75th ANNIVERSARY
NIH RECORD
November 22, 2024
Vol. LXXVI, No. 24

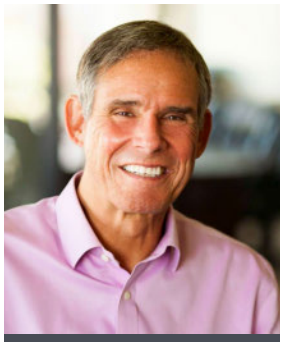
Topol Discusses Potential of AI to Transform Medicine

BY ERIC BOCK

Artificial intelligence (AI) has the potential to shape the future of human health and medicine.

"Machine eyes will see things that humans will never see. It's actually quite extraordinary," said Dr. Eric Topol, executive vice president and professor of molecular medicine at Scripps Research Institute and founder and director of the Scripps Research Translational Institute. He spoke at a recent Contemporary Clinical Medicine: Great Teachers Grand Rounds lecture held in Lipsett Amphitheater.

Advancements in graphics processing units (GPUs) have ushered in a new era of computing. Originally designed for rendering 3D graphics and pixels to display on a screen, GPUs can run many, many operations all at once. This trait makes them highly effective at handling large amounts of data and algorithms required for AI models.


Dr. Eric Topol

A few years ago, medical AI models relied on the availability of labeled datasets to predict outcomes and recognize patterns. Typically, these models were trained using a supervised-learning paradigm, where they learn to map an input—usually a medical image like a chest x-ray—to an output—the prediction of a disease. These models are "unimodal supervised AI."

"We learned from that time that every type of medical scan could get an AI interpretation that would be quite good, comparable and complementary to those from clinicians," Topol said.

In 2019, a New York University study found that a chest X-ray AI tool could catch a cancerous nodule in the lung a radiologist missed. The largest randomized trial using AI to date was for breast cancer detection. He said the study of 80,000 people in Sweden found that AI-assisted reading of mammograms helped doctors detect cancer at faster and higher rates compared to an AI reading or a radiologist alone.

Other studies have shown that AI scans of retinal images can now predict the risk of

SEE **TOPOL**, PAGE 6

EQUITY ON AUTOPILOT

Hightower Discusses Responsible AI in Health Care

BY DANA TALESNIK

Artificial intelligence (AI) tools hold great promise for innovating health care. Algorithms can sift through voluminous data to improve diagnostics, drug development and patient care. Such tools can optimize efficiency and reduce administrative burden, which in turn can lessen clinician burnout and potentially lower health care costs. These applications just scratch the surface of what's possible.


Dr. Maia Hightower

But beware of the darker side of AI. Its

SEE **HIGHTOWER**, PAGE 8

CIT Celebrates 25 Years of NIH's Biowulf Supercomputer

BY ROBERT WAXMAN


Biowulf coolers keep its cores at the appropriate temperature.

The name of NIH's supercomputer—Biowulf—was inspired by the namesake hero of the epic poem, "Beowulf," one of the most important works of old English literature. Beowulf becomes known for his great deeds, like slaying monsters. Biowulf, the supercomputer, isn't quite as old as the poem, but the high-performance computing resource

SEE **BIOWULF**, PAGE 4


Anglican Communion visits. See p. 3.

ALSO THIS ISSUE

NCCIH Symposium to Explore Whole Person Health

Dec. 2

The National Center for Complementary and Integrative Health (NCCIH) will celebrate the conclusion of its 25th anniversary year with a symposium, "Exploring the Impact of Whole Person Health." The event will take place on Monday, Dec. 2, from 1:00 - 4:30 p.m., ET in Lipsett Amphitheater. The symposium will feature NCCIH's annual Stephen E. Straus Distinguished Lecture in the Science of Complementary Therapies delivered by Dr. Patricia Herman, senior behavioral scientist at RAND Corporation and a co-director of the RAND Research Across Complementary and Integrative Health Institutions Center. Herman will speak on the "The Economic Impact of Whole Person Health" and make the case for transforming health care from a disease-centric approach to a whole person model. Herman will illustrate how an investment beginning in early middle age to support a healthy diet, physical activity and stress management can plausibly lead to improved health and well-being, as well as reduced health care spending.

Dr. Patricia Herman

In addition, there will be two sessions considering the impact of real-world models of whole person health care. The first session will feature the team from the University of Vermont Medical Center comprehensive pain program that implemented the unique whole person model of pain care. The second will feature presentations from Dr. Emmeline Edwards, NCCIH's director of extramural research, on the Center's real-world research and Dr. Lyn DeBar of Kaiser Permanente who has conducted pragmatic research on nondrug and other approaches for chronic pain.

This event is partially supported by the Foundation for the National Institutes of Health with a generous gift from Bernard and Barbro Osher. To view the agenda, please visit https://go.nih.gov/LoLoASn.

Clemons to Deliver WALS on Antimicrobial Resistance

Dec. 4

Dr. William M. (Bil) Clemons, Jr. will deliver the first of three NIH Director's Lectures of this Wednesday Afternoon Lecture Series (WALS) season, on Dec. 4 at 2 p.m., ET. His talk, "Mechanisms of Phage-Derived Protein Antibiotic" will be held in Bldg. 10, Lipsett Amphitheater.

Ever adaptable and evolving, pathogenic bacteria continue to outsmart and evade our most powerful antibiotic medicines at an alarming rate, leading to a global health crisis. At the 2024 United Nations General Assembly, HHS Secretary Xavier Becerra stated that 39 million people could die from antibiotic resistance (AMR) in the next 25 years.

One way out of our AMR predicament could be by harnessing the power of bacteriophages, or phages for short, which are specialized viruses that seek out and kill bacteria. Locked in an evolutionary arms race with bacteria, phages have evolved different mechanisms for breaking through the bacterial cell wall and eliminating their host. The Clemons' lab investigates those mechanisms and studies how they might be used in developing new antimicrobial therapeutics.

Clemons is the Arthur and Marian Hanisch Memorial Professor of Biochemistry at the California Institute of Technology, division of chemistry and chemical engineering. He received his Ph.D. from the University of Utah and then spent two years as a visiting scientist at the Laboratory of Molecular Biology in Cambridge, England. There, he was part of the team that solved the first atomic resolution structure of a small ribosomal subunit. This work led to a fundamental understanding of the translation of the genetic code and provided molecular details of the mechanism of a number of antibiotics.

Dr. William Clemons, Jr.

Clemons then took a postdoctoral position at Harvard Medical School. Arriving at Caltech in 2006, the Clemons lab has continued its focus on structurally characterizing important biological systems.

To view the event online, see: at https://videocast.nih.gov/watch=55011. **—Michael Tabasko**

Children's Inn Board Tours CC

The Board of Directors for the Children's Inn at NIH recently toured the National Cancer Institute's Pediatric Oncology Branch (POB) laboratory and the Pediatric Day Hospital in the Clinical Center.

During the tour, the 19 board members visited the lab of Dr. Naomi Taylor, a senior investigator in the POB. Her lab focuses on cancer metabolism, cancer immunology, blood and bone marrow transplantation and gene therapy.

Accompanying the group on the tour were NCI Director Dr. Kimryn Rathmell and Children's Inn CEO Jennie Lucca.

Above r, board members hear from Dr. Naomi Taylor (r) in the pediatric oncology lab.

PHOTOS: CHIA-CHI CHARLIE CHANG

Open Enrollment for the Leave Bank

Fall open enrollment for the NIH Leave Bank has started and runs until Dec. 9. The membership period will begin on Jan. 12.

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 2024 Leave Bank member, your membership will automatically continue into 2025, 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.

Anglican Communion Commissioners Visit NIH

Members of the Anglican Communion Science Commission (ACSC) visited NIH on Oct. 30 to learn about research efforts across the agency.

Reverend Philip Wright (r), bishop of the Diocese of Belize, Church of the Province of the West Indies

The ACSC commissioners include scientists, theologians and church leaders from around the world. Their bishops are nominated by each of the 42 churches that make up the Anglican Communion. According to its website, ACSC supports collaboration between faith and science communities to "bring the ethical voice of faith to scientific discovery."

After a Clinical Center (CC) overview led by CC CEO Dr. James Gilman, the group met with NIH Director Dr. Monica Bertagnolli. They then rotated through several labs: neurorehabilitation, led by CC Senior Investigator Dr. Diane Damiano; pediatric oncology, led by Dr. Troy McEachron, head of the integrated solid tumor biology section at the National Cancer Institute (NCI); cellular and molecular therapeutics led by Dr. John Tisdale, senior investigator at the National Heart, Lung & Blood Institute; and an infectious disease lab, led by Dr. Jeffrey Cohen, chief, medical virology section. CC Nurse Theresa Intrater also took them on a tour of an inpatient unit.

Above, the commissioners split into subgroups and rotated through multiple labs. At right, Dr. John Tisdale (second from r) and a colleague describe advances in sickle cell disease treatment.

Their visit concluded with a briefing on cancer treatment and vaccine research and a discussion on bioethics, led by NCI's Dr. James Gulley, Dr. Richard Koup, deputy director of the Vaccine Research Center and bioethics chief Dr. Christine Grady.

Above l, Dr. James Gulley, director of the medical oncology service at NCI and Dr. Christine Grady, the CC's chief of bioethics, lead a discussion with commissioners in an FAES classroom; at right, NIH Director Dr. Monica Bertagnolli briefs the group. Below, Dr. James Gilman provides a CC overview by the building model in the atrium. **PHOTOS: CHIA-CHI CHARLIE CHANG**

ON THE COVER: *A researcher checks western/moisture blots to know if proteins bind to antibodies.*

PHOTO: NIAID

The NIH Record

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

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

Assistant Editor:
Eric Bock • *Eric.Bock@nih.gov*

Staff Writer:
Amber Snyder • *Amber.Snyder@nih.gov*

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

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

NIH National Institutes of Health
Turning Discovery Into Health

Biowulf

CONTINUED FROM PAGE 1

is celebrating its 25th anniversary this year and it has an impressive history of slaying research questions and enabling scientific research.

In honor of Biowulf's anniversary, the Center for Information Technology's (CIT) High-Performance Computing (HPC) team, who manages Biowulf and provides consulting and scientific support services, hosted a series of seminars throughout the year. The series featured scientists discussing how they use Biowulf in their labs to enable and enhance their research.

The Birth of Biowulf

It started in the 1990s when the size of datasets expanded in fields like genomics, biochemistry and microbiology. Biowulf was created and came online in 1999 as a response to the need to analyze such large amounts of data.

That early version of Biowulf seems humble now, a cluster of 40 "boxes on shelves" with 80 compute cores and two file servers. The fledgling supercomputer had just two applications, 14 users, two dedicated staff members and one citation in a scientific paper.

System Upgrades

Over the years, Biowulf has undergone several expansions. Today, the system has more than 100,000 processing cores, is used in more than 650 labs and has over 2,400 active users. It also has 40 large-memory nodes for memory-intensive projects and 1,050 graphics processing unit processors to handle imaging applications.

In addition, Biowulf's data storage capacity has increased by an astounding 1,000% to 60 petabytes. Between 1999 and 2023, more than 5,000 scientific papers were published citing Biowulf usage. In fact, in 2024, 10.8% of all published papers at NIH acknowledged the use of Biowulf.

A Research Powerhouse

Biowulf has proven itself to be a powerful research tool. It has been ranked among the most powerful supercomputers in the world by the TOP500 project and is the world's most powerful supercomputer dedicated to advancing biomedical research.

During the pandemic, the HPC team prioritized Covid-19-related research on Biowulf. These projects used over 87 million CPU hours with over 2 million jobs run, and the system was cited in more than 50 published, peer-reviewed papers.

In March 2022, the Telomere-to-Telomere (T2T) Consortium—an open, global team of scientists led by National Human Genome Research Institute (NHGRI) researchers—reported they had published the first complete human genome sequence with no gaps. It was a landmark achievement, and Biowulf played a critical role by enabling geneticists to sequence and study areas of the human chromosome that contain highly repetitive DNA that had long been a mystery.

Dr. Adam Phillippy

"Biowulf played two critical roles in that project," noted Dr. Adam Phillippy, head of Genome Informatics Section at NHGRI, during a roundtable discussion at CIT's October Town Hall. "First, it was just the compute power we had at our fingertips...It was not uncommon for my group to run 30 million CPU hours a year on Biowulf when we first joined in 2015, and the ability to run that huge amount of CPU was really critical for us in improving the efficiency and the accuracy of our methods."

Biowulf also played a critical role in the Globus share functionality. Globus is a service on Biowulf that simplifies moving, syncing, and sharing large amounts of data.

Phillippy described how this was important to the T2T project. "We opened our Biowulf partitions as a global share for T2T consortium...and it served as the central data hub for that project. We ended up publishing 8 or 10 companion papers in 2022, when the genome was finished, and that was all enabled by this collaborative analysis and collaborative science with Biowulf and Globus serving as the central data hub for that whole project. It was really transformational in the way we were able to do our work and played a critical role in enabling the success of the T2T project and finishing the human genome."

In 2019, an independent assessment of NIH high-performance computing found that "Biowulf stands out as one of the most scientifically impactful and successful cross-IC efforts at the NIH." The system directly supports almost 70% of research projects at the principal investigator, laboratory and institute/center level.

Recruiter Tool

Statistics show Biowulf attracts talent. Early-career recruits beginning tenure-track

Several of Biowulf's towers **PHOTO: ROBERT WAXMAN**


Dr. Andrew Baxevanis

work at NIH are drawn to the resource and its ability to analyze vast datasets.

Dr. Andy Baxevanis, director of computational biology in the NIH Office of Intramural Research, indicated that Biowulf is seen as a competitive differentiator when trying to attract highly sought after investigators with significant high-performance computing needs. The availability of Biowulf has attracted a number of Stadtman Investigator recruitments, the Intramural Research Program's premier faculty recruitment effort intended to bring preeminent researchers to NIH.

"We're extremely encouraged by the number of researchers who want to use Biowulf," said Baxevanis. "High-performance computing is a critical element of modern-day biomedical research, and Biowulf is uniquely positioned to help [NIH investigators] tackle crucial research questions that were previously beyond our reach."

Expert Staff

One of Biowulf's unique assets is the staff that manages the system. The HPC team not only supports the system's hardware and software, but they also help researchers get the most out of the system by providing classes, seminars and walk-in consultations.

The team has the technical and scientific knowledge to handle various concerns, from scripting problems to node allocation to strategies for a particular project. They are dedicated staff and the secret sauce that makes Biowulf a world-class tool for biomedical research.

Looking Ahead

Biowulf is poised to continue its role empowering research for the NIH intramural research community and developing new offerings, such as support for personally identifiable information and personal health information on the HPC systems, which several HPC customers have requested.

For details about Biowulf, including how to get an account, see: https://hpc.nih.gov/docs/accounts.html.

NIBIB Researcher Named to TIME100 Next List

BY JONATHAN GRIFFIN

These days, many medical advances result from collaboration between clinicians, scientists and engineers. As disciplines become increasingly intertwined, the ability to navigate partnerships across fields will only become more essential. Few are perhaps better suited for this future than Dr. Kaitlyn Sadtler.

A bioengineer at the National Institute of Biomedical Imaging and Bioengineering (NIBIB), Sadtler has flourished as a leader of many impactful, interdisciplinary studies. For her role in shaping the future of medical research, *TIME* magazine named her to the TIME100 Next 2024 List.


NIBIB's Dr. Kaitlyn Sadtler named to the TIME100 Next list

PHOTO: CHIA-CHI CHARLIE CHANG

Sadtler got her start in science with immunology and eventually became well versed in regenerative medicine and materials science. The NIBIB lab Sadtler oversees, the Section on Immunoengineering, operates at the crossing of these subjects, examining the immune system's response to medical devices and its role in wound healing.

Her work has revealed mechanisms by which certain medical devices steer the immune system toward wound healing while others trigger inflammation and scarring. The findings could be instrumental in designing medical technology that is safer and longer lasting in the body.

In 2020, Sadtler pivoted her focus to the spread of Covid-19. She took charge of a team that established methods for accurate lab-based serology testing and then analyzed samples from more than 9,000 people, gaining insights into undiagnosed infections across the country.

To answer complex research questions, Sadtler has worked side-by-side with engineers, biologists, chemists and surgeons. Her success stems not only from her interest in science but also her passion for communication.

"Dissemination is a huge part of doing science. It's needed to build public trust but also to reach potential collaborators in other fields that could bring a new perspective to the table," Sadtler said.

Opportunities for formal science communication training as a student were sparse for Sadtler, so she practiced by explaining her studies to friends and family. Then, while a postdoctoral fellow, she applied for an opportunity to grow as a communicator and explain science to a broader audience.

In 2018, Sadtler became a TED Fellow and delivered a talk covering her discovery of the critical role a specific kind of immune cell played in muscle regeneration.

She received coaching from professionals on strategies to convey complex subjects, such as the use of plain language, comparisons to familiar ideas, and structuring a message into a story—skills she continues to use even when communicating with scientists.

A key part of her skillset is knowing her audience.

For example, during the pandemic, she led teams of engineers, clinicians and mathematicians, all of whom brought forth their own terms and methodologies. She worked to familiarize herself with new ideas and convey her own to establish a common language.

When communicating with the public, Sadtler tries to avoid common pitfalls such as overselling new technologies to an eager public. She recalls a time, close to the turn of the century, when regenerative medicine was spoken of as a cure-all solution.

"In reality, science takes time and lots of trial and error," she said.

Now, decades later, she believes regenerative medicine is headed in the right direction by integrating ideas and people from diverse fields and backgrounds.

Topol

CONTINUED FROM PAGE 1

many conditions, including diabetes, high blood pressure, kidney, liver and gall bladder diseases, coronary artery disease, heart attack, stroke, hyperlipidemia, Alzheimer's and Parkinson's.

Topol during the Q&A after his lecture

"Who would've ever thought that through the retina—the gateway to the human body—we could detect all of these things," Topol said.

There are many randomized, controlled trials evaluating AI in clinical practices, he said. The largest proportion of these studies takes place in gastroenterology. There are almost 1,000 Food and Drug Administration-approved AI models. Few of these models, however, are in use.

Since the emergence of the AI chatbot ChatGPT in late 2022, more and more AI models are "multimodal self-supervised." Topol said these models "learn from themselves, rather than requiring annotations by experts." They can handle various data types, such as text, images and audio.

The latest version of ChatGPT has more than one trillion parameters, or connections, and requires more than 24,000 GPUs. Topol said training these models on data can cost millions of dollars because of the massive amount of data needed.

Despite these limitations, the development of multi-modal self-supervised AI is setting up new applications in health care and medicine. For instance, the newest AI models for cancer prognosis and detection can predict the diagnosis, including the genetic mutations involved, and the prognosis.

There are many stories where patients asked chatbots for help with their diagnosis. In one case, a boy with chronic pain saw 17 doctors in three years. No doctor could diagnose him. Finally, his mother asked ChatGPT about her son's symptoms. Within seconds, the chatbot suggested a diagnosis of spina bifida occulta. A neurosurgeon confirmed the diagnosis.

During appointments with patients, he said doctors of all specialties often spend so much time taking notes and compiling data that they don't have the time to ask patients questions or conduct adequate physical exams.

"This is not the right type of medicine that we want to practice," he said. "We want to have presence, trust and a bond that's ameliorated and built upon during a visit."

Many healthcare systems across the country now use AI dictation programs to help doctors with administrative tasks, including note-taking, prescription refills and billing.

> *"Machine eyes will see things that humans will never see. It's actually quite extraordinary."*
>
> -DR. ERIC TOPOL

Doctors must be aware of the downsides of adopting AI technologies, Topol said. The models can generate incorrect or misleading results. These are called AI hallucinations or confabulations. Also, AI models can produce results that reflect human bias. And, finally, some clinicians believe AI could replace them (It won't, Topol noted).

In the future, physicians will be able to use AI to forecast a patient's individual risk for many types of diseases, he said. Right now, pancreatic cancer is almost always diagnosed late, when it has progressed to stage three or four. Studies have shown that these models can be trained to detect the cancer years before it manifests.

"This is a really exciting time in medicine," he concluded. "We've never had this opportunity before."

NIH OCPL's Myles Gets Permanent Post

On Nov. 7, NIH Director Dr. Monica Bertagnolli announced the selection of Renate Myles as the permanent NIH associate director for communications and public liaison and director of the NIH Office of Communications and Public Liaison (OCPL). She previously had been acting in this role for the past three and a half years.

Renate Myles

In a message to OCPL staff, Myles wrote, "It has been a privilege to lead this office and work alongside such a talented group of people who are passionate about communicating the important work of NIH." Going forward, she added, "I feel confident OCPL will continue to deliver and be recognized for our quality work, commitment to the NIH mission, and dedication to ensuring clear, effective communications with our audiences."

The director's statement about this selection can be found here: go.nih.gov/hFSGDIO.

VOLUNTEERS

Volunteers Needed for PFAPA Study

Do you or your child experience recurring fever, mouth sores (canker sores), sore throat and swollen neck glands? These could be symptoms of PFAPA, the most common periodic fever syndrome in children.

Dr. Kalpana Manthiram and her team at the National Institute of Allergy and Infectious Diseases (NIAID) seek volunteers who are one month old and older (parental consent required for minors) to participate in a research study to better understand PFAPA. Compensation is provided.

Participants can join from home, from anywhere in the world. For more information, contact the NIH Clinical Center Office of Patient Recruitment at 866-444-2214 (TTY users dial 7-1-1) or ccopr@nih.gov. Refer to NIH study #001043-I go.nih.gov/L29b0aX.

'THE METHUSELAH OF BLDG. 1'

Meet NIH's Chief of Staff

BY DANA TALESNIK

John Burklow

Have you seen this man around campus? It's likely. He can often be spotted accompanying NIH leaders to meetings and events.

For 25 years, John Burklow has been an indispensable part of communications and planning at NIH. Most recently, after nearly three years as acting chief, Burklow was appointed as the permanent chief of staff to the NIH director in December 2023.

"I am so very lucky to have John in the chief of staff role," said NIH Director Dr. Monica Bertagnolli. "He has a comprehensive knowledge of how NIH works, and he thinks about how to serve not just the Office of the Director, but all of NIH. And, he's a master at the three-dimensional chess that is sometimes required to accomplish important work."

Burklow came to NIH 38 years ago as an intern in the National Cancer Institute's (NCI) communications office. "I thought I'd stay six months," he said.

An opportunity early on shaped his career path. Burklow became deputy to the late Paul van Nevel, who headed cancer communications. "That's where I learned more about the world of media and public affairs," Burklow recounted. "Paul was so talented and fun to work for, and he always had bold ideas."

In 1999, Burklow began climbing the communications ladder when he became deputy associate director of communications in the NIH Office of Communications and Public Liaison (OCPL). When the head of OCPL left in 2002, he became acting associate director for communications. But when then-NIH Director Dr. Elias Zerhouni made that job a senior executive service position, Burklow found himself competing with several communications bigwigs across government.

"I thought, 'Wow, he's really trying to find somebody else,'" Burklow quipped. "But I was happy that he selected me."

Ever since, it's been a whirlwind of managing all kinds of issues big and small, while delicately balancing competing personalities and priorities. The Zerhouni years prepared Burklow well. Together, they navigated a lengthy conflicts-of-interest controversy, which eventually paved the way for the robust ethics program at NIH today. They also navigated proposed restrictions on stem cell research.

By the time Dr. Francis Collins became NIH director in 2009, Burklow was well-seasoned at coping with complex issues.

In that first month alone, Collins made a music video with the guitarist of Aerosmith, appeared on Stephen Colbert's show, had articles appear in *Science* and *Parade*, welcomed President Barack Obama to campus and hosted a Town Hall. "It just sped up from there," remembered Burklow.

Burklow (l) with NIH Director Dr. Monica Bertagnolli at a 2023 Advisory Committee to the NIH Director (ACD) meeting

PHOTO: MARLEEN VAN DEN NESTE

The job has repeatedly tested Burklow's ability to come through in a pinch. Burklow recalled one instance in 2013 while en route to *The Colbert Report* studio, where Collins was set to talk about the BRAIN Initiative. Burkow had to scramble for footage of somebody's—anybody's—brain waves. Colbert would wear an EEG cap and expected to show his audience what brain waves look like. Burklow understood the power of a visual reference and came through.

A year later, on the day His Holiness the Dalai Lama was set to give a lecture on campus with no seats to spare, Burklow was asked if he could accommodate 800 Tibetans who traveled from New York to witness the event.

"I had 90 minutes before they were going to arrive," he said. "I called for all hands on deck and we made it happen." The Tibetans

Burklow (r) performing with former NIH Director Dr. Francis Collins at Dr. Elias Zerhouni's farewell event in 2008

met with His Holiness, entering and exiting from one side of the Natcher Conference Center, while nearly 1,000 NIH'ers entered the auditorium from the opposite side.

"The Dalai Lama is considered a supreme being on Earth," said Burklow, who was grateful to accommodate their visit. "It was quite important for the Tibetans to feel his presence."

Burklow said his busiest, most challenging year was 2020. As communications director during the first year of the pandemic, he and his team were immersed in internal and external communications seemingly around the clock, while dealing with all the changes that come during an election.

"I look at the job as anything and everything," he said, "whatever needs to be done. No job is too big or too small. And, since I'm the Methuselah of Bldg. 1, I can draw on my experience and offer my opinion on various issues."

Every day, Burklow works closely with Bertagnolli to help achieve her priorities. Staff from the Immediate Office of the Director, the Ombuds and Executive Secretariat offices all report to him. A typical day—if there is such a thing—involves working with people from all functions and ranks across NIH, from communications to legislative, intramural to extramural, facilities to IT.

Through the ups and downs, Burklow finds his job endlessly rewarding. "You feel like you're helping to advance the mission of NIH and that's what's kept me here for 38 years," he said. "I'm proud of what we've accomplished and what we're trying to achieve."

Hightower

CONTINUED FROM PAGE 1

tools, methods and the data itself can have unintended consequences, noted Dr. Maia Hightower, a physician and former executive vice president and chief digital transformation officer at the University of Chicago Medicine and former chief medical information officer at the University of Utah Health. Earlier this year, she spoke at the National Library of Medicine (NLM) Joseph Leiter lecture, co-sponsored by the Medical Library Association.

"There's this real concern that AI systems can perpetuate bias based on the datasets they're trained on, the decisions that are made along the development process all the way to the way an AI system is deployed into a care delivery system workflow," Hightower said. "AI can perpetuate and amplify bias that already exists."

While formulating AI strategy, consider the quality and sources of data and whether the sample is representative of the target population, she advised.

"Real-world data has real-world bias," said Hightower, who also is CEO and co-founder of Equality AI. "Bias starts in the moment of data creation."

Who is formulating the questions and deciding what problems to solve? Is data stratified by demographics to ensure accuracy? Is the model fair across subpopulations?

"You can have the perfectly devised model and then you deploy it into an imperfect world," Hightower said.

An ongoing dilemma in AI is "the human in the loop versus autopilot," she said. AI should complement human expertise, not replace it, she said. "How do we ensure... we're not becoming overly reliant on an automated system or a system that has not yet earned that trust?"

Setting standards and guidelines can help. Hightower said regulations are moving fast in the AI space, but in some ways not fast enough, when it comes to intellectual property, data privacy and algorithmic bias.

Hightower cited a study—(Obermeyer et al.) published in 2019—that found racial bias in an AI model deployed in hundreds of health systems around the country, among an estimated 80 million patients. The study

Hightower (l) chats with acting NLM Director Dr. Stephen Sherry, who moderated the lecture.

revealed that, due to the algorithm's bias, Black patients were 62% less likely to be referred to case management despite being equally sick, leading to a significant underestimation of their health care needs.

"When that model was released, I was chief population health officer at a large health system," Hightower said. "This model most likely was deployed in my health system and I didn't have the tools to measure or mitigate it." Developers ultimately fixed the model.

In a systematic review on the impact of health care algorithms on racial and ethnic disparities conducted by the Agency for Healthcare Research and Quality (AHRQ) and NIH, published in 2024, only 63 studies met inclusion criteria out of more than 13,000 citations. Inclusion criteria required measuring stratified performance or outcomes by demographic groups, which is a key requirement for assessing the impact on health disparities. While some of these algorithms perpetuated health disparities, a few decreased health inequities by design.

To Hightower, these results revealed that, "when intentful, AI algorithms can decrease health disparities. But the biggest travesty is that most did not even measure stratified performance, let alone the effect on outcomes."

Nearly 80% of health equity leaders report that they're not involved in their organization's AI strategy.

"Often you'll have your AI strategy on one pillar and your health equity on another pillar, and the two don't meet," said Hightower, emphasizing the need for the two to come together.

"When AI investments are not aligned with health equity goals, this limits AI's transformative potential," she said.

The solution has its own equation: validate, audit and monitor.

A technical audit evaluates performance and can be stratified by population—race, gender, age, disability, among the possible variables. If the model is flawed, consider what inputs could build a better one.

"There are a lot of different ways of rectifying your model, and then recycling it through this whole process," Hightower said.

Librarians, contributors to NLM and staff all can contribute to responsible AI by ensuring AI research is transparent, reproducible and accessible. Science librarians, and all science communicators, play a critical role in translating digital literacy to patients, practitioners and the public.

"We're going to need that in this new AI world," Hightower said. "We need to give the broader community the resources to thrive in AI decision-making."

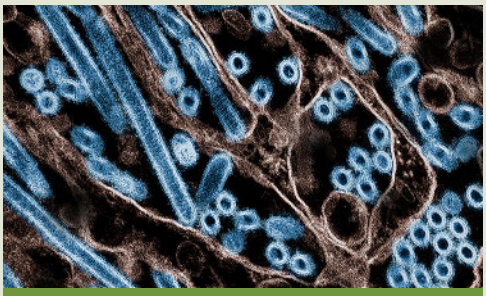
Institutions must be held accountable for the AI systems they deploy, and patients must demand accountability, she emphasized. "Some of the most interesting ways of driving change have come from patient advocates who made visible vulnerabilities that really put patient privacy and safety at risk, and then advocated for responsible AI."

When designing machine-learning models, she urged developers to "have subpopulations in mind, test thoroughly, listen to stakeholders, adopt new methods."

Equity gaps can drive innovation. To health equity advocates, Hightower advised, "when you have that seat at the table, make sure you're expanding that seat to others, including diverse community voices, and recognizing who is missing."

Clinicians also should be involved in AI development and speak up about concerns, she said. Doing so ensures that, as the field of AI forges ahead, clinicians and others in health care remain humans in the loop.

Bovine H5N1 Influenza from Infected Worker Transmissible and Lethal in Animal Models



Colorized transmission electron micrograph of avian influenza A H5N1 virus particles (blue), grown in Madin-Darby Canine Kidney (MDCK) epithelial cells **IMAGE: CDC AND NIAID**

A highly pathogenic avian influenza (HPAI) H5N1 virus, isolated from the eye of a farm worker who became infected through contact with dairy cows, was lethal in mice and ferrets according to a new study in *Nature*. The study investigators also found that the virus isolated from the worker, who experienced mild inflammation of the cornea (conjunctivitis), could be transmitted through the air between separated ferrets and might be capable of binding to and replicating in human respiratory tract cells.

The virus isolated from the worker is called huTX37-H5N1 and has a mutation (PB2-E627K) frequently seen in avian influenza viruses that replicate in mammals, typically making virus replication more efficient. These mutations underscore the need for continued monitoring and evaluation of viruses from the current H5N1 outbreak.

Investigators found huTX37-H5N1 replicated in human cornea and lung cells and also infected each of 15 different mouse tissues tested, with the highest virus levels found in respiratory tissues.

Researchers infected ferrets with a high dose of huTX37-H5N1. Flu infections in ferrets more closely resemble human flu infections than those in mice. All infected ferrets died within 5 days and scientists found huTX37-H5N1 virus in all the tissues sampled, with high levels in the respiratory system.

To evaluate respiratory transmission, the scientists placed healthy ferrets in cages next to ferrets infected one day earlier with one of four decreasing doses of huTX37-H5N1. All directly infected ferrets died within 6 days and between 17% and 33% of the nearby animals became infected via respiratory droplet transmission.

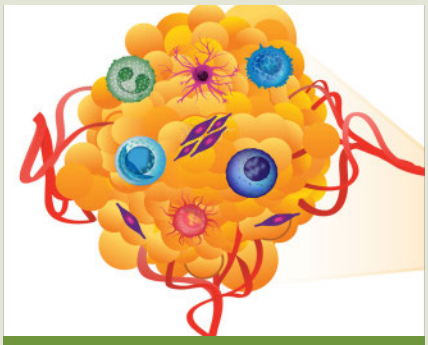
The person infected with the huTX37-H5N1 virus did not develop severe illness. In fact, human cases reported from the current outbreak have mostly experienced conjunctivitis and/or mild respiratory symptoms. Multiple exposures to seasonal human influenza viruses, they say, might provide people with low levels of protection against currently circulating HPAI H5N1 viruses—though additional study is needed.

NIH-Funded Scientists Uncover Clues to Precancer, Tumor Biology

New insights from multiple studies provide critical information on how cancer tumors develop, spread and respond to treatments. The 10 studies from the Human Tumor Atlas Network (HTAN), an NIH-funded Cancer Moonshot initiative to construct three-dimensional maps of human tumors, was published Oct. 31 across several *Nature* journals.

Several studies explore the role of the tumor microenvironment and the immune system in promoting the spread of cancer and its resistance to treatment. Three studies map the trajectory of precancerous colorectal tissues toward cancer by measuring the contributions of multiple molecular and cellular events. Multiple new HTAN papers describe the development of innovative single-cell technology and analysis platforms.

An accompanying research briefing by National Cancer Institute (NCI) Director Dr. Kimryn Rathmell and Dr. Dinah Singer, NCI deputy director for scientific strategy and development, discusses the history, progress and future of HTAN.



The Human Tumor Atlas Network seeks to understand the molecular features of tumors and their microenvironments.

IMAGE: NCI

Launched in 2018, HTAN constructs 3D-maps of human tumors that capture their molecular features and surrounding microenvironments over time. The work is being done by teams of investigators from research institutions across the country using a variety of technologies and computational approaches to study tumors at the single-cell level. This comprehensive, publicly available resource aims to help researchers better understand the development and progression of cancer to inform its prevention and treatment. The first tumor atlas studies from this initiative were published in 2020 and 2021.

Adopting Pediatric Readiness Standards Could Save Thousands of Lives

PHOTO: MONKEY BUSINESS IMAGES/SHUTTERSTOCK

Widespread adoption of standards designed to improve care for children in U.S. hospital emergency departments could save more than 2,000 lives each year, suggests an NIH-funded study. The standards are published by The National Pediatric Readiness Project, an initiative to empower all emergency departments to provide effective emergency care to children, and encompass training for staff, coordination of health care, and the procedures and medical equipment needed to care for ill and injured children. According to the study, adopting the standards would range from no cost to $11.84 per child, depending on the state.

The researchers analyzed data on the readiness standards of 4,840 hospital emergency departments in all 50 U.S. states and the District of Columbia. Their analysis included data on children ranging from birth to 17-years-old who needed emergency services, hospitalization, transfer to another hospital or who had died in the emergency department.

A total of 842 emergency departments (17%) had high pediatric readiness. Based on the cost of emergency department services, the researchers estimated that the annual cost for all U.S. emergency departments to reach high readiness was more than $207 million. The authors concluded that implementing the standards in all U.S. emergency departments may have prevented an estimated 2,143 (28.1%) of the 7,619 U.S. pediatric deaths that occur in emergency departments or following admission to emergency departments each year.

The study was led by Dr. Craig D. Newgard of Oregon Health & Science University, Portland. It appears in *JAMA Network Open*. Funding was provided by NIH's *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD).

Seven NIH Scientists Named to National Academy of Medicine

The National Academy of Medicine (NAM) recently announced election of 100 new members, including seven NIH'ers. Election to the academy is one of the highest honors in health and medicine, recognizing individuals who have demonstrated outstanding professional achievement and commitment to service.

"This class of new members represents the most exceptional researchers and leaders in health and medicine, who have made significant breakthroughs, led the response to major public health challenges and advanced health equity," said NAM President Victor J. Dzau. "Their expertise will be necessary to supporting NAM's work to address the pressing health and scientific challenges we face today."

Current members elect new members through a process that recognizes individuals who have made major contributions to the advancement of the medical sciences, health care and public health. The newly elected members bring NAM's total membership to more than 2,400, which includes nearly 200 international members.

NIH'ers recently elected to NAM and their election citations are:

Dr. Stephen J. Chanock, director of the National Cancer Institute's Division of Cancer Epidemiology and Genetics. For being an international leader in cancer genetics, identifying susceptibility alleles in more than a dozen cancers. He has awards for first describing clonal mosaicism and its relationship to cancer and aging. He created and fostered international consortia on BRCA genetics and Covid-19.

Dr. Janine Clayton, director of the Office of Research on Women's Health. For advancing policy, program, and practice innovations to improve the health of all women by catalyzing integration of sex/gender factors across the biomedical research continuum to galvanize discovery and equity. She is the architect of NIH's high-impact 2016 Sex as a Biological Variable policy, a landmark upgrade for research.

Above, (from l), Dr. Niki Moutsopoulos, Dr. Stephen Chanock, Dr. Nina Schor, Dr. Janine Clayton
Below, (from l), Dr. Avindra Nath, Dr. Jeanne Marrazzo and Dr. Lindsey Criswell

Dr. Lindsey A. Criswell, director, National Institute of Arthritis and Musculoskeletal and Skin Diseases, For defining genetic and epigenetic contributions to development of autoimmune rheumatic disorders and their relationship to specific serologic and clinical phenotypes and to genetic ancestry of patients. Her work has transformed understanding of the pathogenesis of lupus, rheumatoid arthritis, Sjögren's disease, and related diseases.

Dr. Jeanne Marrazzo, director, National Institute of Allergy and Infectious Diseases. For leading transformative research that has redefined our understanding of relationships between the vaginal microbiome and female reproductive tract infections, HIV pre-exposure prophylaxis (PrEP), hormonal contraception, and risk of STI/HIV acquisition. She has had key roles in NIH-funded networks — Infectious Diseases Clinical Research Consortium and HIV Prevention Trials.

Dr. Niki Moutsopoulos, senior investigator, National Institute of Dental and Craniofacial Research. For making seminal contributions toward understanding and treating the prevalent human oral disease periodontitis. Her laboratory has contributed to the understanding of both homeostatic and pathogenic inflammation in the oral cavity, informing interventions for both rare and common forms of aggressive forms of periodontal disease.

Dr. Avindra Nath, clinical director at the National Institute of Neurological Disorders and Stroke. For pioneering research and strong leadership in emerging and persistent infections of the nervous system by studying pathophysiology, developing treatments, and conducting clinical studies. This includes retroviruses, Ebola, Zika, nodding syndrome, and COVID-19 as well as Long COVID, ME/CFS, and Gulf War syndrome.

Dr. Nina Schor, deputy director for intramural research. For pioneering research that has radically improved outcomes for children with tumors of the nervous system. She has been a role model, mentor, and beacon to countless other female physician-scientists throughout her amazing career, from bench scientist to academic dean to NIH leader.

Established in 1970 as the Institute of Medicine, NAM is an independent organization of eminent professionals from diverse fields including health and medicine; the natural, social and behavioral sciences; and beyond. It serves alongside the National Academy of Sciences and the National Academy of Engineering as an advisor to the nation and the international community.

The full list of 2024 class can be found at bit.ly/4hx0dXt.

NCI's Ward Retires

Dr. Mary H. Ward, senior investigator in the Occupational and Environmental Epidemiology Branch (OEEB) of the National Cancer Institute, retired after 30 years of federal service. Ward is an internationally recognized expert in the study of environmental causes of cancer.

Dr. Mary H. Ward

Throughout her career, Ward made important contributions to our understanding of the potential carcinogenic effects of drinking water contaminants, pesticides and persistent pollutants (POPs) in relation to the etiology of childhood leukemia, gastrointestinal cancers, thyroid and other cancers. Her foundational work established the use of geographic information systems (GIS) for exposure assessment of environmental contaminants, a method widely used today. Her research on nitrates in drinking water had important national policy implications under Environmental Protection Agency's (EPA) Safe Drinking Water Act.

Nitrate Ingestion and Cancer Risk

Ward conducted some of the first case-control and cohort studies of nitrate ingestion and cancer risk with individual-level exposure assessment and evaluation of co-factors that affect N-nitroso compound (NOC) formation. Most NOCs are potent carcinogens in animals, causing tumors at multiple cancer sites. She linked large historical databases of measurements from public water supply to residence histories and found increased risk of bladder, kidney, colorectal, stomach, thyroid and ovarian cancers at nitrate concentrations below the EPA maximum contaminant level.

There were no databases of nitrate and nitrite levels in foods at the time Ward initiated her research in this area. To address this need, she developed databases of dietary nitrate and nitrite for food frequency questionnaires, which have been a resource for many investigators.

Ward also led interdisciplinary teams of hydrogeologists and statisticians to develop predictive

models that were applied to the cohort's residence locations to estimate nitrate concentrations from unregulated private wells, which provided drinking water to 70% of the cohort. Together with monitoring data for public water supplies, they were able to estimate long-term average and peak exposure to inform risk analysis.

Pesticides and Other Contaminants

With extramural colleagues, Ward developed methods for using remote sensing data and a GIS to estimate indirect exposure to pesticides in the general population. Later, she and colleagues validated this approach with environmental samples in Iowa and California and in Denmark where they found increased risk of childhood leukemia among offspring of mothers with higher density of agricultural crop fields near their homes during their pregnancies.

Scientific Leadership and Mentoring

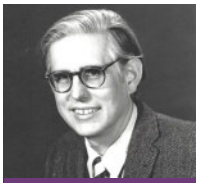
Ward has served the scientific community as part of several important efforts. She chaired the epidemiology review committee of the International Agency for Research on Cancer Monographs Programme on ingested nitrate and nitrite. She served on the National Academy of Sciences Reactive Nitrogen RCN Steering Committee, an interdisciplinary committee whose goal was to assess the ecological and health impacts of humans' disruption of the nitrogen cycle, and on the President's Cancer Panel on Environmental Factors in Cancer as an expert on cancer risk related to nitrate contamination of drinking water.

Ward has served on the Steering Committee for the International Childhood Cancer Cohort Consortium since 2019, and as a liaison to the American Academy of Pediatrics Council on Environmental Health and Climate Change since 2015.

Ward received an M.S. in ecology from the University of Tennessee, Knoxville, and a Ph.D. in epidemiology from The Johns Hopkins University School of Hygiene and Public Health. She has mentored more than 20 post- and pre-doctoral fellows as well as more than 15 master's and undergraduate students. Her role in mentoring and developing junior scientists has been invaluable in establishing the next generation of scientists to carry on critical work in environmental exposures and cancer.

NINDS Mourns the Passing of Reese

Dr. Thomas (Tom) Reese, a senior investigator and chief of the section on structural cell biology of the National Institute of Neurological Disorders and Stroke (NINDS) Intramural Research Program, died on October 11 at the age of 89. His scientific work spanned six decades.


Dr. Thomas Reese

Reese was a world leader in structural neuroscience, developing cutting-edge applications that fundamentally changed the understanding of synapses and cells in the brain, as well as the barrier separating the brain from the bloodstream. His many contributions to neuroscience and cell biology led to his election to the National Academy of Sciences in 1987.

Reese earned his undergraduate degree from Harvard College and his medical degree from Columbia College of Physicians and Surgeons. He then served as a research medical officer at NINCDS (now NINDS) and within four years became head of his laboratory.

In the late 1960s, Reese used electron microscopy (EM) to examine the structural basis of the blood-brain barrier. His experiments with Dr. Morris Karnovsky showed that proteins in the bloodstream are prevented from entering the brain by tight junctions between vascular endothelial cells. This discovery continues to influence the design and delivery of therapeutics for brain diseases.

In the 1970s, Reese and his postdoc Dr. John Heuser carefully examined electron micrographs to delineate the different steps by which the synaptic vesicle membrane is recycled for subsequent reuse at the neuromuscular junction. They went on to develop a revolutionary technique to precisely time rapid tissue freezing with electrical stimulation of motor neurons to capture the fleeting moment when neurotransmitter release occurs. This "freeze-slamming" technique conclusively demonstrated, for the first time, that neurotransmitters are released by fusion of synaptic vesicles with the presynaptic plasma membrane.

While maintaining his appointment at NIH, Reese also set up a lab at the Marine Biological Laboratory (MBL) in Woods Hole, Mass., to study giant axons in squid. He used his rapid-freeze EM methods in conjunction with video microscopy to observe fast axonal transport in real time and then visualize the axons transporting cargo. These techniques enabled Reese and his collaborators to discover kinesins—a class of motor proteins that are critical for axonal transport, mitosis and other cellular functions. Reese maintained his work at Woods Hole full time for most of the 1980s and was active in the MBL community and its educational programs for more than 40 years.

In the 2000s, Reese focused on the structural organization of the postsynaptic density (PSD), a specialized, extensive protein complex associated with the postsynaptic membrane. He discovered that PSD is a dynamic structure that changes shape and protein composition rapidly with synaptic activity. He also discovered that a new subcellular compartment, which he termed the pallium, is a principal site for regulatory machinery that underlies transmitter receptor targeting to and from synaptic microdomains. PSD is now recognized to contain intricate molecular machinery critical to neurotransmitter signaling.

Toward the end of his career, Reese focused on how the nervous system evolves. He worked with his colleague and wife, Dr. Carolyn Smith, on Trichoplax—a tiny disk-shaped marine animal that has no synapses but can perform simple behaviors such as movement and digestion. They used Reese's tried-and-true freezing and microscopy techniques to identify cells that could control locomotion and feeding to gain insights into how animals without synapses can generate behavior. Reese's philosophy to "learn by looking" drove him to develop cutting-edge techniques that were used to achieve fundamental insights into how synapses and cells work.

"Tom will be missed dearly, but his legacy will live on through his family, his seminal contributions to structural neurobiology, and generations of scientists who trained under, worked with, and were inspired by him," said NINDS Scientific Director Dr. Jeffrey Dlamond, who penned the above obituary.

Remembering Wanda Hill

The Office of Disease Prevention (ODP) in the Office of the Director mourns the passing of their long-time colleague Wanda Hill. With more than 40 years of federal service, including 22 years at ODP, Hill quickly became a cornerstone of their staff. Her unwavering commitment and readiness to lend a helping hand made a lasting impact on all who worked with her.


Wanda Hill

Before coming to ODP, Hill supported the director of the Division of Cancer Prevention and Control at the National Cancer Institute, where she prepared protocols for numerous studies and organized essential meetings and conferences. Her attention to detail and skill in fostering connections were evident even then.

At ODP, Hill served as a program support specialist, helping countless programs run smoothly. She played an active role in a multitude of office activities, as well as mentoring, advising and guiding co-workers through complex tasks.

Hill touched so many lives, as seen in the outpouring of positive messages being shared by current and past ODP staff. Colleagues remember her as kind, patient and cheerful—qualities she embodied in her work and interactions with others. Her welcoming smile brightened the office each day.

Many colleagues recall Hill as the first person they met when they joined ODP. But she became more than a reliable co-worker or source of institutional knowledge. Hill was someone you had a cup of coffee with first thing in the morning, when the office was still quiet. She's someone you traded pictures of family with, tracking the milestones and achievements of children and grandchildren as they grew. She was authentic in everything she did and in every interaction.

Hill would give the unvarnished truth, with just the right amount of humor and compassion. Everything she did was in the service of others. Hill's contributions and joyful spirit will be greatly missed, but her legacy will continue to inspire us all.

May the force be with you! NEI senior staff pose in costume on the Bldg. 1 steps. Joining NEI Director Dr. Michael Chiang (second from r) are (l to r) Melanie Reagan, Richard Lee, Santa Tumminia and Anna Han

Clockwise from above, NIH Director Dr. Monica Bertagnolli welcomes event participants. **(PHOTO: CHIA-CHI CHARLIE CHANG)**

The "most decorative" pumpkin winner was created by Reagan, NEI executive officer; (from l) Cheng Rong Yu, Wei Li and John Ball celebrate after finishing the race.

NEI 5K Shows Spirit, Features Halloween Fun

PHOTOS BY DUSTIN HAYS

More than 500 people turned out on Oct. 30 for the fifth annual National Eye Institute 5K Walk/Run/Roll. In addition to racing around the NIH Bethesda campus perimeter, participants competed in costume and carved pumpkin contests.

In attendance to kick off the even were NIH Director Dr. Monica Bertagnolli and NEI Director Dr. Michael F. Chiang. Howard University provided eye health screenings in their mobile clinic. Exhibitors included Prevention of Blindness Society of Metropolitan Washington; The Children's Inn at NIH; the NIH Blood Bank; NIH Office of Equity, Diversity and Inclusion; the NIH Credit Union and Kaiser Permanente.

Above l, finishing the NEI 5K first was Sebastian Relier of NCI (c); second was Yang Shen of NIDDK (l); third was Maxime Donadieu of NINDS (r). Above c, Samantha Johnson of Warrior Canine Connection, a CFC charity, poses with canine ambassador, Eli. Above r, enthused runners at the start of the race.