

EQUITY AS OUR COMPASS

Bertagnolli Begins as NIH Director

Dr. Monica M. Bertagnolli started Nov. 9 as the 17th director of NIH. She is the first surgeon and the second woman to hold the position. Nominated by President Joe Biden, Bertagnolli was confirmed on a bipartisan basis by the U.S. Senate on Nov. 7. She transitioned from her role as the 16th director of the National Cancer Institute, a position she had held since October 2022.

“Dr. Bertagnolli has spent her career pioneering scientific discovery and pushing the boundaries of what is possible to improve cancer prevention and treatment for patients and ensuring that patients in every community have access to quality care,”



Dr. Monica Bertagnolli is the first surgeon and second woman to serve as NIH director.

Biden said in his nomination announcement earlier this year. “Dr. Bertagnolli is a world-class physician-scientist whose vision and leadership will ensure NIH continues to be an engine of innovation to improve the health of the American people.”

Growing up in rural Wyoming, Bertagnolli experienced and saw firsthand the challenges faced by rural communities to access medical

care and participate in medical research. Due to that lived experience, equity is a core value that drives all of her efforts, which include ensuring NIH research is equitable and accessible to all people from all walks of life regardless of income or zip code.

“As a physician-scientist for more than 30 years, I have seen the transformative power of NIH research to produce results that save lives, including my own treatment for breast cancer,” said Bertagnolli. “As NIH director, I look forward to ensuring that NIH continues to be the steward of our nation’s medical research while engaging all people and communities in the research effort that includes informing medical practice that drives equitable access to health care for all.”

“Dr. Bertagnolli has spent her career working to improve the health and well-being of Americans,” said Health and Human Services Secretary Xavier Becerra. “She has

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LARD OF THE FLIES

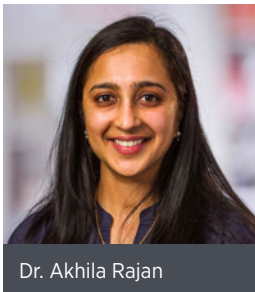
Rajan Studies How Fat Cells Communicate with the Brain

BY ERIC BOCK

Fruit flies have fat—but not too much, said Dr. Akhila Rajan during a recent Judith H. Greenberg Early Career Investigator Lecture.

What little fat there is has helped scientists make unexpected findings about how fat cells communicate with the brain, said Rajan, associate professor in the Fred Hutchinson Cancer Center’s basic sciences division. Fat cells, also referred to as adipocytes, are an organism’s primary energy storage organs.

All organisms are in a constant state of



Dr. Akhila Rajan

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WHEN DEAD CELLS TALK

NCI Investigator Discovers Signals that Spur Metastatic Cancer

BY DANA TALESNIK

One of the toughest challenges in cancer therapy is treating a relapse, when cancer cells become more stubborn and resistant, and the prognosis more precarious.

Earlier this year, Dr. Li Yang and her lab colleagues at the National Cancer Institute discovered a mechanism that may underlie cancer relapse. They found

that dying cancer cells emit signals that can trigger the growth of nearby cancer cells. The implications are vast, and she urges



Dr. Li Yang

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Rosenberg receives presidential medal. See p. 8.

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'Mission First Safety Always' Award Nominations Open

Do you know a superstar in safety? The Office of Research Services Division of Occupational Health and Safety is now accepting nominations for the NIH Mission First Safety Always Award 2023.

The award was created in 2013 to recognize NIH staff who demonstrate leadership, innovation and involvement in their organization's safety culture.

Nominate a superstar by Sunday, Dec. 31 at: <https://go.nih.gov/nDLKjKi>



Federal Benefits Open Season Underway

Ends Dec. 11

The Benefits Open Season runs now through Monday, Dec. 11. If you plan to make an Open Season election, now is the time to do it. Unless you experience a Qualifying Life Event during the year, the annual Open Season is your only opportunity to enroll, cancel enrollment or make a change for the participating programs.

For detailed information, view the announcements at <https://go.nih.gov/VVOD7iY>.

The three participating programs are:

1) Federal Employees Health Benefits (FEHB) Program. To enroll, cancel or change FEHB enrollment, you must use myPay* at <https://mypay.dfas.mil/mypay.aspx>. Elections will be effective on Sunday, Jan. 14, 2024. Current enrollment will automatically continue, if you do not take any action during Open Season.

*Exception: If you will retire between now and Saturday, Jan. 13, 2024, do not use myPay to make your change. Instead, you must submit a hardcopy Health Benefits Election Form, SF 2809, along with your retirement paperwork to your benefits specialist.

2) Federal Employees Dental and Vision Insurance



Cardin Visits NIH for Capital Projects Tour, NIMHD Briefing

U.S. Senator Ben Cardin (D-MD) and staffers visited with several NIH leaders on Oct. 27 to discuss work related to minority health. He asked specifically to chat about accomplishments at the National Institute on Minority Health and Health Disparities (NIMHD) and upcoming needs and goals. Cardin was critical in establishing NIMHD.

In addition, the senator had participated in a buildings and facilities tour in 2019. During this visit, the Office of Research Facilities gave an update on what NIH has accomplished in response to the 2019 National Academies of Sciences, Engineering and Medicine report and highlighted how NIH is managing a backlog of maintenance and repairs (BMAR). The recent tour illustrated what space with high BMAR looks like and the dramatic improvements NIH can achieve with congressional support.



In addition to chatting at a roundtable briefing with NIH leaders (top), Cardin dropped by several areas of the Clinical Center. Here, he takes a tour led by Dr. Constance Noguchi, acting chief of NIDDK's Molecular Medicine Branch. Shown behind them are NIH Associate Director for Budget Neil Shapiro (second from l) and NIDDK Scientific Director Dr. Mike Krause (r).



On hand for the visit are (from l) Dr. Gary H. Gibbons, NHLBI director; Dr. Lawrence Tabak, then-acting NIH director; Cardin; Dr. Tara Schwetz, then-acting NIH principal deputy director; Dr. Gregory Germino, NIDDK deputy director; Dr. Monica Webb Hooper, NIMHD deputy director; Karen Hendricks, constituent services/community outreach representative for Sen. Chris Van Hollen (D-MD), and Sarah Lev, constituent services caseworker for U.S. Rep. Jamie Raskin (D-MD).

Program (FEDVIP). To enroll, cancel or change FEDVIP enrollment, use the BENEFEDS Portal at www.benefeds.com or call 1-877-888-3337 (TTY 1-877-889-5680). Elections effective Monday, Jan. 1, 2024. Current enrollment will automatically continue, if you do not take any action during Open Season.

3) Flexible Spending Accounts (FSA) Program. To enroll in an FSA for 2024, go to the website

at www.fsafeds.com or call 1-877-372-3337 (TTY 1-866-353-8058). Note: Current enrollment will not automatically continue. If you want an account in 2024, you must enroll during Open Season. Elections effective on Monday, Jan. 1, 2024.

Send questions to AskBenefits@nih.gov or your benefits contact. To locate your contact, visit <https://hr.nih.gov/contacts/benefits>.

HEARTFELT ADVANCES

NHLBI Refines Test for Good Cholesterol Function

Routine blood tests at the doctor's office measure the amount of good and bad cholesterol in the body. Research has shown though that measuring how well high-density lipoprotein (HDL)—or “good cholesterol”—functions can better predict heart disease risk. New NIH research is now bringing such testing closer to clinical use.

HDL cholesterol removes extra cholesterol from the arteries by gobbling up early-forming plaque and transporting it to the liver for disposal. Excess plaque in the arteries can narrow blood vessels and impede blood flow, leading to heart attacks and stroke. When HDL cholesterol works well, heart disease risks are reduced.

To date, measuring HDL function has been limited to research labs. The test involves harvesting cells in the lab and can take days to process.

Researchers at the National Heart, Lung and Blood Institute (NHLBI) have developed

of samples you can study. It increases the number of experiments you can do.”

Importantly, they have shown in clinical studies their test can predict cardiovascular disease risk better than HDL concentrations, currently used to assess such risk. They published these findings in the *Journal of Clinical Investigation*.

To perform the test, a person's plasma,



Dr. Edward Neufeld (l) and Dr. Alan Remaley

which contains HDL, is separated from their blood. The plasma is added to donor particles coated with a lipid mixture that resembles plaque, and a fluorescent-tagged phospholipid that can only be removed by HDL. The fluorescent signal obtained by HDL is then measured. A brighter signal reflects optimal HDL lipid removal function. A dim light indicates reduced function.

The test is still years away from potential

• • •
“This is going to quicken the pace of basic research.”

-DR. EDWARD NEUFELD

a diagnostic test that could enable large-scale testing. The cell-free test could be easily replicated in labs, automated to process larger samples and provide readings in about an hour.

“This is going to quicken the pace of basic research,” said Dr. Edward Neufeld, a scientist in NHLBI's Lipoprotein Metabolism Laboratory who, along with Dr. Masaki Sato, developed the test. “It increases the number

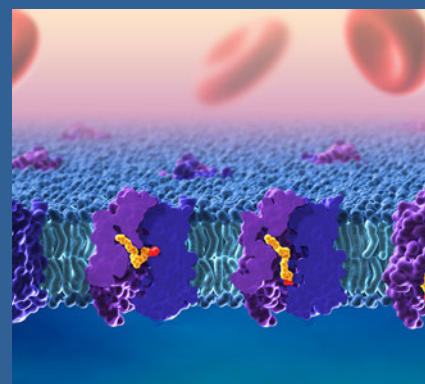
use in a medical setting, but it holds promise for physicians looking to gather additional information that could help inform their treatment decisions. NIH has now patented the test and will work with an outside company to purchase the rights to license and manufacture the diagnostic material.

Basic research over many years has led to advances and novel discoveries in lipoprotein research. Statins, which lower levels of

LDL—“the bad”—cholesterol, were developed decades ago. Despite ongoing research into HDL cholesterol, therapeutic advances so far haven't followed.

“Someday we may have a drug that modulates HDL and turns out to be beneficial, but right now we don't have that,” said NHLBI Senior Investigator Dr. Alan Remaley.

Neufeld said, “This [research] could open up new opportunities to gain further insights, such as with drug development, that have been difficult to achieve.” **R**



ON THE COVER: DHA crossing the blood-brain barrier. Docosahexaenoic acid (DHA) is an essential omega-3 fatty acid that is important for a healthy nervous system. This model shows how DHA and other omega-3 fatty acids cross the blood-brain barrier through the lipid transporter Mfsd2a.

IMAGE: ETHAN TYLER/NIH MEDICAL ARTS

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National Institutes of Health
 Turning Discovery Into Health

New Director

CONTINUED FROM PAGE 1

built a reputation for her willingness to take on the deadliest diseases facing patients and as a powerful advocate for cancer patients, working to end cancer as we know it. That same tireless energy and clear vision will serve her well as NIH director.”



At an Oct. 18 hearing with the Senate committee on Health, Education, Labor and Pensions, Bertagnolli recalled her upbringing in rural Wyoming and the long distances people had to travel for access to health care.

Chief among her key priorities is ensuring clinical trials yield the best results by increasing the diversity of participants; embracing the rapid expansion of new learning-based analytical tools and ensuring their use improves care for all people; and restoring trust in science by making it accessible to all communities, and inspiring the next generation of doctors and scientists.

Bertagnolli also is committed to leveraging commonalities across all diseases—from biology to accessing care—to strengthen collaboration across the 27 NIH institutes and centers.

“My research focused on how inflammation causes cancer,” she said. “We know, however, that inflammation also is a major component behind Alzheimer’s disease, autoimmune disorders, Long Covid, arthritis and many other diseases. As NIH director, I’m excited to drive cross-cutting research to capitalize on such commonalities.”

As NCI director, Bertagnolli initiated efforts to expand and modernize cancer clinical trials to increase the number of people who can participate in

NCI-supported research. Under her leadership, NCI released the National Cancer Plan to galvanize communities to set specific goals to prevent cancer, reduce deaths from cancer and provide the best possible quality of life for people living with cancer.

Bertagnolli has been a cancer surgeon for more than 35 years. Before joining NCI, she specialized in treating and researching gastrointestinal cancers in her roles as the Richard E. Wilson professor of surgery at Harvard Medical School, surgeon at Brigham and Women’s Hospital and member of the Gastrointestinal Cancer Treatment and Sarcoma Centers at Dana-Farber Cancer Institute.

Bertagnolli’s research has advanced the current understanding of the gene mutation that promotes gastrointestinal cancer development and the role of inflammation as a driver of cancer growth. She also has worked to increase responsible access and sharing of

cancer clinical trial data among researchers and has promoted the inclusion of rural communities in clinical studies. She is a past president and chair of the board of directors of the American Society of Clinical Oncology and has served on the board of directors of the American Cancer Society and the Prevent Cancer Foundation. She was elected to the National Academy of Medicine in 2021.

Bertagnolli graduated from Princeton University with a bachelor’s degree in engineering and earned a doctor of medicine degree from the University of Utah in Salt Lake

City. She trained in surgery at Brigham and Women’s Hospital and was a research fellow in tumor immunology at Dana-Farber Cancer Institute.

Dr. Lawrence Tabak, who has served as acting NIH director of NIH since December 2021, has agreed to resume his role as the NIH principal deputy director to assist with the transition. NCI Principal Deputy Director Dr. Douglas Lowy will serve, for the fourth time, as NCI acting director until Biden appoints a new director. **R**

NIMHD Seminar Addresses ‘How to Heal Health Care,’ Dec 7

Dr. Martin Shapiro, general internist and professor of medicine at Weill Cornell Medical College, will present a virtual lecture, “A Broken System: American Health Care Needs Combination



Therapy,” on Thursday, Dec. 7 from 2:30 to 4 p.m. ET. The talk is part of the National Institute on Minority Health and Health Disparities (NIMHD) Director’s Seminar Series.

Shapiro studies accessibility of care and health

disparities. He will discuss how to understand the U.S. health care system. After the lecture, NIMHD Director Dr. Eliseo J. Pérez-Stable and NCI Division of Cancer Control and Population Sciences Director Dr. Katrina Goddard will moderate a Q&A. Virtual audience members will be able to submit questions and comments at NIMHDDSS@mail.nih.gov.

This event, co-sponsored by the NIH Outcomes and Effectiveness Research Interest Group, is open to staff, trainees and external groups.



Advance Care Planning Email Series Launched

The National Institute on Aging has launched a new seven-week email journey, “Ready, Set, Plan! A Step-by-Step Guide to Advance Care Planning.” The series is designed to empower older adults and caregivers to take charge of their health and future care by creating an advance care plan that works for their specific needs.

Using the new resource, people can

- Discover the basics of advance care planning
- Think about their values and care and treatment preferences
- Start conversations with loved ones and health care providers
- Learn how to make an advance care plan official

Sign up for the series at <http://eepurl.com/izXpAg>.

ENGAGEMENT ACROSS DIVERSE ENVIRONMENTS

NIMHD Leads Workshop on Inclusive Participation in Clinical Research

The historical and current underrepresentation of racial and ethnic minority populations in clinical research has resulted in uncertain generalizability of study findings and limited the understanding of health disparities.

In light of greater public recognition around the importance of diversity among research participants during the Covid-19 pandemic, the National Institute on Minority Health and Health Disparities (NIMHD) led a 2-day workshop on inclusive participation in clinical research. Speakers and attendees representing various sectors of the clinical research enterprise explored promising practices and strategies for improving inclusion. The workshop placed particular emphasis on meaningful inclusion of individuals from racial and ethnic minority populations.

NIMHD Director Dr. Eliseo Pérez-Stable, Office of Research on Women's Health Director Dr. Janine Clayton and NIMHD Deputy Director Dr. Monica Webb Hooper opened the event. They shared research enrollment statistics, federal inclusion efforts and the importance of inclusive participation.

"Greater diversity [in clinical research] is needed...largely because of its importance for community confidence, acceptance, trust and overall generalizability," Webb Hooper emphasized.

Keynote speaker Dr. Otis Brawley discussed clinical trials in cancer research and their role in reducing health disparities.

"Clinical trial participation is a way of assuring better care," because individuals who participate in clinical trials receive better health care than individuals who do not, he noted. "[For breast cancer care, compared to White women] Black women are two-thirds as likely to get less than optimal care...and Hispanic [women] are about three-quarters as likely to get less than optimal care."

Brawley invited retired U.S. Army Col. Jimmie Slade of Community Ministry of Prince George's County, Md., to address building trust with local communities and how organizations in them can "translate" trust in the community group to trust in a research institution.

Day 1 focused on steps to improve inclusivity before conducting a study. Panelists discussed appropriate study samples, hiring diverse research teams and engaging communities. Dr. Marvella Ford shared how her cancer center "include[s] community reviewers as score-driving reviewers in [center]-funded research proposals."

Presentations also highlighted factors to consider during the study, such as engaging referring physicians as research partners and the ethics of participant compensation.

To illustrate community-engaged recruitment, Dr. Namratha Kandula presented her work with South Asian populations in Chicago. She described how her



From l, Dr. Eliseo Pérez-Stable, Dr. Debara Tucci and Dr. Leonard Egede

"community and clinical partners provide space for study visits...which means [the] participants can travel to a familiar site, one that is closer to where they work or live."

Dr. Debara Tucci, director of the National Institute on Deafness and Other Communication Disorders (NIDCD), detailed NIDCD efforts to enhance inclusive participation, such as requiring that "investigators...plan for engagement of underrepresented populations up front."

Day 2 began with actions researchers can take after a study that can improve inclusivity in the future. For example, the National Academies of Science, Engineering and Medicine's *Consensus Report on Improving Representation in Clinical Trials and Research* recommended that journals require information on representation in trials and studies submitted for publication.

In his talk on metrics, Dr. Leonard Egede encouraged researchers to evaluate the different recruitment strategies used and examine predictors of non-participation.

Three panels discussed promising practices for conducting clinical research with specific populations:


- Situating research offices in communities and including community representatives on research teams, advisory/governing boards and publications
- Special consent considerations for children, older adults, incarcerated persons and people with limited English proficiency
- Sexual and gender minority groups, pregnant and lactating people, persons with disabilities, rural populations and socioeconomically disadvantaged populations

Panelists raised the importance of offering flexible ways to provide consent, how inclusion builds trust and the need for research teams that include individuals who are members of the populations being studied.

The final session featured perspectives from community and patient advocacy groups, academia, pharmaceutical companies, federal and non-federal funding entities and policy organizations. Panelists discussed funding challenges that limit engagement efforts, emphasizing the importance of building long-term relationships with communities as equal partners.

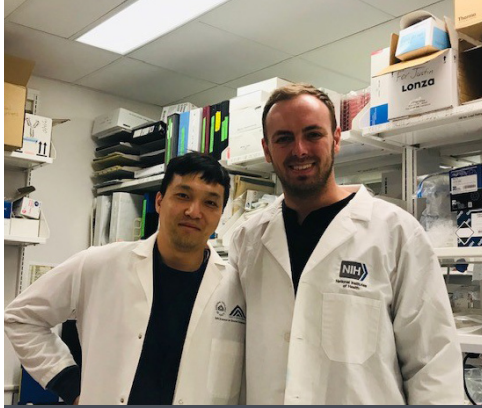
NIH Chief Officer for Scientific Workforce Diversity Dr. Marie Bernard concluded the workshop with a presentation on ongoing NIH efforts to strengthen diversity, equity, inclusion and accessibility (DEIA) in the NIH workforce and in NIH-funded research, including the UNITE Initiative and the newly launched Community Partnerships to Advance Science for Society program.

"One of the things that is really important in helping people to understand the benefit [of DEIA] is the data that show that when you have diverse perspectives, you have better science, greater creativity [and] greater innovation," she said.

Visit <https://go.nih.gov/6gAHlcl> to learn more. 



From l, Col. Jimmie Slade, Dr. Marie Bernard and Dr. Namratha Kandula



NCI postdoc Dr. Woo Yong Park (l) and doctoral student Just Gray were integral to the discovery.

But treatment rarely kills all malignant cells. Some survive, hide and stay dormant, then evolve and resurface, tougher than before, and often resistant to therapy.

“My lab became interested in the epigenetic [how the environment influences genes and cells] component of cancer cells because we believe that understanding these epigenetic changes may provide the answer for how cancer cells change when challenged with treatment and how they create diversity between each other.”

In the lab, her team discovered an epigenetic modifier called PAD4, which they found modifies chromatin—protein-encased strands of DNA.

“We found that dying cancer cells modify their chromatin,” Yang said. “The chromatin becomes expanded and then bursts. When they burst, they’re expunging out their contents.”

She further explained, “Imagine the

cell as a balloon filled with things. When it expands beyond its limits, it bursts. Then all of the stuff inside—the nuclei, chromatin, DNA, proteins—gets spread out, far away.”

This was the start of a groundbreaking discovery. What they found surprised them.

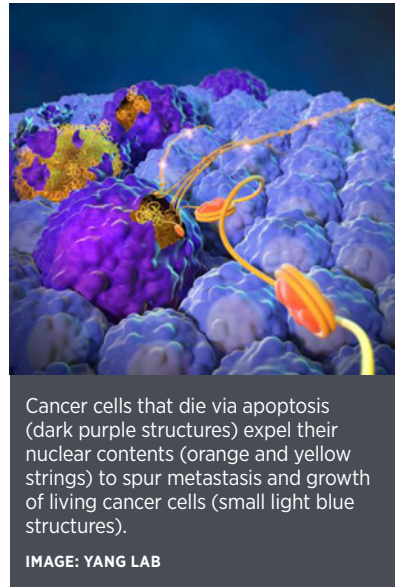
Cancer’s Last Words

Upon further study, “We found out that the dying tumor cells have a way to support their community,” Yang said. “Perhaps they’re not dying in vain. In their death, they communicate to the surviving cancerous cells, ensuring the community’s survival.”

That was an unexpected revelation. They observed dying cancer cells sending signals to surviving cells, making

them more resistant and enabling them to spread. “Cancer cells don’t act alone. Rather, they have quite a sophisticated network of communication,” she said.

Yang’s lab then traced these effects to a



Cancer cells that die via apoptosis (dark purple structures) expel their nuclear contents (orange and yellow strings) to spur metastasis and growth of living cancer cells (small light blue structures).

IMAGE: YANG LAB

Yang

CONTINUED FROM PAGE 1

the cancer research community to follow up.

“We need an effort to investigate how dying cancer cells can also be a problem for the patient,” said Yang, senior investigator in NCI’s Laboratory of Cancer Biology and Genetics. “Our studies show there’s an unexpected side to the story of killing tumor cells, and we need to be aware.”

The Bursting Balloon

It was somewhat of an accidental discovery, Yang recalled. “It was in the back of our minds that dying cancer cells are interesting by themselves,” she said. Many tumor cells die naturally in the body—during circulation or in a hostile immune microenvironment—and many more die during cancer treatment.

The Scientist Behind the Discovery

It’s never too late to follow one’s aspirations, and Yang’s journey to becoming an NCI senior investigator embodies that mantra.

Yang was born and raised in Sichuan province in China. As a child, she dreamed about making scientific discoveries. “When I was 12 years old, my father gave me a book about Madame Curie’s discovery of radium and I always dreamed of being just like her.”

After earning her undergraduate and master’s degrees in China, she emigrated to Raleigh, N.C. For years, she worked as a research technician at North Carolina State University, Duke and later Vanderbilt, where she focused on raising her two young children.

“Many women get their careers established first. I had my babies first,” Yang said.

While she prioritized motherhood, at the same time, she was becoming increasingly bored. Her husband, a professor at Vanderbilt, suggested she go back to school to pursue her doctorate.

“My husband said, ‘I know you want intellectual challenges and need to satisfy your curiosity. I know your mind is wanting more,’” said Yang. She decided to survey a class at Vanderbilt.

“When I sat in on a class, I realized how much I loved it,” she said. “I loved all



Yang dreamed about making scientific discoveries as a child.

of the new intellectual challenges—even taking the tests.” She soon enrolled in the Ph.D. program in cancer biology.

Each day, Yang went to work or class and came home to care for her kids, who were 2 and 9 when she started her graduate studies. “I would get up around 1 or 2 in the morning to finish school coursework until about 4 or 5 a.m.,” she said. After a couple hours of sleep, she would resume her daily activities.

“I was exhausted. But it was my time, and I was using it to do something I love,” she said. “As women, we are good at adapting. The experience we have as mothers, as a family, as major contributors, we have ways to deal with stress and adapt to many different situations.”

In graduate school, Yang studied the role of the COX-2 pathway in regulation, immune response and tumor progression and how host myeloid cells contribute to tumor blood vessel formation. During her studies, she relished the opportunity to do a short stay in Japan, collaborating with a professor at Kyoto University on her dissertation project. “I learned so much about how people do science there and I enjoyed learning about Japanese culture,” she said.

After receiving her Ph.D. and completing postdoctoral work on TGFbeta signaling in breast cancer progression at Vanderbilt, Yang came to work at NCI in 2009.

“NCI was such a great fit, regardless of my different experience,” she said. “I was much older than other applicants, but they loved the way I do science. It’s a good opportunity for me to [have access] to NIH and NCI resources, intellectual as well as technology resources. I was very lucky to come here as a researcher.”—Dana Talesnik

molecule, chromatin-bound S100a4, a factor that can stimulate the outgrowth of the living cancer cells. Is this mechanism of last words, of chromatin releasing from dying tumor cells, responsible for cancer relapse? This opens up an untapped avenue for exploration, toward reducing the chances of cancer recurring after treatment.

“Our investigations have found a molecular pathway containing key components that can be targeted therapeutically so that the cancer cells will not leave out the traces of chromatin that promote metastatic outgrowth,” she said. Building on this research, it might be possible to interrupt the conversation, to prevent dying cancer cells from sending the signals that provoke the spread of remaining cancer cells.

Yang recommends further study toward potential clinical trials. “The importance of our discovery goes beyond what we discovered. We hope that fellow cancer researchers, including principal investigators and young researchers, will join this effort and look into this uncovered area” that could identify new opportunities for cancer treatment and ultimately save lives. **B**

ODP Issues Youth Art Challenge

A new NIH Office of Disease Prevention (ODP) Youth Art Challenge asks young people ages 13–22 to create original artwork that shows how prevention can create better health for everyone.

By sparking creativity and curiosity about how prevention can improve the health of all people, ODP hopes the challenge will stimulate interest in science, technology, engineering and math, as well as prevention and health equity.

Artwork will also provide insights into the perspectives of young people about some of the issues that make it difficult for people to be as healthy as possible and ways to overcome those challenges to improve health for everyone.

Winning entries will be awarded \$500–\$3,500 and artwork will be featured on ODP’s website and social media. Teens and young adults can submit their original art until Wednesday, Jan. 31, 2024. Learn more at prevention.nih.gov/YouthArtChallenge. #ODPArChallenge

Watch a video about the challenge: <https://www.youtube.com/watch?v=Ds3hiKNAfco>.



ORWH Welcomes New Deputy Director

The NIH Office of Research on Women’s Health (ORWH) has named Dr. Vivian Ota Wang as deputy director.

Ota Wang’s background in genomics, psychology, ethics and data science will help to further drive innovative ideas and solutions to advance and improve the health of all women.

She comes to ORWH from the Office of Data Sharing Strategy in the Division of Program Coordination, Planning and Strategic Initiatives. In her previous role, she was responsible for ethics, equity and issues related to data access and sharing policy development and implementation and Covid activities.

Ota Wang established the NIH Covid Rapid Acceleration of Diagnostics (RADx[®]) Data Repository in December 2022. The repository represents one of the largest publicly accessible NIH databases for Covid-19 data in the nation and is considered a gold standard for data management, harmonization and sharing.

In addition, she serves as a subject matter expert in ethics, community engagement, sovereignty, data governance and research participant protections. Her more recent activities include consulting for the National Covid Cohort Collaborative tribal consultation and leading the NIH Tribal Consultation for the RADx Tribal Data Repository, the first NIH-funded, tribally directed and sovereignty-based research data repository for RADx American Indian/Alaska Native research data.

She also served as the inaugural deputy director of the Office of Data Sharing in the Center for Biomedical Informatics and Information Technology at the National Cancer Institute. Additionally, she was the program director for Data Access and Sharing and the Ethical, Legal and Social Implications Research Program at the National Human Genome Research Institute.

Ota Wang received a B.A. in biology from Colorado College, an M.S. in genetic counseling from the University of Colorado, and an M.Phil. and Ph.D. in counseling psychology from Columbia University. She is



Dr. Vivian Ota Wang

a fellow of the American Medical Association (American College of Medical Genetics) and American Psychological Association, diplomate of the American Board of Medical Genetics and American Board of Genetic Counseling, a clinical laboratory specialist in cytogenetics, and a licensed psychologist. **B**

Enrollment Open for NIH Leave Bank

Fall Open Enrollment for the NIH Leave Bank has started and runs until Dec. 11. The membership period will begin on Jan. 14.

The Leave Bank is a pooled bank of donated annual and restored annual leave available to eligible members. It acts like a safeguard for your paycheck and amounts to paid leave for members who have exhausted all of their own sick and annual leave and are affected by a personal or family medical emergency.

To become a Leave Bank member, access the Integrated Time and Attendance System (ITAS) during Open Enrollment and select “Leave Bank Membership” to enroll. If you are a 2023 Leave Bank member, your membership will automatically continue into 2024, unless you opt out in ITAS during Open Enrollment. The yearly membership contribution is one pay period’s worth of annual leave accrual. The membership contribution will be waived automatically if you lack sufficient leave or have an open VLTP and/or Leave Bank recipient account.

For more information, visit <http://hr.nih.gov/leavebank> or contact the Leave Bank Office at (301) 443-8393 or LeaveBank@od.nih.gov.



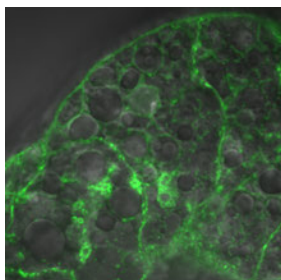
Rajan gives NIGMS's Greenberg Lecture.

PHOTO: CHRIS WANJEK

Flies

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nutritional flux. Their brains communicate with fat cells to constantly balance food intake and nutrient storage with energy requirements. Rajan's lab studies how the nutrient status—whether an organism is sated or starved—affects “our most primal



Adult fly fat (lard of the flies) showing adipokine secretory hubs in green

PHOTO: RAJAN LAB

functions like hunger, movement, sleep and immunity.”

A decade ago, she discovered fruit fly fat cells produce and secrete a protein called Upd2.

The protein is a nutrient sensor. Upd2 communicates with a fly's

brain to control feeding behavior, growth and nutrient status. It affects the areas in the fly brain that are equivalent to the hypothalamus in flies, a region in the brain that regulates energy balance.

Upd2 is similar to leptin, another nutrient sensor that controls appetite in humans and other vertebrates. Signaling satiety is a primary function of these hormones, also known as adipokines. At the time, it was thought that humans and other mammals were the only organisms that produced a leptin-like protein. This proved fruit flies could be a model organism for the study of nutrient sensing.

In one experiment, Rajan fed flies a diet with 30% more sugar. When a fly's sugar intake increased, so did Upd2. Conversely, Upd2 levels decreased when a fly wasn't fed. The researchers also observed that flies cannot accurately sense their nutrient state when Upd2 production is altered.

“Our motivation in this particular work is to leverage this unexpected conservation between humans and flies to uncover

biological principles that govern how organisms adapt to nutrient flux,” she said.

Most people think of leptin as an obesity signal. However, Rajan believes “we should be thinking about leptin during starvation.”

Studies in flies and mice have shown that adipokine levels drop when an animal doesn't eat. In this starvation state, organisms begin conserving energy. A fly, for instance, won't perform energy-consuming activities, such as laying eggs. This process must happen. Experiments have shown that flies that overproduce Upd2 have a shorter lifespan compared to control flies.

“We don't fully understand how starvation status controls the release of adipokines,” she noted.

When a cell is starving, it begins a nutrient-scavenging process called autophagy. A

protein called Atg8-LC3 plays an important part in the process. Right now, Rajan and her colleagues are trying to identify what happens when this process begins. She hopes to publish

more on Atg8-LC3's role in managing nutrient flux soon.

After her talk, Rajan participated in a brief question and answer session with Dr. Jon Lorsch, director of the National Institute of General Medical Sciences (NIGMS).

In 2021, NIGMS renamed its Director's Early Career Investigator Lecture Series to honor former deputy director Greenberg. The series was established in 2016 to encourage undergraduate students

to pursue careers in biomedical research. The scope has since broadened to include graduate through postdoctoral students and other early-career scientists.

To watch the lecture, visit: <https://www.youtube.com/watch?v=JhzTApI-OBI>. **R**



Fruit fly image generated in DALL.E with prompt “fruit fly in a dark background in Seurat's stylistic representation”

PHOTO: DALL.E

Rosenberg Receives Presidential Medal

NCI Chief of Surgery Dr. Steven Rosenberg received the National Medal of Technology and Innovation on Oct. 24 at a ceremony in the East Room of the White House.

“For this year's recipients, outstanding may be an understatement,” said President Joe Biden in opening remarks, welcoming the distinguished honorees receiving the nation's highest award for science, technology and innovation.

Rosenberg was honored “for transforming the way we treat cancer and advancing our progress toward ending cancer as we know it. By leading the development of the first effective immunotherapies, he has saved countless lives and inspired a generation of scientists. His work powerfully illustrates that we can do big things as Americans.”

Biden thanked the honorees for their courage, perseverance and integrity. “They have paved the way for [future] generations of scientists and innovators to pursue their own discoveries, to unlock our nation's full potential,” he said.

“I've long said America can be defined by a single word...possibilities,” Biden said. Beyond economic and military might, “the strength of a nation is also measured



NCI's Dr. Steven Rosenberg (l) shakes hands with President Joe Biden during the medal ceremony at the White House in October.

by the boldness of its science, the quality of its research and the progress it helps bring forth for not only the country but for the whole world.”

Biden referenced the Cancer Moonshot initiative he launched as vice president and reignited upon becoming president.

“If there's one thing I wish as president I could do, it would be ending cancer as we know it,” he said. “For those who have lost [loved ones] and for the ones we can save, I don't just hope we can do it, I know we can do it. There's nothing beyond our capacity if we set our minds to it and do it together.”



For more on Rosenberg's career, see <https://go.nih.gov/GgAvxoD>.

25-YEAR SCIENTIFIC QUEST Hope Offered for Patients with Rare Disorder

BY TIFFANY CHEN

Seven-year-old Jianna Monchais was an enigma to doctors as an infant. Physicians struggled to explain the large birthmarks across her body and puzzled over why she started menstruating as a baby. Some years earlier, Kelly Cohen had noticed similar birthmarks on her son, Liam, who, by his fifth birthday, had broken his femur—the strongest bone in the body—multiple times.

Jianna and Liam have fibrous dysplasia/McCune Albright Syndrome (FD/MAS), a rare disease of the skeleton, skin and endocrine system. Marked by weak, malformed bones, early puberty and birthmarks, the disease can cause immense pain, disability and diminished quality of life.

Both families found answers and expert care over the years from clinician-scientists at NIH. Recently, several families visited NIH to participate in a symposium “Fibrous Dysplasia/McCune-Albright Syndrome: Celebrating 25 Years of NIDCR Research.”

“I’ve never felt so cared for,” said Jianna’s mother Voncia Monchais, about their first consultation with Dr. Alison Boyce, pediatric endocrinologist at the National Institute of Dental and Craniofacial Research (NIDCR). “Dr. Boyce said, ‘We have this team for her and she’s going to have this team for her life’ and that has brought all the comfort.”

Boyce and her colleagues at NIDCR are world-renowned leaders in FD/MAS research and key members of the NIDCR scientific program that has focused on the disease for 25 years.

As part of NIDCR’s 75th anniversary, the symposium celebrated the program’s legacy and highlights its future. The event featured talks from Nobel Laureate Dr. Brian Kobilka of Stanford University; former Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Dr. Allen Spiegel; FD/MAS scientific leaders; patients; and patient advocates.

Tracing the Root

Spiegel recounted his work on diseases that arise from mutations in a family of proteins called G proteins, and their corresponding receptors, called G-protein-coupled receptors.



Scientists and members of the patient community gathered to celebrate NIDCR’s 25-year legacy of research on fibrous dysplasia/McCune-Albright syndrome.

In 1991, Spiegel’s team at NIDDK found that a mutation in one member of the G protein family — $G\alpha_s$ —causes the skin and hormonal effects of FD/MAS. But, he wondered, does it also cause the skeletal abnormalities, and if so, how? To find out, Spiegel visited NIDCR Bone Stem Cell Biologist Dr. Pamela Robey with a box full of bone samples collected from patients with FD/MAS.

“My first impression when I was looking down the microscope was ‘This is a disease of bone [stem] cells that have gone wild,’” Robey recalled during her presentation. Unlike healthy bone, the diseased bone was disorganized, poorly mineralized and riddled with scar-like fibrous tissue.

Soon after Spiegel’s visit, Robey and her colleagues discovered that the $G\alpha_s$ mutation impairs skeletal stem cells’ ability to develop into mature bone cells. The mutation-carrying cells multiply rapidly and form immature bone that doesn’t quite harden, resulting in weak, breakable regions

throughout. These faulty patches, or lesions, can also expand and press against organs and nerves, impairing vision, hearing and breathing.

Currently, there are no approved drugs to slow or curb the growth of bone lesions.

The Search for a Bone Treatment

Given NIDCR’s expertise in bone biology, Robey saw an opportunity to better understand the skeletal aspects of FD/MAS and develop treatments. Along with NIDCR Endocrinologist Dr.

Michael Collins, she launched a research project called a natural history study to document the nature and progression of the disease.

Since its launch in 1998, the study has enrolled more than 300 patients ages 1 to 102.

Collins explained how the study has revealed that bone lesions tend to develop before age 15, suggesting that an effective treatment, if administered early, may help prevent the most serious impacts of FD/MAS. Results from the study have also led to better standards of care, including showing that certain surgical procedures might be unnecessary and even harmful.

Patients with FD/MAS also have excessive bone turnover,

the process by which old bone is continually replaced with new bone. Dr. Mara Riminucci from Sapienza University, Italy, showed that blocking RANKL, a protein responsible for excessive bone turnover, can prevent the formation of new bone lesions in mice. The study added to evidence that an FDA-approved RANKL-blocking osteoporosis drug called denosumab might hold promise for patients.

Boyce shared how that hypothesis was tested in a recent NIDCR clinical trial. Eight adults with FD/MAS were given denosumab, which markedly reduced abnormal bone turnover—an indication of improved bone quality and strength. Her team is now testing whether early intervention with denosumab in children can prevent FD/MAS lesions from forming in the first place.

Beyond FD/MAS Research

The final speaker, Kobilka, described his Nobel-winning research on the receptor family at the heart of FD/MAS—G-protein-coupled receptors. About half of all approved drugs act on this group of receptors, including antihistamines, antidepressants and opioids.

Citing his research to develop nonaddictive opioids as an example, Kobilka highlighted the progress, challenges and opportunities in G-protein-coupled receptor drug discovery. These principles may help guide the discovery of therapeutic molecules that act on the faulty $G\alpha_s$ protein underlying FD/MAS.

“We move from a place of uncertainty to one of hope, from limited treatment options to a future where personalized therapies are within reach,” said NIDCR Director Dr. Rena D’Souza, who closed out the event. “Fibrous dysplasia/McCune-Albright is no longer an insurmountable challenge but a field ripe with possibilities.”

To watch the event in full, visit <https://videocast.nih.gov/watch=49386>. 



Drs. Michael Collins (l) and Alison Boyce (r) spoke with patient community members (from l to r) Voncia Monchais, Jianna Monchais and Lucy Gerhart about their experiences with FD/MAS.

SEVEN-YEAR CYCLE OF CHANGE

NLM Celebrates Brennan's Contributions to Data-Driven Discovery

BY FELICITY FOX

If you've ever met Dr. Patricia Flatley Brennan, you know she speaks quickly and thinks even quicker. She's swift to innovate and swifter to collaborate—the very embodiment of “accelerate.” And during her time at the National Library of Medicine, she set NLM's trajectory to speed into the future as a leader of biomedical informatics and computational health science research, even well after handing off the baton.

Recently, Brennan gathered with family, colleagues and friends in Natcher Conference Center to celebrate her retirement. As she took to the podium, she acknowledged her inclination to speak fast as well as an important attribute she developed as NLM director.

“Fundamentally, the job of a director at NIH is to learn through listening—whether it's to other colleagues, to the needs of our scholars, our researchers, the public, our investigators,” she said. “Working at the National Library of Medicine has taught me a lot about shutting up and *listening*.”

In September 2016, shortly after she was sworn in as NLM director, Brennan began building on the work of previous trailblazers such as former NLM Director Dr. Donald Lindberg by positioning NLM as a global scientific research library with visible and accessible pathways to universally actionable, meaningful, understandable and useful research and information. Her goal? To prioritize discovering new analytic and data science advances.

“The future will be defined by data,” Brennan predicted at her swearing-in ceremony. As director of the primary source of biomedical data that serves science, research and society, she knew “we need to be ready.”

Brennan's unique experience as the first nurse, industrial engineer and woman named to lead NLM guided her approach to integrate health

information management with artificial intelligence (AI), machine learning and deep learning.

She made enormous progress towards a vision of making NLM the epicenter of data science at NIH. For one, NLM strengthened its literature and data resources, including moving the Sequence Read Archive, the largest publicly available biological database, into commercial cloud platforms. NLM also shared its expertise across NIH, helping colleagues improve systematic data collection, embrace modern approaches to curation and discovery and progress towards interoperability.

Her work never went unnoticed.

“Patti is known throughout the NIH community for her commitment to data science and we have worked to amplify the impact of data science for biomedical and behavioral

research,” said Dr. Susan Gregurick, NIH associate director for data science and director of the Office of Data Science Strategy. “If you have had the opportunity to work with Patti, as I have, you will realize that her commitment to her colleagues is as passionate as her commitment to data science. She is truly an amazing and inspiring leader.”

Brennan developed extraordinary bonds with colleagues, leading to frank conversations around data science, medical informatics, AI and other topics in a rapidly growing, data-centered discovery landscape.

“The most important part about my interactions with Patti have been the honesty and candor,” noted Dr. Lawrence Tabak, then-NIH acting director. “She was honest and secure enough to reach out to me—regardless of what position I was holding—and tell me what she felt I needed to know as opposed to what I wanted to hear. As a result, Patti became a very trusted counselor for me, providing truly significant insight on how to navigate several challenges far beyond the things that the NLM director would need to worry about.”

Her talent for building collaborative relationships extended well beyond NIH; in fact, it was those forged with outside research professionals and organizations that positioned NLM as a global resource for advanced biomedical science, informatics and data-centered research.

“While I'm going to miss your valuable leadership and perspective in interagency contexts and your efforts to bring our agencies closer together to collaborate on a whole host of fronts in data, AI, and beyond—I think NLM and NIH really have

huge shoes to fill on that front—most of all, I am going to miss what a wonderful friend and person you have been in shaping all this work together,” said Dr. Erwin Gianchandani of the Directorate for Technology, Innovation and Partnerships at the National Science Foundation, via video recording. “I'll miss our chats on the margins of meetings, I'll miss the incredible wisdom and advice you've offered, and I'll miss the personal touch that you have brought forth.”

Brennan's attitude also served as “one-NLM” glue.

Dianne Babski, associate director of library operations, said Brennan helped NLM “truly become a united and collaborative team...Patti's emphasis on teamwork, collaboration and open communication has been key to achieving our collective goals. Perhaps one of the most amazing things about her is her ability to bring our organization together.”

Dr. Shannon Zenk, director of the National Institute of Nursing Research (NINR), also spoke to Brennan's NIH-wide collaborations and contributions.

“Patti will be sorely missed at NIH and across the nursing research community, especially for her support and mentoring of women leaders,” she said. NINR hosted Brennan's Advanced Visualization Lab. “We were proud to support her trailblazing research in using cutting-edge technology—including interactive virtual reality simulations—to improve health outcomes.”

“She has placed us on a trajectory to do amazing things,” said Dr. Richard Palmer, acting director of NLM's Division of Extramural Programs. “She has not only changed the culture of an organization, which is not easy; she also helped all of us reach further than we thought we could and achieve more than we ever thought possible.”

Dr. Jeffrey Reznick, chief of the History of Medicine Division, appreciated how Brennan positioned NLM as the steward of globally respected collections and resources for modernized data-driven research.

“This history and the future of NLM as it approaches its third century of public service helps us appreciate the solid progress of NLM thanks to Dr. Brennan's leadership,” Reznick explained.

He presented Brennan with a brick from NLM's previous home on the National Mall. Handed down from generation to generation, the unique artifact remains preserved in the collections of the library.

On announcing her retirement, Brennan said she considered not just her career, but also the entire NLM team.

“Most of all, I'm very proud of NLM's greatest asset—you,” she concluded. “It's been a great honor and privilege to serve NLM all these years and learn from you.”



Dr. Patricia Brennan at Connell School of Nursing in 2017

PHOTO: JUSTIN KNIGHT



Brennan (l) with NLM panel (from l) Dr. Bart Trawick, Joyce Backus and Dr. Mike Huerta at a 2019 Data Science Open House.



Brennan (r) and other NIH leaders with HHS Secretary Becerra (fourth from l) in 2021

PHOTO: CHIA-CHI CHARLIE CHANG

NINDS's Mamounas Retires After 22 Years of Service

BY SHANNON E. GARNETT

After 22 years of federal service at NIH Dr. Laura Mamounas, a program director in the Neurogenetics Cluster of the Division of Neuroscience at the National Institute of Neurological Disorders and Stroke (NINDS), retired from full-time work on Oct. 31.

"I have immensely enjoyed my career at NIH—helping students and junior scientists navigate the NIH system to achieve grant funding and working to advance research progress in neurodevelopmental disorders (NDDs) and autism," said Mamounas. "NINDS is an amazing place to work."

Mamounas earned her undergraduate degree in biology from the University of California, Irvine, in 1979, and her Ph.D. in neuroscience from Stanford University in 1986. Upon completion of postdoctoral training in the department of neuroscience at Johns Hopkins University (JHU) School of Medicine, she continued at JHU as a research associate for several years. From 1993 to 1995, she was a National Institute of Mental Health-funded research scientist at the Neuroscience Center at St. Elizabeth's Hospital in Washington, D.C.

Prior to joining NINDS, Mamounas conducted basic research at the National Institute on Aging's Gerontology Research Center located on the JHU School of Medicine campus and was a JHU faculty member in the division of neuropathology of the department of pathology. There, she directed an NIH-funded research program that investigated the role of neurotrophic factor mechanisms in brain plasticity during neurodevelopment and aging.

"Although I loved my research, I was frustrated with my career prospects and the near-total dependency on obtaining grant funding," Mamounas explained. "One weekend, while revising a grant application (that was not funded), I happened to look at NIH job openings. NINDS had an opening for a program director that fell squarely within my interests and background. On a whim, I decided to apply. I wanted to have a broader impact on neuroscience research."

In 2001, she joined NINDS as a program director in the Neurogenetics Cluster where she managed a portfolio of research grants and programs focused on childhood neurodevelopmental disorders (NDDs). Many NDDs involve rare genetic mutations that are often associated with intellectual disability, autism and epilepsy.

For more than 10 years, Mamounas also helped direct and manage the Undiagnosed Diseases Network (UDN)—a 10-year, \$300 million NIH Common Fund program that recently transitioned to NINDS. And she played a significant role in NIH-supported clinical trials for NDDs including those designed to explore fragile X syndrome and tuberous sclerosis complex.

"It's been very rewarding to work with the patient community and advocacy groups, as well as my NIH colleagues and other federal agencies, in our mutual goal to find a cure for these devastating disorders," she said.

Throughout her career, Mamounas organized or co-developed more than 20 workshops or conferences, chaired or served on many NIH-wide and federal coordinating committees, and authored and co-authored a number of publications and journal articles. Over the years,

her work garnered her numerous accolades and awards, and she was frequently invited to speak at national and international conferences and meetings.

In retirement, Mamounas plans to spend more time with her two grandsons, work on home renovation projects and travel. She also will work part-time as a contractor, starting this month, helping to manage the UDN.

Lei Departs NIGMS Division for Research Capacity Building

Dr. Ming Lei left the National Institute of General Medical Sciences (NIGMS) Division for Research Capacity Building in early August to become senior associate vice president for research and graduate education at West Virginia University (WVU) Health Sciences. He also joined the faculty in WVU's School of Medicine as vice dean for research and professor in the department of microbiology, immunology and cell biology.

Lei had been part of the NIH community since 2008, serving in key positions at the National Cancer Institute before joining NIGMS in 2018.

During his time at NIGMS, he led numerous initiatives to enhance existing programs and to create



Dr. Laura Mamounas



Dr. Ming Lei

new ones, including the Institutional Development Award (IDeA) Regional Entrepreneurship Development Program and expanded opportunities for IDeA states to build capacity for clinical and translational research.

During the Covid-19 pandemic, he created grant programs to support vaccine hesitancy research and variant surveillance studies, and to document patient outcomes in underserved communities.

Additionally, he led NIGMS's participation in the Rapid Acceleration of Diagnostics for Underserved Populations (RADx-UP) program, a \$500 million NIH-wide initiative to understand and reduce morbidity and mortality disparities for vulnerable and underserved populations disproportionately affected by Covid-19. **R**

VOLUNTEERS

EBV Vaccine Trial Recruits

NIAID researchers seek to enroll healthy volunteers ages 18-29 living in D.C., Maryland and Virginia in an investigational Epstein-Barr virus (EBV) vaccine clinical trial. If you are eligible, consider joining to help stop the spread of EBV, the most common cause of infectious mononucleosis (mono) and associated with some cancers. Compensation will be provided, up to \$2,220 over the course of the trial. For more information, contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #21-I-0005. Online: <https://go.usa.gov/xsYK5>.

Severe Aplastic Anemia Study Seeks Volunteers

NHLBI seeks adults with severe aplastic anemia (SAA) for a research study determining viability and safety of early initiation of oral therapy with cyclosporine and eltrombopag in patients with SAA. All patients will receive standard treatment with cyclosporine, eltrombopag and horse antithymocyte globulin (h-ATG) unless there is complete count recovery with oral therapy. Compensation will be provided. For more information, call the Office of Patient Recruitment at 1-866-444-2214 (TTY users dial 711). Refer to study 20-H-0033. Online: <https://go.nih.gov/KnIRlpY>.

Washington Commanders Come for a Visit

Players from the National Football League's Washington Commanders visited the Clinical Center pediatrics unit on Oct. 23, just in time for Halloween festivity planning.

After greeting patients and staff and posing for photos, the players dropped in at the Children's Inn at NIH, where they participated in a fall party and autograph and photo session.

At right, Washington Commanders players (back row, from l) Mason Brooks, Casey Toohill, Efe Obada, James Smith-Williams and Antonio Gibson gather for a photo op with several of the CC nursing staff in the atrium.



At the Clinical Center with several Washington Commanders players are Avery Brink (l) and Natasia Patterson.

PHOTOS: CHIA-CHI CHARLIE CHANG



At left, Commanders defensive ends Smith-Williams (l) and Obada paint pumpkins with families at the inn. At right, Commanders mascot Major Tuddy high fives a child and preps for pumpkin painting.