

## NIH’s Work With Native Communities Drives Diabetes Research

BY MICHAEL TABASKO, OD

**IN GUADALUPE, ARIZONA, A MIX OF** Yaqui Indian and Hispanic families stepped off the sunbaked street and gathered in the annex building of a small NIH research clinic. It’s a space reserved for education where, for the past 10 years, clinical research participants have been collaborating with scientists. The families were eager to discuss the health issues that mattered most to them and wanted to know how biomedical research could be applied to help the community.

Today’s session, on how lifestyle and diet can help prevent childhood obesity and early-onset type 2 diabetes (T2D), was led by **Madhumita Sinha**, a physician with the National Institute of Diabetes and Digestive and Kidney Diseases’ (NIDDK) Phoenix Epidemiology and Clinical Research Branch (PECRB), and her staff. The families are particularly vulnerable to developing these diseases and participate in research because they have a stake in ensuring a healthy future for themselves and their children. This community-based approach is just one of the multifaceted tools being used to stem the rising tide of obesity and T2D.

Other investigators at PECRB are zeroing in on biological elements. The Chronic Kidney Disease Section, headed by **Robert Nelson**, is identifying molecular

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## Francis Collins To Step Down As NIH Director

Will Continue His Research at NHGRI

FROM OCTOBER 5, 2021, NIH NEWS RELEASE



CREDIT: NIH

Francis S. Collins, who has served as NIH Director since 2009, announced that he will be stepping down from that post by the end of the year, but will continue to lead his lab at the National Human Genome Research Institute.

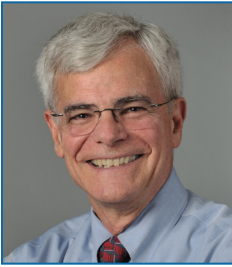
**ON OCTOBER 5, 2021 FRANCIS S. COLLINS ANNOUNCED HIS DECISION TO END HIS** tenure as the director of the National Institutes of Health by the end of the year. Collins is the longest serving presidentially appointed NIH director, having served three U.S. presidents over more than 12 years.

“It has been an incredible privilege to lead this great agency for more than a decade,” said Collins. “I love this agency and its people so deeply that the decision to step down

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## Saluting the Unseen NIH Heroes Among Us

BY MICHAEL GOTTESMAN, DDIR

**THE NIH IS A CITY UNTO ITSELF.** THE Bethesda campus alone is home to more than 30,000 NIH citizens. So, when the COVID-19 pandemic hit in March 2020 and threatened our ability to conduct research, simply shutting down the NIH was not an option. As in New York, the famed city that never sleeps, hundreds of our colleagues sprang to work to ensure that the rest of us could perform our duties remotely and, if allowed, enter our workplace safely.

I speak of the animal caretakers, security guards and police, IT support, cleaning staff, health care workers, food service providers, and many others who were very much on the frontlines, reporting to the physical workplace at the height of the pandemic at no small risk to their own health. We owe these colleagues our deep gratitude. They rose to the occasion in ways many of us may not fully realize.

Consider NIH Security. To account for personnel shortages, the security team needed to switch from three 8-hour shifts to two 12-hour shifts, all while still processing an average 6,550 visitors and 3,524 patients per month. The NIH Police were exceptionally busy as well. Since the start of the pandemic, there have been 15 demonstrations on or near NIH property, compared with the one or two we normally experience per year. These required them to operate with heightened vigilance. Even the dogs had their paws full. K9 teams conducted more than 1,000 building patrols necessitated by the sparse activity on campus.

Our animal-care staff also faithfully reported to work at facilities on the main campus in Bethesda, at Research Triangle Park in North Carolina, and at Rocky Mountain Labs in Hamilton, Montana. They had a pressing task of global importance in supporting animals used in vaccine development and related COVID-19 research. They also were busy keeping novel animal lines healthy for that day when we would all return to the labs. They, too, were stretched thin as many needed to enter quarantine and could not report to work during times when a “close contact” contracted COVID-19, transferring the burden of labor to colleagues, sometimes in other buildings.

The cleaning crew struggled similarly through quarantine-triggered staff shortages. Yet they were essential in our decision early into the pandemic to allow for laboratory shift work. We knew we could count on them to clean between shifts, and we factored in their dependability into our decision to reopen labs in mid-2020.

The facilities staff performed admirably as well in multiple ways. In addition to providing continuation of basic services such as water, steam, and heat, they were called upon to alter air flow in buildings and construct physical barriers to help keep SARS-CoV-2 from spreading. On top of this, they pushed through the pandemic to make astounding progress on key construction projects, such as the TIL Cell Processing Modular Facility, the Center for Alzheimer’s and Related Dementias, and the Central Utility Plant.

Behind the scenes, more than 200 of your colleagues volunteered to be part of the COVID-19 response teams, comprising the Call Center, Contact Investigations, and the Occupational Medical Services Return-to-Work teams. From March to October 2020, most were working out of FAES classrooms in Building 10. Collectively, they interacted by phone with thousands of people who had been in contact with the more than 1,600 NIH employees who have been infected with COVID-19. This was important but often stressful work. Additionally, NIH personnel and others recruited from the U.S. Public Health Service staffed both the symptomatic and asymptomatic testing stations and then the COVID-19 vaccination booths.

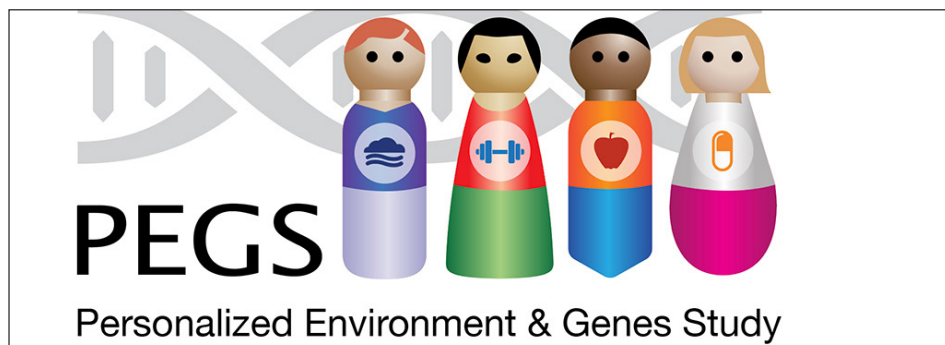
And let’s never forget the very foundation we all relied upon these past 18 months: the NIH network. IT staff in the Center for Information Technology, Office of Research Services, Office of Research Facilities, and in your own institutes and centers toiled to strengthen the NIH network to enable remote work. They developed creative solutions to keep a diverse workforce fully connected via Webex, Teams, Zoom, VideoCast, and other tools that were new to most of us.

‘Tis the season for thanks. NIH Director **Francis Collins** is on a “gratitude tour” to express his admiration for these and other staff who have kept the NIH research enterprise alive and well. When we return to our labs and office, let’s also give them a big thanks for their giving. ●

## Personalized Environment and Genes Study

NIEHS Initiative Focuses on Gene-Environment Interactions

BY KELLEY CHRISTENSEN, NIEHS



A NATIONAL INSTITUTE OF Environmental Health Sciences (NIEHS) initiative called the Personalized Environment and Genes Study (PEGS) integrates genetic and environmental data to understand disease etiology, identify disease risk factors, and improve disease prevention. PEGS merges genetics data with study participants' in-depth health history, including information about environmental exposures. The effort is unique because scientists can eventually follow up with individuals who donated biological samples and completed surveys, potentially providing them with tailored feedback about their disease risk factors.

“The combination of state-of-the-art genetic analysis and in-depth information on participants' medical conditions and environmental exposures will allow researchers to define environmental risks in a way that has never before been possible,” said NIEHS Clinical Director and PEGS co-PI **Janet Hall**.

PEGS began in 2002 as the NIEHS Environmental Polymorphisms Registry (EPR), an effort that collected DNA samples from nearly 20,000 people living in North Carolina. The goal of EPR was to determine whether genes associated with disease in mice were also linked to disease in humans and whether polymorphisms, or small variations in these genes, may increase

the risk of negative health outcomes in people. Scientific advances and new research methods have allowed researchers to expand the original EPR effort into PEGS.

Hall and co-PI **Alison Motsinger-Reif**, head of the NIEHS Biostatistics and Computational Biology Branch, created a database that provides researchers access to aggregate and summary information. Several other investigators played critical roles in transitioning EPR to PEGS. The study's leadership now includes experts in medicine, genetics, genomics, data science, and other fields.

### Using PEGS data, scientists will be able to:

- Identify novel genetic and environmental factors that increase risk of common diseases, such as diabetes, heart disease, stroke, multiple sclerosis, psoriasis, rheumatoid arthritis, allergies, asthma, and cancer.
- Understand how multiple genetic and environmental factors jointly increase disease risk.
- Use data in combination with clinical information to improve disease-risk prediction.
- Discover differences in risk factors for people of different ages, races, or ethnicities.
- Enhance knowledge about the causes and mechanisms of various diseases.

In addition, PEGS will soon have data on epigenetic changes, the modifications to DNA that affect gene expression without altering the underlying genetic code.

Many scientists have used PEGS in their research. One of them is **Dmitry Gordenin**, head of the NIEHS Mechanisms of Genome Dynamics Group. Gordenin and his team measured the various types of DNA changes that arise across all genes in human skin cells. They found that even skin normally shielded from the sun had mutations from ultraviolet light. The findings were published in the journal *PLoS Genetics* (*PLoS Genet* 17:e1009302, 2021).

NIEHS Scientific Director **Darryl Zeldin** has also used the PEGS database. He likes another important feature of the study.

“Investigators have the ability to call participants back to the clinic for follow-up studies to test specific hypotheses of interest,” Zeldin said. “Most other prospective cohorts lack the ability to do this.”

PEGS welcomes collaborations with intramural researchers from all NIH institutes and centers as well as with outside researchers who wish to leverage PEGS data in their work. All projects using these data are conducted as collaborations with PEGS investigators. For details, visit the PEGS website (<https://www.niehs.nih.gov/research/clinical/studies/pegs/index.cfm>) or contact Janet Hall ([janet.hall@niehs.nih.gov](mailto:janet.hall@niehs.nih.gov)) or Alison Motsinger-Reif ([alison.motsinger-reif@niehs.nih.gov](mailto:alison.motsinger-reif@niehs.nih.gov)). ●

*Kelley Christensen is a contract writer and editor for the NIEHS Office of Communications and Public Liaison. Outside of work, she enjoys hiking, skiing, gardening, knitting, and devouring science fiction novels.*

## From the Fellows Committee

### Are You on Twitter Yet?

BY ALISON JANE MARTINGANO, NHGRI

**EVEN IF YOU'RE NOT ON TWITTER**, you're likely still aware of its vast impact on public life. Twitter boasts more than 200 million active users including celebrities, politicians, and journalists. Among them is a thriving group of scientists who tweet about research and job openings and joke and commiserate about the quirks of scientific research. Twitter is particularly useful for early-career researchers who wish to promote their work and network with other scientists.

**How to start?** As an NIH trainee, when you make a Twitter account you should use your personal email address. You'll choose a unique Twitter handle (such as @girlscientist, used by **Chris Gunter** in the National Human Genome Research Institute) and a display name. Putting key terms into your Twitter bio (examples: virologist, Ph.D. student, health policy, etc.) enables Twitter's algorithms to connect you to users with similar interests. But feel free to add personality to your bio (examples: dog mom, Lakers fan, etc.) to make it more authentic.

#### Should you list your NIH affiliation on personal social media accounts?

The United States Office of Government Ethics makes it clear in their 2015 guidance that trainees and employees may list their NIH position in their Twitter bio, but encourages them to include a disclaimer (such as "All views are my own") indicating that their social media communications reflect only their personal views and do not necessarily represent the views of NIH, the Department of Health and Human Services, or the federal government. You must also be careful not to violate the Hatch



Act, (https://ethics.od.nih.gov/hatch-act) which refers to restrictions placed on certain political activities of government employees.

The Office of Intramural Training and Education (OITE) suggests, however, that to be especially safe, trainees can choose not to list their NIH affiliation at all. "Although omitting your NIH affiliation may seem like you are hindering networking, plenty of tweeters have been able to effectively use Twitter without an affiliation," said

**Lori Conlan**, director of OITE's Office of Postdoctoral Services and Career Services Center. "And [they] also have the liberty to express their personal and political views."

**Who to follow.** You can curate your Twitter feed to focus on scientific content by being discerning about whom you follow. Use the search feature to find leaders in your field and follow them. You can also follow journals, magazines, and official NIH accounts to stay up to date on recent developments.

To broaden your network, you can



follow popular Scientific Twitter hashtags such as #AcademicChatter, #WithAPhD, #AcademicLife, #ScholarSunday, and #scicomm. Just reading tweets that use these hashtags can give you a better sense of how other scientists use Twitter and enable you to find users you admire.

Early-career scientists and graduate students can feel isolated. Scientific Twitter can provide a virtual support network via the hashtags #PhDAdvice, #PhDChat, and #WriteThatPhD. There are also hashtags that provide support and discussion for women and other underrepresented groups in science such as #WomeninSTEM, #BlackAcademics, #BlackAndSTEM, #LatinaProfessor, #QueerSTEM, #TransInSTEM, and #WomenInAcademia.

**What to tweet.** Twitter is known for its strict character limit (280 characters). To be sure, Twitter values wit and pithiness, but it is also possible to link tweets together (called a thread) and share links to longer



articles. That said, brevity isn't always a bad thing and it can be useful to practice sharing your ideas succinctly.

**Share links.** If you've found a journal article or podcast that is particularly interesting, share a link to it. Comment on why it was useful to you or the thoughts it prompted.

**Share your research.** Many scientists join Twitter to promote their own research. If you are presenting at a conference or have published something, tweet about it and be available to respond to comments. You may even find that your work is picked up by journalists who prowl Twitter looking for breaking news. Most conferences have their own hashtags, and you can live-tweet updates and share photos of posters, but first make sure that this practice is allowed by the conference's social media policies.

**Share your experiences and advice.** Some of the most popular tweets simply share relatable anecdotes, advice, and scientific "shower thoughts." Be genuine, humble, and open to conversation. Showing the person behind your research can be a great way to engage nonscientists. Feel free to discuss when things didn't go as planned, when life got in the way, or just what you're watching on Netflix this morning.

**Be careful about what you tweet.** Although humanizing science and authenticity are important, you should still be careful about what you tweet. A simple rule of thumb is to act as you would in any other public setting such as a conference or networking event, with the understanding that what you say publicly can be seen by anyone, forever. Gunter suggests "that if you think it might

be controversial, you can save it as a draft for a few hours and think about it."

Overall, Twitter can revolutionize how you interact with science. For those who use it regularly, it can be a source of inspiration and support. Twitter networking allows you to broaden your perspectives. You may find that when you attend your next academic conference or job interview, you meet people that you already know. Your tweets may also inspire the next generation of researchers to pursue science, safe in the knowledge that NIH researchers are human too. ●

**Check out this OITE video in which Chris Gunter (@girlscientist) offered tips on how to use Twitter successfully:** <https://www.youtube.com/watch?v=5EZIJYGFmPQ>. **For more on the use of personal social media, check the NIH guidance at** <https://employees.nih.gov/pages/social-media>.

*Alison Jane Martingano is a postdoctoral fellow in the Immersive Stimulation Research Program, Social and Behavioral Research Branch, at the National Human Genome Research Institute. Her research involves using virtual reality to evaluate how providers communicate genomic concepts and show empathy during physician-patient interactions. She is the Outreach Liaison on the NIH Fellows Committee.*

## KUDOS

### National Academy of Medicine

Four NIHers are among the 100 New Members of the National Academy of Medicine.

**Carolina Barillas-Mury** (NIAID) for discovering how plasmodium parasites manipulate the mosquito immune system to survive, and how these interactions maintain global malaria transmission.

**Jessica Gill** (formerly NINR, now at Johns Hopkins University School of Nursing) for her team's reporting that acute plasma tau predicts prolonged return to play after a sport-related concussion.

**Mariana Julieta Kaplan** (NIAMS) for seminal contributions that have significantly advanced the understanding of the pathogenic role of the innate immune system in systemic autoimmune diseases, atherosclerosis, and immune-mediated vasculopathies.

**Shannon Nicole Zenk** (Director, NINR) for research on the built environment in racial/ethnic minority and low-income neighborhoods that enriched understanding of the factors that influence health and contribute to health disparities.

### Sammies (Samuel J. Heyman Service to America Medals)

**2021 COVID Response Award:** NHLBI Director **Gary Gibbons** and NIMHD Director **Eliseo Pérez-Stable** were honored for addressing the higher COVID-19 rates in the nation's underserved communities.

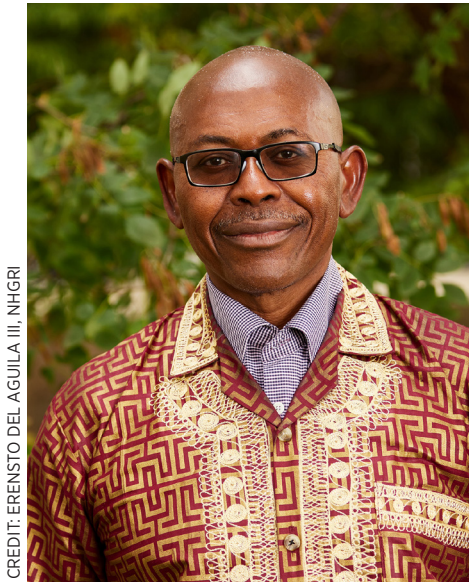
**2021 Federal Employee of the Year Award:** **Barney Graham**, deputy director of NIH's Vaccine Research Center (VRC), and **Kizzmekia Corbett**, formerly with the VRC and now at Harvard University T.H. Chan School of Public Health (Boston) received this honor for leading the groundbreaking research that led to an mRNA vaccine for COVID-19.

**Finalist:** **Brigitte Wideman** (NCI) for her work on neurofibromatosis.

## Charles Rotimi, Ph.D., Is NHGRI's New Scientific Director

Genetic Epidemiologist and Genomics Researcher to Lead NHGRI Intramural Research Program

BY SARAH A. BATES, NHGRI



CREDIT: ERENSTO DEL AGUILA III, NHGRI

Charles Rotimi, new scientific director at NHGRI.

ON OCTOBER 10, 2021, CHARLES ROTIMI became the new scientific director of the National Human Genome Research Institute (NHGRI), succeeding **Dan Kastner** who had served as scientific director since October 10, 2010. Rotimi is a leading genetic epidemiologist and genomics researcher with expertise in statistical genetics, computational science, biochemistry, health disparities and scientific management. He will be the first African-born scientist to hold the position of scientific director at the NIH.

Rotimi, an NIH Distinguished Investigator and chief of the NHGRI Metabolic, Cardiovascular, and Inflammatory Disease Genomics Branch, joined NIH in 2008 as the founding director of the trans-NIH Center for Research on Genomics and Global Health. He has designed and led major basic science and clinical research projects in human genomics. Rotimi is also a leader in the development of global genomics expertise and resources, acting as a vocal advocate for increased ancestral diversity in research participants

and in the international scientific workforce.

“His work has led to multiple transformative success stories in human genomics,” said NHGRI Director **Eric Green**. “It has been my privilege to watch his ever-increasing impact on genomics world-wide and the global recognition of his achievements.”

The NHGRI Intramural Research Program supports more than 50 investigators who conduct a wide range of research at the forefront of genomics, such as implementing new genomic technologies and approaches, developing treatments for rare genetic diseases, and promoting innovative research collaborations. Since its founding in 1993, the program has established a well-respected track record of seminal research accomplishments and has disseminated genomics across the broader NIH Intramural Research Program.

“With Charles’ extensive leadership within the program, ability to inspire and forge collaborations and creativity in applying genomics to improving human health, he is superbly qualified to become the program’s next leader,” said Green.

Rotimi established many scientific endeavors that grew out of his research efforts and into a worldwide revolution for expanding access to genomic data, knowledge, and technologies.

“My vision for the NHGRI Intramural Research Program builds on a deep understanding of the synergic integration of basic science, genomic technologies and clinical activities that have produced an outstanding NHGRI research enterprise with a highly regarded international reputation,” Rotimi said.

His expertise in the unique genomic diversity of African populations has contributed to the advancement of several

key genomics initiatives. Notably, Rotimi engineered the successful engagement of African communities for the International Haplotype Mapping Project (HapMap), which revolutionized scientific understanding of the global distribution of common genomic variants and facilitated the large-scale implementation of genome-wide association studies. He was an active scientist in the 1,000 Genomes Project, which led a revolution in DNA sequencing technologies. He is perhaps most well known for being a key architect and major participant in the Human Heredity and Health in Africa Initiative, which is funded by the NIH and Wellcome Trust and has greatly expanded genomics-based studies of human disease on the African continent.

“I strongly believe that increasing diversity in genomics is a scientific and a social justice imperative,” Rotimi said. “The lack of diversity hinders our understanding of biology, exacerbates already unacceptable health disparities and raises the question of whether genomic-derived therapeutics will serve all human populations equally.”

Rotimi earned a bachelor’s degree in science from the University of Benin (Benin City, Nigeria); a master’s in health care administration from the University of Mississippi (Oxford, Mississippi); and a Ph.D. in epidemiology from the University of Alabama at Birmingham. He is a member the U.S. National Academy of Medicine, the American Academy of Arts and Sciences, and the African Academy of Sciences. He was the founding president of the African Society of Human Genetics and the president-elect of the American Society of Human Genetics. He has received dozens of awards and recognitions, contributed to several books, and co-authored more than 300 scientific papers. ●

## Outgoing NHGRI Scientific Director Dan Kastner, M.D., Ph.D.

Met Challenges and Helped NHGRI Researchers Succeed

BY ETHAN SMITH, NINR

“As scientific director, the most important accomplishment that you can have is for the people who work for you to succeed,” said **Daniel Kastner**, the outgoing scientific director (SD) for the National Human Genome Research Institute (NHGRI). “If they succeed, you succeed.” Kastner, who joined NIH in 1985 as a rheumatology fellow in the National Institute of Arthritis and Musculoskeletal and Skin Diseases, became the NHGRI SD on October 10, 2010. He’s proud that over the past decade, NHGRI has achieved a high level of scientific productivity, with a major impact on the field of genomics. In addition, right now at the end of Kastner’s tenure as SD, almost half of NHGRI’s 22 senior investigators are members of the National Academy of Medicine and/or the National Academy of Sciences “That’s pretty darn good,” he said.

That doesn’t mean Kastner’s time has been without challenges. Almost immediately after settling into his role as SD, he faced a dilemma: Congress was discussing across-the-board federal budget cuts. Kastner had to prepare for the worst by reorganizing NHGRI’s budget. During difficult moments like these, Kastner tried to ensure that the wants and needs of NHGRI staff were considered at the same time that hard budget decisions were being made. A cut did eventually happen in 2013, but NHGRI’s budget had been tightened so it could withstand the cut without compromising scientific pursuits. Kastner also fostered a culture of collegiality in NHGRI by prioritizing the little things: ordering

lunch for faculty meetings; bringing in doughnuts on the mornings when the division of intramural research seminar series was held; and hosting holiday parties in his home every winter.

In the 1980s many inflammatory diseases were not well understood. In his role as a physician–scientist, NIAMS clinical director, and head of NHGRI’s Inflammatory Disease Section, Kastner made important contributions to the field of immunology. He helped to uncover the genomic causes of rare and debilitating autoinflammatory diseases such as familial Mediterranean fever (FMF), a genetic autoinflammatory disorder that causes recurring fever and intense inflammation in the abdomen, chest, and joints. His work has also led to advancements in therapies that are used for treating FMF and several other autoinflammatory diseases.

Kastner knows that the NHGRI intramural program will be in good hands with **Charles Rotimi**, who became the new SD on October 10, 2021, exactly 11 years after Kastner assumed that role. From humble origins in Nigeria, Rotimi has become one of the leading genetic epidemiologists in the world and has been “the indispensable man in the field of African diaspora genomics for the last two decades,” said Kastner. Rotimi has been “leading projects ranging from HapMap [International Haplotype Mapping Project] to H3Africa [Human Heredity and Health in Africa Initiative].”

Kastner plans to make himself available to help his successor, if needed, during the transition. He



Dan Kastner, former scientific director at NHGRI.

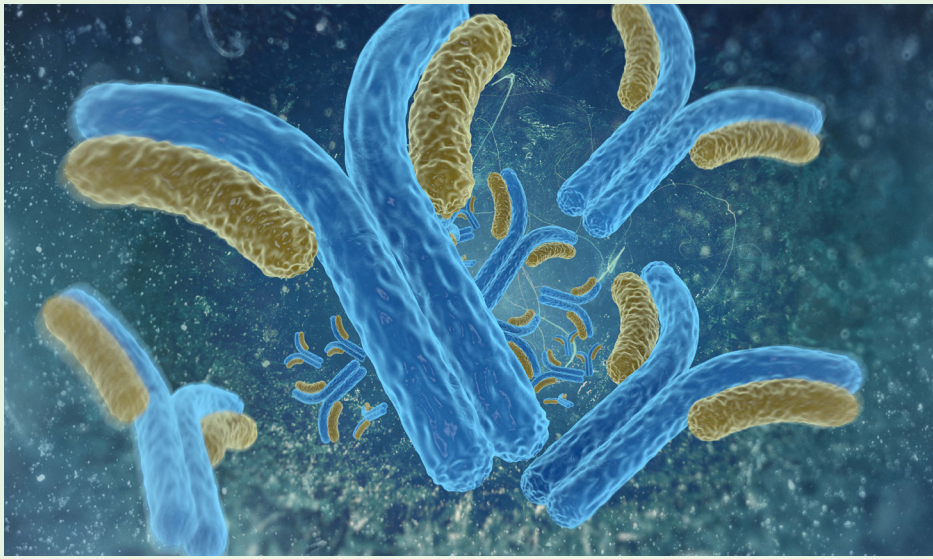
also looks forward to spending more time on his own research and working in the clinic, where he sees and cares for patients with undiagnosed inflammatory diseases.

“There are lots of puzzles yet to be solved,” Kastner said. “That’s what I plan on spending my time doing.” ●

*Ethan Smith, a postbaccalaureate fellow in the National Institute of Nursing Research, is studying blood-based biomarkers for traumatic brain injury. He’s applying to graduate programs in clinical psychology. Outside of work he enjoys watching television and talking with friends.*



## Intramural Research Briefs



CREDIT: STOCK

NIA researchers recently found that monoclonal antibodies that target and bind to beta-amyloid may slightly improve cognitive function in people with Alzheimer disease. Shown: Digital illustration of cell antibodies.

### NIA: ANTIBODY DRUGS MAY IMPROVE SYMPTOMS IN ALZHEIMER DISEASE

A hallmark of Alzheimer disease (AD) is the buildup, in the brain, of beta-amyloid proteins, which clump together to form plaques that disrupt neuronal communication. Scientists at NIA recently examined data from 17 phase 3 clinical trials and found that monoclonal antibodies that target and bind to beta-amyloid may slightly improve cognitive function in people with AD.

The clinical trials assessed the effectiveness of five beta-amyloid antibodies: aducanumab, bapineuzumab, crenezumab, gantenerumab, and solanezumab. The researchers found that aducanumab and solanezumab slightly improved thinking, memory, and performance of daily activities. Aducanumab also reduced the amount of beta-amyloid plaques. Three of the drugs, however, increased the chance of developing certain abnormalities such as fluid buildup or even bleeding in the brain.

These findings may help researchers better assess the merits of beta-amyloid antibodies to treat AD. (NIH authors: K.I. Avgerinos, L. Ferrucci, and D. Kapogiannis, *Ageing Res Rev* 68:101339, 2021)

[BY SATABDI NANDI, NIA]

### NCI, NIEHS: UNLOCKING THE ORIGINS OF LUNG CANCER IN NEVER-SMOKERS

A large international study led by NCI researchers and their collaborators at NIEHS has found three distinct types of lung cancer in people who have never smoked. The investigators characterized molecular changes in tumors from 232 people with no history of smoking who were diagnosed with non-small-cell lung cancer.

The genomic analysis revealed three new subtypes of lung cancer in never-smokers, which the researchers assigned musical names correlating with the magnitude of genetic changes in the tumor. The most common “piano” subtype had the fewest mutations and grows slowly over many years but is difficult to treat. The “mezzo-forte” subtype grew faster and had specific chromosomal changes as well as mutations in a gene commonly altered in lung cancer. The “forte” subtype also grows quickly and exhibited whole-genome doubling, a genomic change that is often seen in lung cancers in smokers.

The findings may inform future treatments tailored to specific types of cancers. (NIH authors: T. Zhang...S.J. Chanock, and M.T. Landi, *Nat Genet* 53:1348–1359, 2021)

[BY MANJU BHASKAR, NINDS]

### NICHD: DRINKING JUICE BEFORE 6 MONTHS LINKED TO SUGARY BEVERAGE CONSUMPTION

In 2017, the American Academy of Pediatrics recommended that children younger than a year old should not have 100% fruit juice. Early juice consumption is suspected to be associated with obesity and tooth cavities in later childhood, and a recent NICHD-led study has shed new light on this theory.

The researchers analyzed data from a study with 4,067 children and their parents. Parents answered periodic questionnaires about when they first introduced juice to their child and reported their child’s juice, soda, water, and milk intakes at 24 months, 30 months, 36 months, and seven years.

Across all age intervals, children introduced to juice before they were 6 months old drank more juice and soda and less water than children given juice after they were one year old. Markers of socioeconomic risk such as younger parenthood, lower educational attainment, and smoking during pregnancy were related to earlier juice introduction.

The authors concluded that early introduction of juice in infancy may predispose children to a preference for sweet tastes. The findings suggest behaviors that exacerbate health disparities begin early in life, and more research is needed to identify drivers of these associations. (NIH authors: S.L. Robinson, R. Sundaram, D.L. Putnick, J.L. Gleason, and E.H. Yeung, *J Nutr* 2021; DOI:10.1093/jn/nxab260)

[BY JANETTE NORRINGTON, OITE]

### NINDS: INFECTION AFTER BRAIN INJURY IMPEDES BLOOD-VESSEL REPAIR

NINDS researchers found that infections hindered blood-vessel repair after injury to brain tissue as well as the meninges, the protective sheath that covers the brain. Injuries to the blood vessels in the brain and meninges, such as traumatic brain injury (TBI) and stroke, are a major cause of disability and death worldwide. Systemic infections (viral, bacterial,





or fungal) are common in hospitalized patients with brain injuries, and the NINDS team found that these infections can distract the immune system, delaying essential repair of blood vessels and leading to worse outcomes.

Using a mouse model previously developed for mild TBI, investigators found that some immune cells stopped repairing the injury site after infection, resulting in far slower healing in infected mice. This effect was temporary, as infected mice eventually did heal unless a second infection was introduced. Additional experiments revealed that a class of proteins called type I interferons (IFN-I) disrupt the repair process after infection by shifting the focus of the immune response—a new mechanistic insight that may help guide future therapeutic interventions.

Researchers then tested how infection influences recovery from cerebrovascular injury (CVI) using a second mouse model. They found a similar delay in blood-vessel repair, with IFN-I activity again playing a large role. And in the case of the infected CVI mice, the slower recovery led to permanent brain damage. (NIH authors: P. Mastorakos, M.V. Russo, T. Zhou, K. Johnson, and D.B. McGavern, *Nat Immunol* 22:1280–1293, 2021)

[BY HENRY DIECKHAUS, NINDS]

#### NIAID: UNDERSTANDING HCV PROTEIN STRUCTURE MAY AID IN VACCINE DEVELOPMENT

Hepatitis C virus (HCV) is one of the most common bloodborne infections in the United States, affecting an estimated 2.4 million people. Chronic infections can lead to liver disease, cancer, cirrhosis, and death. HCV is usually transmitted through blood, such as during childbirth or when sharing drug-injection equipment.

A team of NIAID-led researchers described the mechanics behind HCV infection of human cells. Their findings build on prior research suggesting that a protein on the surface of HCV known as E2 engages with a receptor on liver

cells called CD81, allowing the virus to enter its host. The investigators studied how the two proteins interact under different conditions. They found that an acidic environment promoted HCV E2 binding to the CD81 receptor. Once associated, the viral protein changed shape, facilitating infection by bringing the virus closer to the host cell membrane. This discovery may lead to a future vaccine against HCV. (NIH authors: A. Kumar, R.A. Hossain, W. Bu, Y. Wang, A.D. Dearborn, J.I. Cohen, and J. Marcotrigiano, *Nature* 598:521–525, 2021)

[BY MANJU BHASKAR, NINDS]

#### NIDA: DRAMATIC INCREASE IN METHAMPHETAMINE OVERDOSE RATES

Methamphetamine overdose deaths have escalated nationwide in recent years. To better understand this concerning trend, NIDA researchers completed a cross-sectional analysis of a nationally representative survey and national overdose mortality data. They assessed patterns of methamphetamine use and methamphetamine-involved overdose deaths in individuals aged 18–64. The study showed that use of the drug increased 43% between 2015 and 2019, but overdose deaths rose from 5,526 to 15,489, an 180% increase. In parallel with rising overdose mortality, survey respondents reported riskier patterns of use such as injected methamphetamine, co-use with cocaine, and/or increased rates of methamphetamine use disorder (MUD), a psychiatric condition characterized by compulsive drug taking despite negative consequences.

Moreover, the study found that populations using methamphetamine diversified in the time period analyzed. While middle-aged white individuals have historically been at greatest risk for methamphetamine use, populations with socioeconomic risk factors and comorbidities (such as HIV, hepatitis B or C, and depression) are increasingly being affected.

“What makes these data even more devastating is that currently, there are no approved medications to treat methamphetamine use disorder,” said study co-author Emily Einstein. “NIDA is working to develop new treatment approaches.” (NIH authors: B. Han, W.M. Compton, E.B. Einstein, and N.D. Volkow, *JAMA Psychiatry* 2021; DOI:10.1001/jamapsychiatry.2021.2588)

[BY TAMAR JACOBSON, NICHD]

#### NCI: BLOOD TEST REVEALS WHEN BENIGN TUMORS TURN CANCEROUS IN COMMON GENETIC DISORDER

NCI scientists and collaborators at Washington University (St. Louis) have developed a blood test that allows for early cancer detection in people with neurofibromatosis type 1 (NF1), a genetic disorder that causes the development of benign tumors along nerves, which can turn into an aggressive cancer called malignant peripheral nerve sheath tumor (MPNST). Current standards (such as a biopsy or positron-emission tomography scan) to differentiate MPNST from benign tumors can be challenging and impractical, and the researchers conducted a study in 53 people, including 16 healthy volunteers, to determine whether blood markers could have diagnostic potential.

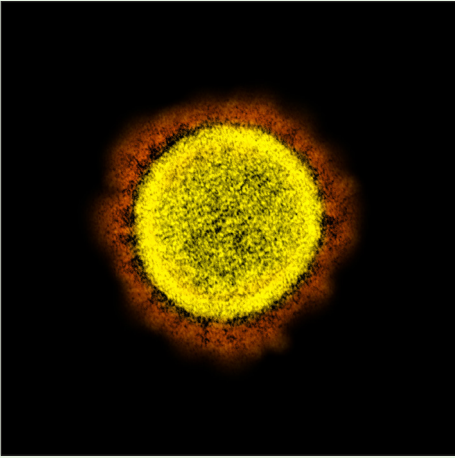
The team is now working to increase the accuracy of the current test and planning to conduct the study with more patients. They hope the technology can be further developed to improve early detection and monitoring of other cancer-predisposing genetic disorders. (NIH authors: R.T. Sundby, H. Lei, L. Hoffman, M. Spencer, B.C. Widemann, and J.F. Shern, *PLoS Med* 18:e1003734, 2021; DOI:10.1371/journal.pmed.1003734)

[BY LEANNE LOW, NIAID]

Read longer versions of these briefs at: <https://irp.nih.gov/catalyst/v29i6/research-briefs>.



## COVID-19 Timeline at NIH (September–October 2021)



CREDIT: NIAID

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

**September 1:** A phase 2 clinical trial led by NHLBI scientists finds that the drug fostamatinib was well tolerated and showed early signs of clinical efficacy when used to treat patients with COVID-19 with severe disease. The drug is currently used as an immune therapy to treat adults with a rare bleeding disorder. (*Clin Infect Dis* ciab732, 2021; DOI:10.1093/cid/ciab732)

**September 3:** In his all-staff email, NIH Director Francis Collins reports that COVID-19 cases have reached their highest levels since winter, while U.S. vaccination rates continue to rise with 900,000 doses on average administered each day. He notes that NIH is developing a plan to provide booster doses to employees.

**September 7:** In his NIH Director's Blog, Francis Collins shares research that the number of Americans infected with SARS CoV-2 by December, 2020, was likely five times as great as initially thought. (*Nature* 598:338–341, 2021)

**September 9:** President Joseph Biden issues a six-point action plan to end the pandemic that focuses on vaccinating the unvaccinated. The plan mandates that all federal executive branch employees and employees of contractors who do business with the federal government be vaccinated against COVID-19, except in limited circumstances. Vaccine requirements

also extend to companies with greater than 100 employees and health care facilities that participate in Medicare and Medicaid.

**September 10:** NIH Director Francis Collins hosts the 8th Virtual Town Hall with NIH Deputy Director for Management Alfred Johnson, NIAID Director Anthony Fauci, NIH Chief People Officer Julie Berko, and NIH Office of Research Services Director Colleen McGowan, with over 14,000 staff attending online. The NIH leaders answer questions and provide an update on the state of the pandemic, treatments and vaccinations; new vaccination and testing requirements; and return to the physical workplace plans.

**September 10:** Deputy Director for Management Alfred Johnson authorizes an extension to the excused absence policy for those caring for a dependent family member. The policy is now effective through March 9, 2022, and the ability to telework with dependents at home remains in place.

**September 14:** In his blog, NIH Director Francis Collins highlights a new study by investigators in the United Kingdom that found breakthrough infections in vaccinated people were less likely to cause long COVID syndrome. (*Lancet Infect Dis* 2021; DOI:10.1016/S1473-3099(21)00460-6)

**September 15:** NIH's Researching COVID to Enhance Recovery Initiative awards nearly \$470 million to New York University (NYU) Langone Health, New York. NYU will make subawards to more than 100 researchers at over 30 institutions to support new and existing studies on the long-term effects of COVID-19.

**September 17:** HHS Assistant Secretary for Administration Cheryl Campbell emails all HHS staff with a timeline to comply with the new federal requirement to be fully vaccinated by November 22, 2021. She announces that HHS will launch an electronic form for employees to confirm their COVID-19 vaccination status.

**September 17:** In his weekly email, NIH Director Francis Collins reminds all staff of the government-wide vaccination requirement.

He reports today's FDA recommendation that individuals 65 years of age and older and those at high risk of exposure or severe symptoms be administered a booster. He mentions the ongoing application process for group C employees to return to the physical workspace as well as updated COVID-19 safety guidance. He expresses gratitude to the police officers and emergency communications dispatchers running the 911 system at NIH.

**September 23:** NIH Deputy Director for Management Alfred Johnson announces that starting October 1, 2021, conference attendance requests will no longer require NIH leadership approval. Staff should work with their IC administrative staff and supervisors.

**September 24:** HHS Assistant Secretary for Administration Cheryl Campbell announces HHS will begin COVID-19 vaccination verification efforts as early as next week.

**September 24:** At least three promising antiviral pills for COVID-19 are being tested in clinical trials. Like tamiflu, which is given after a flu diagnosis, the antivirals would conceivably stop symptoms from developing after exposure and limit the duration of the infection. The top contender is a medication from Merck & Co. and Ridgeback Biotherapeutics called molnupiravir. Results from clinical trials are expected by late fall or winter, according to Carl Dieffenbach, director of the Division of AIDS at NIAID.

**September 28:** NIAID awards approximately \$36.3 million to three academic institutions to fuel vaccine research for a diverse family of coronaviruses.

**October 1:** In his all-staff email, NIH Director Francis Collins reminds everyone of the requirement for federal employees to be fully vaccinated by November 22, 2021, and contractors by December 8, 2021. He also points to a promising unpublished phase 3 trial reporting that the oral antiviral drug molnupiravir reduced hospitalizations by 50% when given to high-risk outpatients with a recent diagnosis of COVID-19.



**October 4:** A large surveillance study led by scientists from NCI and NIMHD finds that the global COVID-19 pandemic caused more deaths in Black, American Indian and Alaska Native, and Latino groups in the United States than in white or Asian individuals. (*Ann Intern Med* 2021; DOI:10.7326/M21-2134)

**October 5:** Francis Collins announces that he will end his tenure as NIH director by the end of this year. Appointed in 2009 by President Barack Obama, Collins is the longest-serving director in NIH history. President Joseph Biden recognizes Collins as one of the most important scientists of our time for his achievements ranging from mapping the human genome to fighting the COVID-19 pandemic.

**October 5:** The NIH Director's Blog highlights a new study that found most vaccine-hesitant people are willing to change their minds. (*JAMA Netw Open* 9:e2126882, 2021)

**October 6:** A study led by NIDA scientists finds that fully vaccinated people with substance-use disorders may be at higher risk for SARS-CoV-2 breakthrough infections. The results suggest that the increased risk was likely due to co-occurring diseases and adverse socioeconomic characteristics. (*World Psychiatry* 2021; DOI:10.1002/wps.20921)

**October 7:** An NIDA-led study finds that more than 140,000 U.S. children lost a primary or secondary caregiver due to the COVID-19 pandemic and highlights stark disparities in caregiver deaths by race and ethnicity. (*Pediatrics* 2021; DOI:10.1542/peds.2021-053760)

**October 14:** The NIH Rapid Acceleration of Diagnostics initiative announces \$77.7 million in contract awards to develop and manufacture 12 new rapid diagnostic tests for SARS-CoV-2.

**October 15:** NIH Director Francis Collins marks his 100th coronavirus update to all staff. He directs employees vaccinated outside NIH to report their status online through the COVID-19 Vaccination Status Form. He reports that the FDA's Vaccines and Related Biological Products Advisory Committee voted to expand the

emergency use authorization of the Moderna vaccine for the administration of an additional booster dose for higher-risk individuals: people older than 65 years of age; 18–64 year olds at high risk of severe COVID-19 or with frequent occupational exposure. He expresses gratitude to NIH's Animal Care and Use Program staff, who have played a critical role in caring for research animals throughout the pandemic.

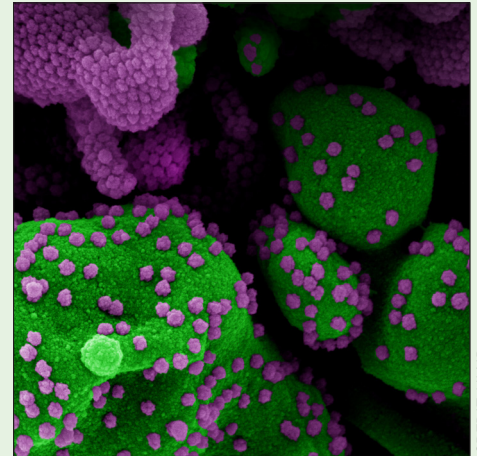
**October 15:** An NIH-funded study finds that antibody treatment for multisystem inflammatory syndrome (MIS-C) in children works by depleting inflammatory immune cells. MIS-C is a rare condition that usually affects school-age children who initially had only mild COVID-19 symptoms or no symptoms at all. (*J Clin Invest* 131:e147076, 2021)

**October 18:** A clinical trial supported by NIH finds that the immunomodulator interferon beta-1a does not improve outcomes for hospitalized adults with COVID-19. (*Lancet Respir Med* 2021; DOI:10.1016/S2213-2600(21)00412-4)

**October 19:** In his blog, NIH Director Francis Collins features a Swedish study that found vaccination is a key strategy for reducing transmission of SARS-CoV-2 within families. (*JAMA Intern Med* 2021; DOI:10.1001/jamainternmed.2021.5814)

**October 20:** NIH Director Francis Collins releases a statement addressing the NIH-supported research (funded through a subaward from NIH-grantee EcoHealth Alliance) to understand naturally occurring bat coronaviruses at the Wuhan Institute of Virology (Wuhan, China). Analysis of published genomic data and other documents from the grantee demonstrate that the coronaviruses studied under the NIH grant are genetically far distant from SARS-CoV-2 and could not have caused the COVID-19 pandemic.

**October 21:** NIAID scientists and colleagues find that a booster dose of the mRNA-1273 COVID-19 vaccine given to rhesus macaques about six months after their primary vaccine series significantly increased concentrations of



CREDIT: NIAID

Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-CoV-2 virus particles (purple), isolated from a patient sample. Image at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

neutralizing antibodies against all known SARS-CoV-2 variants of concern. (*Science* 2021; DOI:10.1126/science.abc18912)

**October 29:** In his weekly email, NIH Director Francis Collins reports that over 88% of NIH federal employees are fully vaccinated against COVID-19. Effective today, fully vaccinated staff can submit requests for non-mission-critical travel for approval. He also mentions that the FDA's Vaccines and Related Biological Products Advisory Committee met and voted to recommend emergency use authorization of Pfizer's COVID-19 vaccine for children ages 5 through 11. Beginning November 1, NIH will offer Pfizer (now known as Comirnaty) and Moderna COVID-19 boosters to a limited portion of the NIH staff who received their second dose, at NIH, at least six months ago.

**October 29:** The NIH Clinical Center announces its updated patient/visitor screening process. ●

Read a more detailed version of this timeline, complete with links, at <https://irp.nih.gov/catalyst/v29i6/covid-19-timeline-at-nih-november-december-2021>.

## Collins

CONTINUED FROM PAGE 1

was a difficult one, done in close counsel with my wife, Diane Baker, and my family. I am proud of all we've accomplished. I fundamentally believe, however, that no single person should serve in the position too long, and that it's time to bring in a new scientist to lead the NIH into the future. I'm most grateful and proud of the NIH staff and the scientific community, whose extraordinary commitment to lifesaving research delivers hope to the American people and the world every day."

A physician-geneticist, Collins took office as the 16th NIH director on August 17, 2009, after being appointed by President Barack Obama and confirmed by the U.S. Senate. In 2017, he was asked to continue in his role by President Donald Trump, and in 2021, by President Joe Biden. Prior to becoming the NIH director, Collins served as the director of the National Human Genome Research Institute (NHGRI) from 1993 to 2008, where he led the international Human Genome Project, which published the full sequence of human DNA in 2003.

"It takes an extraordinary person to tackle the biggest scientific challenges facing our nation—and under three presidents, amidst three distinctly different chapters of American history," said Health and Human Services Secretary Xavier Becerra. "Dr. Collins, master of scientific breakthroughs and scientific reason—from mapping the human genome to fighting the most devastating pandemic of a century—has routinely broken ground to save countless lives, while unleashing innovation to benefit humanity for generations to come."

Known for his accessible, plain-spoken manner, Collins garnered broad bipartisan Congressional support for NIH research. During his 12-year leadership, NIH's budget grew by 38%, from \$30 billion in 2009 to \$41.3 billion in 2021. Collins proposed and established bold initiatives—extending from fundamental basic science to translational

science to focused projects—to tackle some of the most pressing health issues facing Americans, including Alzheimer disease, cancer, opioid use disorder, rare diseases and the COVID-19 pandemic.

Collins long envisioned that knowledge gained from the mapping of the human genome would be used to develop treatments tailored to every person's unique genetics, environment and lifestyle. To spur research in the emergent area of precision medicine, Collins launched the All of Us Research Program, which is well on its way to enrolling one million people across the U.S. to provide their health data so that researchers can improve the way we prevent illness as well as treat the full spectrum of diseases and conditions. He also is the architect of several strong public-private partnerships such as the Accelerating Medicines Partnership.

In concert with the Obama administration, Collins launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative,

a multi-billion-dollar effort to develop sophisticated technologies to understand the neuronal networks of the brain and what goes wrong to cause Alzheimer disease, schizophrenia, psychosis, and other serious brain diseases. He worked closely with then Vice President Biden to launch the Cancer Moonshot Initiative to fuel innovation and speed new treatments to reduce cancer incidence and improve patient outcomes.

Under the leadership of President Trump, Collins launched and galvanized the research and addiction communities around the HEAL (Helping to End Addiction Long-term) Initiative to address the national opioid crisis by improving treatments for opioid misuse and addiction and enhancing pain management.

Working with both the Trump and Biden administrations to respond to the COVID-19 pandemic, Collins helped launch several game-changing initiatives, including the Accelerating COVID-19 Therapeutic Interventions and Vaccines



As NIH Director, Francis Collins worked hard to build relationships with members of Congress, meeting with them one-on-one and inviting them to the NIH campus in Bethesda, Maryland, to learn about NIH research. On May 17, 2021, a bipartisan contingent of United States senators and staff members visited NIH for science briefings, a lab tour, and biotech demonstrations. Shown: Vaccine Research Center Director **John Mascola** (right) describing vaccine research; Collins is on the far left.

CREDIT: CHIA-CHI "CHARLIE" CHANG



Francis Collins enjoys playing with his band and performing solo for NIH audiences “I think there’s a lot we can learn there about how music touches us in ways that can be uplifting and even healing,” he said. The Sound Health Initiative (an NIH-Kennedy Center for the Performing Arts-National Endowment for the Arts partnership) is funding \$20 million worth of research that brings music therapists together with neuroscientists to explore how music can be effective in healing.

(ACTIV) public-private partnership that developed a coordinated research strategy for prioritizing and speeding development of promising treatments and vaccines; the Rapid Acceleration of Diagnostic (RADx) program to create an innovation funnel for COVID-19 testing technologies; the Community Engagement Alliance (CEAL) Against COVID-19 Disparities to support partnerships in communities hardest hit by the pandemic and reduce health disparities; and the Researching COVID to Enhance Recovery (RECOVER) Initiative to identify why some patients don’t fully recover from the effects of COVID-19 disease and develop ways to treat these patients or even prevent long COVID altogether.

All these efforts have set the stage for a new component of NIH, known as the Advanced Research Project Agency for Health (ARPA-H), proposed by President Biden and strongly supported by Collins. ARPA-H is currently under consideration by the U.S. Congress. Modeled after DARPA in the Department of Defense, ARPA-H is envisioned to support and conduct high-risk, high-reward biomedical and health research in a way that is radically different than NIH’s grant-based system.

On the policy front, Collins has tackled many long-standing issues that have hampered science. He bolstered policies and activities to address sexual harassment and structural racism, enhance accountability and transparency in clinical trials and ensure broad data sharing. He has been a champion of early-stage researchers, implementing numerous policies to enable their success in a hyper-competitive research environment.

He is an avid supporter of science communication, and the importance of making the findings of NIH research accessible to the public. He shares information about the latest NIH research via his blog, Twitter handle, and through many social media events. He is known for using music to convene people with different perspectives and for his parodies about science.

Collins will continue to lead his NHGRI research laboratory, which is pursuing genomics, epigenomics and single-cell biology to understand the causes and means of prevention for type 2 diabetes. His lab also seeks to develop new genetic therapies for the most dramatic form of premature aging, Hutchinson-Gilford progeria syndrome. ●

## A Conversation with NIH Director Francis Collins

Staff from *The NIH Catalyst*, the *NIH Record*, and the “I Am Intramural” Blog, conducted a joint interview, on Zoom, with NIH Director **Francis Collins**, on October 27, 2021. We knew we’d only have 30 minutes with him so we worked hard beforehand to distill our 50+ questions into just a few. Here’s what we asked him:

- What did you tackle successfully during your tenure as NIH director and in hindsight, is there anything that you might have done differently?
- What were some of the top accomplishments for intramural research and for extramural research during your time as NIH Director?
- What advice do you have for explaining science in ways that anyone can understand?
- Can you tell us about your passion for music and its potential as a therapy for healing?
- What advice did the previous director (**Elias Zerhouni**) give you, and what insights might you share with the next director?
- What research areas do you see as being particularly important in the next decade, and what do you think NIH’s role will be in that work?
- Is there anything else you’d like to add?

NIH Director Francis Collins’s responses to these all but the last questions begin on page 14 ; all responses appear in *The NIH Catalyst* online edition: <https://irp.nih.gov/catalyst/v29i6/a-conversation-with-nih-director-francis-collins>.

## A Conversation with Outgoing NIH Director Francis Collins

Reflecting on Accomplishments, Advice, Music, and More

INTERVIEW WITH STAFF FROM THE NIH CATALYST, NIH RECORD, AND "I AM INTRAMURAL" BLOG



CREDIT: NIH

NIH Director Francis Collins

ON OCTOBER 5, 2021, FRANCIS S. Collins, M.D., Ph.D., announced his decision to end his tenure as the director of the National Institutes of Health by the end of the year. He is the longest serving presidentially appointed NIH director, having served three U.S. presidents over more than 12 years.

He will continue to lead his National Human Genome Research Institute (NHGRI) research laboratory, which is pursuing genomics, epigenomics, and single-cell biology research to understand the causes and means of prevention for type 2 diabetes. His lab also seeks to develop new genetic therapies for the most dramatic form of premature aging, Hutchinson-Gilford progeria syndrome.

Collins spoke recently with staff from *The NIH Catalyst*, the *NIH Record*, and the "I am Intramural" Blog. Following is an edited version of his comments.

**Q.** When you took this job in 2009, you penned an article in *Science* magazine (*Science* 327:36-37, 2010) in which you identified five areas you wanted to focus on as NIH director: 1) high-throughput technologies; 2) translational medicine; 3) benefitting health care reform; 4) a greater focus on global health; and 5) the reinvigoration and empowerment of the biomedical research community. What do you think you tackled successfully? And in hindsight, is there anything that you might have done a little differently?

**COLLINS:** I thought pretty hard about those themes. I consulted with [former NIH Directors] **Harold Varmus** and **Elias Zerhouni** about it. In each of those areas, we've made some real progress. Much of this has been assisted since 2015 by Congress supporting our need for sustainable and predictable increases in budgets. This has made it possible to start new projects that otherwise would have been hard to do.

**High-throughput technologies:** I'm pretty excited about the way in which technology has evolved to enable things such as the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative. Additionally, some breathtaking advances have been happening with stem cells and single-cell biology.

**Translational medicine:** A big push for me in the first couple of years as NIH director was to create a specific entity at NIH that was focused on translational science. So we created the National Center for Advancing Translational Sciences, which has been remarkably successful in providing capabilities for NIH-funded researchers to take basic science discoveries into clinical applications. I am now hoping that President Biden's proposed Advanced

Research Projects for Health (ARPA-H) will be established at NIH in the next few months. ARPA-H could speed up the process of funding use-driven projects that could translate biomedical research into outcomes that would improve the health of all Americans.

**Benefitting health care reform:** I wrote in the *Science* article that reinventing health care is an urgent national priority and that NIH could make substantial contributions in such areas as comparative-effectiveness research, prevention and personalized medicine, and health-disparities research. That's been happening in a big way.

**Global health research:** NIH is the largest public supporter of global health research in the world, more than any other agency. I wanted to be sure we were doing whatever we could to optimize it. We are co-leaders of a project called Human Heredity and Health in Africa that has supported more than 30 different African institutions working together in a network that has made it possible for a lot of cutting-edge science to emerge. Previously, there wasn't a lot of research opportunity in those places and there was a real risk of losing a lot of the African talent. Although we've made progress, there are still challenges. We wish we'd been able to encourage more research capacity in low- and middle-income countries, as we're facing a COVID crisis and would have benefited from better molecular surveillance, clinical-trial opportunities, and expanded vaccine manufacturing.

**Reinvigorating and empowering the biomedical research community:** We are investing in training and diversity. We are also trying to be sure that the necessary resources are there for people who are trying to do great science but were struggling a few

years ago because the percent success rates for grant applicants was in the teens. It is better now at about 21 percent, but to fund all of the most meritorious research it should be even higher. Furthermore, diversity is a hugely important issue for our workforce, our grantee community, and our clinical-trials participation. Several years ago I put together a diversity working group of my advisory committee, and out of that came the creation of a new position, the Chief Officer for Scientific Workforce Diversity. The initial holder of that post was **Dr. Hannah Valantine**, and now **Dr. Marie Bernard** leads the office. In addition, we have made real strides in increasing diversity in our intramural program through the Distinguished Scholars Program.

In the extramural arena, we are starting the FIRST [Faculty Institutional Recruitment for Sustainable Transformation] program, which aims to inspire institutions to recruit cohorts of tenure-track faculty with specific interests in diversity. Here at NIH, we founded the UNITE program, which



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"The Vaccine Research Center's development of the COVID-19 mRNA vaccines will be seen historically as one of the most significant scientific advances of this decade," said Collins. At the HHS/NIH COVID-19 Vaccine Kickoff event, held at NIH on December 22, 2020, he received the Moderna COVID-19 vaccine.

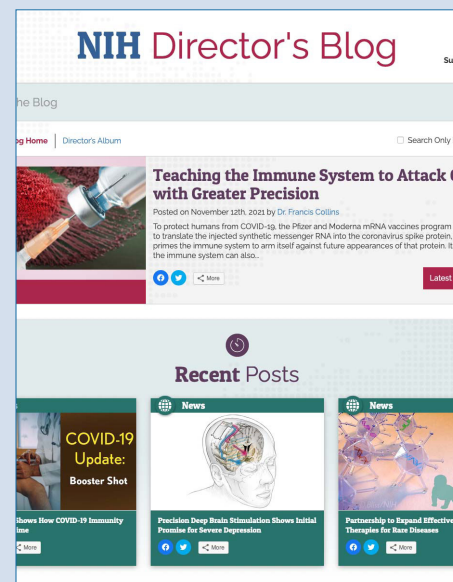
seeks to address structural racism within the NIH-supported scientific community. We are also revamping our health-disparities research effort to be more intentional and more focused on interventions.

**Q.** What were some of the top accomplishments for intramural and extramural research during your time as NIH Director?

**COLLINS:** There are many examples of intramural achievements. I could start with the remarkable work being done by **John Tisdale's** team on using gene therapy to cure sickle-cell disease and by **Steve Rosenberg's** team on cancer immunotherapy efforts that have shown how activating the immune system can provide dramatic responses to cancer, even for people with stage four disease. A bricks-and-mortar achievement was getting the funding for the new Surgery, Radiology, and Laboratory Medicine wing of the Clinical Center. Finally, the Vaccine Research Center's development of the COVID-19 mRNA vaccines will be seen historically as one of the most significant scientific advances of this decade.

Extramural achievements include boosting the success rate for early-stage investigators (ESIs) to receive RO1 grants; we funded more than 1,300 first-time ESI applicants last year compared with 600 in 2015. Now the top 25% of ESI applicants receive grants (before it was only the top 15%). I'm proud of that.

Successful new programs include the BRAIN Initiative, which as I mentioned earlier, is a remarkable interdisciplinary effort to try to figure out how the cells and circuits in the human brain do what they do. There's been an outpouring of papers in *Nature* describing for the first time the cell census of the motor cortex in mouse and human at a level of detail unimaginable a few years ago.



Collins is an avid supporter of science communication, and the importance of making the findings of NIH research accessible to the public. He shares information about the latest NIH research via his NIH Director's blog (shown here), Twitter handle, and through many social media events.

I'd also like to point to the "All of Us" program, the effort to recruit a million Americans (we have about 430,000 so far) to serve as partners in a detailed study of all the factors that play out in health or illness. They are making their electronic health records accessible to researchers, getting their genomes sequenced, answering questionnaires about their health behaviors, wearing ambulatory sensors, and doing a lot of laboratory measurements. This is going to be a foundation for discoveries for decades to come.

**Q.** What advice do you have for explaining science in ways that anyone can understand?

**COLLINS:** Communicating our research is an important part of what all scientists are called upon to do. To be successful, a scientist needs to be aware of whether the information is actually getting across. One of the things that helped me was growing up in the theater. My father was a director and producer, my mother was a playwright,

CONTINUED ON PAGE 16 ►

## Conversation With Collins

CONTINUED FROM PAGE 15

and I ended up on the stage at an early age. It was a small theater where you could see your audience and you knew if you were connecting.

Before coming to NIH, I taught medical students at the University of Michigan (Ann Arbor, Michigan). If you want to be humbled by your own communication deficiencies, this is a great way to discover them [laughs] because med students will turn you off really quickly if you're not making sense on their level. I always try to imagine the typical background of the person in the group to whom I'm speaking, and how I could put forward a complicated scientific concept in a way that would resonate. I use analogies a lot, because they often help people anchor a scientific finding within a more familiar, everyday experience. I try as best I can to avoid using the jargon terms that science is famous for. Most importantly, I check out the body language of the person or group I'm speaking with to see whether I'm coming across, or whether I need to modify the approach. This is harder to do in the era of everything being virtual.

**Q.** You are our rock star! You started the Sound Health Initiative. For these last 12-plus years, you've been entertaining us with solo performances and with your band. Could you tell us about your passion for music and music as a potential therapy for healing?

**COLLINS:** We live pretty intense, stressful lives, especially under COVID. We all need opportunities to get away from that intensity sometimes and experience something that's uplifting and re-energizing. For me, music lifts my spirits and is just good therapy. It's also an enjoyable way to share an experience with others. When the band is really in the groove, and we're playing a song that's rocking the house, you can't help but feel



Opera singer Renée Fleming visited NIH in 2019 as the featured guest at the annual J. Edward Rall Cultural Lecture. She talked about the Sound Health initiative, an NIH–Kennedy Center partnership in association with the National Endowment for the Arts, and had an on-stage conversation with NIH Director Francis Collins. Afterwards she and Collins sang together.

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good. Of course, under COVID, the band has not had any gigs because it has not been safe. I've really missed that. Right now, my musical experiences have been more of the solo variety, sitting down at the piano or playing my guitar just to change the dynamic after a very intense and busy day. That's helped me a lot.

I do think there's a lot we can learn about how music touches us in ways that can be uplifting and healing. And that's what the Sound Health Initiative (an NIH–Kennedy Center for the Performing Arts–National Endowment for the Arts partnership) is all about. I started this with Renee Fleming, the best-known operatic soprano of our era. She's become extremely knowledgeable and highly effective in this area of connecting science and music. And now NIH, through the Sound Health Initiative, is funding \$20 million worth of research that brings music therapists together with neuroscientists to try to understand each other's approach to how music can be effective in healing. I love the idea of bridging what is often seen as a gap between the humanities and the sciences.

**Q.** What advice did previous directors give you? And what insights about the job might you share with the next director?

**COLLINS:** I mentioned earlier the five themes that I put forward in 2009 when I became NIH director. A couple of long talks with **Harold Varmus** helped those ideas to come into focus. I also had a long conversation with **Elias Zerhouni** when I was nominated by President Obama. The thing that sticks with me most was [Zerhouni] saying, "You have one critical priority that you must never let slip down the list: that is supporting the next generation of scientific talent." This was in 2009 when funding was pretty tight. Elias was deeply worried that we were in such a discouraging place for young investigators that we were going to lose a whole generation of that group, never to return. I heard that message loud and clear and a lot of what I did in the course of these 12 years was to try to address it. I mentioned earlier that one response to this situation is to prioritize applications from early-stage investigators. That has





more than doubled the number of such investigators who join our community of grantees each year.

Elias and I also talked about whether we were doing enough to build on the scientific capabilities that occur in the private sector. Elias had some familiarity with that and went on to be a major player in the private sector at Sanofi. That conversation inspired me to think a bit more about what could be done to accelerate progress in our complicated research ecosystem. As a result of that thinking and by getting to know some of the senior scientists in pharmaceutical and biotech companies, the Accelerating Medicines Partnership (AMP) emerged. It brought together the remarkable talent in both the public and private sectors to figure out ways to work together to identify biological markers of disease and the development of treatments that target those pathways. AMP initially focused on Alzheimer disease, diabetes, and rheumatoid arthritis and lupus. Later projects have added on Parkinson disease and schizophrenia. Even more recently, AMP has launched another project on gene therapy for rare diseases. AMP is a really powerful collaborative effort that didn't exist before. As co-chair of the AMP Executive Committee with Mikael Dolsten of Pfizer, I am proud to see what has been accomplished. The level of trust that was developed between the public and private sectors through AMP turned out to be critical for the ability to establish rapid and effective collaborations on COVID-19, particularly the Accelerating COVID-19 Therapeutic Interventions and Vaccines public-private partnership.

If I was trying to advise the next NIH director, I would emphasize the importance of focusing on relationships with members of Congress. If you want NIH to flourish, you need Congress' support and trust. You want Congress to have confidence in the NIH

director, to know that straight answers will be provided when asked for. I've probably had close to 1,000 one-on-one visits with members of Congress in the past 12 years. And those usually go really well. Although members of Congress may seem to disagree about everything right now, they all see the value of medical research. Provided with a bit of information about NIH, they see what a remarkably important contribution we make to finding answers to all those conditions that they're worried about on behalf of themselves, their families, and their constituents.

Those personal relationships are crucial. The fact that we have seen our budget increase in the last six years has a lot to do with a few bipartisan heroes in the Congress. We've done everything we can to help them get to know us. They accept our invitations to come to NIH to visit us, they see what's going on in research labs, they meet with patients in the Clinical Center, and they develop a real personal knowledge of what medical science is all about right now. So I'd say to the next NIH director: Never turn down an invitation to meet with a member of Congress, even if you're really busy.

**Q.** What research areas do you see as being important over the next decade, and what do you think NIH's role will be in those areas?

**COLLINS:** Well, it's always hard to see much beyond a year or two because so many things happen that we didn't expect. I never imagined that CRISPR gene editing would emerge so dramatically during my time as director and make a wide variety of scientific advances possible, from basic science to clinical applications. Certainly, there will be other advances nobody can predict.

There are areas that I know will be full of potential that we'll want to invest in: One example is neuroscience, in which new technologies will open up new insights

to normal function and to the basis of brain disorders. Another area of rapid progress is likely to be artificial intelligence and machine learning.

I hope we'll also make major progress in dealing with the opioid crisis and the need to find better answers for chronic pain. At NIH, the Helping to End Addiction Long-term Initiative aims to speed scientific solutions to stem the national opioid public-health crisis. This is urgent: We lost 90,000 people to opioid overdoses in the past 12 months.

In the area of immunology, mRNA vaccines have provided safe and effective vaccines for COVID-19 in a breathtaking 11 months. But mRNA vaccines might also advance the effort to prevent HIV, malaria, and tuberculosis—and might also lead to major progress in vaccines for cancer in the next few years.

Single-cell biology has transformed our ability to understand how life works and how disease happens, and this technology is just going to get better and better. Combined with a range of -omics approaches, it is now possible to ask a single cell, "What are you doing there?" by assessing RNA expression, chromatin structure, and, increasingly, proteomics.

Therapeutically, I'm really excited about where we're going with gene therapy. In the next few years many of those 7,000 genetic diseases for which the DNA misspelling is known might be amenable to a scalable approach using in vivo gene therapy.

These are just a few examples of areas to watch—but there are dozens of other areas of investigation that are showing great promise right now. This is just a fabulous time to be involved in biomedical research. ●

**Check online for the answer to one more question:** <https://irp.nih.gov/catalyst/v29i6/a-conversation-with-nih-director-francis-collins>.

## Native Communities

CONTINUED FROM PAGE 1



CREDIT: NIDDK

Phoenix Indian Medical Center Campus: PEICRB's Clinical Research Center is located on the top floor of the Indian Hospital (large white building). The epidemiology groups operate out of the old Indian hospital shown in the foreground.

mechanisms responsible for diabetic kidney disease and finding new ways to detect and prevent this complication. Its work resulted in a study published just this year (*Diabetes* 8:1603–1616, 2021). An ongoing legacy of knowledge continues to be generated by PEICRB and their research participants.

“Since 1965, the branch has probably contributed more to the understanding of T2D than any other group in the world,” said Branch Chief **Clifton Bogardus**.

T2D now affects an estimated 6% of the global population and 13% of all U.S. adults—a prevalence nearly fourfold that of 40 years ago, according to the Centers for Disease Control and Prevention. Previously known as adult-onset diabetes, T2D typically started in middle and late adulthood. But since the 1990s, the obesity epidemic has fueled a shift to younger ages worldwide, increasing the risk for complications such as heart disease and kidney failure within 15 years of diagnosis.

Yet, we already know of effective

methods to mitigate this disease. Decades ago, research at PEICRB in Phoenix, Arizona, as part of a multicenter clinical trial, demonstrated how weight loss and exercise can have a powerful effect on preventing or delaying T2D. A cure, however, has remained elusive. Researchers today are studying the genetic playbook of diabetes, which has revealed a complex interaction of biology and environment. And helping to unlock the mysteries of T2D for us all are minority groups that are disproportionately affected by the disease—including Hispanics, Alaska Natives, and American Indians, such as the Pimas.

### A Changing Landscape

The Pimas call themselves Akimel O’odham, which means “River People.” Using irrigation farming techniques, their ancestors cultivated the arid Gila and Salt River valleys of Arizona’s south-central territory into a riparian green ribbon of agriculture. Adapted to an active, traditional lifestyle, the Pimas

were both successful and generous. The Maricopa Tribe—driven from their homes in the 16th century by tribal conflict along the lower Colorado River—found refuge with the Pimas, where they continue to live today in the Gila River Indian Community (GRIC).

At the turn of the 20th century, nonnative farmers began settling the region. A series of upstream dams and irrigation projects diverted the waters of the Gila River, depriving the GRIC desert farmers of an agrarian way of life that had defined them for generations. Famine was followed by federal aid in the form of food such as canned goods, flour, and lard. The abrupt change in diet and forced change to a sedentary lifestyle led to a surge of obesity and diabetes. While the Arizona Water Settlements Act of 2004 would later restore water rights to the GRIC, disruptions to traditional ways of life had lasting health consequences: Two-thirds of Pima adults over the age of 45 now suffer from T2D.

Modern-day Phoenix is a diverse

patchwork of ethnicities, including individuals from several tribal nations, and many choose to be invaluable participants in clinical research at PECRB. Staff here both conduct research and provide care for people with diabetes at clinics on the Phoenix Indian Medical Center campus, downtown Phoenix, and Valleywise Health Medical Center. Clinical trials are also run out of five sites in Arizona and New Mexico.

PECRB has been leading the charge of universities and biomedical institutions working on a cure for T2D. The branch has produced over 1,000 papers and generated discoveries that have benefitted both tribal communities and the growing number of people living with the disease. Indeed, PECRB's work with the Pimas led to a unified definition of diabetes based on a glucose tolerance test that was adopted in 1980 by the World Health Organization. Since then, PECRB's criteria for modifying or treating factors that put people at high risk for T2D and its complications have become standard practices of care.

### Setting the Standard

**Peter Bennett**, scientist emeritus and former Chief of PECRB, and subsequently **William Knowler**, until recently chief of the Diabetes Epidemiology and Clinical Research Section, led a longitudinal population study that began in 1965 and would eventually span 43 years. This work, in collaboration with Bogardus, NIDDK Senior investigator **Robert Hanson**, and others, established obesity, insulin resistance, and inadequate insulin secretion as primary risk factors for developing T2D. Further investigation revealed evidence of heritability. T2D incident rates increased dramatically in individuals whose parents developed the disease before age 45. An even higher risk was associated with full Pima Indian heritage, yet another genetic indicator. But the strongest determinant they found was in children born to mothers who had diabetes during pregnancy—they were nearly certain to develop T2D by age 30.

Knowler's work laid the foundation for the Diabetes Prevention Program

(DPP). This landmark study, started in 1996, set an international standard for diabetes care and prevention in high-risk individuals. A lifestyle-change group reduced their risk of developing T2D by 58% when provided with intensive training on modest weight loss, eating less fat and fewer calories, and exercising at least 150 minutes per week. A second group reduced their risk by 31% with metformin, a drug that lowers blood glucose levels and improves how the body handles insulin. These participants took 850 milligrams twice a day and were provided standard advice about diet and physical activity. About half of the DPP's nearly 4,000 participants were from minority groups—such as African American, Alaska Native, American Indian, Asian American, Hispanic, or Pacific Islander—and most of these original participants continue to be followed today in the DPP Outcomes Study.

### Traditional Lifestyle May Offer Protection

The notion that environment can exacerbate—or protect against—susceptibility to disease is well exemplified by the Pima Indians in Sonora, Mexico. Genetically similar to their Arizona counterparts, this geographically isolated group has largely maintained a traditional subsistence lifestyle. Living around the village of Maycoba in Mexico's rugged Sierra Madre Mountains, the Mexican Pimas are primarily farmers and ranchers who maintain high levels of physical activity while providing for their families. They grow much of their own food consisting of beans, potatoes, and whole grains—a high-fiber, low-fat diet that contrasts sharply with their American relatives. NIH-funded studies here found drastically lower rates of T2D



CREDIT: NIDDK

In the early 1960s, NIDDK, then known as the National Institute of Arthritis and Metabolic Diseases, began research working out of facilities located in the Gila River Indian Community.

CONTINUED ON PAGE 20 ►

## Native Communities

CONTINUED FROM PAGE 19



CREDIT: MADHUMITA SINHA, NIDDK

Research study visit at the Guadalupe clinic. Ten years ago, NIDDK set up a research clinic—in Guadalupe, Arizona—which has become a model for community-based participatory research.

and obesity compared with the GRIC, offering further evidence of the protective role that a traditional lifestyle imparts (*Curr Obes Rep* 4:92–98, 2015).

### Genetic Connections and Targeted Treatments

However, some forms of T2D have a strong genetic component. “If we can understand genetically which different pathways are being affected, we can find drugs that are better suited for an individual’s diabetes,” said **Leslie Baier**, chief of PECRB’s Diabetes Molecular Genetics Section, who has uncovered several genetic variants related to diabetes. In 2013, her group in collaboration with Hanson identified a common variant in the gene *KCNQ1* that increases risk for T2D in the Pima population by impairing insulin secretion from pancreatic beta-cells. Because the GRIC studies can draw from generations of family data, the variant was traced to inheritance from the mother (*Diabetes* 8:2984–2991, 2013).

Rare monogenic causes of T2D are being discovered, too. Established tribal

research partnerships led to the creation of a genetic data array that uncovered a risk factor affecting some parents and their newborn children (*Diabetes* 64:4322–4332, 2015). As a result, the research team reached out to educate community physicians on providing valuable interventions and care to these individuals in the hospital after delivery. In a separate study, altered function of *MC4R*—a gene known as a genetic variant hotspot—was associated with an extremely high body-mass index early in life (*Hum Genet* 133:1431–1441, 2014).

Discovering diversity in genetic architecture can help communities direct prevention resources to those who need it most—and moves the science forward. Baier sees potential for work in the genomic arena to benefit all those affected by T2D. “Even though a genetic variant might be unique to a specific ethnic group, we’re understanding physiology that will translate to other populations,” she said.

PECRB’s molecular genetics lab is also delving further into disease-causing mechanisms using engineered beta-cell

lines. This exciting new research may guide investigators closer to personalized drug targets for T2D. “We can take [a variant] and look at what genes and pathways are affected at each stage of development and where is the best stage to intervene,” said Baier.

### Building Community

Between the urban bustle of Phoenix and Tempe lies Guadalupe, a one-square-mile town that is home to 5,000 Hispanics and Yaqui Indians. The tight-knit community maintains many of its cultural traditions that blend Catholic rites with centuries-old Yaqui rituals, such as the festival of Our Lady of Guadalupe. Ten years ago, NIDDK set up a research clinic here, which has become a model for community-based participatory research.

“We are reaching out to the community as equal partners,” said Sinha, who is an associate research physician at PECRB’s Diabetes Epidemiology and Clinical Research Section. “If obesity is a problem, you’re trying to engage the community and translate your research findings to a practical environment so it can frame health-policy decisions that are more acceptable to the people.” Her team has presented its research at town council meetings, the local elementary school, and even the fire station.

Since 2019, the Tribal Turning Point Study has been recruiting American Indian children, between 7 and 10 years old, who have obesity but not diabetes. Sinha is the principal investigator at Guadalupe, while two other sites in the Navajo Nation (a 17.5-million-acre territory that spans portions of Arizona, Utah, and New Mexico) at Chinle, Arizona, and Shiprock, New Mexico, are overseen by the University of Colorado (Denver, Colorado). The intervention group participates in a structured lifestyle behavior

program—tailored by native leaders—while the control group receives educational information on general diets and activities. Researchers study how these interventions affect a variety of biomarkers such as adiposity, lipids, glucose, and indicators of liver disease. The clinic at Guadalupe also happens to be part of the town's church campus. “The people saw that we were working with children in their backyard, doing physical activity,” said Sinha. “I think that creates community awareness.”

This year, NIDDK will open a new research clinic in the Valleywise Health Medical Center (Phoenix, Arizona). Here, Sinha will oversee the Early Tracking of Childhood Health Determinants Study, an ambitious 23-year longitudinal and observational study backed by NIH's Intramural Research Program. The study will follow 750 American Indian and Hispanic mothers and their children through 18 years of age to identify the intrauterine and early-life risk factors that contribute to obesity and metabolic risk in children. Sinha's team plans to collect comprehensive medical data in addition to examining other socioeconomic and demographic influences during pregnancy. Diet, stressful experiences, sleep, and physical activity are among the many factors being tracked. The study aims to link these prenatal risk factors to a spectrum of health markers in the children such as adiposity, gut microbiome, and even cognitive development. “Obesity is not just biological, it's shared environment, too,” said Sinha. “And the environment may be adverse.”

There are 574 federally recognized tribes in the United States. Each is a sovereign nation with an independent government and culture and the potential to contribute to scientific discovery in an authentic way. NIH's Tribal Health Research Office (THRO) is the central hub for coordinating

tribal health research throughout NIH and serves as the single point of contact for both researchers and tribes.

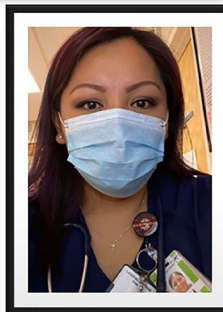
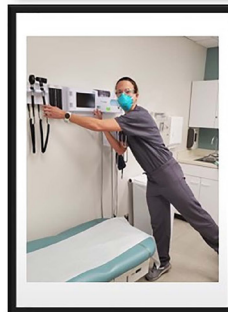
“We can help create strategies and identify areas where tribes have unique differences,” said THRO Director **David Wilson** in a recent videocast on the ethical conduct of research with American Indians. That way researchers “have a better understanding of the community they are going into, and [these strategies] help get them off on the right foot.” He pointed to tribal institutional review boards and formal consultations between tribal leadership and NIH as ways to align expectations and ensure that research is meaningful to each community. “Tribes are very interested and willing to participate in biomedical research,” said Wilson. “But we have to offer them opportunities to be involved as true partners in the process.” ●

*Michael Tabasko is a science writer–editor for The NIH Catalyst.*

## Recent Videocasts

**Clinical Center Grand Rounds: Physiologic and Genetic Studies of Diabetes in the Akimel O'odham (Pima Indians):** <https://videocast.nih.gov/watch=41794> (April 28, 2021)

**Office of Human Subjects Research Protections Education Series: Ethical Conduct of Research with American Indian and Alaska Native Participants: Extending Protections through Respect for Tribal Sovereignty (NIH only):** <https://videocast.nih.gov/watch=42651> (September 2, 2021)



CREDIT: NIDDK

Shortly after the pandemic began, the PIMC sent out a call for volunteer health care workers to provide extra clinical care as the hospital prepared for the COVID-19 patient surge. Several PECCB staff members, including the branch's clinical research nursing staff, medical director, and supervisory nurse practitioner, rose to the challenge. They've been continuously volunteering since the early stages of the pandemic to provide patient care, including for those with COVID-19.

## NIH Volunteers During the 1960s Civil Rights Movement

### Visiting Hospitals in the South to Certify Desegregation

BY GORDON MARGOLIN, OD

CREDIT: NATIONAL LIBRARY OF MEDICINE



President Lyndon Johnson signing the 1965 Medicare bill in a ceremony held in Independence, Missouri. From left: President Johnson, Lady Bird Johnson, Vice President Hubert Humphrey, President Harry S. Truman, and Bess Truman.

**WHILE SERVING AS A FACILITATOR IN** the Oral History program in the Office of NIH History, I have met many accomplished NIH scientists. I have recorded the personal stories of scientists who volunteered in the mid-1960s (a turbulent period during the Civil Rights Movement) to travel to the Southern states to mitigate and help resolve the Jim-Crow-like incursions into the medical care of Black citizens. The recognized problems were that Black patients were hospitalized only in segregated and physically inadequate facilities, that the medical care offered to these individuals was substandard and outdated, and that there was refusal to recognize and support the limited number of Black physicians. Five young faculty members, all registered with the U.S. Public Health Service, responded to a call for volunteers to offer their services in confronting these difficult issues, despite the known dangers of such involvement at that time.

### Background

Two Federal laws had been passed. The first was the Hospital Survey and Construction Act of 1946, which provided funds for new hospital construction in an effort to provide better care for all Americans contingent upon the guarantee of equal treatment of people of all races, colors, creeds, or national origins. The second was the Civil Rights Act of 1964, which outlawed discrimination on the basis of race, color, religion, sex, or national origin; required equal access to public places and employment; and strengthened the enforcement of voting rights and the desegregation of schools. But neither law led to the desegregation of medical care and facilities.

In 1965, the Medicare Act became law and provided federal oversight as well as an incentive to hospitals to integrate. Medicare funds would be withheld from hospitals that failed to comply with the new law and its explicit requirement of equal treatment and care for all Americans.

### Call for Volunteers

President Lyndon Johnson, concerned about hospital compliance and failure to desegregate, sent some 700 federal workers into the South to do on-site surveillance and assess whether hospitals had complied with desegregation requirements.

Five Public Health Service officers who were NIH scientists volunteered: **Stanley Rapoport, M.D., Paul Plotz, M.D., Norman Robbins, M.D., Ph.D., Jesse Roth, M.D., and Robert Perlman, M.D., Ph.D.** Plotz and Roth were already active in the Civil Rights Movement and were members of the Medical Committee for Human Rights. Perlman, however, never received an assignment and was unable to go.

The volunteers received several days of instruction to learn how to detect evidence of racial discrimination in hospitals. Then they were sent in pairs to evaluate hospitals in varying locales, focusing on the importance of desegregation of care. They first met with former patients and many knowledgeable community members to obtain information regarding segregation in each hospital, so they were knowledgeable and positioned to circumvent false information during their visits. Later in the 1960s and beyond, these physicians continued to combine their professional work with volunteering to help communities in need. Following is a summary of the NIH scientists' experiences.

**Stanley Rapoport, M.D.** (*National Institute of Mental Health; later National Institute on Aging; he specialized in understanding the blood-brain barrier*) stimulated this project of assembling information from all who had gone to the South. After volunteering and waiting six months for approval, Rapoport was assigned in March 1965 to report on the circumstances in Bogalusa, Louisiana,

a center of resistance in the Civil Rights Movement. He bravely went by himself, was sheltered in homes of members of the Deacons for Defense and Justice (an armed resistance force of Black citizens), evaluated the medical conditions, and saw the brutality by white citizens and the response by the Deacons. He was arrested for his participation. He submitted a highly regarded report on his findings to the Medical Committee for Human Rights and to the Congress of Racial Equality (an African American civil rights organization), which brought attention to these serious discriminatory concerns of citizens throughout Louisiana. Recently, Rapoport was appointed to the board of the Robert Hicks Foundation, which is converting the house of a Bogalusa civil rights leader into a museum.

**Paul Plotz, M.D.** (*National Institute of Arthritis and Musculoskeletal and Skin Diseases; his research focused on understanding autoantibodies, autoimmune disease, and inflammatory muscle diseases*) was assigned, in 1966, to rural hospitals along the Mississippi Gulf Coast and in the southwest corner of Tennessee, finding various forms of noncompliance at all sites. He was never injured, but was often followed by pickup trucks with rifles sticking out the windows. He also noted that the phones in his hotel were tapped. Among his other volunteer activities, he went with a group from NIH to the West African country of Liberia to help during the Ebola outbreak.

**Norman Robbins, M.D., Ph.D.** (*National Institute of Neurologic Disorders and Strokes; studied neuromuscular synaptic plasticity*) was assigned to Jackson, Mississippi, and surrounding areas after an extraordinary



Stanley Rapoport was assigned in March 1965 to report on the circumstances in Bogalusa, Louisiana, a center of resistance in the Civil Rights Movement. Pictured: Rapoport (center) with some members of the Deacons for Defense and Justice.

crash course in negotiation in Dallas, Texas. He was invited to attend the March Against Fear in 1966 (an attempt to walk from Memphis, Tennessee, to Jackson, Mississippi, to promote black voter registration and defy entrenched racism), described the brutality of the police, and was himself threatened at gunpoint when he offered medical help to an injured participant. He was impressed with the bravery of the Black individuals who were involved, was constantly badgered by trucks with exposed firearms, and found his phone lines monitored. Later on, he volunteered with nonprofits that were working on environmental, peace, social justice, and voting issues.

**Jesse Roth, M.D.** (*National Institute of Diabetes and Digestive and Kidney Diseases; he elucidated much of what is known about the structure and intracellular mechanisms of the insulin receptor and other endocrine receptors*) inspected hospitals in West Virginia for

compliance with the Medicare Act. He relied on reports from scouts who were hospital workers and in danger of losing their jobs if their employers knew what they were doing. He was also a pro bono physician for Head Start programs in the Washington, D.C., area, manned a clinic in Anacostia, Maryland, helped to assure the fair distribution of food stamps in Alabama, and served the injured and jailed during race riots Washington, D.C. (in 1968 after the assassination of Martin Luther King Jr.). ●

For more details, read the oral histories of each of these physicians at <https://history.nih.gov/display/history/Medicare+Hospital+Certificati+Program+Oral+Histories/>.

*E. Gordon Margolin, M.D., a retired internist and nephrologist, has been a volunteer in the Office of NIH History and Stetten Museum since 2011. He was the director of medicine at Cincinnati Jewish Hospital and a professor of medicine at the University of Cincinnati.*

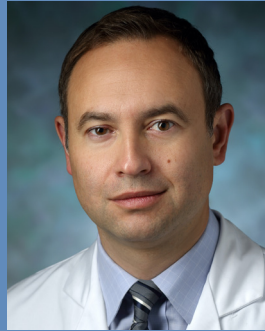
## Recently Tenured



JILL BARNHOLTZ-SLOAN,  
NCI-DCEG



HYOKYOUNG GRACE HONG,  
NCI-DCEG



DIMITRIOS KAPOGIANNIS, NIA



PETER W. SCHUCK, NIBIB



MEREDITH SHIELS, NCI-DCEG

### JILL BARNHOLTZ-SLOAN PH.D., NCI-DCEG

*Senior Investigator, Trans-Divisional Research Program, Division of Cancer Epidemiology and Genetics, National Cancer Institute; Associate Director for Informatics and Data Science, NCI Center for Biomedical Informatics and Information Technology*

**Education:** University of Florida, Gainesville, Florida (B.S. in mathematics); University of Texas at Austin, Austin, Texas (M.S. in statistics); University of Texas School of Public Health, Houston (Ph.D. in biostatistics)

**Before coming to NIH:** Various roles at Case Western Reserve University School of Medicine and University Hospitals of Cleveland (Cleveland) including director, Research Health Analytics and Informatics, University Hospitals Health System; professor, of population and quantitative health sciences; associate director for Translational Informatics at Cleveland Institute for Computational Biology; and associate director for Data Science at Case Comprehensive Cancer Center.

**Came to NIH:** In May 2021

**Outside interests:** Walking outside with her dog (a chocolate Labrador retriever named Duke) and her family; listening to music; having friends over for meals

**Website:** <https://dceg.cancer.gov/about/staff-directory/barnholtz-sloan-jill>

**Research interests:** Because brain tumors are uncommon and subdivided into many subtypes, with distinct etiologies and outcomes, multisite, multidisciplinary team science approaches are essential for advancing the field. I am facilitating collaborations in data science and in the study of brain tumors by leveraging my experience in multi-institutional team science and the use of large, complex health care datasets to enhance the data assets available in the NCI Cancer Research Data Commons and throughout NCI.

My team's work has contributed to a better understanding of the population burden of disease (*Neuro Oncol* **2**(12 Suppl 2):iv1–iv96, 2020) and identified risk factors and biomarkers (*Nat Genet* **49**:789–794, 2017; *N Engl J Med* **372**:2481–2498, 2015; *Cell* **155**:462–477, 2013), and we are working toward uncovering biological mechanisms underlying known sex differences in brain tumors (*Sci Transl Med* **11**:eaa05253, 2019), all of which significantly improve the diagnosis, treatment, and management of brain tumors.

I was a founding member of the Brain Tumor Epidemiology

Consortium, which resulted in two highly successful international collaborations, including the first studies to assess genetic risk factors for familial and sporadic brain tumors at the genome-wide level (*Nat Genet* **49**:789–794, 2017; *Cancer Res* **71**:7568–7575, 2011).

Given my dual roles in NCI's Center for Biomedical Informatics and Information Technology and the Division of Cancer Epidemiology and Genetics (DCEG), I envision bringing data science to all research domains within DCEG, helping to move toward 1) use of cloud resources for computing and data sharing via the NIH Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability Initiative, and 2) use of the Findability, Accessibility, Interoperability, and Reuse principles (FAIR) for research in DCEG. In addition, I am developing and facilitating closer links with all divisions across the NCI and more generally across NIH, especially with the NIH Office for Data Science Strategy, to fully leverage data assets and data analytics for cancer research.





**HYOKYOUNG GRACE HONG, PH.D., NCI-DCEG**  
*Senior Investigator, Biostatistics Branch,  
 Division of Cancer Epidemiology and  
 Genetics, National Cancer Institute*

**Education:** Sungkyunkwan University, Seoul, Korea (B.S. in mathematics education); University of Illinois at Urbana-Champaign, Champaign, Illinois (M.S. in actuarial science; M.S. and Ph.D. in statistics)

**Before coming to NIH:** Associate professor (tenured), Department of Statistics and Probability, Michigan State University (East Lansing, Michigan)

**Came to NIH:** In January 2021

**Outside interests:** Traveling and tasting new cuisines (some favorite travel destinations are Italy, Spain, and China); painting; healthy cooking; reading

**Website:** <https://dceg.cancer.gov/about/staff-directory/hong-grace>

**Research interests:** As a statistical scientist, my goal is to advance scientific knowledge in population-based cancer epidemiology and genetics studies through the development and use of novel statistical methodology. I am developing cutting-edge statistical methods for analyzing complex large-scale datasets, and applying these methods to the fields of public health, medicine, and health-policy research.

Throughout my career, my team and I have led the development of methods in high-dimensional data analysis by proposing a series of novel and innovative ideas. We have made important advances in statistical theory and methodological development in the areas of quantile regression analysis, classification, and time-to-event analysis. Quantile regression has emerged as both an efficient way of linking the whole distribution of an outcome to the covariates of interest and an important alternative to commonly

used regression models. In a recent study, we used quantile regression to identify clinical and molecular predictors associated with high-risk lung cancer patients. (*Precis Clin Med* **2**:90–99, 2019).

I have also contributed to statistical methodology for classification problems with high-dimensional covariates. For example, many classification problems emerge from analyses of gene expression and imaging data to identify individuals with disease or at high risk of developing disease. To circumvent these issues, I proposed a novel high-dimensional classification method that could predict clinical diagnosis of autism spectrum disorder using imaging predictors, integrating known different sources of anatomical information, correlation among imaging predictors, and spatial information (*Biometrika* **104**:785–800, 2017).

**DIMITRIOS KAPOGIANNIS, M.D., NIA**

*Senior Investigator, Human Neuroscience  
 Section, National Institute on Aging*

**Education:** National University of Athens Medical School, Athens, Greece (M.D.)

**Training:** Internal medicine internship at Evanston Hospital/Northwestern University (Evanston, Illinois); neurology residency at Massachusetts General Hospital/Brigham and Women's Hospital/Harvard Medical School (Boston); clinical fellowship in behavioral neurology at the National Institute of Neurological Disorders and Stroke.

**Came to NIH:** In 2006 for training; staff clinician in NIA; then investigator and chief of NIA's Human Neuroscience Unit; adjunct associate professor in neurology at Johns Hopkins School of Medicine

**Outside interests:** Is passionate about history, archaeology, and philosophy; enjoys traveling and swimming

**Website:** <https://irp.nih.gov/pi/dimitrios-kapogiannis>

**Research interests:** My lab and I are identifying biomarkers for neurodegenerative diseases, particularly Alzheimer disease (AD) and related dementias (ADRD), as well as neurologic and psychiatric diseases that may affect the aging brain. Our ultimate goal is to arrive at precision-medicine treatments for AD and ADRD by characterizing individual patients for multiple pathogenic processes simultaneously and using biomarkers to predict their response to experimental treatments. The bulk of our work has focused on the analysis of extracellular vesicles (EVs) in plasma.

A limitation of many AD biomarkers measured in the soluble phase of blood is their tenuous link to brain pathology, because they are often produced by multiple tissues and their brain-derived fraction has to cross multiple barriers before reaching the blood.

To address this limitation, my lab and I have taken a new approach to biomarker discovery in AD: harvesting EVs enriched for neuronal and astrocytic origin from blood. These EVs are akin to a brain “liquid biopsy” and can be used to interrogate pathogenic processes that were previously inaccessible in vivo. We have identified EV biomarkers that reflect many pathogenic processes involved in AD and other neurodegenerative diseases. (*JAMA Neurol* **76**:1340–1351, 2019; *Annals Neurol* **83**:544–552, 2018). We have also pioneered the use of these EVs to demonstrate target engagement and biomarker responses in clinical trials for various neurological and psychiatric disorders (*JAMA Neurol* **76**:420–429, 2019).

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**Recently Tenured**

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We are currently in the process of conducting large-scale studies using longitudinal study cohorts to further validate EV biomarkers, demonstrate their ability to predict AD or ADRD diagnosis at the preclinical stage, and assess whether they can identify disease subgroups with different biologies and clinical trajectories.

We are also busy clinically. We are conducting early-phase interventional studies targeting brain metabolism to ameliorate pathogenic processes leading to AD or ADRD. We conducted a pilot double-blind placebo-controlled randomized clinical trial of the antidiabetic agent exendin-4 in early AD. In addition, we are conducting controlled randomized clinical trials in middle-aged individuals at risk for cognitive impairment—testing a 5:2 calorie restriction diet (eating regularly for five days and very little for two) and an oral ketone ester—and will be looking at changes in EV and magnetic resonance spectroscopy biomarkers as well as cognitive outcomes.

**PETER W. SCHUCK, PH.D., NIBIB**

*Senior Investigator and Chief, Laboratory of Dynamics of Macromolecular Assembly, National Institute of Biomedical Imaging and Bioengineering*

**Education:** Goethe University, Frankfurt am Main, Germany (B.S. in physics; Ph.D. in biophysics)

**Training:** Postdoctoral fellowship, Laboratory of Biochemical Pharmacology, National Institute of Diabetes and Digestive and Kidney Diseases

**Came to NIH:** In 1994 for training; became a staff scientist in 1999; chief, Protein Biophysics Resource, Division of Bioengineering and Physical Science, Office of Research Services (2003–2007);

and chief, Dynamics of Macromolecular Assembly Section, Laboratory of Cellular Imaging and Macromolecular Biophysics, NIBIB (2007–2021); appointed an Earl Stadtman Tenure-Track Investigator in 2014  
**Outside interests:** Enjoying jazz music—listening and playing bass guitar; playing carom billiards; cooking; bicycling  
**Website:** <https://irp.nih.gov/pi/peter-schuck>

**Research interests:** It's exciting to determine how macromolecules are assembled and interact with each other and to apply that knowledge to understanding the inner workings of a cell. My group and I are developing biophysical methods to study protein interactions and the assembly of multiprotein complexes.

We are developing quantitative hydrodynamic methods using analytical ultracentrifugation in conjunction with mathematical modeling of reaction, diffusion, and sedimentation processes. Although analytical ultracentrifugation is a classical biophysical discipline, it has undergone a renaissance in the last decade due to new computational capabilities that allow us to fully exploit mass-based separation in solution to obtain macromolecular size distributions and measure interactions.

There are increasing applications in structural biology and immunology for the study of protein interactions and multiprotein complexes, and in the biotechnology industry for the characterization of protein pharmaceuticals and nanoparticles for drug delivery. In a recent study, we used a suite of biophysical methods including analytical ultracentrifugation to gain insights into the molecular mechanisms of SARS-CoV-2, the virus responsible for COVID-19 (*iScience* **24**:102523, 2021).

Recently, we embarked on the extension of analytical ultracentrifugation to concentrated macromolecular solutions to better mimic conditions in cytosol, serum, and pharmaceutical formulations. In crowded solutions, ultraweak attractive and even repulsive interactions can play key roles in controlling dynamic assemblies that would fall apart in more dilute solutions. Developing new experimental and computational strategies, we have achieved unprecedented resolution of transient macromolecular complexes at protein concentrations close to those in serum.

In the other extreme, using a fluorescence detector in combination with newly developed computational tools and exploiting properties of photo-switchable fluorescent molecules, we have achieved unprecedented sensitivity in characterizing architectural principles and driving forces of protein assemblies in the low picomolar concentration range. These methods have great potential to provide information on macromolecular organization complementary to structural and microscopy methods.

In addition, we are involved in several collaborative applications in various fields including immunological protein complexes, viral proteins, membrane receptor complexes, and eye lens crystallins.


**MEREDITH SHIELS, PH.D., NCI-DCEG**

*Senior Investigator, Infections and Immunoepidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute*

**Education:** The Pennsylvania State University, Schreyer Honors College, State College, Pennsylvania (B.S. in biobehavioral health); Johns Hopkins Bloomberg School of Public Health, Baltimore (M.H.S. and Ph.D. in cancer epidemiology)

**Training:** Postdoctoral fellow and research fellow, Infections and Immunoepidemiology Branch, NCI-DCEG

**Came to NIH:** In 2009 for training; became a tenure-track investigator in 2016

**Outside interests:** Spending time with her three daughters, ages 3, 6, and 9

**Website:** <https://irp.nih.gov/pi/meredith-shiels>

**Research interests:** My research program uses a combination of innovative contemporary approaches—using descriptive analyses, population-based databases, and real-world data—to confront high-impact public health questions. My work focuses on 1) quantifying cancer risk and burden in people with HIV; 2) estimating the impact of risk factors on changing cancer rates; and 3) using careful investigation of population-based surveillance data to provide insights into emerging public health crises, including the opioid epidemic and the COVID-19 pandemic.

People with HIV have a higher risk of certain types of cancer. I am the co-principal investigator of the HIV/AIDS Cancer Match Study, an observational study of nearly one million people with HIV across the United States. We have projected future

cancer rates and burden among U.S. adults with HIV, showing a decline in the number of cases of Kaposi sarcoma and non-Hodgkin lymphoma and an increase in the number of lung and prostate cancers (*Ann Int Med* **168**:866–873, 2018).


My work uses linked databases and statistical modeling to disaggregate cancer-risk rates based on etiology, which is important for targeted prevention efforts. For example, we estimated the role of the impact of the increasing prevalence of overweight and obesity on rising rates of papillary thyroid cancers (*J Nat Cancer Inst* **112**:810–817, 2020).

I have applied my expertise to interrogating large, population-based data to address specific public health questions related to the underlying drivers of premature mortality rates (deaths among 25- to 64-year-olds) in the United States. Some of this work has focused on the evolving drug-overdose epidemic, which is a main contributor to rising premature mortality rates in some groups. In 2020, I expanded my research program to include descriptive analyses of COVID-19. This includes recent work that estimated excess deaths in the United States during the pandemic (*Ann Intern Med* **174**:437–443, 2021).

**NIH ABBREVIATIONS**

**CBER:** Center for Biologics Evaluation and Research, FDA  
**CC:** NIH Clinical Center  
**CCR:** Center for Cancer Research, NCI  
**CIT:** Center for Information Technology  
**DCEG:** Division of Cancer Epidemiology and Genetics, NCI  
**DIPHR:** Division of Intramural Population Health Research, NICHD  
**FAES:** Foundation for Advanced Education in the Sciences  
**FARE:** Fellows Award for Research Excellence  
**FelCom:** Fellows Committee  
**FDA:** Food and Drug Administration  
**FNHI:** Foundation for the NIH  
**FNL:** Frederick National Laboratory  
**IRP:** Intramural Research Program  
**HHS:** U.S. Department of Health and Human Services  
**NCATS:** National Center for Advancing Translational Sciences  
**NCBI:** National Center for Biotechnology Information  
**NCCIH:** National Center for Complementary and Integrative Health  
**NCI:** National Cancer Institute  
**NEI:** National Eye Institute  
**NHGRI:** National Human Genome Research Institute  
**NHLBI:** National Heart, Lung, and Blood Institute  
**NIA:** National Institute on Aging  
**NIAAA:** National Institute on Alcohol Abuse and Alcoholism  
**NIAD:** National Institute of Allergy and Infectious Diseases  
**NIAMS:** National Institute of Arthritis and Musculoskeletal and Skin Diseases  
**NIBIB:** National Institute of Biomedical Imaging and Bioengineering  
**NICHD:** Eunice Kennedy Shriver National Institute of Child Health and Human Development  
**NIDA:** National Institute on Drug Abuse  
**NIDCD:** National Institute on Deafness and Other Communication Disorders  
**NIDCR:** National Institute of Dental and Craniofacial Research  
**NIDDK:** National Institute of Diabetes and Digestive and Kidney Diseases  
**NIHES:** National Institute of Environmental Health Sciences  
**NIGMS:** National Institute of General Medical Sciences  
**NIMH:** National Institute of Mental Health  
**NIMHD:** National Institute on Minority Health and Health Disparities  
**NINDS:** National Institute of Neurological Disorders and Stroke  
**NINR:** National Institute of Nursing Research  
**NLM:** National Library of Medicine  
**OD:** Office of the Director  
**OITE:** Office of Intramural Training and Education  
**OIR:** Office of Intramural Research  
**ORS:** Office of Research Services  
**ORWH:** Office of Research on Women's Health  
**OTT:** Office of Technology Transfer

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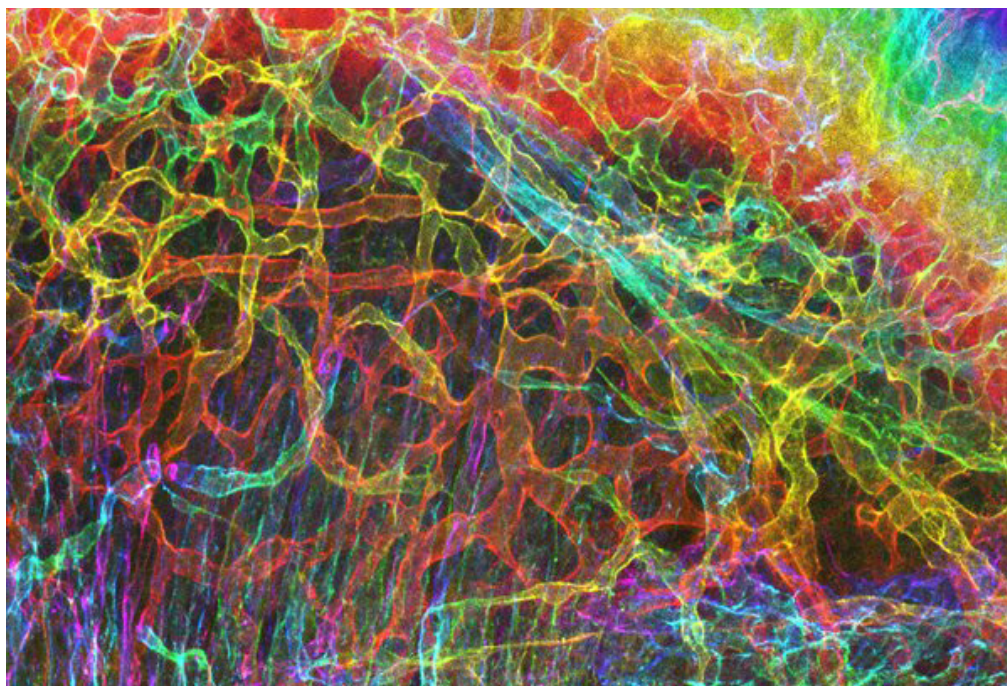
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## PHOTOGRAPHIC MOMENT

### Skin-Muscle Interface



CREDIT: SARAH LIPP AND SARAH CALVE, PURDUE

NIAMS: A 3D color projection of the developing skin-muscle interface of an embryonic mouse forelimb stained for LAMA1, a basement membrane. Understanding how the limb develops can help engineer new options to treat musculoskeletal injuries. This image was a winner in the 2020 BioArt Scientific Image and Video Competition of the Federation of American Societies for Experimental Biology.

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