptors send signals through a complex network of other retinal neurons that converge at the optic nerve before traveling to various centers in the brain. The RPE sits beneath the photoreceptors as a monolayer, one cell deep.

Age and disease can cause metabolic changes in RPE cells that can lead to photoreceptor degeneration. The impact on vision from these RPE changes varies dramatically by severity and where the RPE cells reside within the retina.

Using AI, the team analyzed RPE cell morphometry, the external shape and dimensions of each cell. They trained a computer using fluorescently labeled images of RPE to analyze the entire human RPE monolayer from nine cadaver donors with no history of significant eye disease.

"Overall, the results suggest that AI can detect changes of RPE cell morphometry prior to the development of visibly apparent degeneration," said NEI research fellow Dr. Davide Ortolan.

These findings could potentially be used to predict changes in RPE health in living patients.



At left, Covid-19 vaccination campaign posters produced by ORS's Medical Arts. Above, senior designer Jeffrey Everett stands by a UNITE Initiative diversity poster installed in a Clinical Center hallway. Designers of these and several other works were among 700 projects awarded by Graphic Design USA.

Medical Arts Produces Award-Winning Designs

Several designers in ORS's Medical Arts recently were honored by Graphic Design USA. Winning pieces included posters, flyers, visual branding and murals for several NIH institutes, centers and offices.

Awards went to Jessica Jackson, Jeffrey Everett, Bonnie Hamalainen, India Taylor, Maiu Romano-Verthelyi, Ethan Tyler and Erina He, as well as creative director Martha Blalock for projects that included:

- Covid-19 vaccination campaign posters
- NIMH Director's Innovation Speaker Series posters
- ORS strategic plan and work-life@NIH branding
- NHLBI workplace innovations flyers and office artwork and murals
- NIAMS GCgx scientific web app identity mark
- UNITE Initiative diversity posters

The GDUSA Awards showcase 700 projects out of more than 11,000 entries that reflect how graphic design shapes business, society, culture and causes.



Meet the awardees (top from l) acting branch chief Martha Blalock, production lead India Taylor, art director Bonnie Hamalainen; (center) senior designer Jessica Jackson, medical illustrator Ethan Tyler; (bottom) senior designer Jeffrey Everett, designer Maiu Romano-Verthelyi and medical illustrator Erina He.

NHLBI Seeks Adults with B-Cell Malignancies

NHLBI opens a new clinical trial testing the drug NX-2127 for adults with relapsed/refractory B-cell malignancies. NX-2127 is an oral drug that degrades a protein in B-cell malignancies, Bruton's tyrosine kinase, instead of inhibiting or blocking it like other drugs. NX-2127 may also stimulate the body's immune T-cells to attack cancer cells. The study enrolls adults 18 years or older diagnosed with a B-cell malignancy that progressed after prior systemic therapies. Participation is at no cost and travel assistance may be available. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email: ccopr@nih.gov. Refer to study #00326-H. Online: <https://go.usa.gov/xuPDr>.

Have Psoriasis? CC Needs Volunteers

Do you or someone you know have mild to moderate psoriasis? Researchers at the Clinical Center are testing a form of vitamin B3 dietary supplement to help improve immune system function in the blood and skin of people with mild to moderate psoriasis. Treatments and research procedures are provided at no cost. Refer to study #20-H-0044. Online: <https://go.usa.gov/xdH2Y>. For more information, call the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email ccopr@nih.gov.

Have Recurrent Prostate Cancer?

Join a clinical study looking to find a safer radiation treatment dosage. The standard treatment for recurrent prostate cancer after surgical removal of the prostate is radiation to the prostate bed delivered over 6-7 weeks. NCI's Dr. Deborah Citrin is conducting a study to see whether a shortened or compressed radiation treatment schedule of 2, 3 or 4 weeks can be as effective as the standard. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Online: <http://go.usa.gov/xtHdD>. Refer to study #18-C-0028.

Adults with Covid-19 Sought

NIMHD researchers are recruiting adults newly diagnosed with Covid-19 (within 72 hours) for a remote study. This is a remote study with no in-person visits. The study will collect physical health data using a temperature patch and digital wristband that will be provided to each patient. The collected data will be uploaded to an app using a smartphone and will help researchers gain a better understanding of how Covid-19 progresses in patients and its long-term effects in patient groups with different demographics and risk profiles. To learn more, contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #000315. Online: <https://go.usa.gov/x676m>.



Participants take part in "Stump Dr. Sciencehead," an ORWH activity.

Take Your Child to Work Day Held Virtually Once Again

NIH's "Take Your Child To Work Day" (TYCTWD) was held virtually on Apr. 22.

The day offered students in grades 1 through 12 an opportunity to experience the diversity of research and careers that makes the NIH what it is.

TYCTWD is sponsored by the Office of Research Services.

"People here at NIH do many different things, but all of it has the goal of helping everyone live longer and healthier lives," said NIH acting director Dr. Lawrence Tabak during the day's welcome video.

Although many students are back in the classroom, organizers

stuck with the virtual format for another year because the Clinical Center cares for many patients with underlying medical conditions associated with higher risk for severe Covid-19.

Next year, Tabak is looking forward to hosting *NIH Jeopardy* in person once again to test young contestants' science and health knowledge.

Over 20 institutes offered more than 100 engaging virtual activities to all NIH locations.

Live and recorded events were available throughout the day in addition to Earth Day activities.

"I'm excited to see how many kids, parents and volunteers have signed up to take part in today's impressive list of activities," Tabak enthused.—**Eric Bock**



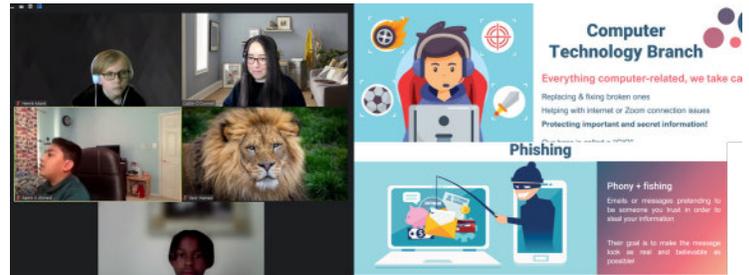
Dr. Laura Campello (top l), a research fellow at NEI, and Dr. Jayshree Advani (r), a postdoctoral fellow at NEI, demonstrate how to extract DNA from a strawberry using everyday household items.



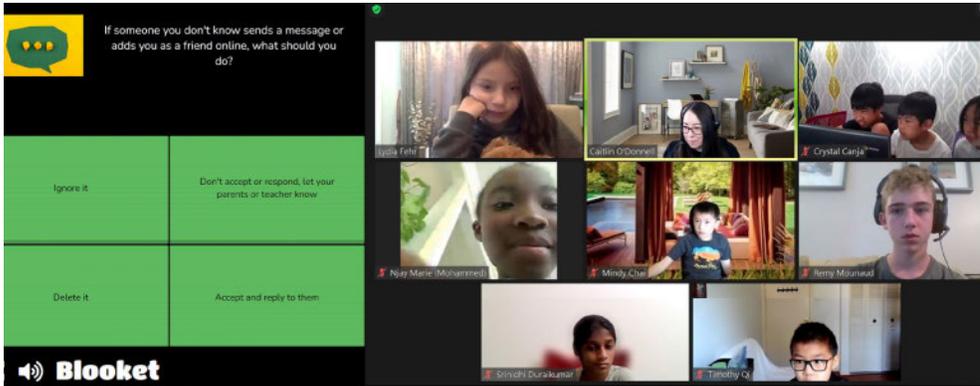
Leo, 2nd Grade



Stephanie Morrison's and Masaki Terabe's kids get ready to begin the Healthy Living Scavenger Hunt game with Carrie Hoskins and Toni Waldron.



Above, NIDDK's Computer Technology Branch gave kids a brief lesson on cyber safety such as detecting phishing, cyberbullying and password security. Afterward, the youngsters played a game based on what they'd learned.



ABOVE: Kids played a fun Blooquet quiz game testing their knowledge from NIDDK's Computer Technology Branch's short lesson. AT RIGHT: Dr. John Rohde, AAAS science and technology policy fellow at NINDS, models a nerve signal with a fire tornado. The pressure and motion of air molecules help viewers see what ions are doing when a nerve sends a signal.

