

## Diagnosing Traumatic Brain Injuries

BY FRANCES FERNANDO, NICHD

It's ALWAYS BEEN TRICKY TO DIAGNOSE mild traumatic brain injuries (TBIs) because there are no reliable blood, neuroimaging, or other tests. In three papers that were recently published in *Neurology*, NIH researchers reported that a blood biomarker called neurofilament light chain (NfL) may hold the most promise for predicting, diagnosing, and following up on TBIs. When compared with three other blood biomarkers and with neuroimaging, NfL was better at identifying patients who had mild, moderate, or even severe brain injury.

After injury to brain tissue, indicators of cellular damage are released into the blood and cerebral spinal fluid (CSF). NfL is one such indicator.

Computed tomography (CT) scans and magnetic resonance imaging (MRI) are some of the current testing mechanisms, but each imaging method has its limitations. Imaging is expensive and imprecise.

“For mild events without much trauma, imaging is less useful,” said **Leighton Chan**, chief of the Rehabilitation Medicine Department at the NIH Clinical Center, and senior author on two of the papers. “Scans show images of anatomic abnormalities, without providing much insight into brain function.”

In one study—“Neurofilament Light as a Biomarker in Traumatic Brain Injury”—the researchers found that in a group of Swedish hockey players, “that serum NfL

CONTINUED ON PAGE 12 ➤

## NIH and Howard University Partnership Building a Foundation for Scientific Collaboration

BY MICHAEL TABASKO



CREDIT: DALE LEWIS, NCI

Students and faculty from Howard University have been conducting research with NIH principal investigators for decades, but in March a formal partnership was established. Shown (pre-COVID-19 photo): NIH Distinguished Investigator Susan Gottesman (NCI) and Howard undergraduate Abbigale Perkins. Gottesman has been working with one of Perkins's professors (Karl Thompson) for 20 years. Perkins will join Gottesman's lab as a postbac this fall.

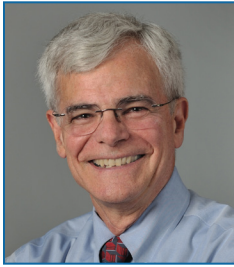
**ONE SUMMER NEARLY 20 YEARS AGO, KARL THOMPSON CAME TO NIH FROM** Howard University (Washington, D.C.) as a student aspiring to a career in science. “I was the most junior trainee, at a time when there weren't many Ph.D. students at NIH, but they treated me like family,” said Thompson.

His mentor was NIH Distinguished Investigator **Susan Gottesman** (National

CONTINUED ON PAGE 14 ➤

### CONTENTS

**FEATURES** • **|1|** Diagnosing Traumatic Brain Injuries **|1|** NIH and Howard University Partnership **|7|** Meet the Newest Members of NAS **|10|** COVID-19 Timeline (July–August) **|13|** Using Flatworms to Study Stem Cells **|24|** Sad News: NIH PI Herb Tabor Dies at 101  
**DEPARTMENTS** • **|2|** DDIR: Safety First in the Age of COVID-19 **|3, 4, 5|** Training: Reflections on returning to the workplace; Train-the-Trainer Workshop; New Policy on Family Leave **|6|** News Briefs: Five New IC Directors **|8|** Research Briefs **|17|** SIG Beat: COVID-19 SIG **|18|** Colleagues: Recently Tenured **|23|** Abbreviations



## Safety First in the Age of COVID-19

BY MICHAEL GOTTESMAN, DDIR

**THE COVID-19 PANDEMIC HAS** brought dramatic changes to the way we operate our laboratories and clinics. We are continually making adjustments as the pandemic progresses and we learn more about how COVID-19 spreads. Although NIH leaders have to respond to a variety of challenges, I want to assure you that there is one overriding principle: **Safety first!**

As government employees, trainees, and contractors we have a primary mission, and an obligation to the taxpayers who support our research, to carry out research to improve the public health and train the next generation of researchers. But we must first ensure that the conditions under which we do this work are safe. As I always point out in my annual safety memo each spring: **Safety is my primary concern.**

NIH does its best to assure the safety of our staff. First, we restricted attendance in the workplace to mission-critical employees (clinical, animal-care, security, and maintenance staff) and, more recently, to scientists whose work cannot be done through telework. The goal is to keep the density of people low, ensuring physical distancing that reduces the risk of transmitting COVID-19. Added protections include mandatory safety training, masks that cover the nose and mouth, and appropriate sanitizing of shared working surfaces and high-touch areas. These precautions create low-risk circumstances for transmission of the virus. The vast majority—and quite possibly all—of the cases detected in NIH employees have resulted from community transmission.

Recently, the NIH Clinical Center has

begun to offer free testing for SARS-CoV-2 infection to asymptomatic D.C.-area staff whether they are working onsite (members of Groups 0, A, or B) or are not yet eligible to return to the physical work space.

Certainly, anyone experiencing COVID-19-like symptoms should *not* schedule an appointment for asymptomatic testing. Instead, follow the procedures outlined on the “What to Do if You Have Symptoms” page: <https://employees.nih.gov/pages/coronavirus/what-to-do-feel-sick.aspx>. NIH’s Occupational Medical Service will determine whether you need to be tested and will provide instructions.

The asymptomatic testing service is voluntary and was initially available only to on-site staff to allow the Clinical Center time to expand its capacity to be able to test all NIH staff. These tests involve taking samples using a nasal mid-turbinate swab (inserted about an inch into the nose); the samples are analyzed using a highly sensitive and specific reverse-transcription polymerase chain reaction (RT-PCR) assay at the Clinical Center. In general, the results are available within 24 to 48 hours. Testing is by appointment only; to schedule one, go to <https://clinweb.cc.nih.gov/cct>.

Other NIH locations in Baltimore, Maryland, Montana, and North Carolina have also begun conducting asymptomatic testing for staff and shipping the samples to the Clinical Center for RT-PCR analyses. The mode and location of testing may be changing in the future to make it easier, so keep an eye on notices to NIH staff.

There is good epidemiological evidence and data indicating that individuals who

are completely asymptomatic or pre-symptomatic are responsible for up to 40% of the transmission of COVID-19. By finding such individuals and having them leave the workplace temporarily, we can reduce the risk of transmission.

**Carson Chow**, a biostatistician in NIDDK and a leader of our COVID-19 scientific interest group, has demonstrated that the efficacy of testing to prevent transmission depends on how effective our physical distancing and mask-wearing is, and whether there is herd immunity in our population. If we assume that there is less than 100% efficacy of the physical protections (or the failure of some to abide by these requirements) and no significant herd immunity, then testing every 7 to 10 days appears to be optimal in preventing disease transmission in the workplace.

Our recent survey indicated that about 95% of our staff are willing to be tested. I urge all NIH staff, especially those coming to the workplace, to be tested to help reduce the risk of transmission at our facilities.

But safety is more than just physical safety. We are also concerned about your sense of well-being. Lack of child care, schools not opening, loss of personal interactions that drive so many transactions at the NIH—all of these are stressful and affect mental health. The Office of Research Services (including the Division of Occupational Health and Safety and the Occupational Medical Service), the Office of Acquisition and Logistics Management, and the Office of Human Resources are working to provide the support needed to address these issues.



## From the Fellows

### Reflections on Returning to Work During a Pandemic

BY THU-LAN LILY NGUYEN, NCI

Our staff, particularly trainees, are anxious about the effects of the prolonged hiatus in their research. To ensure that you are not penalized for this enforced pause, the Office of Intramural Research and supervisors have provided flexibilities needed by extending appointments, delaying Boards of Scientific Counselors reviews, and providing a means to fund enforced quarantine requirements. In addition, the Office of Intramural Training and Education has provided sessions aimed at reducing stress on trainees and their principal investigators. The results of the recent survey that most of you filled out about how the pandemic is affecting your life will be very helpful as we develop new strategies for dealing with stress in the workplace.

I am proud to say that you all have demonstrated your adaptability and willingness to suffer inconvenience to keep all of us safe. Compliance with safety requirements is very high, and patience with the other impediments to a more normal existence is impressive. I have not listed everyone whose hard work has kept us safe, but I can assure you that this is a full-time job for quite a few dedicated individuals.

Please stay safe, and continue to show concern and respect for your colleagues by physical distancing, wearing masks, washing your hands, sanitizing public spaces, and getting tested. ●

For more information and resources, please visit the “NIH Guidance for Staff on Coronavirus” intranet site at <https://employees.nih.gov/pages/coronavirus>.

**I WOKE UP ON MONDAY MORNING, JUNE 22**, feeling excited and nervous as if it were the first day of school. It was my first day back since March 16 when the COVID-19 pandemic forced most NIH labs and offices to shut down.

Most of us had been teleworking. But here I was, part of Group A, the first employees allowed to return to campus. Before leaving my apartment, I triple-checked my bag to make sure I wasn't forgetting anything: phone, check; wallet, check; laptop, check; Metro card, check; earbuds, check; water bottle, check; lunch, check. And facemask. Let's not forget that!

Wearing my mask, I joined a few riders on the Metro. Before the pandemic, the train would have been packed and I would have been swept into a dense sea of commuters exiting at the Medical Center stop. Today, only four of us got off at the station.

At the NIH entry gate, I scanned my badge and walked through the turnstile. As I headed to Building 37, I felt as if I were walking through a ghost town with empty parking lots and few signs of life. Posted signs urged me to go home immediately if I had any symptoms of COVID-19.

The first things I did when I walked into the lab were wash my hands and sanitize my workspace. I swapped out my homemade fabric mask for a disposable surgical one. I was briefed on new waste-disposal protocols to reduce risks to custodial staff and on the required advance sign-ups for shared rooms and equipment.

Every few days I would come to work and encounter a new safety measure. One day the door to my lab was outfitted with a plastic forearm shield so you could open the door with your arm instead of your hands. Another day, stickers appeared on the elevator floor to mark where people should stand to avoid being too close. Soon, we had

to complete a daily self-assessment to report whether we had COVID-19 symptoms or had been exposed to someone who had, or was suspecting of having, the disease. Anyone who responded “yes” was instructed not to return to work, to notify their supervisor, and to fill out an Occupational Medical Service screening form.

The most exciting part of returning to work was being able to see my co-workers. The only other person in my lab was our research biologist. We did our best to stay at least six feet apart while navigating the lab space and using shared equipment. The only time we would talk was to discuss results.

Eating lunch with co-workers was reimagined as well. Before the pandemic, we would squeeze around a small table. Now the few of us who were part of Group A sat outside, at least six-feet apart, around a gazebo. We ate quietly with our masks off but grew livelier once we finished eating and had our masks back on. Squinted eyes signaled smiles as we discussed everything from new hobbies picked up while working from home to our plans for applying to grad school.

With Group B's return the week of July 20, three people at a time are allowed in my workspace now and we often make small talk from opposite corners of the lab. I saw more people eating together outside (while maintaining the proper distance) and chatting in the hallways.

Although working at the NIH looks very different from when I started a year ago, I'm thankful to be working among scientists who continue to do important work while maintaining a safe environment. ●

*Lily Nguyen, a postbaccalaureate fellow in NCI, plans to pursue a Ph.D. in molecular biology when she completes her NIH training in 2021.*



## From the Office of Intramural Training and Education

### Train-the-Trainer Workshop

BY CHARLESICE HAWKINS, OITE

**DURING THE COVID-19 PANDEMIC**, research universities, scientific institutions, and other high-stress organizations have begun to pay closer attention to the mental-health needs of their workers. Many have come to appreciate that prioritizing good mental health and wellness practices can enhance productivity and success rather than diminish it.

At NIH, the Office of Intramural Training and Education (OITE) has always run programs and activities that support trainees and help them as they advance in their careers. In this time of stress and uncertainty, fellows and employees alike are dealing with unique issues that may affect their ability to be productive. One of the ways that OITE is helping fellows to reach their potential is by training the trainers (including PIs, supervisors, mentors, and advisors). In July, OITE offered a virtual, five-day train-the-trainer workshop that was open to people from the NIH as well as from other organizations throughout the country.

Training the trainers is an important step for creating a productive research culture that also supports the wellbeing of everyone in the research community, according to the Wellcome Trust (London), which conducted a survey of more than 4,000 researchers at different stages in their careers. Most supervisors reported that they had not received managerial training, much less guidance on supporting trainees in difficult situations. Concurrently, trainees reported that conversations about their career aspirations and support for their wellbeing overall were lacking.

OITE's workshop integrated good mental-health strategies and professional development to teach effective techniques for helping trainees succeed. PIs, program

administrators, and other career-development professionals attended seminars on career advising, mental health, wellness, and resiliency strategies for helping their biomedical trainees navigate the stresses of life, science, and research. The training outlined the fundamental components needed to develop a wellness program, to recognize substantial personal and cultural changes, and to consider the interplay of stress and executive functioning.

In addition, the current COVID-19 pandemic warranted emphasis on topics of critical importance—responding to trauma; preventing suicide; and discussing how the issues of anti-Black racism and xenophobia affects trainees. In virtual break-out rooms, registrants were separated into groups of three-to-eight people and worked with a facilitator to share their ideas and experiences and to role-play scenarios that might occur with trainees who are experiencing different types of distress.

“My partner and I took turns offering the perspective of the trainee or the training director,” said **Jackie Lavigne**, chief of the Office of Education in the National Cancer Institute's Division of Cancer Epidemiology and Genetics. Having a mental-health counselor offer feedback and support “helped me build confidence in having these difficult and important conversations.”

Other participants expressed their appreciation for the opportunity to discuss difficult topics, the support for PIs and trainees, and the chance to rehearse those hard conversations.

“These are hugely important topics, and I feel like I learned a lot, but also that I have a lot to learn,” said Brian Mitchell, an associate professor at the Northwestern University Feinberg School of Medicine (Chicago). “It was both humbling to think about all the

mentoring mistakes I have made but also really exciting to see the effort that NIH is putting into these issues. Just yesterday [a trainee] came into my office needing some career advice, and I feel like I was already able to implement some of what I learned.”

“I found it very supportive and insightful. I especially enjoyed the mental-health break-out group,” said Karin Lawton-Dunn, director of Graduate and Postdoctoral Career Services at Iowa State University (Ames, Iowa), who had a difficult virtual meeting with a trainee later that day. “It was nice to have just revisited this topic in the morning. I had more energy to support [the trainee].”

A growing body of literature and recent events highlight the need to intentionally work toward a healthier and more sustainable work environment, especially within the biomedical-research enterprise. Support for mental well-being and the training of those in managerial, advising, and mentoring positions is essential for success as well as for collaborative and innovative science.

“Thank you for providing a space (on a national level) to discuss racism [and] xenophobia and other topics such as suicide,” said **Erika Barr**, director of OITE's Community College Programs, in an email after the workshop.

“Please keep reading. Please keep discussing. Please keep [learning],” one of the participants suggested. “Let's keep challenging ourselves.” ●

*Charlesice Hawkins received her M.S. in biology before joining OITE as an Undergraduate Scholarship Program fellow in early 2020. She will continue her career in communications within OITE beyond this year while also exploring her interests in creative writing and other forms of expression.*

## From the Fellows

### New Policy Extends Paid Family Leave Benefits for NIH Trainees

BY SOFIYA HUPALO, NIGMS

**A RECENT SHIFT IN POLICY EXTENDS** paid family leave from eight to 12 weeks for NIH trainees. The new policy, which started in March 2020, provides any trainee—appointed under the Intramural Research Training Award (IRTA), the Cancer Research Training Award (CRTA), visiting fellow (VF) award, or Title 42 clinical or research fellow mechanisms—a 12-week paid excused-absence related to the birth, adoption, foster-care placement of a child, or other family medical needs (such as serious illness or an illness of a close family member). If both parents are NIH trainees, each of them are entitled to take paid leave.

**Charles Dearolf**, director of Program Development and Support at the Office of Intramural Research, advises fellows to communicate their intent to take leave in a memo to their PI; if trainees disagree with the PI response, they can appeal to their institute's scientific director.

This change was enacted to align with new paid family-leave policies for federal civilian employees under the 2020 National Defense Authorization Act. However, the application of this law for full-time NIH employees won't take effect until October 2020, and the implementation is still being finalized.

Although federal laws have guaranteed 12 weeks of job-protected family and medical leave to employees since 1993, only eight states and Washington, D.C. have implemented legislation to ensure employees are paid during this time. In other states, paid-leave policies are largely determined by employers and are variable.

In science, technology, engineering,

and math (STEM) fields, barriers to paid family leave can lead to attrition and augment the male-female imbalance in leadership positions. A recent study examining career trajectories of STEM professionals found that 43% of women and 23% of men leave full-time STEM positions after their first child, opting for part-time STEM work or full-time careers outside of STEM (*Proc Natl Acad Sci USA* **116**:4182–4187, 2019).

Meanwhile, there is ample evidence to suggest that paid family leave boosts employee morale and retention (2012 Report of the Center for Women and Work, Rutgers the State University of New Jersey in New Brunswick). Science stands to benefit from fair paid-leave policies by minimizing the male-female imbalance, improving job satisfaction, and attracting and retaining competitive candidates (*Proc Natl Acad Sci USA* **116**:4182–4187, 2019).

The increase in the length of paid leave is one of several policies the NIH has implemented to alleviate setbacks that fellows face as new parents. For example, trainees applying for career-development awards (such as the K99/R00 mechanism) can extend their eligibility window if they've experienced a lapse in productivity due to family and/or medical leave. The Keep the Thread Program allows IRTAs and CRTAs the flexibility to modify work schedules and temporarily reduce hours in times of family need. Together, these policies signal the NIH's commitment to supporting and retaining scientists as they start families.

Despite these progressive initiatives, financial hurdles remain a challenge for many intramural fellows. Although

Title 42 clinical and research fellows are eligible for the NIH Child Care Subsidy Program, trainees appointed under the IRTA, CRTA, and VF mechanisms are not. Childcare costs in the Washington, D.C., metropolitan area are among the most expensive in the country, ranging from \$17,000 to \$24,000 annually, according to a January 9, 2020, report from the local NPR station, WAMU. That accounts for a substantial percentage of a fellow's take-home stipend.

Therefore, although the NIH leads in the quality of health and paid-leave benefits it provides for trainees, bolstering other benefits such as child care subsidies and retirement plans would create a more holistic and competitive package.

As the NIH continues to expand family-friendly benefits for trainees, the impact of these policies must be monitored to determine how they influence measures of success including research productivity and equal gender representation among grant submissions, independent investigator hires, tenure approval, and leadership positions. ●

*Sofiya Hupalo is a fellow in the Postdoctoral Research Associate Training (PRAT) program at the National Institute of General Medical Sciences. She works in Joshua Gordon's lab at the National Institute of Neurological Disorders and Stroke, where she studies the neurophysiological bases of cognition in animal models of genetic susceptibility to schizophrenia.*

## New Directors Named at Five Institutes

NIEHS, NINR, NEI, NIAMS, and NIDCR Welcome New Directors

FROM NIH NEWS RELEASES

### NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES

**New Director:** Rick Woychik, Ph.D.

**Started:** In June 2020 (was acting director)

**Research:** His laboratory was the first to identify a gene associated with polycystic kidney disease, the first to connect a protocadherin gene to hearing loss in Cushing disease patients, and the first to clone an obesity-related gene called *agouti*.

**Before NIH:** President and CEO, Jackson Laboratory (Bar Harbor, Maine); came to NIH in 2010 as NIEHS deputy director.

### NATIONAL INSTITUTE OF NURSING RESEARCH

**New Director:** Shannon Zenk, Ph.D., M.P.H., R.N., F.A.A.N.

**Will start:** In September 2020

**Research:** Identifying effective approaches to improve health and eliminate racial, ethnic, and socioeconomic health disparities. Through pioneering research, she and her colleagues helped bring national attention to the problem of inadequate access to healthful foods in low-income and Black neighborhoods.

**Before NIH:** Professor at University of Illinois at Chicago (UIC) Department of Population Health Nursing Science and a fellow at the UIC Institute for Health Research and Policy.

### NATIONAL EYE INSTITUTE

**New Director:** Michael Chiang, M.D.

**Will start:** In late 2020

**Research:** Using telemedicine and artificial intelligence for the diagnosis of retinopathy of prematurity and other ophthalmic diseases, implementation and evaluation of electronic health-record systems, modeling of clinical workflow, and data analytics. His clinical practice focuses on pediatric ophthalmology and adult strabismus.

**Before NIH:** Practicing ophthalmologist; professor of ophthalmology and medical informatics and clinical epidemiology at Oregon Health and Science University, OHSU (Portland, Oregon), and associate director of the OHSU Casey Eye Institute.

### NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES

**New Director:** Lindsey Criswell, M.D., M.P.H., D.Sc.

**Will start:** In early 2021

**Research:** She is interested in the genetics and epidemiology of human autoimmune disease, particularly rheumatoid arthritis and systemic lupus erythematosus. Using genome-wide association and other genetic studies, her research team contributed to the identification of more than 30 genes linked to these disorders.

**Before NIH:** Vice chancellor of research at University of California, San Francisco; a professor of rheumatology in the Department of Medicine; and professor of orofacial sciences in the School of Dentistry.

### NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

**New Director:** Rena N. D'Souza, D.D.S., M.S., Ph.D.

**Will start:** Later in 2020

**Research:** Her research focuses on developmental biology and genetics; matrix biology; biomaterials, tissue engineering, and stem cells; and clinical research. Her group's discovery that a novel mutation in *PAX9* was responsible for a severe form of human tooth agenesis opened a new field of research to discover genes and mutations as well as therapies for common human inherited disorders of the craniofacial complex.

**Before NIH:** Assistant vice president for academic affairs and education for health sciences at the University of Utah (Salt Lake City); is also a licensed dentist and holds faculty positions at the university's School of Medicine and the Department of Biomedical Engineering; and was the inaugural dean of the University of Utah's School of Dentistry (established in 2012). ●



Rick Woychik, NIEHS

Shannon Zenk, NINR

Michael Chiang, NEI

Lindsey Criswell, NIAMS

Rena N. D'Souza, NIDCR



## Meet the Newest NIH Members of the National Academy of Sciences

Mini Symposium Held to Honor John Schiller and Robert Tycko

BY THU-LAN LILY NGUYEN, NCI

ON JULY 21, 2020, THE NIH HOSTED A virtual mini symposium to honor the two NIH investigators who were elected to the National Academy of Sciences (NAS) this year: NIH Distinguished Investigator **John Schiller** (National Cancer Institute, NCI) and Senior Investigator **Robert Tycko** (National Institute of Diabetes and Digestive and Kidney Diseases, NIDDK). The NAS is a private, nonprofit organization of the country's leading researchers and is committed to furthering science in America. Its 2,404 members and 501 foreign associates are active contributors to the international scientific community. The number of current NIH colleagues who have been elected to the prestigious NAS is 50.

### John T. Schiller, Ph.D., NCI

John Schiller has made fundamental contributions to our understanding of the human papillomaviruses (HPV), the most common sexually transmitted infections in the United States. He helped develop the HPV vaccines for the prevention of cervical cancer and other tumors caused by HPV and is developing treatments for other sexually transmitted infections and chronic diseases, including cancer.

Schiller earned a Ph.D. in microbiology from the University of Washington (Seattle) before coming to NIH to work in Douglas Lowy's lab at NCI in 1983. The two have worked together for more than 30 years and have been honored countless times for their pioneering work studying HPV and developing the HPV vaccines, with awards including the National Medal of Technology and Innovation from President Barack Obama and the Lasker-DeBakey Clinical Medical Research Award. Lowy is also a member of the NAS.

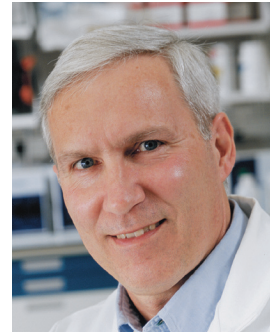
During the mini-symposium, Schiller described his research as well as his efforts to bring cancer treatments to low-income countries with limited resources and health-care infrastructure. These countries need simple, inexpensive, and safe interventions for disease. In one project, his research group is attempting to harness preexisting antiviral immunity to treat cancers.

In another project, he is collaborating with the National Institute on Aging to study the effects of injecting peptides derived from viral epitopes (molecular regions on the surface of antigens) into naturally occurring tumors in mice. The idea is that the immune system will recognize the viral epitopes expressed in cancers and recruit T cells that can fight the tumors. The initial results in mouse tumor models are promising, and he hopes that such general therapies can be used as off-the-shelf treatments for many types of cancerous tumors.

### Robert Tycko, Ph.D., NIDDK

Robert Tycko, a biophysicist, uses solid-state nuclear magnetic resonance (NMR) to investigate the structural properties of molecules important to human biology and disease. His work has provided new insights into the structure and physical behavior of proteins associated with Alzheimer disease, type 2 diabetes, and AIDS.

Tycko completed a Ph.D. in chemistry at the University of California at Berkeley (Berkeley, California) and did his postdoctoral training at the University of Pennsylvania (Philadelphia). He then worked as a member of the technical staff at AT&T Bell Laboratories (Murray Hill, New Jersey) for eight years before coming to



John Schiller



Robert Tycko

CREDITS: RHODA BAER; SASHA K. TYCKO

NIH as a senior investigator in 1994. His development of NMR technology served as a way to bridge his interests in math, physics, chemistry, and building things. At NIH, he roped in biology, too, and explored the biological applications of NMR.

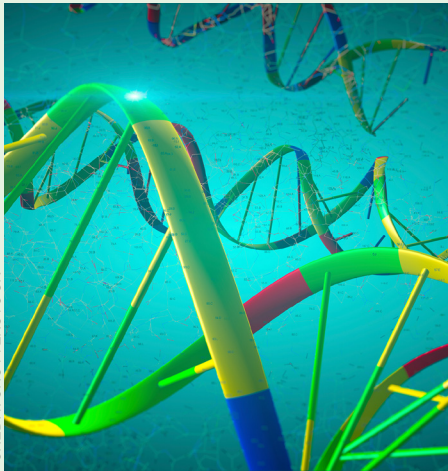
He recognized the potential of using solid-state NMR and electron microscopy to study protein structures such as the amyloid-beta fibrils that develop in brain tissue of people with Alzheimer disease. Not much was known about the fibrils when Tycko began studying them. Over the years, he has been able to characterize the structure and identify distinct morphologies of amyloid-beta fibrils. Now examining the implications on human health, his lab studies fibrils extracted from patients with Alzheimer disease to see how differing morphologies may affect pathogenesis. Tycko continues to play an instrumental role in developing technologies in structural biology to shed light on the molecular world. ●

To watch a videocast of symposium, go to: <https://videocast.nih.gov/watch=38191>.

*Lily Nguyen is a postbaccalaureate fellow in the National Cancer Institute's Laboratory of Molecular Biology. After she completes her training in 2021, she hopes to go to graduate school to pursue a Ph.D. in molecular biology.*



## Intramural Research Briefs



CREDIT: SHUTTERSTOCK

NIEHS: A new study highlights *BRCA1-2* and *APEX2* synthetic lethality, which means that the combined lack of both gene products is lethal to breast cancer cells. Shown: DNA strands.

### NIEHS: DNA REPAIR DISCOVERY HOLDS PROMISE FOR PRECISION CANCER THERAPY

NIEHS researchers and collaborators in Canada discovered that cancer cells with mutated *BRCA1* and *BRCA2* genes died when they lacked a protein called apurinic or apyrimidinic endonuclease (APE2), which promotes the repair of damaged DNA. APE2 is encoded by *APEX2* gene. The mechanism behind *BRCA1-2* and *APEX2* synthetic lethality (when the combined lack of both gene products is lethal) to breast-cancer cells highlights a vulnerability that may lead to a precision-medicine approach to treating *BRCA1-2*-deficient breast cancers. (NIEHS authors: J.L. Wojtaszek, T. Patel, C.D. Appel, B.D. Wallace, and R.S. Williams, *Mol Cell* 78:1152–1165.E8, 2020; DOI:10.1016/j.molcel.2020.05.021)

[KELLY LENOX, NIEHS]

### NIA: GUM DISEASE LINKED WITH DEMENTIA

Periodontal (gum) disease has been linked with heart disease, preterm labor, and many other health conditions including Alzheimer Disease (AD). Lab studies have suggested that both bacteria and the toxins they produce can travel through the bloodstream to the brain, causing inflammation and other

neurotoxicities. NIA researchers were the first, however, to conduct a large retrospective analysis of population data to examine the association between periodontal pathogens, as well as antibodies against certain oral pathogens, with the incidence and mortality of AD and other dementias.

The NIA research team used data from the National Health and Nutrition Examination Survey, Medicare, and the National Death Index to examine whether periodontal disease and antibodies against 19 bacteria might be linked to dementia diagnoses and deaths. The study provides evidence for an association between periodontal pathogens and AD, which was stronger for older adults. The authors called for further investigations, including randomized controlled trials, on the effectiveness of periodontal treatment against the onset and progression of neurodegenerative disorders such as AD. (NIA authors: M. Beydoun, S. Hossain, and A.B. Zonderman, *J Alzheimers Dis* 75:157–172, 2020; DOI:10.3233/JAD-200064.)

[GERI PIAZZA, NIA]

### NIDDK, NIEHS, NIDA: THE LURE OF HIGH-FAT DIETS

The brain may be wired to drive the intake of high-fat foods, according to a study conducted in mice by an international team of scientists including researchers from NIDDK, NIEHS, and NIDA. The investigators found that after exposure to high-fat, calorie-rich foods, mice no longer wanted a nutritionally balanced, standard diet, even when they were hungry and no longer had access to the high-fat foods. The high-fat diet was the only way to “switch off” the neurons responsible for the unpleasant sensations linked to hunger.

The researchers also looked at the neurons associated with the sense of reward that comes with food discovery. They found that these neurons showed significantly decreased responses to the nutritionally balanced foods after the mice were exposed to the high-fat

foods. Because the neurons the researchers studied in mice have nearly identical functions in people, these findings suggest a neural basis behind the challenges of human dieting. (NIH authors: C.M. Mazzone, J. Liang-Gualpa, C. Li, N.S. Wolcott, M.H. Boone, M. Southern, N.P. Kobzar, I. De Araujo Salgado, D.M. Reddy, G. Cui, and M.J. Krashes, *Nat Neurosci* 2020; DOI:10.1038/S41593-020-0684-9)

[LISA YUAN, NIDDK]

### NHGRI, NCBI: COMPLETE HUMAN X CHROMOSOME SEQUENCE GENERATED

Researchers from NIH and other institutions have produced the first end-to-end DNA sequence of a human chromosome. Because a human genome is incredibly long, consisting of about 6 billion bases, DNA-sequencing machines cannot read all the bases at once. Instead, the genome is chopped into smaller pieces; each piece is analyzed to yield sequences of a few hundred bases at a time; and then these sequences are reassembled in much the same way that a jigsaw puzzle is reconstructed. The scientists chose to complete the X chromosome sequence and capitalized on new technologies that leave DNA molecules largely intact. Being able to generate a precise, base-by-base sequence of a human chromosome will enable researchers to produce a complete sequence of the human genome. (NIH authors: S. Koren, A. Rhie, S. Brooks, V.A. Schneider, E. Pak, V. Maduro, A. Dutra, G.G. Bouffard, A.M. Chang, N.F. Hansen, F. Thibaud-Nissen, A. Young, J.C. Mullikin, and A.M. Phillippy, *Nature* 585:79–84, 2020; DOI:10.1038/S41586-020-2547-7)

### NINDS: TURNING OFF “JUNK DNA” MAY FREE STEM CELLS TO BECOME NEURONS

Over the course of evolution, the human genome has absorbed thousands of human endogenous retrovirus genes. As a result, nearly eight percent of the DNA that lines our chromosomes includes remnants of these genes. Although once thought to be





inactive, or “junk,” recent studies have shown that these genes may be involved in human embryonic development, the growth of some tumors, and nerve damage during multiple sclerosis. Previously, NINDS researchers showed that amyotrophic lateral sclerosis may be linked to activation of the *HERV-K* gene. In the new study, the team showed that deactivation of the gene may free stem cells to become neurons. In the future, the team plans to explore how *HERV-K* genes may shape the wiring of a nervous system. (NINDS authors: T. Wang, M. Medynets, K.R. Johnson, T.T. Doucet-O’Hare, B. DiSanza, W. Li, Y. Xu, A. Bagnell, R. Tyagi, K. Sampson, N. Malik, J. Steiner, Alina Hadegan, J. Kowalak, J. O’Malley, D. Maric, and A. Nath, *Proc Natl Acad Sci U S A* 117:17842–17853, 2020; DOI:10.1073/pnas.2002427117)

#### **NICHD: STARVING A MALARIA PARASITE**

In 2018, there were 228 million cases of malaria worldwide, leading to more than 400,000 deaths, 67% of which were among children under 5, according to the World Health Organization. One way to stop the infections would be to starve the malaria parasite, *Plasmodium falciparum*, once it infects a person but before it can do any damage. NIH researchers are making discoveries about how the parasite gets its nutrients as it infects red blood cells. In 2000, NIH researchers found a set of porelike holes in the membranes of red blood cells. The parasite uses those holes to supply itself with *non-fatty* nutrients. In a recent study, NIH researchers discovered another set of channels—ones that enable the transport of *fatty* nutrients between the blood cell and the parasite. Together the discoveries may lead to treatments that would starve the parasite and keep it from proliferating in the body. (NIH authors: M. Garten, T. Tenkova-Heuser, J. Heuser, and J. Zimmerberg, *Nat Commun* 11:article number3825, 2020; DOI:10.1038/s41467-020-17506-9)

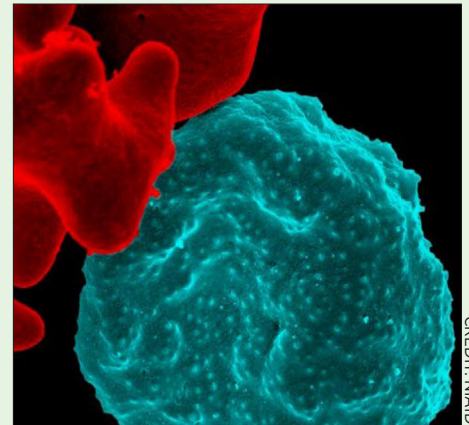
#### **NIAMS, NCI: REDUCTIONS IN SMOKING AND HEAVY DRINKING MAY MEAN FEWER HIP FRACTURES**

A new study, conducted by researchers from NIH and other institutions, analyzed 40 years of Framingham Heart Study data (including information from 4,918 men and 5,634 women) and found an association between lowered rates of hip fractures and decreases in smoking and heavy drinking. The rates of hip fractures in the United States have been declining over the past few decades. Although some experts attribute this change to improved treatments for bone health, the new study suggests that modifiable lifestyle factors may be beneficial, too.

Between 1970 and 2010, the rates for hip fractures dropped by 4.4% each in both men and women. In addition, the rate of smoking decreased from 38% in the 1970s to 15% in 2006–2010. During the same period, heavy drinking fell from 7% to 4.5%. The authors noted limitations in the study, however: data were exclusively from white individuals; participants had lower rates of obesity than the national average; and measurements of bone mineral density were not included because such testing was not available until the 1990s. (NIH authors: J. Swayambunathan, A. Dasgupta, P.S. Rosenberg, and T. Bhattacharyya, *JAMA Intern Med* 2020; DOI:10.1001/jamainternmed.2020.2975)

#### **NEI: DUAL ROLE FOR MOLECULE INVOLVED IN AUTOIMMUNE EYE DISEASE**

The inflammatory molecule interleukin-17A (IL-17A) triggers immune cells that in turn reduce IL-17A’s pro-inflammatory activity, according to a study by NEI researchers. The finding could explain why IL-17-targeted treatments for conditions like the eye disease autoimmune uveitis and multiple sclerosis have failed. (NIH authors: W.P. Chong, M.J. Mattapallil, K. Raychaudhuri, S.-J. Bing, P.B. Silver, Y. Jittayasothorn, C.-C. Chan, R. Horai, and R.R. Caspi, *Immunity* 53:384–397.e5, 2020; DOI:10.1016/j.immuni.2020.06.022)



CREDIT: NIAID

NICHD: Starving malaria parasites may be one way to stop malaria. Shown: Colorized scanning electron micrograph of red blood cell infected with malaria parasites (blue) and uninfected cells with a smooth red surface (red).

#### **NIMH: SEX DIFFERENCES IN HUMAN BRAIN**

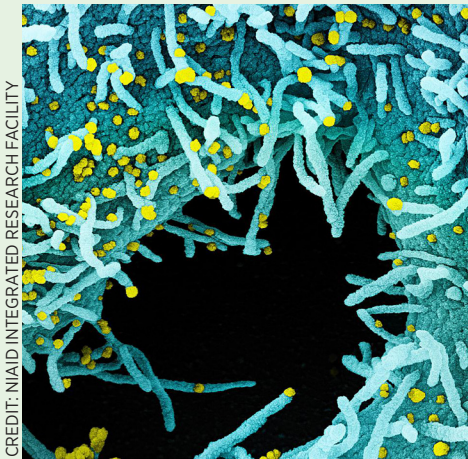
A scientific analysis of more than 2,000 brain scans found evidence for highly reproducible sex differences in the volume of certain regions in the human brain, according to an NIMH-led study. The data, obtained from 976 healthy adults between the ages of 22 and 35, revealed consistent sex differences in the volume of certain cortical structures.

On average, females had relatively greater cortical volume in the medial and lateral prefrontal cortex, orbitofrontal cortex, superior temporal cortex, and lateral parietal cortex. Males had relatively greater cortical volume in ventral temporal regions and occipital regions including the primary visual cortex. Specifically, regions of the cortex with relatively high expression of sex-chromosome genes tended to have greater cortical volume in males than females. Sex differences in brain organization are theoretically important for our understanding of sex differences in human cognition and behavior, according to the authors. (NIH authors: S. Liu, J. Seidlitz, J.D. Blumenthal, L.S. Clasen, and A. Raznahan, *Proc Natl Acad Sci U S A* 117:18788–18798, 2020; DOI:10.1073/pnas.1919091117)

Read more at: <https://irp.nih.gov/catalyst/v28i5/research-briefs>.



## COVID-19 Timeline at NIH (July–August 2020)



CREDIT: NIAID INTEGRATED RESEARCH FACILITY

Colorized scanning electron micrograph of a cell heavily infected with SARS-CoV-2 virus particles (yellow), isolated from a patient sample. The black area in the image is extracellular space between the cells.

**July:** Since May 21, the NIH Clinical Center has been performing weekly, voluntary testing to screen for SARS-CoV-2 infection in asymptomatic clinical staff approved to work on site in Building 10. In July, the Clinical Center expanded access to this testing to nonclinical staff approved to work on site in Building 10. Other NIH locations in Maryland, North Carolina, Massachusetts, and Arizona also have begun conducting asymptomatic testing of approved onsite staff; the samples are sent to the Clinical Center for analysis.

**July 1:** In a “Perspective” for the *New England Journal of Medicine*, members of NIH’s Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) Vaccines Working Group assess practical considerations and prerequisites for using controlled human infection models (CHIMs), which can be used for human challenge studies, to support SARS-CoV-2 vaccine development. In the article, the authors determine the timeline for developing robust CHIMs that meet the essential criteria for limiting risk for study volunteers, and the process could take one to two years. The authors conclude that large, randomized, controlled trials of SARS-CoV-2 are the fastest and most effective path forward for establishing vaccine safety and efficacy. (*N Engl J Med* 383:e63, 2020; DOI:10.1056/NEJMp2020076)

**July 2:** NIH Director Francis Collins, in testifying before the Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies, estimates that \$18.8 billion in emergency funding would be needed for the NIH to respond to COVID-19 including approximately \$10 billion to offset expenses associated with lab disruptions. He described the financial difficulties faced by universities and medical centers because of the shuttered labs in addition to reduced income from elective surgeries and other medical procedures.

**July 8:** NIAID announces the launch of a new clinical-trials network called the COVID-19 Prevention Trials Network. The network aims to enroll thousands of volunteers in large-scale trials testing a variety of investigational vaccines and monoclonal antibodies (mAbs) intended to protect people from COVID-19.

**July 10:** In his all-staff email, NIH Director Francis Collins announces that NIAID is enrolling NIH staff who have recovered from COVID-19, and have been cleared to return to work, in the NIAID Antibody Research Study.

**July 14:** A study by NICHD and outside investigators finds the placental membranes that contain the fetus and amniotic fluid lack the messenger RNA molecule required to manufacture the angiotensin-converting enzyme 2 receptor, the main cell-surface receptor used by the SARS-CoV-2 virus. (*eLife* 9:e58716, 2020; DOI:10.7554/eLife.58716)

**July 14:** An mRNA-1273 investigational vaccine, co-developed by researchers at Moderna, Inc., and NIAID’s Vaccine Research Center (VRC), was generally well tolerated and prompted gratifying titers of neutralizing antibodies in healthy adults in a NIAID-supported phase 1 trial. Plans are underway to launch a phase 3 efficacy trial for this vaccine soon. (*N Engl J Med* 2020; DOI:10.1056/NEJMoa2022483)

**July 14:** The “NIH Workforce COVID-19 Impact Survey” for all staff including employees, contractors, students, fellows, and volunteers is launched to help assess the impact of COVID-19 on the NIH workforce.

**July 20:** Group B begins coming back to the workplace.

**July 22:** Several NIH institute and center directors and NIH Director Francis Collins outlined the efforts of the Rapid Acceleration of Diagnostics (RADx) initiative in a special report in the *New England Journal of Medicine*. They explained the urgent need for nationwide deployment of low-complexity, point-of-care molecular diagnostics with rapid results, and described the critical need to ensure testing is available to diverse, vulnerable, and underserved populations, which are disproportionately affected by the virus. (*N Engl J Med* 2020; DOI:10.1056/NEJMs2022263)

**July 27:** A phase 3 clinical trial designed to evaluate whether an investigational vaccine can prevent symptomatic coronavirus disease 2019 (COVID-19) in adults begins. The vaccine, known as mRNA-1273, was co-developed by NIAID and Moderna, Inc. The trial, which will be conducted at U.S. clinical-research sites, is expected to enroll approximately 30,000 adult volunteers who do not have COVID-19.

**July 27:** NIH Director Francis Collins’s email to employees shares the news that Pfizer and BioNTech announced the launch of their combined phase 2/3 vaccine trial for their experimental coronavirus vaccine.

**July 28:** Two doses of an experimental vaccine to prevent COVID-19 induced robust immune responses and rapidly controlled the coronavirus in the upper and lower airways of rhesus macaques exposed to SARS-CoV-2, the virus that causes COVID-19. (*N Engl J Med* 2020; DOI: 10.1056/NEJMoa2024671)

**July 30:** Group B staff at the Baltimore County, Maryland, locations begin returning to their physical workspaces.

**July 31:** NIH announces that it is investing \$248.7 million in new technologies to address challenges associated with COVID-19 testing. NIH’s RADx initiative has awarded contracts to seven biomedical diagnostic companies to support a range of new lab-based and point-of-care tests that could significantly increase



the number, type, and availability of tests by millions per week as early as September 2020. These technologies are expected to make a significant contribution to expanding the nation's testing capacity.

**July 31:** NIAID Director **Anthony Fauci** and other health experts testify before a House subcommittee on the coronavirus crisis. He says he is “cautiously optimistic” the United States could have a safe and effective vaccine by the “end of this year and as we go into 2021.” He also says the NIH’s strategic plan is focused on addressing: the improvement of fundamental knowledge of COVID-19; the development of diagnostics; the testing of therapeutics; and development and testing of vaccines.

**August 4:** NIH launches a phase 3 clinical trial to test mAb treatment in hospitalized COVID-19 patients at select hospitals. The new study is one of four ongoing or planned trials in NIH’s Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) program, a public-private partnership to speed development of the most promising treatments and vaccine candidates. It also is receiving support through Operation Warp Speed the U.S. government’s multiagency effort to develop, manufacture, and distribute medical countermeasures to fight COVID-19.

**August 4:** NIH-supported researchers launch a phase 2 clinical trial for outpatients with mild and moderate COVID-19 to test whether mAbs and other experimental therapeutics can reduce the severity of symptom. The first therapeutic to be tested will be LY-CoV555, an investigational mAb made by Eli Lilly and Company. The antibody emerged from Lilly’s collaboration with AbCellera Biologics, which, together with NIAID’s VRC, discovered the antibody when it was isolated from a blood sample from a recovered COVID-19 patient.

**August 5:** The NIH-Moderna investigational COVID-19 vaccine, mRNA-1273, protected mice from infection with SARS-CoV-2, the virus that causes COVID-19, according to research published in *Nature*. Scientists at NIAID,

Moderna, and other institutions conducted the preclinical research. NIAID VRC scientists worked with investigators from the University of Texas at Austin to identify the atomic structure of the spike protein on the surface of the novel coronavirus. This structure was used by VRC and Moderna in the development of the vaccine candidate. (*Nature* 2020; DOI:10.1038/s41586-020-2622-0)

**August 5:** NIH launches the Medical Imaging and Data Resource Center (MIDRC), which will harness the power of artificial intelligence and medical imaging to fight COVID-19. The multi-institutional collaboration, led by NIBIB, will create new tools that physicians can use for early detection and personalized therapies for COVID-19 patients.

**August 6:** An NIAID-sponsored clinical trial testing the antiviral remdesivir plus the immunomodulator interferon beta-1a for COVID-19 treatment begins. The study, called the Adaptive COVID-19 Treatment Trial, is anticipated to enroll more than 1,000 hospitalized adults with COVID-19 at as many as 100 sites in the United States and abroad.

**August 10:** Two phase 3, randomized, placebo-controlled, double-blind clinical trials testing whether experimental mAbs can prevent infection by SARS-CoV-2 coronavirus are now enrolling healthy adults at clinical-trial sites in the United States. The trials are enrolling adults who are at risk of infection due to close contact at work or home to persons with SARS-CoV-2 infection. One trial, being conducted jointly by NIAID and trial sponsor Regeneron Pharmaceuticals, will evaluate Regeneron’s investigational double mAb combination, REGN-COV-2, which is designed to bind to two points on the SARS-CoV-2 spike protein and prevent it from entering healthy cells. The other trial, sponsored by Eli Lilly and Company and implemented in collaboration with NIAID, will evaluate LY-CoV555, isolated from a recovered COVID-19 patient by scientists at AbCellera and the NIAID VRC, and developed by Eli Lilly and Company.

**August 10:** An email to DC area staff announces that the NIH Clinical Center has begun testing asymptomatic staff for SARS-CoV-2 in Groups O, A, and B working on site. The program is voluntary but strongly encouraged. Other NIH locations in Baltimore, Maryland, North Carolina, and Montana also have begun conducting asymptomatic testing of approved on-site staff; lab analyses are done at the Clinical Center.

**August 21:** New FAQ section on child care is added to the NIH intramural site for coronavirus guidance.

**Aug 26:** The Clinical Center announces that asymptomatic testing is available for all DC-area staff; appointments are needed.

**August 28:** The COVID-19 pandemic has taken a disproportionate toll on people with intellectual and developmental disabilities, write the directors of the Intellectual and Developmental Disabilities Research Centers network, a nationwide group funded by NICHD, in the *American Journal of Psychiatry*. (*Am J Psychiatry* 2020; appiajp202020060780; DOI:10.1176/appi.ajp.2020.20060780)

**Aug 31:** Staff approved to work on site will no longer receive a message from Alert NIH to self-assess for COVID-19 and will instead start using the SAFER-COVID tool.

**August 31:** Phase 3 clinical testing of the AstraZeneca investigational COVID-19 vaccine known as AZD1222 begins. The trial will enroll approximately 30,000 adult volunteers at 80 sites in the U.S. to evaluate whether the candidate vaccine can prevent symptomatic COVID-19. AstraZeneca is leading the trial as regulatory sponsor; NIAID and the Biomedical Advanced Research and Development Authority (part of HHS) are providing funding support. Scientists at NIAID’s Rocky Mountain Laboratories, based in Hamilton, Montana, conducted a preclinical study of AZD1222. ●

Read more at: <https://irp.nih.gov/catalyst/v28i5/covid-19-timeline-at-nih-july-august-2020>.



## Diagnosing Traumatic Brain Injuries

CONTINUED FROM PAGE 1

concentrations highly correlated with CSF NfL levels, showing that serum NfL reflects CSF NfL,” said **Pashtun Shahim**, a staff scientist in the Rehabilitation Medicine Department and first author on the two papers. (*Neurology* Jul 2020, DOI:10.1212/WNL.0000000000009983)

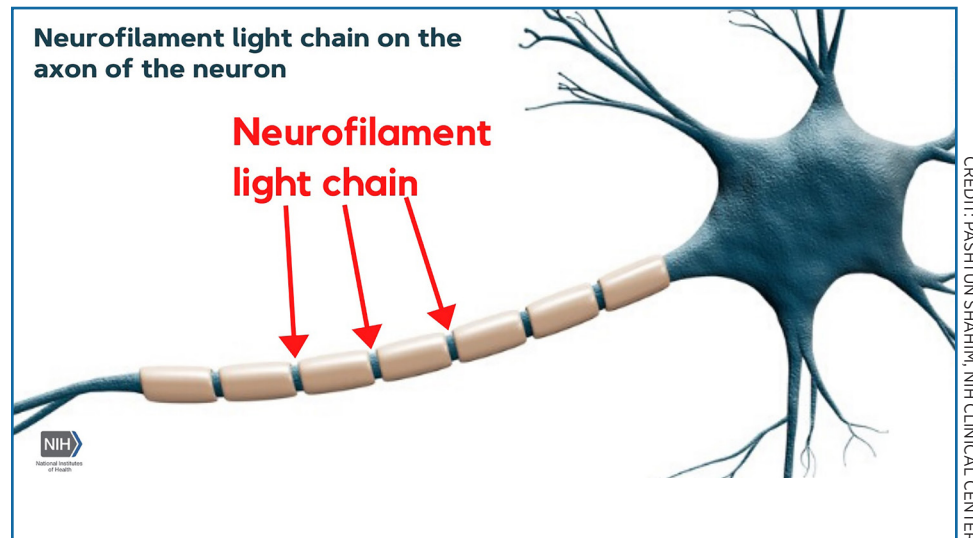
That’s good news for people who would prefer a simple blood test over the lumbar puncture needed to obtain the CSF.

The researchers also observed that NfL concentrations were associated with more concussions and greater severity of post-concussion symptoms after a year. NfL predicts how long professional hockey players would be symptomatic from acute concussions and distinguishes which players could return to play from those who could not. Ultimately, the study showed that, compared with concentrations in control subjects, blood NfL concentrations in hockey players with TBIs presented strong diagnostic capabilities in identifying mild, moderate, and severe TBIs.

In the article—“Time Course and Diagnostic Utility of NfL, tau, GFAP, and UCH-L1 in Subacute and Chronic TBI”—the scientists studied four proteins, including NfL, that collect in the brain after a TBI from patients at the NIH Clinical Center. The results showed that blood NfL was better than the other proteins at distinguishing patients with mild, moderate, and severe TBI from each other; NfL remained elevated five years post-TBI. (*Neurology* Jul 2020; DOI:10.1212/WNL.0000000000009985)

“While no biomarker reliably detects subtle brain injury over time, the study shows serum NfL elevates after injury and remains high five years after a TBI event, suggesting ongoing axonal degeneration years after the initial event,” said Shahim.

The study also showed that blood NfL had the strongest association with results



CREDIT: PASHTUN SHAHIM, NIH CLINICAL CENTER

NIH researchers reported that a blood biomarker called neurofilament light chain (NfL) may hold the most promise for predicting, diagnosing, and following up on traumatic brain injuries. Shown: The location of neurofilament light chain on the non-myelinated section of the neuron’s axon.

from advanced brain imaging than did the other proteins.

In another *Neurology* paper—“Exosomal Neurofilament Light: A Prognostic Biomarker for Remote Symptoms After Mild Traumatic Brain Injury?”—that came out a month before the other two, Senior Investigator and Acting Scientific Director **Jessica Gill** (National Institute of Nursing Research) compared NfL concentrations in military veterans who had no history of TBI with those who had one or more TBIs. She led a team of researchers (including Shahim) that found a significant correlation between higher NfL concentrations in veterans with a history of repetitive TBIs, with length of time in years since the last TBI, and with increased severity of neurological and behavioral symptoms. The results indicate that NfL has superior diagnostic performance for mild, moderate, and severe TBI. (*Neurology* 94:e2412–e2423, 2020)

In addition, blood serum NfL captures subtleties in brain function that may not

be reflected in CT scans and MRIs and predicts long-term outcomes. NfL has important applications in hospitals and for fields ranging from sports to the military.

“By developing a better understanding of the neuronal underpinnings that contribute to chronic symptoms following a brain injury, clinicians can intervene proactively and anticipate symptom onset if NfL peaks at a certain level or a certain time point following the injury,” said Gill.

The findings from all three studies suggest that—compared to advanced brain imaging or with other blood biomarkers, measuring NfL concentrations may offer an easier, faster, and more cost-effective way to diagnose TBI and predict outcomes even years after the event occurred. ●

*Frances Fernando, a postbaccalaureate fellow in the Eunice Kennedy Shriver National Institute of Child Health and Human Development, plans to pursue a doctorate in public health after completing her NIH training in 2021. Outside of work, she gardens and explores Washington, D.C., by bike..*

## Using Flatworm Regeneration To Study Stem Cells

Erin Davies Brings Flatworm Animal Model to NIH

BY MEGAN KALOMIRIS, NIAID

**THE KEY TO UNLOCKING MYSTERIES** surrounding regenerative medicine could lie within worms—tiny, flat, cross-eyed worms. Recently hired Stadtman Investigator **Erin Davies** (National Cancer Institute, NCI) is the first in the NIH intramural research program to use flatworms (*Schmidtea mediterranea*), or planaria, as an animal model to explore stem cells at various developmental stages.

Planarians are flatworms that possess an amazing ability to regenerate themselves. If you cut one planarian down the middle, each half would reform its missing parts, and you would have two planarians in a matter of weeks. Although humans and other mammals possess some regenerative ability, such as the ability to heal wounds, we are not nearly as capable as these flatworms. Davies is determined to figure out why.

She was introduced to the planarian model by her postdoctoral advisor, Alejandro Sánchez Alvarado, at the Stowers Institute for Medical Research (Kansas City, Missouri). Sánchez Alvarado provided a unique opportunity for Davies to study the planarian *S. mediterranea*, a long-lived species that can reproduce both sexually and asexually and has a seemingly inexhaustible capacity to regenerate itself.

During her postdoctoral training, she pioneered molecular and functional studies of embryogenesis in *S. mediterranea* and observed the cellular mechanisms that guide development through the planarian's life cycle. When she finished her training, she was eager to continue that research in her own lab. She applied to NIH's competitive Earl Stadtman Investigator program and was hired by NIH in 2020 to work in NCI's Cancer and Developmental Biology Laboratory, where she heads the Potency and Developmental Plasticity Section.

Planarians have adult pluripotent stem cells (PSCs) that fuel tissue homeostasis and regeneration. In most animals (including mammals), however, PSCs are only present in embryos and are responsible for the development of organs, limbs, and tissues.

“The planarian has found a way to sustain embryonic pluripotency programs throughout [its] life cycle,” Davies explained. What's more, planarian PSCs can readily proliferate without causing the organism to age or develop cancer.

Through her research, Davies is exploring whether the nature of planarian pluripotency changes throughout the life cycle and just how that pluripotency is maintained. A greater understanding of the planarian regenerative system could have implications for treating cancer, degenerative diseases, and other conditions.

“I think that there are a number of unique opportunities in not only planarians, but other lower invertebrates...to address key concepts and principles, like the evolution of tumor suppression or other facets,” she said. “Simpler models like planarians,

sponges, [and] hydra...can offer a unique evolutionary perspective [on] how some of these systems evolved...and how some embryonic developmental programs can be repurposed.”

“Planarians are a remarkable model system,” said NCI-CCR Scientific Director **Tom Misteli**. “Its arrival in the intramural program offers a powerful new tool to study regeneration, differentiation, and stem-cell biology, all processes that are highly relevant to many diseases including cancer.”

Although setting up her NIH lab during the COVID-19 pandemic has been challenging, Davies is brimming with enthusiasm at the prospect of getting back to work investigating the mysterious abilities of these cross-eyed creatures. ●

*Megan Kalomiris is a postbaccalaureate fellow in the National Institute of Allergy and Infectious Diseases, where she studies noroviruses. After completing her training in 2021, she plans to pursue a master's degree in science writing with hopes of working in science communications some day.*



Erin Davies is using the flatworm *Schmidtea mediterranea*, which has an amazing ability to regenerate, to study pluripotent stem cells. Shown: adult worm (left); Stage 3 embryo stained with riboprobes (right). The blue belly button-like structure is the embryonic pharynx; the small blue circles are undifferentiated embryonic cells. Embryogenesis lasts for approximately two weeks for this flatworm species. Scale bar: 100 microns.

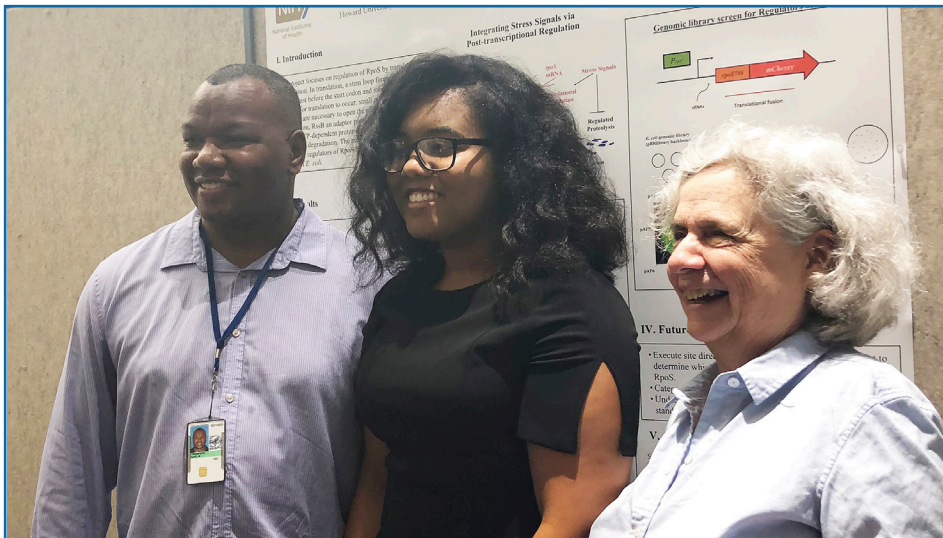
BOTH: ERIN DAVIES, NCI





## NIH-Howard Partnership

CONTINUED FROM PAGE 1



Karl Thompson (left) started working with NCI Distinguished Investigator Susan Gottesman (right) 20 years ago as a trainee from Howard. Today he is an associate professor in microbiology at Howard University College of Medicine and runs his own lab. One of Thompson's undergraduates—Abbigale Perkins (center)—will begin working as a postbac in Susan Gottesman's lab this fall. (Photo was taken in summer 2019.)

Cancer Institute, NCI), who was already an established leader in the field of bacterial genetics. Today, Thompson is an associate professor in microbiology at Howard University College of Medicine and runs his own lab. He has reestablished ties with NIH and Gottesman under a new formalized partnership between the two institutions. Their collective work is shedding new light on gene regulation at the post-transcriptional level to improve our understanding of human disease.

That new partnership was established in March 2019 when the NIH Intramural

Research Program (IRP) and Howard University, a historically Black university, launched a joint venture to share resources and expertise. Although students and faculty from Howard have been conducting research with NIH principal investigators for decades, the new NIH-Howard University partnership centrally coordinates and broadens the investigators' professional networks. Now, in its second year, the NIH-Howard partnership is opening new doors for Howard junior faculty, postdoctoral fellows, medical residents, and graduate and medical

students to become successful investigators and is helping NIH foster diversity in its labs and in clinical research.

“Our original vision was to create a network that could accomplish what no one institution could do by itself,” said **John Gallin**, chief scientific officer at the NIH Clinical Center and NIH associate director for clinical research. He was instrumental in establishing the partnership.

Back in December 2017, leaders from the IRP and academic biomedical centers began exploring the idea of regional alliances, unions that would enable new and distinct research possibilities. The program's architects decided that the best way to move forward was to cultivate one relationship at a time, focusing on training and mentorship. They created a master agreement that serves as a model of how to partner with NIH. Howard was the first to sign on.

“When we launched this collaboration with the NIH, we hoped to bring together bright scientists who could innovate and expand the research experience between the two institutions,” said Hugh Mighty, dean and vice president of clinical affairs at Howard University College of Medicine. There are now five junior faculty from Howard as well as two graduate students and one medical resident working with



Behind the scenes: These are some of the people behind-the-scenes who are helping to make the NIH-Howard Partnership a success. From left: John Gallin (NIH), Hugh Mighty (Howard), Anne Zajicek (NIH), Celia Maxwell (Howard), and Roland Owens (NIH).



IRP labs. NIH and Howard hope the ongoing project will continue fostering many quality partnerships.

In addition, many Howard students considering a future in science are using this relationship as a gateway to enrich their professional development. In 2019, with the encouragement of Howard leadership, NIH hosted Howard undergraduate, graduate, and medical students on campus through summer programs and internships, laying the groundwork for the next generation of exceptional investigators.

The new partnership also makes it easier for people from other institutions to work with NIH. “NIH can be daunting to navigate,” said Deputy Director of NIH’s Office of Clinical Research **Anne Zajicek**, who, along with Howard University’s medical school Associate Dean for Research **Celia Maxwell**, was very involved in building the partnership. “With this agreement, there is now an open flow of communication, and people are better able to understand the process of how to collaborate at NIH,” Zajicek said.

“The partnership...provides access to NIH content-matter experts that Howard may not have due to our small number of faculty,” said Maxwell. It also allows “access to equipment that may be needed to further research by junior faculty or students receiving mentorship.”

Howard Associate Professor **Sudha Sharma** appreciates having access to NIH’s equipment and cutting-edge genetics technologies, such as advanced next-generation sequencing. She has been working with NCI Senior Investigator **Ashish Lal** to explore the role that enzymes known as helicases play in genome stability. Sharma was able to sequence her lab’s samples at NCI, resulting in some of the first evidence of how these enzymes may contribute to the development of—and



Howard Associate Professor **Sudha Sharma** (right) has been working with NCI Senior Investigator **Ashish Lal** to explore the role that enzymes known as helicases play in genome stability.



Howard graduate student **Raechel McKinley** (right) and NIH Stadtman Tenure-Track Investigator **Ariel Levine** (NINDS) have just begun working together.

susceptibility to—breast cancer.

The partnership master agreement also addresses legal and administrative hurdles in an effort to make research relationships easier to establish and maintain. For example, the new master agreement brings relief to partner investigators from a longstanding NIH policy: that outside investigators who come to NIH and use NIH resources to make inventions must assign those inventions to NIH. Now, when non-NIH investigators covered by the new partnership master agreement make discoveries at NIH, they can retain their intellectual property rights

when they leave. Gallin noted that this arrangement has been transformative in making collaborations attractive to scientists outside of the government.

Other roadblocks that are being worked out include making sure that malpractice insurance coverage meets federal requirements and identifying appropriate institutional review boards to oversee human clinical studies taking place between institutions.

Setting up the right combination of people for success is a key element of this

CONTINUED ON PAGE 16

## NIH-Howard Partnership

CONTINUED FROM PAGE 15



NIDDK Senior Investigator Anne Sumner (left) and Howard Assistant Professor Peter Whitesell are exploring the connection between sleep disturbance and the high rate of cardiometabolic disease in people of African descent.

arrangement. Although some partnerships occur organically, others require a bit of matchmaking. That's where IRP Director of Research Workforce Development **Roland Owens** comes in. "My job is faculty recruitment and development," he said. "I get to know people from my research and training interactions and learn who might be a good match and research partner for a particular mentee from Howard." He pointed to a brand-new connection between Howard graduate student Raechel McKinley and NIH Stadtman Tenure-Track Investigator **Ariel Levine** (National Institute of Neurological Disorders and Stroke), who studies how the molecules, neurons, and circuits of the spinal cord mediate normal behavior. Owens hopes McKinley will follow the path of previous trainees—going on to faculty positions and eventually returning to NIH to initiate new roads of discovery with their mentors.

Finding mentors by sorting through the vast pool of talent at NIH is no simple task. "I look for scientists who want to stretch themselves, who are open minded, and enjoy one-on-one teaching, and have an open-minded attitude about how to contribute to the NIH mission," explained Owens. In turn, Howard internally evaluates

applications for mentees twice a year, selecting the most promising candidates—ranging from junior faculty, to graduate and medical students, to medical residents and postdoctoral fellows—who demonstrate a strong interest in pursuing research careers. An NIH team then reviews the applications before a final pairing is made.

The Howard University College of Medicine has a long history of service to underserved communities surrounding their urban hospital setting, offering an opportunity for NIH to contribute to research addressing health-care disparities in minority populations. For example, Howard Assistant Professor Peter Whitesell and NIH Senior Investigator **Anne Sumner** (National Institute of Diabetes and Digestive and Kidney Diseases) are exploring the connection between sleep disturbance and the high rate of cardiometabolic disease in people of African descent. Whitesell noted that access to a carefully collected database generated by NIH has been invaluable to his research efforts. His work has resulted in several important abstract presentations and publications.

"The partnership has gone wonderfully, with many of our junior investigators getting opportunities that may otherwise

have eluded them," said Mighty. "We look forward to continued growth for both institutions."

Beyond this initial pilot phase, the exchange will encompass other academic programs at Howard, such as dentistry, arts and sciences, pharmacy, and even law (to explore bioethics).

"The framework that we have created with Howard is a model for how NIH and other institutions can work together to advance science and improve health," said Gallin.

Other organizations are entering into partnerships with NIH. Virginia Commonwealth University School of the Arts (Richmond, Virginia) expressed interest in using their media expertise to help NIH enhance community engagement and outreach. The University of Maryland's partnership will include the schools of medicine, dentistry, nursing, pharmacy, law, and social work as well as the graduate school. And MedStar, the largest health-care provider in Maryland, has access to data that could assist research on the current COVID-19 pandemic.

The vision laid out three years ago was to create a network of partners positioned to address our modern health challenges. Following a successful journey with Howard, this goal seems well on its way to being realized.

As the journey with Howard continues, a new generation of researchers has already begun to partner with NIH: One of Karl Thompson's undergraduates—Abbigale Perkins—will begin working as a postbac in Susan Gottesman's lab this fall. ●

*Michael Tabasko is an orthopedic physical therapist and writer, having lived in California and Colorado before coming to Bethesda. In his spare time, he is a competitive cyclist and enjoys adventures with his family in the mountains.*



## COVID-19 SIG: What Autopsies Have Taught Us About COVID-19

NCI's David Kleiner and Stefania Pittaluga Discuss Their Findings at a COVID-19 Lecture

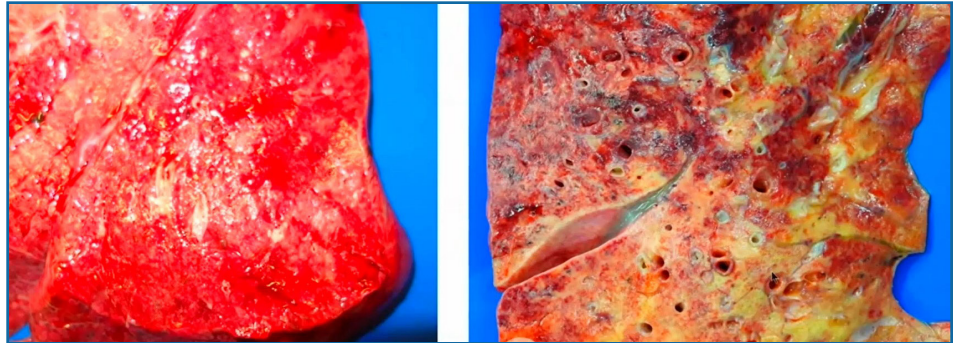
BY EMMA ROWLEY, NIAID

**AUTOPSIES CAN OFFER A BETTER** understanding of the underlying pathophysiology of COVID-19, the disease caused by the severe acute respiratory-syndrome coronavirus 2 (SARS-CoV-2). But few autopsies have been performed partly because of logistical issues such as shortages of appropriate personal protective equipment, reluctance of medical staff to conduct autopsies on these patients, difficulty in obtaining consent from the families of the deceased, and lack of transportation for the bodies. In addition, patients are frequently hypoxic at the time of death and have underlying conditions that interfere with the quality of tissue obtained during autopsy.

Two NIH researchers, however, have collaborated with colleagues who performed autopsies on COVID-19 patients at New York University's Winthrop Hospital (Mineola, New York). **David Kleiner** and **Stefania Pittaluga**, senior research physicians in the National Cancer Institute's Laboratory of Pathology, reported their findings at a July 22, 2020, virtual lecture sponsored by the COVID-19 SIG.

Kleiner highlighted histopathological findings in 18 autopsies of which 16 were sent to NCI for a second review. The most common finding, diffuse alveolar damage (DAD), was present in 15 of the 18 patients. Once DAD reaches the fibrotic stage, the oxygenation of blood and tissue is severely impaired and the lungs cannot recover. Lungs with end-stage DAD are pale yellowish due to the fibrosis, and they take on a honeycomb appearance in which open-air spaces are lined by fibrotic tissue.

Some patients also experienced severe pneumonia before they died. Such superinfections occur in some COVID-19



Diffuse alveolar damage (DAD) in the lungs was a common finding in the COVID-19 autopsies conducted by the NCI researchers and their NYU colleagues. Shown: early-stage DAD lung (left); late-stage DAD lung (right).

patients even when antibiotics were administered. In several patients, Kleiner noted a striking finding of bacterial overgrowth in the lungs and in multiple extrapulmonary sites 24 hours after death, equivalent to what would be expected in a body that had been unrefrigerated for a week. The full effects of SARS-CoV-2 on the immune system remain unclear.

Other autopsy findings included microthrombi composed of platelets in both the lungs and other tissues; enlargement of the liver sinusoids; and damaged kidneys, heart, and neuromuscular systems.

Pittaluga's talk focused on localization of the virus and cytokine and chemokine expression. SARS-CoV-2 was detected in five of the 16 cases sent to NCI for review, but greater viral loads were found in patients who had died early in the disease. Two of the patients died in the emergency room and had had symptoms for only three to seven days. Autopsy findings from these patients are helpful in separating what the virus is doing from the cascade of events triggered by the activity of the immune system in patients who died later during the disease. Unfortunately, many COVID-19 patients die at home or have died before they reach the hospital, making autopsies of patients

who died early almost impossible.

One patient who died early in the disease had strikingly high interleukin-6 (IL-6) expression with IL-6 present throughout the lungs and in the endothelial cells and macrophages of several organs. Although the sample size for this observation was small, further investigations into the role of IL-6 in disease progression will help determine whether anti-IL-6 drugs such as tocilizumab are an appropriate course of treatment.

"Autopsies are still important," Pittaluga concluded. Despite the challenges, the information gained plays an essential role in understanding the pathophysiology of COVID-19. ●

To view a videocast of this lecture, go to <https://videocast.nih.gov/watch=38104>. For more information about the COVID-19 SIG as well as links to resources and to other COVID-19 lectures, go to <https://oir.nih.gov/sigs/covid-19-scientific-interest-group>.

*Emma Rowley is in her second year as a postbaccalaureate fellow in the National Institute of Allergy and Infectious Disease. She is investigating the impact of oxidative stress on a parasite that causes malaria.*



## Recently Tenured



ALEXANDER CHESLER, NCCIH



DIMA HAMMOUD, CC



ZAYD M. KHALIQ, NINDS

JAMES KOCHENDERFER,  
NCI-CCRJADRANKA LONCAREK,  
NCI-CCR

### ALEXANDER CHESLER, PH.D., NCCIH

*Senior Investigator and Head, Sensory Cells and Circuits Section, National Center for Complementary and Integrative Health*

**Education:** Bard College, Annandale-On-Hudson, New York (B.A. in biology); Columbia University, New York (Ph.D. in biology)

**Training:** Postdoctoral training at the University of California at San Francisco (San Francisco)

**Came to NIH:** In 2013 as a Stadtman Investigator

**Outside interests:** Drinking coffee; cooking; traveling; hiking; camping

**Website:** <https://irp.nih.gov/pi/alexander-chesler>

**Research interests:** The central question guiding my research is how sensory input is detected and processed by the brain to evoke experiences and behaviors. My work focuses on identifying peripheral somatosensory neurons tuned to specific types of stimuli (such as touch, temperature, and pain), the molecules they use for transduction, and the neural circuits that they activate. Through my research I seek to understand the basis by which some stimuli are perceived as innocuous while others noxious, and how these distinctions are modulated by someone's physiological state or prior experience. The hope is that improving our knowledge of

these basic mechanisms will be useful in developing new therapeutic approaches for treating acute and chronic pain.

My group uses mouse genetics, electrophysiology, in vivo imaging, and behavior to study how stimuli are detected and encoded. Together, these approaches help us to better understand the importance of specific molecules for the responses of defined classes of sensory neurons and to map neural pathways for touch and pain. In parallel, together with **Carsten Bönnemann's** group (National Institute of Neurological Disorders and Stroke), we have identified and characterized patients with a rare inherited disorder that selectively affects mechanosensation (the process by which mechanical stimuli are translated into neuronal impulses) due to damaging mutations in the gene for the stretch-gated ion channel *PIEZO2*. Studying these patients allows us to probe basic questions about the senses of touch, proprioception (sense of body position), interoception (sense of the internal state of the body), and mechanical pain. Through our research, we are gaining insight into human experiences that, by definition, are impossible to answer using animal models. We are now positioned to take what we learn from these patients to guide our studies in the lab and vice versa.

### DIMA HAMMOUD, M.D., CC

*Senior Investigator and Deputy Director, Center for Infectious Disease Imaging, Radiology and Imaging Sciences, Clinical Center*

**Education:** American University of Beirut, Beirut (B.S. in biology; M.D.)

**Training:** Residencies in medicine and diagnostic radiology at American University of Beirut-Medical Center (Beirut, Lebanon); fellowships in neuroradiology and PET imaging at Johns Hopkins Hospital (Baltimore)

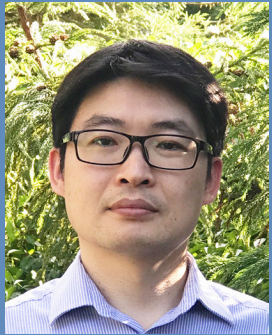
**Before coming to NIH:** Assistant professor of neuroradiology at Johns Hopkins University School of Medicine (Baltimore)

**Came to NIH:** In 2006 as a staff radiologist; in 2011 became a tenure-track investigator

**Outside interests:** Painting; building ship models; hiking; cooking; spending time with family

**Website:** <https://irp.nih.gov/pi/dima-hammoud>

**Research interests:** Infectious diseases remain a leading cause of mortality in the world. Molecular imaging, including positron-emission tomography (PET) scanning, can provide valuable insights into disease mechanisms in a noninvasive manner that is very difficult to replicate with other methods. In my lab, we use molecular imaging to better understand the pathophysiology of infection and inflammation by developing novel ligands



WEI LU, NINDS



NEHAL MEHTA, NHLBI



JORDAN MEIER, NCI-CCR



ANANT PAREKH, NIEHS



ARMIN RAZNAHAN, NIMH

and testing existing PET probes in animal models of several major infections. The ultimate goal is to translate what is learned into clinical practice.

We have already used those imaging modalities to delineate changes occurring in the brain in the early stages of HIV, including neuronal loss and microglial infection, as well as changes occurring upon starting and stopping antiretroviral therapy. Using PET imaging, we also demonstrated that although HIV-specific changes are still seen in the brains of optimally treated HIV-infected subjects, cognitive dysfunction is probably also due to comorbidities, especially cardiovascular disease.

Another interest is developing and validating fungal-specific imaging ligands in animal models. We are exploiting metabolic pathways and cellular constituents that are present in fungi but not in mammalian cells or bacteria. We have already identified many promising PET ligands that we are now testing in animal models of fungal infection. We hope we can eventually apply what we've learned to patients.

Finally, we are also using molecular imaging to understand high-consequence viral infections and how they affect the brain and other major organs. This work includes evaluation of Ebola-infected monkeys and small-animal models of SARS-CoV-2 disease pathology.

#### ZAYD M. KHALIQ, PH.D., NINDS

*Senior Investigator, Cellular Neurophysiology Section, National Institute of Neurological Disorders and Stroke*

**Education:** Dartmouth College, Hanover, New Hampshire (B.A. physics); Northwestern University, Evanston, Illinois (Ph.D. in neuroscience)

**Training:** Postdoctoral fellowship at Harvard Medical School (Boston)

**Came to NIH:** In 2011 as an Earl Stadtman Investigator

**Outside interests:** Spending time with his family; running; listening to music; watching documentary films; playing Bach pieces for solo violin

**Website:** <https://irp.nih.gov/pi/zayd-khalik>

**Research interests:** I am interested in the dopamine system and its contributions to reward and motor learning. Dysfunction of dopamine-releasing neurons in the midbrain has been linked to a variety of brain disorders including addiction, schizophrenia, depression, and Parkinson disease. Although early work established that dopaminergic neurons respond robustly to unexpected rewards, recent studies have revealed that these neurons are engaged by a broader range of behaviors—including novelty and aversion—suggesting that multiple dopaminergic circuits exist. My lab has focused primarily on defining distinct

dopamine subcircuits and determining how they contribute to incentivized learning.

We are interested in how dopaminergic neurons located in the substantia nigra (a region of the midbrain) are controlled by projections from the basal ganglia (clusters of neurons in the brain). Dopamine neurons are innervated by the dorsal striatum, which is a structure involved in an animal's choice of future movements. This structure relies on reciprocal input from dopaminergic neurons, which enable movement; the lack of dopamine release in the dorsal striatum leads to Parkinsonism. Although the dorsal striatum is believed to quiet the activity of dopamine neurons, a recent circuit-mapping study from our lab identified a striato-nigral circuit in which striatal input can lead to an increase in activity in a subset of dopaminergic neurons that enhance dopamine release [*bioRxiv* 2020; DOI:10.1101/856617 (preprint server)].

We believe that this dopamine circuit may be a useful way to signal relief from an unpleasant stimulus and may reinforce escape behaviors.

I am also interested in how motor-learning circuits control dopamine release by directly targeting dopaminergic neuron axons. Substantia nigra dopaminergic neurons have axons that branch extensively

CONTINUED ON PAGE 20



## Recently Tenured

CONTINUED FROM PAGE 19

compared with other central neurons, a feature that increases their energetic cost and may factor in their susceptibility to neurodegeneration.

Our lab provided the first direct recordings from the thin dopaminergic axon processes within the striatum [*bioRxiv* 2020; DOI:10.1101/2020.02.09.941179 (preprint server)]. We hope that these studies will help us identify therapeutic targets for disorders—such as addiction and Parkinson disease—that compromise the dopamine system.

### JAMES KOCHENDERFER, M.D., NCI-CCR

*Senior Investigator, Surgery Branch, Center for Cancer Research, National Cancer Institute*

**Education:** West Virginia University, Morgantown, West Virginia (B.A. in chemistry); West Virginia University School of Medicine, Morgantown, West Virginia (M.D.)

**Training:** Clinical training in internal medicine at Vanderbilt University (Nashville); oncology fellowship at the University of Texas M.D. Anderson Cancer Center (Houston) and hematology fellowship at Baylor College of Medicine (Houston); further training in tumor immunology and stem-cell transplantation as a clinical fellow at NCI

**Came to NIH:** In 2002 for training; in 2010, became an assistant clinical investigator; in 2013, became a tenure-track investigator

**Outside interests:** Exercising; spending time with his family

**Website:** <https://irp.nih.gov/pi/james-kochenderfer>

**Research interests:** My team and I develop T-cell therapies for blood cancers including lymphoma, leukemia, and multiple myeloma. T cells normally play a critical role in fighting infections. But in some cancers, the T cells are ineffective. With gene therapy, T cells can be modified to attack a cancer target and

exert a powerful and specifically targeted anticancer effect.

My lab genetically engineers T cells with genes encoding chimeric antigen receptors (CAR) that target malignancy-associated antigens. When I was a post-doctoral fellow in **Steven Rosenberg's** lab, I designed and constructed a novel anti-cluster of differentiation (CD19) CAR that led to the first FDA-approved CAR T-cell therapy for lymphoma.

We also designed the first chimeric antigen receptor targeting B-cell maturation antigen (BCMA). I led the first clinical trial of T cells expressing an anti-BCMA CAR as a treatment for multiple myeloma. My group played a central role in the first multicenter trial of anti-BCMA CAR T cells for multiple myeloma (*N Engl J Med* **380**:1726–1737, 2019)

We have ongoing clinical trials investigating novel CAR T-cell therapies in multiple myeloma and lymphoma. We are also developing new methods to improve the cancer-fighting ability of CAR T cells.

A barrier to widespread use of CAR T-cell therapy is toxicity, primarily cytokine-release syndrome (CRS) and neurologic toxicity. In a recent paper, we reported a new anti-CD19 CAR that was shown to be less toxic than prior anti-CD19 CARs already in clinical use. (*Nat Med* **26**:270–280, 2020)

### JADRANKA LONCAREK, PH.D. NCI-CCR

*Senior Investigator and Head, Centrosome Biology Section, Laboratory of Protein Dynamics and Signaling, Center for Cancer Research, National Cancer Institute*

**Education:** Faculty of Sciences at Zagreb

University, Zagreb, Croatia (B.S. in molecular biology; M.S and Ph.D. in cell and molecular biology)

**Training:** Postdoctoral training at Wadsworth Center, New York State Department of Health (Albany, New York)

**Came to NIH:** In August 2011 as an Earl Stadtman Investigator

**Outside interests:** Reading; watching movies; gardening

**Website:** <https://irp.nih.gov/pi/jadranka-loncerek>

**Research interests:** Abnormalities of centrosomes are the hallmark of most tumors, especially aggressive ones. Understanding the molecular mechanisms that regulate centrosome number, structure, and function is paramount for understanding centrosome-related diseases.

A typical dividing human cell has two centrosomes, organelles that organize bipolar mitotic spindle poles and facilitate the segregation of chromosomes during cell division. In the heart of each centrosome is the centriole, a structure that organizes a proteinaceous matrix into a centrosome. The number of centrosomes depends on the number of centrioles.

Aberrant centriole amplification, which destabilizes chromosomes, correlates with a loss of tumor-suppressor proteins, the triggering of oncogenic-virus infections, and DNA damage. Because we lack basic knowledge about how the centriole assembly is regulated during the normal cell cycle, we don't yet understand the molecular mechanisms that promote centriole amplification.

My lab aims to unravel cellular





regulatory pathways that control centrosome formation in normal and pathological conditions such as human tumors. We use biochemical and genetic approaches in combination with conventional, super-resolution, and electron microscopy in our investigations.

In our latest study, we used expansion microscopy (a recently pioneered imaging approach) in combination with electron and super-resolution microscopy to explore the mechanisms that lead to the formation of structurally aberrant centrioles. We discovered that centrioles do not have an elongation-monitoring mechanism. The lack of this mechanism makes them prone to over-elongation in some situations. To the best of our knowledge, ours was the first report showing how centriole over-elongation can occur in cells without chemical or genetic manipulation of centrosomal proteins. Our data can explain the origin of centriole structural variability within cell populations and demonstrates why numerical and structural centriole abnormalities often coincide in tumors. (*J Cell Biol* **219**:e201910019, 2020)

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**WEI LU, PH.D., NINDS**

*Senior Investigator, Synapse and Neural Circuit Section, National Institute of Neurological Disorders and Stroke*

**Education:** Sichuan University, Chengdu, China (B.S. in biochemistry); New York University, New York (Ph.D. in neuroscience and physiology)

**Training:** Postdoctoral training in neuroscience at the University of California at San Francisco (San Francisco)

**Came to NIH:** In 2012 as an Earl Stadtman Investigator

**Outside interests:** Traveling; playing weiqi (go); engaging in family-oriented activities

**Website:** <https://irp.nih.gov/pi/wei-lu>

**Research interests:** My lab is exploring how the synaptic connections between neurons are formed, how synaptic strength is regulated, what the role of neuronal activity is in the regulation of synapse formation and synaptic plasticity, how the regulation of synaptic strength influences animal behavior, and what the molecular mechanisms underlying synaptic dysfunctions in brain disorders are.

We mainly rely on the rodent hippocampus as our model system for our work. Currently we use molecular, biochemical, and genomic approaches to identify novel players in synaptic function; molecular, genetic, optical, and pharmacological approaches to manipulate synapses; and electrophysiological, genetic, and behavioral approaches to examine synaptic and neural-circuit function and dysfunction.

In a recent study, we found that the *Shisa7* gene plays a critical role in the regulation of inhibitory neural circuits and the sedative effects some benzodiazepines have on circuit activity. Before this study, it was thought that benzodiazepines worked alone to calm nerves. But we discovered that the drugs and the neural circuits they affect need the assistance of *Shisa7*. We hope the results will help researchers design more-effective treatments for a variety of neurological and neuropsychiatric disorders that are caused by problems with these neural circuits. (*Science* **366**:246–250, 2019; DOI:10.1126/science.aax5719)

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**NEHAL MEHTA, M.D., M.S.C.E., F.A.H.A., NHLBI**

*Lasker Senior Investigator and Head, Section of Inflammation and Cardiometabolic Diseases, National Heart, Lung, and Blood Institute*

**Education:** George Washington University Washington, D.C. (B.A. in neuropsychobiology; M.D.); University of Pennsylvania, Philadelphia (M.S.C.E. in genetic epidemiology)

**Training:** University of Pennsylvania: residency and chief residency in internal medicine; fellowship in cardiovascular diseases, nuclear cardiology, and preventive cardiology; postdoctoral fellowship in genetic epidemiology (focus on human translational studies of inflammation and lipoproteins)

**Before coming to NIH:** Assistant professor, Perelman School of Medicine at the University of Pennsylvania; attending cardiologist and director, Inflammatory Risk in Preventive Cardiology, Hospital of the University of Pennsylvania

**Came to NIH:** In 2012 as the inaugural Lasker Clinical Research Scholar

**Outside interests:** Spending time with his wife and their two daughters; cooking; skiing; surfing; traveling

**Website:** <http://irp.nih.gov/pi/nehah-mehta>

**Research interests:** I am interested in inflammation's role in the development of cardiovascular and metabolic diseases. Using a transdisciplinary approach that involves human translational studies, novel cardiovascular-imaging approaches, and a diverse set of applied laboratory-based techniques, my team and I study how inflammation affects the development of insulin resistance, metabolic syndrome, and lipoprotein dysfunction, all of which are factors for developing subclinical atherosclerosis and subsequent cardiovascular events.

My interest in this research was triggered by seminal studies demonstrating that inducing acute inflammation through exposure to lipopolysaccharide could cause insulin resistance in otherwise healthy people. To better understand the mechanism, I used the chronic inflammatory state in psoriasis to study the development of cardiometabolic diseases. I direct the world's first and largest study on the effect of psoriasis on

CONTINUED ON PAGE 22



## Recently Tenured

CONTINUED FROM PAGE 21

cardiometabolic diseases. For more than five years, we have followed over 300 patients who have undergone whole-body cardiovascular imaging as well as flow cytometry for blood. This work has allowed us to do serial evaluation of atherosclerosis over time.

We demonstrated that people with psoriasis display abnormal lipoprotein particle composition and impairment in high-density lipoprotein efflux capacity, a measure of reverse cholesterol transport. We have also used positron emission tomography to show that patients with psoriasis have early onset of vascular disease and systemic inflammation, an observation confirmed by coronary computed-tomography angiography. We also recently described the important role of neutrophils, in the development of atherosclerosis in psoriasis.

Finally, my lab provided the first-in-human proof of concept that treating psoriasis with biologic therapy reduces coronary-artery inflammation and improves coronary-artery disease over time. We now have studies ongoing in Sweden, Spain, and Australia to assess how new biologic therapy for psoriasis affects coronary disease and cardiovascular events in other populations.

### JORDAN MEIER, PH.D., NCI-CCR

*Senior Investigator and Head, Epigenetics and Metabolism Section, Chemical Biology Laboratory, Center for Cancer Research, National Cancer Institute*

**Education:** Creighton University, Omaha, Nebraska (B.S. in chemistry); University of California at San Diego, San Diego, California (Ph.D. in chemistry)

**Training:** Postdoctoral fellow at the California Institute of Technology (Pasadena, California)

**Came to NIH:** In 2013

**Outside interests:** Playing and watching basketball; drinking coffee; hoisting children over streams

**Website:** <https://irp.nih.gov/pi/jordan-meier>

**Research interests:** My laboratory aims to understand how metabolites influence epigenetic signaling pathways involved in the development, progression, and treatment of cancer. In the past decade enormous evidence has demonstrated that metabolites can serve as critical drivers of cellular adaptation. In particular, they have been found to interact with enzymes that establish epigenetic protein and nucleic-acid modifications crucial to gene expression. These metabolite-protein interactions occur in all living organisms and represent an essential interface between chemistry and our biological code.

Our lab has defined this interface through a chemical approach. We have developed proteomic technologies to characterize how metabolites physically interact with enzymes on a proteome-wide scale. We have discovered new protein-metabolite interactions that link metabolism to protein synthesis and also contribute to hereditary kidney cancer. In addition, we have developed technologies—such as nonenzymatic malonylation and RNA cytidine acetylation—for defining the landscape of novel epigenetic modifications. As we better explain the underlying logic linking gene expression and metabolism, we hope to apply this knowledge toward new approaches to cancer therapy, diagnosis, and chemoprevention.

### ANANT PAREKH, D.PHIL., NIEHS

*Deputy Chief of the Signal Transduction Laboratory and Head of the Calcium Signaling in Health and Disease Group, National Institute of Environmental Health Sciences*

**Education:** University of Oxford, Oxford, England (D. Phil. in pharmacology)

**Training:** Postdoctoral fellowship at the Max Planck Institute for Biophysical Chemistry

(Goettingen, Germany) with Nobel Laureate Erwin Neher (discoveries concerning the function of single ion channels in cells)

**Before coming to NIH:** Professor of physiology, director of the Centre of Integrative Physiology, and fellow of Merton College, University of Oxford

**Came to NIH:** In December 2019

**Outside interests:** Listening to classical music (particularly Wagner); reading English literature; gardening; playing squash and cricket

**Website:** [https://www.niehs.nih.gov/research/atniehs/labs/stl/pi/calcium\\_signaling/index.cfm](https://www.niehs.nih.gov/research/atniehs/labs/stl/pi/calcium_signaling/index.cfm)

**Research interests:** Ever since I attended a physiology lecture in medical school, I've been fascinated by the underlying mechanisms of how different biological systems communicate with one another. Communication between and within cells is essential for the development and survival of any complex organism. In particular, I am interested in intracellular calcium signaling, which plays a fundamental role inside cells as a universal regulator of cell function. The calcium ion activates many cellular responses including fertilization, neurotransmitter release, muscle contraction, energy production, cell growth, and cell death.

My group at NIEHS studies how aberrant calcium signals may contribute to disease in humans, particularly allergies and asthma. We are using various cell model systems and human tissue to study store-operated calcium-channel proteins. Store-operated calcium channels are so called because they are activated by physiological or pharmacological processes that deplete calcium from bones and other places where it is stored in the body. Once opened, calcium enters the cell and triggers important physiological responses.



Previously, my group at Oxford demonstrated that store-operated calcium channels in the plasma membrane were central to immune-cell activation by specific allergens from the house dust mite.

Drugs that target calcium channels show efficacy in various animal models of asthma. My hope is that by using these compounds to control the channels, we might find an effective means of reducing the severity of airborne allergens and pollutants that damage the lungs.

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**ARMIN RAZNAHAN, M.D., PH.D., NIMH**

*Senior Investigator and Chief, Section on Developmental Neurogenomics, Human Genetics Branch, National Institute of Mental Health*

**Education:** King's College University London, London (M.D.; Ph.D. in biological psychiatry)

**Training:** Residencies in pediatrics and psychiatry, and a specialty fellowship in child and adolescent psychiatry at the Maudsley Hospital (London, England); postdoctoral training at NIMH

**Came to NIH:** In 2008 for a year as visiting Ph.D. student; in 2010 returned as a postdoc; in 2012 became a staff scientist; in 2014 became a NIH-Lasker Clinical Research Scholar

**Outside interests:** Spending time with his wife and daughter; practicing tai chi; cooking; listening to music; honing the “Dad Joke”

**Website:** <https://irp.nih.gov/pi/armin-raznahan>

**Research interests:** I am interested in achieving a better understanding of the biology of childhood-onset neuropsychiatric disorders in ways that might ultimately help to improve disease prediction, detection, and treatment. Together with our collaborators, my

team and I work toward this goal in two mutually informative ways.

First, we use in vivo neuroimaging to study the architecture of human brain organization in healthy volunteers. We also link in vivo neuroimaging maps to complementary molecular and cellular surveys of the human brain. By modeling how human brain organization varies with age, sex, and behavior in health, we hope to advance basic developmental neuroscience while also refining how we ask questions about atypical development.

Second, we use a genetics-first clinical-research strategy to study the relationship between atypical brain development and neuropsychiatric symptoms. This effort involves gathering deep-phenotypic data (spanning measures of gene expression, brain structure and function, cognition, and behavior) in diverse genetic disorders that increase the risk for neuropsychiatric impairment.

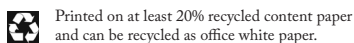
These two main research themes are closely interwoven at theoretical, methodological, and empirical levels. For example, we recently developed new ways of linking in vivo neuroanatomical and post-mortem gene expression data in healthy groups (*Science*, **360**:1222–1227, 2018; DOI:10.1126/science.aar25780; *Neuron* **97**:231–247, 2018; DOI:10.1016/j.neuron.2017.11.039). We then used these approaches to show that regional neuroanatomical changes in neurogenetic disorders can be partly explained by intrinsic cell-type patterning of the human brain (*Nat Commun* **11**:article number 3358, 2020; DOI:10.1038/s41467-020-17051-5).

## 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  
**FNIH:** 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  
**NHGR:** 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  
**NIAID:** 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  
**NIEHS:** National Institute of Environmental Health Sciences  
**NIHGS:** 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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## CATALYTIC REACTIONS?

IF YOU HAVE A PHOTO OR other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via e-mail: [catalyst@nih.gov](mailto:catalyst@nih.gov); fax: 301-402-1434; or mail: *The NIH Catalyst*, Building 60, Room 232.

Also, we welcome “letters to the editor” for publication and your reactions to anything on the *Catalyst* pages.

**READ MORE ARTICLES, AND EXPANDED VERSIONS OF THE ONES IN THIS ISSUE, ONLINE AT <https://irp.nih.gov/catalyst/v28i5>.**

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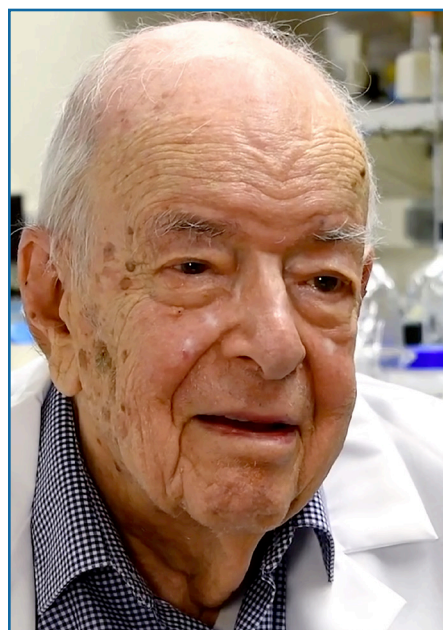
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## SAD NEWS

### Herbert Tabor (1918-2020)

**WE ARE SAD TO RELAY NEWS OF** the passing of **Herbert Tabor, M.D.**, the world’s foremost authority on the enzymatic pathways of polyamines, as well as an esteemed editor of the *Journal of Biological Chemistry* for 40 years, and, until his death at age 101, a senior principal investigator in the NIDDK Laboratory of Biochemistry and Genetics, where he had served as lab chief until 1999. He died peacefully in his sleep on August 20, 2020, at his home on the NIH campus. ●

Read more at <https://irp.nih.gov/catalyst/v28i5/herb-tabor-1918-2020>.



Herb Tabor being interviewed for an oral history in 2019.

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