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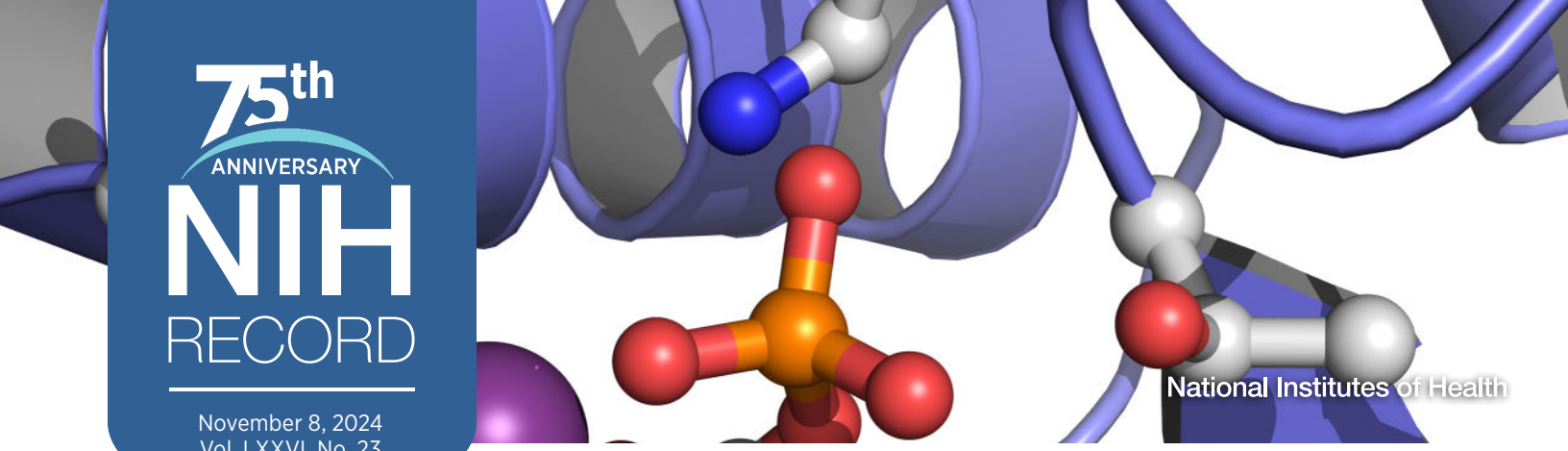


NIH Research Festival Showcases Innovative Science

Exploring the NIH Research Festival

It's the premier event of NIH's Intramural Research Program. As in years past, the 2024 NIH Research Festival spanned several days, featuring lectures, workshops, poster sessions, a vendor expo and a green labs fair.

This year though another event snuck in: a lecture featuring an extramural researcher. It was a first. But organizers concurred that Dr. Manu Prakash's topic—a low-cost scientific innovation that's gone global—captured the spirit of the festival.

Read on about Prakash's invention and another signature talk: Dr. Stephen Whitehead's efforts to develop a dengue vaccine. They are among the many NIH-funded innovations changing the world.

Frugal Science Can Change the World

BY ERIC BOCK

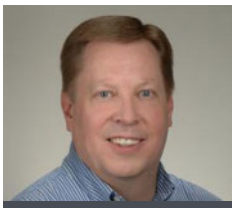
Curiosity is the seed of all science, said Dr. Manu Prakash during a recent Wednesday Afternoon Lecture in Masur Auditorium.

"It's important for us, as scientists, to think about how to share that sense of curiosity we all experience and practice

SEE **PRAKASH**, PAGE 6

Whitehead Recounts Journey to Developing Dengue Vaccine

BY DANA TALESNIK


Dr. Stephen Whitehead

Anyone who lives in, or travels to, areas where dengue fever is prevalent knows the fear of getting bitten by a dengue-carrying mosquito. The dengue virus, spread by a certain mosquito species in tropical climates, can cause severe illness. If not treated properly, it can be deadly.

Dr. Stephen Whitehead has been developing vaccine candidates for dengue and other arboviruses at NIH for 25 years. One of

SEE **VACCINE**, PAGE 4


NIH director gets knighted in Italy. See p. 2.

ALSO THIS ISSUE

SERENDIPITY, SYMBIOSIS STRIKE

Basser Experiences Eureka Moment at NIH Research Festival

BY CARLA GARNETT


Dr. Peter Basser

Dr. Peter Basser's eldest brainchild is an invention that keeps on giving. Now after more than 33 years, new adaptations and applications of diffusion tensor magnetic resonance imaging (DTI) continue to spring forth from myriad scientists and disciplines. Conceived by chance at an NIH Research Festival, DTI serves as the poster child for the ingenuity of NIH's Intramural Research Program.

"As a postdoc, I stumbled on a poster that

SEE **BASSER**, PAGE 5

OUT OF SIGHT

NEI Scientists Publish Cell-Making Recipe for Research

BY DANA TALESNIK


NEI's Dr. Tea Soon Park

Dr. Tea Soon Park and colleagues at the National Eye Institute (NEI) published a step-by-step protocol that uses human induced pluripotent stem cells (iPSCs) to produce key components of capillaries (tiny vessels that carry blood, oxygen and nutrients throughout the body). Now, they're combining these capillary cell types to make tissues to study eye diseases and potential new approaches for treatments.

"Throughout the years, my research has

SEE **PARK**, PAGE 8

Chakrapani to Deliver Stetten Lecture

Nov. 20

The 2024 DeWitt Stetten Jr. Lecture will be held on Wednesday, Nov. 20, from 2 to 3 p.m. ET, in Lipsett Amphitheater, Bldg. 10, and virtually, via videocast. Dr. Sudha Chakrapani will present "Molecular Mechanisms Underlying Glycinergic Neurotransmission."

This NIH Director's Wednesday Afternoon Lecture Series event is sponsored by the National Institute of General Medical Sciences.

Chakrapani is the director of the Cleveland Center for Membrane and Structural Biology and the John H. Hord Professor and Chair of the department of pharmacology at Case Western Reserve University in Cleveland, Ohio. She has dedicated her career to investigating ion channels that mediate fast synaptic transmission at the neuronal and neuromuscular junction.

She will discuss glycine receptors (GlyRs), including the conformational changes they go through based on different factors, their regulation and the potential to develop subtype-specific therapies for various disease states.

GlyRs at the inhibitory synapses in the spinal cord and brainstem are key players in regulating motor and sensory signals. Differential expression of GlyR subunits governs their widely differing physiological functions, ranging from muscle tone and respiratory rhythm to pain mediation. GlyR dysfunctions are associated with epilepsy, chronic pain, addiction and autism. Targeted regulation of specific GlyR subtypes will require a detailed understanding of their structure, function and pharmacology.

Dr. Sudha Chakrapani

Chakrapani's scientific approach combines cutting-edge, multidisciplinary tools that include cryo-electron microscopy (Cryo-EM) and X-ray crystallography for high-resolution structure determination, electron paramagnetic resonance (EPR) spectroscopy for protein dynamic measurements, and electrophysiology for functional characterization of ion channels. These techniques provide an atomic description of how structure and dynamics govern protein functioning.

The lecture series was established in 1982 in honor of NIGMS' third director. Read more about Stetten at https://go.nih.gov/YzlvJUw.

To watch online, go to https://videocast.nih.gov/watch=55010.

People who require sign language interpretation or other reasonable accommodation to participate should email: WALSoffice@od.nih.gov.

Bertagnolli Knighted By the Republic of Italy

Above, NIH Director Dr. Monica Bertagnolli with Her Excellency Mariangela Zappia; below, Bertagnolli, Zappia and former NIAID Director Dr. Anthony Fauci

NIH Director Dr. Monica Bertagnolli received the Knight of the Order of Merit of the Republic of Italy from Mariangela Zappia, the Italian Ambassador to the United States, at the ambassador's residence on Oct. 8.

"I was humbled to recently receive the honor of becoming a Knight of the Order of Merit of the Republic of Italy," Bertagnolli said in a recent Linkedin post. "My paternal grandparents, Alfonso and Maria, immigrated to Wyoming from northern Italy in the early 20th century, eventually settling on the sheep ranch where I grew up. I'm so proud of their courage and that the agency I now lead continues to nurture many valuable collaborations with Italian researchers."

Food and Drug Administration Commissioner Dr. Robert Califf and senior officials from NIH attended the ceremony.

NIAID ClinRegs Updates Its Resource for Clinical Research Professionals

ClinRegs—a free, online database that provides a central resource for country-specific clinical research regulatory information for 23 countries—has added new features to its website.

Recent updates to the site include a tabular dashboard on every country page, providing easy access to new requirements as they are issued, quick facts, current research and sites, and details on profile updates. Also, users can now compare up to four countries side-by-side and filter search results by country and topic.

The website, https://clinregs.niaid.nih.gov/, was first launched by the National Institute of Allergy and Infectious Diseases (NIAID) in 2014.

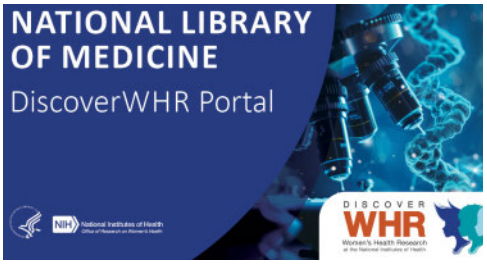
Each country profile has 36 topic areas that are updated at least annually and provide a summary of the applicable requirements and links to official regulatory and ethics guidance documents and forms. In the past year alone, nearly 68,000 users in 166 countries have visited ClinRegs.

To learn more, watch this webinar, recorded earlier this year: bit.ly/4e0zDTM. If you have related questions or comments, email the ClinRegs team at NIAIDClinRegsSupport@mail.nih.gov.

ORWH, NLM Launch Women's Health Portal

The NIH Office of Research on Women's Health (ORWH), in collaboration with the National Library of Medicine (NLM), has launched the first phase of a novel discovery resource for women's health research called DiscoverWHR. This resource enables researchers, health care providers, patients, caregivers and the public to easily find the latest discoveries and current research funded by NIH on topics that affect women's health.

Visit the portal at https://discoverwhr.nih.gov/.



Former NCI Lab Chief Visits Display Featuring Her Work

BY MICHELE LYONS

On Oct. 3, Dr. Jacqueline Jia-Kang Whang-Peng visited the new display in the Clinical Center featuring her work and life and reflected on more than three decades as a researcher at the National Cancer Institute (NCI). Accompanied by family members, NIH scientists, former colleagues and the curatorial staff of the Office of NIH History and Stetten Museum who created the display, Whang-Peng remembered her time as chief of NCI's cytogenetic oncology section from 1960 to 1994. An expert in cytogenetics—the study of chromosomes and their effect on cell behavior—she expanded scientific understanding of many cancers.

Susan Wong (NHLBI/ORS), Dr. Jacqueline Whang-Peng, and Dr. Emily Chin-Hsien Tai (NCI) at the display. Tai arranged the visit and escorted the family. Wong contacted the NIH history office, which set the wheels for the display in motion.

In 1960, the role of chromosome (gene) changes as a cause of cancer was not recognized because no established technique existed yet for observing chromosome changes in the laboratory. Whang-Peng and her mentor Dr. Joe Hin Tjio developed the technique to prepare mammalian cells for chromosomal research, observing and analyzing the chromosomes inside the cell. Their 1962 paper described a "squash" method and an "air-dry" method. One of her first related efforts was to study leukemia in tissue culture.

Whang-Peng quickly became the primary consultant on chromosomal abnormalities and cancer at NIH and collaborated with scientists within NCI—helping to research many different cancers—as well as researchers across NIH and outside the agency.

In 1972, Whang-Peng became one of the first two women to win the Arthur S. Flemming Award, which honors outstanding young federal workers. She was recognized for her chromosomal and leukemia research.

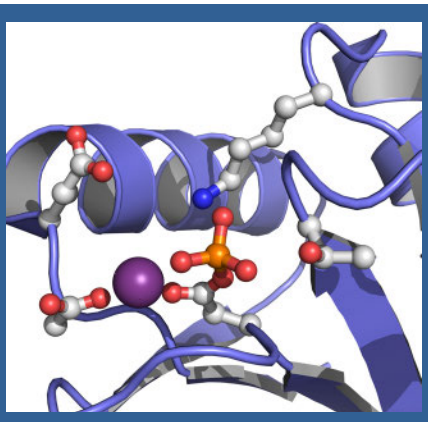
Whang-Peng was born in mainland China in 1932, but in 1949 her family fled to Taiwan to escape the Chinese civil war. She was the first woman trained in surgery at National Taiwan University's Medical College, earning her M.D. in 1956, and the first female surgeon from Taiwan to do an internship in the United States. During her internship at Boston's New England Hospital, the plight of people with cancer inspired her to change her focus, leading to her career at NCI.

After retiring from an over three-decade career at NIH, Whang-Peng returned to Taiwan. A human dynamo, she has had a fruitful second career establishing research programs, training investigators and conducting public education in cancer prevention and treatment. She is now in her early 90s and still working.

In 2008, Whang-Peng added the L'Oréal-UNESCO Award to her long list of honors. She was the first Taiwanese national to receive the award, which celebrates the accomplishments of women scientists.

The display about Whang-Peng is located on the first floor of the NIH Clinical Center, near the entrance to the Bioethics Office.

Whang-Peng, her daughter Sarah Freedman, and her son-in-law Scott Freedman at the display. Sarah Freedman described how her mother would bring home chromosome sheets for the children to help her cut up.



ON THE COVER: *Active site of E. coli response regulator PhoB*

IMAGE: ANN STOCK/RUTGERS UNIVERSITY

The NIH Record

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Turning Discovery Into Health

Vaccine

CONTINUED FROM PAGE 1

those vaccines recently completed a Phase-3 clinical trial in Brazil.

Whitehead, a senior investigator in the Arbovirus Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID), discussed efforts toward developing a dengue vaccine at this year's NIH Research Festival, where he delivered the Philip S. Chen Jr. Distinguished Lecture on Innovation and Technology Transfer.

Some arboviruses (arthropod-borne viruses), such as West Nile and Zika, have short and sporadic outbreaks, making them difficult to study, he said.

"This low disease incidence makes it very difficult to do efficacy trials for vaccines," Whitehead noted. "By the time you have a vaccine candidate ready and proceed to clinical testing, the virus has moved on; it's no longer circulating. But dengue is different."

There are more than 390 million dengue infections each year. The virus is endemic in more than 100 countries. Some 3 billion people live in an area of frequent or sporadic outbreaks across Africa, Central and South America and Asia.

"Dengue is both an established disease and an emerging and re-emerging disease," Whitehead said.

Symptoms of a dengue infection can include fever, vomiting, rash, lethargy and, in more severe cases, shock, hemorrhage and respiratory distress.

"The case fatality is probably less than half a percent, but that is with proper case management," he said.

In developing a vaccine, an envelope protein on the outside of the virus particle is the main target of neutralizing antibody. The challenge, though, is that dengue consists of four different serotypes. A person can get infected with more than one serotype throughout their life.

Exposure to each type elicits antibodies that provide natural immunity. But that can be a double-edged sword.

"Preexisting immunity to one dengue serotype is the greatest risk factor for more severe disease when you get your second infection," Whitehead said. That incoming virus from a different serotype can be bound by antibodies that aren't effectively neutralizing, which ultimately can enhance infection and increase the viral load.

"This is why partial immunity to dengue can be dangerous," he said. Therefore, "we need a vaccine to provide effective tetravalent immunity."

In the streets of Bangkok, millions of adults are walking around immune to all four dengue serotypes due to sequential exposure throughout their lifetime. "This is what natural immunity looks like," Whitehead said. But what about people with no previous exposure? "Can we safely induce this immunity in children?"

Whitehead set out on a long journey to develop a live, attenuated dengue vaccine. Live vaccines tend to induce lifelong immunity, can be highly immunogenic with just one dose and they're cost-effective to produce.

"For live vaccines, infection is required for immune stimulation," Whitehead explained. "For an effective, live, tetravalent vaccine, all four serotype components need to replicate. That's the foundation for developing the NIH vaccine."

Currently, there are two commercially available dengue vaccines. Sanofi's vaccine shows efficacy as high as 93% against serious dengue but it's recommended only for those who have had a previous infection and has not proven effective for certain serotypes. Takeda's vaccine is also not for use in 'dengue-naïve'—haven't previously been infected—children. It too does not effectively protect against all four strains.

"We worked for 25 years, moving hundreds of different virus constructs through preclinical studies, most of them made in the laboratory," Whitehead said. They then put forward the best candidates in monovalent clinical studies.

Whitehead (r) with the lecture's namesake, Dr. Philip S. Chen, Jr., who held multiple positions in NIH's Intramural Research Program over 41 years and had established NIH's Office of Technology Transfer.

"Why our vaccine works is because we went and tested each serotype individually in human Phase-1 trials." That took about a decade. "We wanted to make sure [each] was going to work so we could come up with this final tetravalent formulation."

They conducted 31 different trials to tweak this vaccine. A winning candidate was tested in Thailand and Bangladesh that has proven uniformly immunogenic, even in dengue-naïve subjects; it's safe in older adults up to age 70 and in infants and children. And it's protective as early as 30-days post-vaccination, which is important for protecting those planning to travel to dengue-endemic regions.

The vaccine study in Bangkok showed high antibody responses in children who, prior to vaccination, had little or no immunity. "The immune profile of these children now looks very similar to what you see after natural infection in adults," Whitehead noted. And in adults, "We have 100% protection demonstrated in our controlled human-infection model."

Whitehead discusses technology transfer of NIH's dengue vaccine, which multiple companies are developing in the U.S. and abroad. **PHOTOS: MARLEEN VAN DEN NESTE**

The next step was technology transfer. NIAID licensed this technology—including the patent rights, biological materials and methods, and data to date—to multiple companies to develop in the U.S. and abroad.

The Phase-3 study in Brazil, conducted in more than 16,000 participants at 16 clinical sites across Brazil by Instituto Butantan, showed 88% efficacy overall against severe dengue for two years. After more than three years, a single dose still showed 67% overall efficacy against any severity of dengue, including good protection even among the youngest children. Overall, Whitehead noted, the NIH vaccine outperforms the two others currently on the market.

One caveat is that two of the four serotypes were not circulating in Brazil during the study. Merck, Inc., which would distribute the vaccine in the U.S., China and across Europe, is currently running its own trial and found one dose elicited neutralizing antibodies for all four serotypes.

Another Phase-3 trial began this summer with DengiAll, the brand name of the NIH vaccine produced by Panacea Biotec in India. The trial will enroll 10,000 healthy Indian adults, ages 18-60, at 19 clinical sites. Whitehead expects stellar results from this trial when data becomes available.

"How did we get here? By technology transfer," said Whitehead. "What started on the bench, moved to the bedside and then [we] are moving into implementation."

Basser

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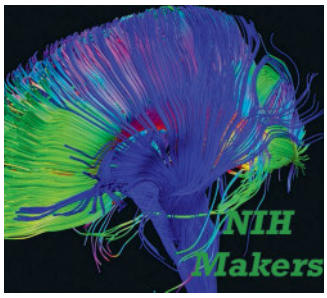


my future colleague, [Dr.] Denis Le Bihan, and his colleagues in Radiology had presented at the 1991 NIH Research Festival...a venue for people in the Intramural Research Program to communicate ideas," recalled Basser, NIH senior investigator and head of NICHD's section on quantitative imaging and tissue sciences. "I wasn't working on nuclear magnetic resonance [NMR] *per se* before that, although I had a patent issued from the late '80s on an NMR method. The invention of DTI was a happy accident. The work that I had been doing in the Biomedical Engineering and Instrumentation Program required high quality *in vivo* data—we had great models to describe important biophysical transport processes, but we needed better data to be able to inform these models."

Now a principal investigator in NICHD's Intramural Research Program, Basser uses noninvasive MRI methods to describe relationships between structure and function in living tissues—how their microstructure, hierarchical organization, composition and material properties affect the way they work...or don't work.

In 2016, Basser (l) traveled with Dr. Carlo Pierpaoli (r), also of NICHD, to Wales to celebrate the opening of the Cardiff University Brain Research Imaging Centre (CUBRIC). Basser's former postdoc and mentee, Dr. Derek Jones (c), was named CUBRIC director. Basser and his lab have been instrumental in developing the field of microstructure imaging.

In 1991, Basser had been at NIH for four years and had already established himself as a "serial inventor." However, many models he and his group were producing leapt ahead of the technology to characterize them.

"Our biophysics-bioengineering models outstripped the methods that were available to provide parameters for them," Basser recalled. "So I stumbled upon MRI as a methodology to fill this gap."

He invented DTI after encountering Le Bihan's group's work while wandering through the back tent of Research Festival. It was serendipity.

Diffusion tensor MRI addresses many problems. In neuroscience, for example—specifically neuroradiology clinical imaging applications—the concept can "better describe and understand the architecture of the brain and how different parts of the brain are connected...the gross wiring diagram of the brain," Basser explained.

DTI also helps neurologists diagnose brain diseases and neurosurgeons navigate procedures.

"Neurosurgeons who are planning operations can use this information to avoid areas so that the patient doesn't leave the surgery blind, or unable to hear or unable to understand language," Basser said.

Radiation oncologists use the technology to kill tumors while sparing important brain areas that would cause disability. "They need to know what areas to avoid, that would leave the patient worse off," Basser pointed out. Developmental biologists use DTI to understand how the brain forms and changes at different stages of life."

Over the next several decades, Basser's invention sprouted a number of other technologies that have become fields in themselves. "Tractography," for example, allows scientists to discover how different areas of the brain are connected to one another, Basser added.

"[DTI] is used to look at the structure of the heart now and not just inside the brain, but also in other tissues and organs in the body to see muscle architecture in the heart and tubule architecture in the kidney," he noted. "It's become a very sensitive indicator of tumor growth, not only in the brain, but in the rest of the body. It's become built into a lot of clinical systems to diagnose cancer, and monitor therapy effectiveness. It's used in a lot of specialties and subspecialties in medicine more and more."

Basser and colleagues have continued to finetune DTI technology, even as dozens of applications for the method in various medical disciplines develop every few years. That it was born in-house on the Bethesda campus is a source of pride for intramural investigators in particular.

"I really feel fortunate that I was in the right place at the right time," Basser concluded. "NIH has been a partner in all of this. Had we not had the Research Festival and had NIH not brought together these diverse groups of scientists, this invention never would have happened here."

Prakash

CONTINUED FROM PAGE 1

with the broadest sets of communities," said Prakash, associate professor of bioengineering, senior fellow at the Woods Institute for the Environment and associate professor, by courtesy, of Oceans and Biology at Stanford University.

His curiosity has taken him around the world. During one of his most recent expeditions, Prakash spent 35 days at sea. While there, he sampled 150 million liters of water.

"It's a lot of water, but it's still a drop in the ocean," Prakash said. And from those millions of liters, he found one single cell that's only been seen once, back in 1898. These expeditions illustrate how little scientists really know once they step outside the lab.

One challenge to expanding a curiosity-driven approach to science is that many parts of the world don't have access to health care and education. Some communities in Madagascar, for instance, are a 12-hour walk from their nearest health clinic. Educational opportunities for children in developing countries are also limited.

"Unless technical tools and technologies reach these communities, we might never tackle these sets of problems," he said.

Prakash's solution to these challenges is what he calls "frugal science," or the practice of using creative methods to achieve scientific goals with limited resources. His lab invents, builds and scales up medical devices as cheaply as possible so amateur and professional scientists can work together.

"I believe we can and have, as a humanity, the capacity to dramatically change the course of our trajectories," he said.

Before starting a new project, he always thinks about how to build access into its design. From his experiences of working in the field, he's learned, "it's very important to understand the context and the sets of challenges and problems." Many of the tools he's designed have been inspired by feedback he received from people who have firsthand knowledge of problems, such as community health workers.

There are many devices Prakash's lab could invent. However, the infrastructure to manufacture these devices at scale doesn't exist in many parts of the world. Manufacturing pipelines must be built from scratch. Recently, they partnered with an airplane engine manufacturer in India to make medical devices.

Fun with Foldscopes around the world

PHOTOS: FOLDSCOPE

"They had never touched a medical device before, but I knew they had the capacity because they were already making a sophisticated device," he said.

A decade ago, Prakash co-invented a paper microscope called a Foldscope that could be manufactured for less than one dollar. This light microscope has a standard magnification of 140x. He then shipped 100,000 Foldscopes around the world.

With this invention, Prakash created a network of amateur scientists from more than 150 countries. Today, more than 2.5 million Foldscope users share what they discover on Microcosmos, Foldscope's online community. They can study organisms that Prakash would never have access to. Roughly 700 papers have been published using data collected from Foldscopes.

"One of the things I've been thinking a lot about is how do we translate the principles we learned using this approach to other products," he said.

For example, he is trying to increase access to diagnostic services, particularly since much of the world doesn't have access to them. Diagnostic services are vital for the prevention, screening, diagnosis, case management, monitoring and treatment of diseases. His lab is currently working on creating a factory in a small box to manufacture diagnostic tests. They have also created a molecular test that only needs hot water to function.

"We like to joke that if you can make a cup of tea, you can do diagnostics," he said.

Malaria is one of the most severe public health problems worldwide. Spread by certain types of mosquitos, it is one of the leading causes of death in developing countries. And yet, "surveillance systems for mosquitos are just absolutely abysmal," Prakash said. His lab developed an app that can quickly identify the species of a mosquito by its buzzing sound.

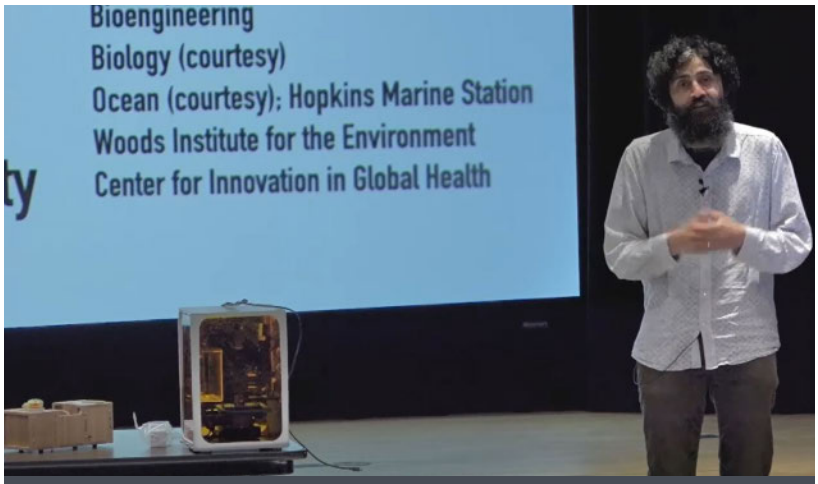
Health workers typically diagnose the disease using a microscopic examination of blood film, a time-consuming process. His lab has devised an alternative method to detecting the disease. They developed Octopi, a low-cost and reconfigurable autonomous microscopy platform capable of automated slide scanning and correlated bright-field and fluorescence imaging. Using machine learning, Octopi can analyze blood samples 120-times faster than a traditional microscope.

"We have so many of these instruments in the field now," he said. "We're starting to collect the largest digital malaria database."

Working with people from all over the world has given Prakash insights he would never have had if he worked alone.

"If you have the chance to engage with broader sets of communities, please do," he concluded.

The full talk is available to view at https://videocast.nih.gov/watch=55005.



Dr. Manu Prakash discusses his innovative research.

EVERY DOLLAR COUNTS

Annual CFC Effort Launches

BY ERIC BOCK

NIH employees work hard every day to advance medical research. "Your work affects the lives of so many," said NIH Director Dr. Monica Bertagnolli during the 2024 Combined Federal Campaign (CFC) virtual kickoff on Oct. 9. "Your generous support of the CFC is another way you can help make the world a better place."

The CFC is the annual workplace fundraising drive among federal employees that serves more than 4,500 charities, said Ila Flannigan, the Clinical Center's (CC) acting executive officer and 2024 CFC campaign manager.

'Give Happy' is this year's theme. "The theme echoes what happens when we give generously to those in need to enrich the quality of life for all," said Flannigan.

While the CC is taking the lead this year, it takes an even bigger team to run a successful CFC campaign. She thanked other institutes, centers and CFC coordinators for their efforts in making the campaign the most successful workplace fundraising program in the world.

Cecelia "Cece" Henry, scientific diversity advisor at the CC and award-winning vocalist and songwriter, opened the program by singing the National Anthem.

CC CEO Dr. James Gilman said he is excited to be co-chairing the 2024 campaign with Bertagnolli because of NIH's strong CFC tradition. Over the past 19 years, NIH employees have contributed more than $2 million during every campaign year.

"While NIH traditionally meets and exceeds our dollar goal, we have another goal this year. That's to increase the number of NIH federal employees who participate in the CFC," Gilman said. "With over 18,000 employees, we encourage each of you to dig deep and consider making a pledge to your favorite charity."

Two CFC charities sent representatives to the kickoff to talk about the campaign's impact on their organizations.

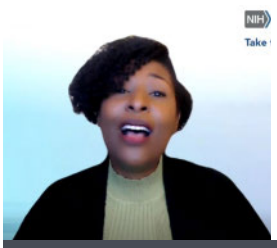
RAINN, a non-profit that carries out programs to prevent sexual violence, help victims and ensure that perpetrators are brought to justice, is one charity that benefits from the CFC, said Zach Larkin, a development associate there. Since its founding 30 years ago, the organization has helped nearly 5 million people.

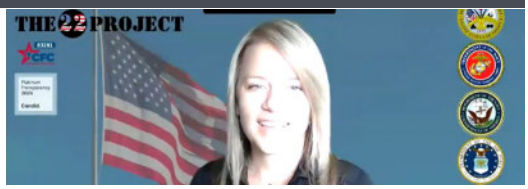
Over the past three years, RAINN's National Sexual Assault Hotline has reduced its average wait time to 3.1 minutes. Through June, the non-profit has helped 54% more people through its victim service program compared to last year.

"We urgently need your support to help RAINN keep up with the increase in sexual assault survivors that are in crisis and needing help," said Larkin.

A representative from the 22 Project also spoke at the kickoff. Since Sept. 11, 2001, more than 2 million military personnel have served in Iraq and Afghanistan. Roughly 10 percent of those who returned have been diagnosed with a traumatic brain injury, said Ashley Williams, executive director at the 22 Project. These injuries are linked to post-traumatic stress disorder and suicidal ideation.

Named after the average of 22 veterans who commit suicide each day, the 22 Project supports veterans in need after receiving the diagnosis of a TBI from a combat tour. Veterans from across the country travel to south Florida, where they receive single-photon emission computed tomography and hyperbaric oxygen therapy.





Above, Cecelia Henry (l) sings National Anthem; CC CEO Dr. James Gilman offers welcoming remarks at the virtual kickoff. Below, Ashley Williams of the 22 Project

"We take care of travel and accommodations," Williams said. "We try to eliminate any potential barriers to veterans being able to receive these treatments."

Concluding the kickoff, Flannigan said, "Your participation today and throughout the campaign will help make a crucial difference in many, many lives." The CFC officially started on Sept. 1 and will end on Jan. 15, 2025. For more information about the campaign, visit https://cfc.nih.gov/.

BATTER UP!

CIT's Night Out at the Ballpark is a Home Run

BY LILY BISSON

The NIH Center for Information Technology (CIT) executive leadership team, along with CIT staff, attended the HHS Night Out at the Ballpark on Sept. 27 at Nationals Park. Dr. Sean Mooney, CIT's new director, recently transplanted to the Washington, D.C. metro area from Washington state earlier this year and was excited to take in his first game in his new city.

CIT Executive Officer Kevin Davis was also excited to share in the game's camaraderie, despite the slower pace of baseball compared to his preferred sport of football. CIT Deputy Director Ivor D'Souza wore his Stone Garrett jersey to the park, which seemed to bring the player good luck as he hit a home run!

Despite intermittent showers, which kept some people away, the park was electric, with fans from across HHS cheering on the home team. That night, the Nats scored 9 runs to beat the Phillies 9-1.

After the game, some CIT staffers stuck around to watch the Lady A concert. A new annual CIT tradition was born, though many staff also would enthusiastically support an HHS Night Out at an NFL game.

(Top, r) CIT Chief Information Security Officer Jothi Dugar; (front row, from l) CIT Director Dr. Sean Mooney, Deputy Director Ivor D'Souza, Executive Officer Kevin Davis

Park

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been closely related to blood vessels and blood progenitor cells," said Park, a scientist in NEI's ocular and stem cell translational research section and lead author of the protocol. "During my postdoc, I studied the inner-retinal blood vessels using iPSC-derived regenerative therapy. Then came the idea of combining cell types to generate vascularized tissues using stem cell-derived cells."

The protocol, published last year, details a system of how to produce three cell types necessary to generate capillary structure: endothelial cells—which line the capillaries; pericytes—which encase endothelial cells and stabilize the capillaries; and fibroblasts—which support and connect tissues. Park's reproducible recipe takes the researcher through the steps to seed, differentiate and separate progenitor cells, and explains how to freeze and thaw them when ready for use.

NEI Research Associate Devika Bose (l) with Park

Led by Drs. Kapil Bharti and Ruchi Sharma, the team is using this process to study tissue in the back of the eye, called the choroid. Dr. Andrea Barabino, a postdoctoral fellow in the lab and Casey Cargill, a postbaccalaureate fellow, are collaborating with Park on 3D-bioprinting technology to make vascularized choroid tissue [made from capillary cells].

The 3D-bioprinted choroid is combined with iPSC-derived functional ocular cells, called retinal pigmented epithelial (RPE) cells. These replicated, lab-made tissues allow researchers to study age-related macular degeneration (AMD) and other eye diseases in which capillary atrophy occurs during the disease progression.

"Our current project focuses on how the wet type of AMD begins, which occurs due to abnormal capillary growth under the macula," Cargill said. AMD, which affects millions of elderly Americans, can lead to vision loss.

AMD "is a disease that's hard to mimic in animal models," Barabino said, because only humans and primates have a macula. "That's why we use human iPSCs to do in vitro modeling."

Cargill explained, "We can use our iPSCs protocol to differentiate cells, make the choroid layer of the eye and mimic this disease."

"One advantage of using iPSCs is we can target specific proteins or genes," noted Park. "When studying AMD, we know the genetic risk factors so we can target those genes in specific cell types. With that, this protocol, will allow us to combine cells with genetic variants and investigate which types of cells are more damaged under stress conditions. That way we can trace back to where the degeneration of the retina is starting from."

Park (r) and fellows Dr. Andrea Barabino (l) and Casey Cargill pose with the bioprinter used to make vascularized tissue of the choroid. It takes about 10 million of combined endothelial cells, fibroblasts and pericytes to make 24 tissues, each 9 mm in diameter. **PHOTOS: DANA TALESNIK**

Park (r) with colleagues at the 2024 Research Festival **PHOTO: MARLEEN VAN DEN NESTE**

It's an intricate system. "If any one cell type is not good in the system, we have to start all over again," noted Devika Bose, an NEI stem-cell research associate who has regularly supplied members in OSCTR with iPSCs for the project.

Another challenge, said Barabino, is that iPS cells can behave differently depending on their donor.

"It takes a lot of work to find the right concentration of all the molecules you want [in a way] that's consistent across all cell lines," he said. "Sometimes you have to change the parameters and tweak them to adapt to the new donor iPS cell line."

Scientists from across the field developed this technology over many years. Bharti and Sharma's group, though, is the first to publish a detailed recipe, based on prior research and their own, so others can reproduce the process.

The procedure also can be expanded beyond studying the eye, added Park. It can be used for any type of organ studies or condition involving the vascular system.

"This work requires close teamwork," she emphasized. "It's always helpful and inspirational to work together, especially on different parts of cells and specialized functions in the eye, because the eye is such a complex organ."

"People in the industry are very interested in this 3D-bioprinted choroid/RPE tissue and want to know if it's possible to make a product," Park said. It might be possible to one day put the choroid and RPE together to make a treatment for late-stage AMD, she noted, but there is still a long way to go.

"I think that's the future," Bose said.

NIH Launches Large Study to Tackle Type 2 Diabetes in Youth

NIH has launched a nationwide consortium to address the dramatic rise in youth diagnosed with type 2 diabetes over the past two decades, a trend that is expected to continue. The effort aims to advance understanding of the biologic, social and environmental drivers of youth-onset type 2 diabetes to help determine which children are at highest risk and how to better prevent, screen for and manage the disease in young people.

A doctor tests a child's blood sugar with a glucometer.

PHOTO: ANDREY POPOV/SHUTTERSTOCK

The observational study builds on previous research indicating that youth-onset type 2 diabetes is more challenging to treat and progresses more aggressively compared to the adult form. In youth with type 2 diabetes, good blood glucose control is harder to achieve, and the ability of the pancreas to secrete insulin declines much more rapidly. Many young people with this disease also don't respond well to metformin, the most common first-line treatment for diabetes in adults. In addition, youth-onset type 2 diabetes is associated with earlier development of diabetes-related complications.

The study will aim to identify unique drivers of the disease to help clinicians better understand risk and guide more effective, targeted prevention and intervention strategies. Study sites across the country will recruit 3,600 participants, ages 9 to 14, who are considered at risk for developing type 2 diabetes, including people from diverse racial and ethnic, socioeconomically disadvantaged and underserved rural populations.

The research team is also seeking input from youth, young adults and parents with lived experience of type 2 diabetes on both study design and conduct.

In addition to looking at biological factors, the study team will gather comprehensive data from participants and their families to understand what social and environmental factors may be adversely contributing to health disparities and poor outcomes among these youth.

First Wave of Covid-19 Increased Risk of Heart Attack, Stroke up to Three Years Later

Covid-19 infection may have significantly increased the risk of heart attack, stroke and death for up to three years among unvaccinated people early in the pandemic when the original SARS-CoV-2 virus strain emerged. The NIH-supporting findings confirm previous research showing an associated higher risk of cardiovascular events after a Covid-19 infection but are the first to suggest the heightened risk might last up to three years following initial infection, at least among people infected in the first wave of the pandemic.

Compared to people with no Covid-19 history, the study found those who developed the virus early in the pandemic had double the risk for cardiovascular events, while those with severe cases had nearly four times the risk. The findings were published in *Arteriosclerosis, Thrombosis, and Vascular Biology.*

The study also showed blood type may increase the risk of heart attack and stroke in patients with severe Covid-19. Researchers found that hospitalization for Covid-19 more than doubled the risk of heart attack or stroke among patients with A, B, or AB blood types, but not in patients with O types.

The researchers analyzed data from 10,000 people enrolled in a biomedical database of European patients, who were ages 40 to 69 at the time of enrollment, including 8,000 who had tested positive for Covid-19 and 2,000 who were hospitalized with severe infection between February and December 2020.

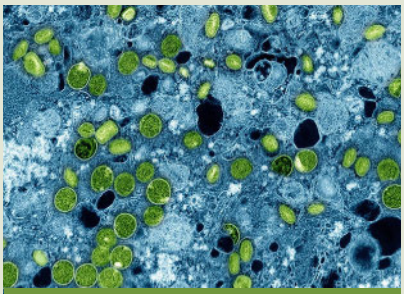
The researchers compared the two Covid-19 subgroups to a group of nearly 218,000 controls. They then tracked the patients from the time of their diagnosis until the development of either heart attack, stroke or death, up to nearly three years.

It is unclear whether the risk of cardiovascular disease is persistent for people who have had severe Covid-19 more recently.

The study was limited due to inclusion of patients from only the UK Biobank, a group that is mostly White. Future studies will be needed to determine whether vaccines influence cardiovascular risk, and on the connection between blood type and Covid-19 infection.

Mpox Vaccine is Safe and Generates Robust Antibody Response in Adolescents

An NIH-funded clinical trial of an mpox vaccine in adolescents found it was safe and generated an antibody response equivalent to that seen in adults, according to a planned interim analysis of study data. Adolescents are among the population groups affected by mpox in the current Clade I mpox outbreak.



Mpox virus particles

CREDIT: NIAID

Two types of the virus that causes mpox have been identified. Clade I is endemic in Central Africa and can cause severe illness. Clade II, endemic in West Africa, caused the global mpox outbreak that began in 2022 and tends to result in milder illness.

People with compromised immune systems, children and pregnant individuals are especially vulnerable to severe mpox regardless of the virus clade. A large proportion of people affected in the current Clade I outbreak in the DRC and other African countries are adolescents and children. The modified vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine is approved in several countries for the prevention of mpox and smallpox in adults, but insufficient data are available to support licensure for people younger than 18.

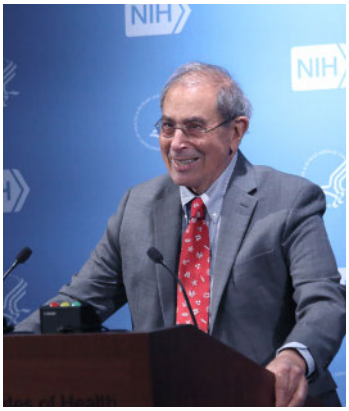
NIAID is sponsoring a mid-stage study in the U.S. to evaluate the safety and immune response generated by two doses of MVA-BN in adolescents aged 12-17 years, comparing outcomes to those in adults aged 18-50 years.

In a planned interim analysis, study investigators measured antibody levels two weeks after the second dose (study day 43) and monitored safety through 180 days after the second dose (study day 210). The analysis showed that the vaccine generated antibody levels in adolescents equivalent to those observed in adults at day 43 and found that the vaccine was well tolerated through study day 210.

The overall frequency of adverse events was comparable between the study groups. Reports of dizziness were more common in adolescents than adults, but similar to the frequency of dizziness reported when other vaccines are administered in adolescents. The authors underscored the need to evaluate the vaccine in younger children.

NIH Mourns Loss of Former CC Director Gallin





Above, Gallin (l) and CC CEO Dr. James Gilman; Smithsonian geologist Dr. Michael Wise hands Gallin a gem at the 2016 "Minerals in Medicine" exhibit; Gallin at podium **PHOTOS: CHIA-CHI CHARLIE CHANG; ERNIE BRANSON**

Dr. John Gallin, the 10th and longest-serving director of the NIH Clinical Center (CC), died at his home on Oct. 10 of multiple myeloma with his wife Dr. Elaine Gallin by his side. He was 81.

Gallin's illustrious career at NIH spanned more than 50 years, but he will be most remembered for leading NIH's research hospital for 23 years from 1994-2017. He often said that his time at the CC was his most special because of the hospital's partnership with patients.

"My father was passionate about NIH's mission and how it has expanded the frontiers of biomedical research," said Gallin's daughter, Alice Gallin-Dwyer. "He was particularly devoted to the Clinical Center and its role helping patients, who often present with few other options, and that is why he called it the 'House of Hope.' He was honored to serve as its director for over two decades."

At Gallin's retirement event last year (from l): longtime CC scientist and Nobel laureate Dr. Harvey Alter, Dr. Elaine Gallin and grandchildren Nathaniel Dwyer, Mitchell (Mick) Dwyer and Miriam (Mira) Dwyer, Gallin, former NIAID Director Anthony Fauci, Alice Gallin-Dwyer and Stephen Dwyer **PHOTO: CHIA-CHI CHARLIE CHANG**

Gallin developed the CC's research portfolio, created the Patient Advisory Group and established the Department of Bioethics. He was instrumental in the creation of the Edmond J. Safra Family Lodge for adult patients and their families, a complement to the Children's Inn at NIH.

He also led efforts to build the addition to the hospital, the Mark O. Hatfield Clinical Research Center, which opened to patients in 2005. He started the Bench-to-Bedside Awards to integrate the work of basic and clinical investigators. His years of work led to the CC receiving the 2011 Lasker-Bloomberg Public Service Award.

One of his greatest passions was training the next generation of clinical researchers. In 1995, he created a curriculum in clinical research that started as a seminar with 15 students and today reaches 25,000 students in 168 countries annually. In 2018, the Gallins personally launched and funded the Trailblazer Prize for Clinician-Scientists at the Foundation for the National Institutes of Health. The prize is awarded to early-career clinician-scientists whose work has the potential to, or has led to, innovations in patient care.

Gallin was born in 1943 in New York City. He graduated from Amherst College and earned his M.D. from Weill Medical College of Cornell University. He then completed his residency at New York University's Bellevue Hospital. He joined NIH in 1971 for postdoctoral training in basic and clinical research in infectious diseases in the National Institute of Allergy and Infectious Diseases (NIAID), where he and his close friend, former NIAID Director Dr. Anthony Fauci, were mentored by Dr. Sheldon "Shelly" Wolff.

In 1976, he became a senior investigator and went on to serve as NIAID's scientific director for intramural research activities and the founding chief of NIAID's Laboratory of Host Defenses. Later in his career, Gallin served as the NIH associate director for clinical research where he oversaw CC independent investigators, clinical research training and the scientific review process for all clinical protocols at the NIH. He also served as the chief scientific officer of the CC where he provided leadership for ongoing research, oversaw the research budget process and developed policies and procedures for the scientific review of all intramural clinical protocols, research funding opportunities and the CC Board of Scientific Counselors. He retired from NIH in March 2023.

Throughout his career, Gallin remained committed to his own research on rare immune disorders of phagocytes, with a focus on chronic granulomatous disease (CGD). His laboratory described the genetic basis for several forms of CGD and other disorders of phagocytes and did pioneering research that has reduced life-threatening bacterial and fungal infections in patients with these disorders. Gallin was a member of the National Academy of Medicine, the Association of American Physicians, the American Society for Clinical Investigation, the American College of Physicians (Master) and the Royal College of Physicians of London.

"John left an incredible legacy that lives on in the important work at the NIH Clinical Center and in generations of clinician-scientists," said NIH Director Dr. Monica Bertagnolli. "On behalf of NIH, I extend our deepest condolence to his wife Elaine, his two children Alice and Michael, and the rest of his family, friends and colleagues. John was a treasure and will be greatly missed."

Symposium Celebrates Rosenberg's 50th Anniversary at NCI

Dr. Steven Rosenberg, chief of the Surgery Branch at the National Cancer Institute, recently celebrated his 50th anniversary with the institute. NCI marked the occasion with a two-day symposium honoring Rosenberg's pioneering work in cellular immunotherapy.

Dr. Steve Rosenberg poses with NIH Director Dr. Monica Bertagnolli, a fellow oncologist, at the symposium.

Speakers at the symposium discussed the development of cell therapy for the treatment of cancer, from early studies to the current state-of-the-art basic, clinical and translational research utilizing T cells, T-cell receptors and chimeric antigen receptors.

"Dr. Rosenberg really wanted to focus on the science of what he has been able to accomplish," said Dr. Stephanie Goff, senior research physician at the Surgery Branch and committee co-chair for the symposium. "So we designed the symposium to have a session that will briefly focus on the initial studies, where we are now, and where we are looking to [for] the future to make cellular therapy better for patients with cancer."

Most of the speakers were either trained in the Surgery Branch or collaborated with the Surgery Branch in important ways. In her speech introducing Rosenberg prior to his lecture, NIH Director Dr. Monica Bertagnolli noted that he has mentored more than 400 trainees over the course of his career.

NCI Director Dr. Kimryn Rathmell presents Rosenberg with award for 50 years of service.

Rosenberg was also presented with a milestone award for 50 years of excellent service to NCI. His revolutionary work in cancer immunotherapy has touched countless lives, inspired researchers and transformed the field.

To read more about Rosenberg's research and career, see: go.nih.gov/zqYfWZu.

Rosenberg (front, 6th from l) poses with colleagues, mentees, friends and family at his 50th anniversary symposium. **PHOTO: CHIA-CHI CHARLIE CHANG**

Biostatistician Honored with Prestigious Mentoring Award

BY SAM TYLER

Dr. Clarice Weinberg received the 2024 Jeanne E. Griffith Mentoring Award—the highest honor of its kind to a statistician in federal, state or local government—in recognition of a mentor's support and development of junior staff. The annual award is presented by the American Statistical Association.

Weinberg, a principal investigator in the Biostatistics and Computational Biology Branch at the National Institute of Environmental Health Sciences, has mentored nearly 40 students and postdoctoral fellows and served on the thesis committees of more than 20 Ph.D. students during her career at NIEHS.

She also has published and worked with biostatistics and epidemiology trainees on nearly 200 scientific articles. These articles explored such topics as reproductive and hormonal risk factors in women, gene-by-environment effects on disease risk, and intimate care products and hormone-related cancers.

"One of her biggest contributions to the growth and development of her trainees is to teach them how to think about a problem by engaging in deep thought-provoking conversations, and working with them to identify and solve important scientific questions," said Dr. Shyamal Peddada, an NIEHS senior investigator who nominated her. "I cannot think of anyone who deserves this award more than Dr. Weinberg."

To read a Q&A with Weinberg about her award and the joy of mentoring junior staff, see: bit.ly/3zQre79.

Dr. Clarice Weinberg
PHOTO: STEVE MCCAW/NIEHS

SAME Tours NIH Construction Sites

PHOTOS: ERIC BOCK

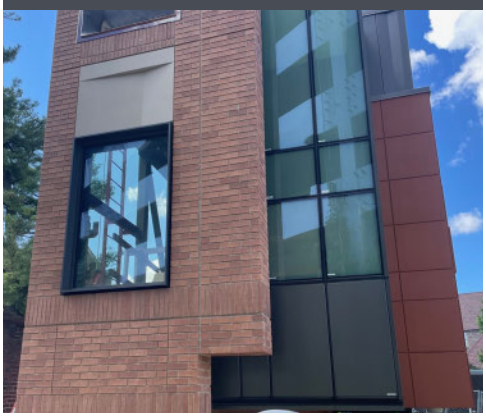
The Society of American Military Engineers (SAME) visited NIH's campus on Oct 3 to get an update and up-close look at several construction sites.

The tour, led by the NIH Office of Research Facilities, began in the Clinical Center's north atrium with a brief presentation about the Surgery, Radiology and Laboratory Medicine (SLRM) wing construction project. Scheduled to open in 2029, the wing will house three departments—perioperative medicine, radiology and imaging sciences, and laboratory medicine—as well as National Cancer Institute and National Heart, Lung and Blood Institute labs and patient service areas.

The tour stopped by several construction sites across NIH's campus, including the SRLM observation platform, Electrical Switching Station and Emergency Generators project, and the Vaccine Research Center laboratory expansion. Members of ORF concluded the tour with an update about future construction projects.

Above, construction for the Clinical Center's surgery, radiology and laboratory medicine (SRLM) tower continues. Currently, workers are building the wing's fourth floor. Below, SAME members gather on the SRLM observation platform, which overlooks the construction site.

Above, Susan Roberts (l), chief of the Planning and Programming Branch in the Office of Research Facilities' Division of Facilities Planning, updates the group about future construction projects. Below is a mock-up for the exterior of the SRLM. Once built, the new wing will blend into the existing red brick building.



Members of the Society of American Military Engineers listen to an update on the Vaccine Research Center laboratory expansion. Once completed, the expansion will double the available laboratory space.