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PIs Pursuing Their Passions

From Pencils to Pinnacles

BY VICTORIA TONG, OD

NIH SCIENTISTS HAVE A VARIETY OF interests outside of work. Many enjoy hiking, dancing, running, gardening, and other activities. Here are a few PIs we thought had particularly interesting "extramural" pursuits, which we feature starting on page 12.

Elodie Ghedin (NIAID), who develops tools to define the genetic structure and mechanisms of evolutionary change in respiratory viruses, loves to cartoon in her spare time. **Sergi Ferré** (NIDA), who studies receptors as targets for drug development in neuropsychiatric disorders, is an operatic tenor and sings with his wife (who's a soprano and a scientist) at all kinds of venues. **Katie Kindt** (NIDCD), who uses zebrafish in her investigations of hair cells in the inner ear, loves to rock climb. **Joseph M. Ziegelbauer** (NCI), who studies Kaposi's sarcoma-associated herpesvirus, has a telescope equipped with a special camera that takes out-of-this-world photos of the stars. And a pair of NIH investigators summit alpine mountains together all over the world: **Edward Giniger** (NINDS), who studies how neural wiring develops and disassembles during neurodegenerative disease; **Adrian R. Ferré-D'Amaré** (NHLBI), who investigates the function of RNA imolecules in their many guises.

Read on to learn more about them.

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Health Effects of Environmental Disasters

GuLF Study Assesses Exposure After Oil Spills

BY CATHERINE ARNOLD, NIEHS

CREDIT: ROB SCHRADER, U.S. COAST GUARD

The U.S. Coast Guard fire response team battles a fire on the Deepwater Horizon offshore oil rig in 2010.

ON APRIL 20, 2010, THE DEEPWATER HORIZON OFFSHORE OIL RIG EXPLODED, burned, and sank in the Gulf of Mexico, about 40 miles off the coast of Louisiana. Eleven of the 126 workers on board were killed in what is still considered one of world's worst environmental disasters and the largest marine oil spill in United States history. The underwater well, almost a mile below the surface, spewed more than 200 million gallons of oil for the next 87 days before it was capped and sealed. Over the next year and a half, the many thousands of people who helped with the cleanup were exposed to toxicants related to crude oil, burning oil, dispersants, and other pollutants.

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Charting the Future of the Intramural Research Program

BY NINA F. SCHOR, M.D., PH.D., ACTING DDIR

I AM EXCITED TO WRITE THIS, MY FIRST essay for *The NIH Catalyst*. As the new Acting NIH Deputy Director for Intramural Research (DDIR), I have incredibly big shoes to fill. My predecessor, **Michael Gottesman**, who was DDIR for 29 years, launched and nurtured many initiatives that enhanced biomedical workforce diversity, created NIH-wide core facilities, and established the laboratories of extraordinarily talented new scientists on the NIH campus. I am grateful, not only for the foundation he has laid for the future, but also for his gracious welcome, encouragement, and mentorship.

I came to science from an upbringing in Queens, New York, and schooling in the New York City public school system. My father was a scientist–engineer; he shaped my love for and approach to science. My mother was an avocational actress and singer who spent many years earning a living in the fashion industry. She shaped my approach to people and my passion for music and poetry.

I earned my B.S. in molecular biophysics and biochemistry at Yale University as a Scholar of the House in Chemistry Research, a designation that afforded me a year in the laboratory of the late Julian Sturtevant, a pioneer in collecting thermodynamic and kinetic data for important biochemical reactions; I earned my Ph.D. in medical biochemistry from The Rockefeller University in the laboratory of Anthony Cerami, who has led research programs in genetic, metabolic, and infectious diseases.

I received my M.D. from Cornell University Medical College (now Weill Cornell Medicine) and completed residency training in pediatrics and child neurology at Boston Children's Hospital and Harvard's Longwood Area Neurology Program. I then rose through the academic ranks at the University of Pittsburgh, where, over 20 years' time, I became chief of the Division of Child Neurology and associate dean for Medical Student Research. I left Pittsburgh for the University of Rochester in 2006 to become chair of the Department of Pediatrics and pediatrician-in-chief of Golisano Children's Hospital in Rochester.

My passions and the substance of my career have been laboratory-based research and the nurturing of the next generation of biomedical scientists. During 20 years in Pittsburgh and 11 years in Rochester, the dual privilege of creating new knowledge by challenging dogma and seeing my trainees become my colleagues made all the hard work worthwhile.

In January 2018, when I left Rochester to become deputy director of the National Institute of Neurological Disorders and Stroke (NINDS), I wanted to apply all I had learned in institutional leadership across a national platform and to repay my enormous debt of 27 years of NIH funding.

With NIH funding, my laboratory defined the role of the p75 neurotrophic receptor in cellular life-and-death decision-making in the neural crest and the importance of protein methylation in the virulence of a childhood tumor, neuroblastoma; and hosted more than 80 students and trainees. I fervently wanted to give back to the system that nurtured and sustained me.

Since coming to NIH, I have had the privilege of leading the NINDS strategic-planning and career-development programs; spearheading the Ultra-Rare GENe Therapeutics Network in its extramural enterprise; and serving as acting scientific director of the NINDS intramural program. These experiences have given me a 30,000-foot view of the entire multifaceted institute and afforded me the opportunity to work with diverse and dedicated colleagues to build synergies and create initiatives that make a whole greater than the sum of its parts. I think this experience and this approach have equipped me well for the exciting opportunity to serve the NIH intramural community as acting DDIR.

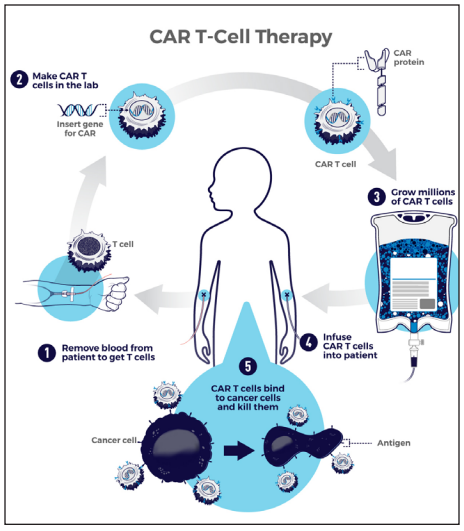
I am hoping to build on the robust foundation Michael Gottesman and his colleagues in the Office of Intramural Research have created. Think, for example, of the ways in which we can synergize as the NIH intramural research program (IRP) to bring the individual approaches and talents of each of the institutes and centers to bear on solving the messy, interdisciplinary and multidisciplinary health problems that face real people. Think of the recruitment power of making mentors and trainees in the extramural biomedical community more aware of our collective resources and capabilities. And think of how we can better prepare our trainees for science as it will be long into the future.

I am so looking forward to working with all my NIH colleagues to chart the future of the NIH IRP. ●

Celebrating 10 Years of CAR T-cell Therapy at NIH

Reflecting on a Landmark Treatment Program for Childhood Leukemia

BY ANINDITA RAY, NINDS



CREDIT: NCI

Avery was a pioneer. On July 13, 2012—his 13th birthday—he became the first pediatric patient to be treated with CAR T-cell therapy at NIH. He had acute lymphocytic leukemia (ALL), the most common form of childhood cancer. Standard treatments—immunotherapy, chemotherapy, and bone-marrow transplant—had failed him. Desperate to save their son, his parents brought Avery to NIH's Clinical Center (CC) where scientists from the National Cancer Institute's (NCI's) Pediatric Oncology Branch (POB) tried the then-experimental therapy that involved re-engineering his T cells to attack his cancer. Although Avery is no longer with us, his legacy lives on through the success of POB's CAR T-cell program that has represented hope for so many families over the past decade.

CAR T-cell therapy works by extracting T cells (infection-fighting white blood cells) from a patient via an apheresis machine, which collects blood, removes the T cells, and then sends the blood back to the patient. Scientists then genetically modify the T cells to produce chimeric antigen receptors (CARs) that can recognize and bind to specific proteins, or antigens, on the surface of cancer cells. Millions of CAR T cells are grown and infused back into the patient to seek out and destroy blood cancers such as leukemia, lymphoma, and multiple myeloma.

Lasker Clinical Research Scholar **Nirali Shah** heads POB's Hematologic Malignancies Section and leads today's CAR T-cell program. When she was a clinical fellow, she was part of the program's founding team of clinicians 10 years ago that included former NIH'ers **Alan Wayne**, **Crystal Mackall**, **Terry Fry**, **Daniel "Trey" Lee**, and **Kristin Baird**. In those early days CD19 CAR T-cell therapy was often used in patients who were already enrolled in high-risk treatments for ALL at the CC. When standard treatments fail or a patient's disease returns, CAR T-cell therapy may help.

In 2012, few clinical sites were using the technology, but groundbreaking work at the POB would change that. CAR T-cell treatment was FDA-approved in 2017, and clinical trials around the world are now exploring and improving personalized cell-based therapies to treat a variety of cancers. The POB program has launched several new CAR T-cell clinical trials, and the therapy is being further developed to treat other types of rare hematological malignancies.

The program traces its roots back to 2010, when a clinical trial led by NCI Senior Investigator **Steven Rosenberg** and Oncology Fellow (now Senior Investigator) **James Kochenderfer** was the first to successfully treat lymphoma with CD19 CAR T cells in an adult (*Blood* **116:**4099–4102, 2010). Rosenberg approached Alan Wayne at the POB about expanding the therapy to treat childhood cancers and a new pediatric-specific protocol was subsequently developed.

Hundreds of children and young adults with leukemia have been treated by the POB's CAR T-cell program at the CC. A long-term follow-up study of 50 patients with relapsed or refractory ALL who were treated with CD19 CAR T-cell therapy found that 62% of those patients had a complete remission of the disease (*J Clin Oncol* **39:**1650–1659, 2021). At the CC today, there are half a dozen patients who have either just received the therapy or are being evaluated for enrollment.

Drawing on insight from the past 10 years, the POB is also improving the treatment protocol by addressing complications such as cytokine-release syndrome, a life-threatening inflammatory reaction that can arise after infusion with CAR T cells and cause injury to multiple organs. Prompt organ-specific treatment is essential and the CC's intensive care unit clinicians have become an obligatory part of delivering the potentially life-saving therapy.

Targeting CD19 does not always work, however. Ongoing clinical trials are exploring how CAR T cells can bind to other tumor markers expressed by ALL such as CD22 and be used to treat other types of cancers such as acute myeloid leukemia, another form of childhood leukemia. The technology is also being optimized to treat osteosarcomas, neuroblastomas, and other solid tumors in children.

Today's POB CAR-T cell program continues to evolve and add to its expert team of clinicians. It's been "a bench-to-bedside journey," said Shah, adding that we now know many of the important factors that influence CAR T-cell response and efficacy that were not known 10 years ago. "There is still a long way to go, and we must continue to push forward to make these therapies better, safer, and easier to access." ●

Anindita Ray is a postdoctoral visiting fellow in the National Institute of Neurological Disorders and Stroke.

From the Fellows Committee

Beyond the Bench: Translational, Clinical, and Market Research Training Opportunities at NIH

BY LARISA GEARHART-SERNA, NCI

Gone are the days when being a scientist always meant doing benchwork day in and day out. Here at NIH, trainees are part of an extensive workforce dedicated to public service, following NIH's primary motto, "Turning discovery into health." Not only do trainees contribute by doing basic research, but they can learn how to contribute in other ways by taking courses in translational, clinical, and market research.

Translational Research Training

Among the translational research training programs at NIH is the National Cancer Institute's (NCI's) Translational Research in Clinical Oncology course, which is designed for NIH staff and trainees who want to learn about cancer biology and the different forms of cancer therapy.

Doctoral graduate students or early-career investigators are eligible to take the NIH Summer Course in Clinical and Translational Research, offered by the NIH Office of Clinical Research. The course includes lectures, discussions, and small-group activities about the role of Ph.D. scientists in clinical and translational research, provides an overview of how basic science and clinical observations are translated into practice, and increases awareness and access to Ph.D. role models, resources, and career opportunities at NIH. It provides a foundation in study design, protocol development and implementation, scientific and ethical review of research, special topics in training and research opportunities, and medical-product development and FDA regulations.

The Office of Intramural Training and Education (OITE) offers a Translational Science Training Program (TSTP) for postdoctoral fellows and Ph.D. graduate students. The TSTP intertwines interdisciplinary scientific content, understanding of the drug-development process, professional skills development, clinical trial terminology, and career exploration.

You have probably received emails regarding the Methods: Mind the Gap webinar series, which explores research design, measurement, intervention, data analysis, and other methods of interest in prevention science. There was also a Medicine: Mind the Gap series, which explored issues in translational research (videocast recordings are still available).

The Demystifying Medicine course is worth considering, too, and is offered every year from January through May (past sessions are available on videocast). The course helps bridge the gap between advances in biology and their application to human diseases.

Finally, the NIH Foundation for the Advancement of Education in the Sciences (FAES) offers hundreds of courses in various fields such as technology transfer, business, and industry, including TECH 528 Preclinical Evaluation of Novel Drugs and Beyond and TECH 584 Translational Medical Product Development.

Clinical Research Training

The NIH Office of Clinical Research offers clinical research training for NIH staff and trainees involved or interested in clinical research. Several of these opportunities are offered separately or comprehensively provided via the Clinical Research Curriculum Certificate (CRCC). To receive a CRCC, you must complete the Introduction to the Principles and Practice of Clinical Research course, the Ethical and Regulatory Aspects of Clinical Research course, and specific modules in the Collaborative Institutional Training Initiative; and attend at least two institutional review board meetings.

The National Institute of Child Health and Human Development offers Principles of Pediatric Clinical Pharmacology and Therapeutics webinars. And the NIH Summer Course in Clinical and Translational Research includes clinical research material.

Market Research Training

The NCI Advancing Innovations through Mentorship program, offered by the NCI Technology Transfer Center, uses experiential education to help researchers gain valuable insight on how to translate technologies from the lab into the marketplace.

FAES offers the course TECH 491 Market Assessment for Innovative Technologies in Biomedical Sciences, which delves into the financial and business aspects of the biomedical sciences.

Other Training Opportunities

For information about other training programs, visit NCI's Courses and Fellowships for Trainees and Fellows web page, or reach out to OITE to find opportunities specific to your institute or center. ●

For links to these programs and courses, check out the online version of this article at https://irp.nih.gov/catalyst/v30i5/the-training-page.

Larisa Gearhart-Serna, a postdoctoral fellow in the NCI's Technology Transfer Center, is a member of The NIH Catalyst *Editorial Board.*

Saliva Suspected in Transmission of Intestinal Viruses

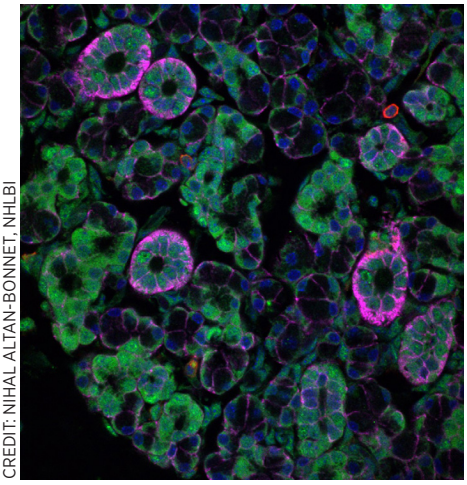
Nihal Altan-Bonnet's Research on Host-pathogen Dynamics

BY STEPHEN ANDREWS, NIAID

Why do outbreaks of gastrointestinal illnesses spread so rapidly among passengers on cruise ships? How can norovirus, which the Centers for Disease Control and Prevention lists as a leading cause of acute gastroenteritis, infect nearly 700 million people each year worldwide? A newly discovered route of enteric (intestinal) virus transmission may be the culprit. Enteric viruses such as norovirus and rotavirus reproduce in the intestines and are known to spread via the fecal-oral route (when fecal-contaminated food or water is ingested). The viruses often cause vomiting and acute diarrhea and can sometimes be deadly.

A trans-NIH team of researchers, led by Senior Investigator **Nihal Altan-Bonnet** (National Heart, Lung, and Blood Institute), has learned that saliva can be a transmission vehicle, too. Their findings were published in *Nature* (*Nature* **607:**345–350, 2022).

Health experts have traditionally recommended regular hand washing and sanitizing surfaces as ways to mitigate transmission of common enteric diseases. But the new findings suggest that talking, coughing, sneezing, and kissing could also contribute to disease spread and that extra precautions, such as wearing masks, might also be indicated.



CREDIT: NIHAL ALTAN-BONNET, NHLBI

Enteric viruses, which can cause severe diarrheal diseases, can spread through saliva. Shown: microscopic view of salivary gland acinar epithelial cells (pink) infected with rotavirus (green) in a mouse.

Previous research by Altan-Bonnet's team uncovered mechanisms whereby norovirus and rotavirus egressed from cells. In the new study, the team used female mice and their infant pups as a model to study disease transmission between animals.

First, infant mice were orally inoculated with a norovirus or rotavirus and then allowed to suckle their virus-free mothers. Shortly after, the scientists noticed something unusual—a rapid and large spike in secretory immunoglobulin (sIgA, a disease-fighting antibody found on mucous membranes) in the immature mice intestines. The immune systems of the mouse pups were not expected to make their own antibodies at this young age. Moreover, the mammary tissue and the milk of the mothers whose infants were infected had high concentrations of sIgA and were found to be infected with the same virus.

It seemed that the infant mice had passed their infection to their mothers' breasts through saliva while suckling, which then boosted the production of virus-fighting sIgA antibodies in the breast milk. The curious results prompted further experiments.

Mouse pups were again orally inoculated with a virus and allowed to breastfeed on their birth mothers. Then, these pups were replaced with a litter of noninfected pups that were permitted to suckle from the newly infected mothers. To the surprise of the research team, the previously uninfected pups now became infected and had high viral loads not only in their intestines but also in their saliva and salivary glands. This supported the notion that suckling had caused both pup-to-mother and mother-to-pup viral transmission. Notably, the pup salivary glands replicated these viruses to concentrations on par with what's in their gut. Additionally, removing the pups' salivary glands allowed for a quicker clearance of infection in their gut, suggesting that the salivary glands may be reservoirs for these viruses.

CREDIT: NHLBI

NHLBI Senior Investigator **Nihal Altan-Bonnet** found that saliva is an unexpected route of transmission for gastrointestinal illnesses such as norovirus.

The new discovery may have important implications for therapeutics and diagnostics for enteric diseases and inform sanitation measures to reduce transmission through saliva.

"Follow where the data [lead] you and don't make any assumptions," said Altan-Bonnet, adding that naming these viruses "enteric" may draw an incomplete picture of how they spread. She looks forward to future research to uncover how these viruses replicate in humans. ●

Stephen Andrews, a postbaccalaureate research fellow in the National Institute of Allergy and Infectious Diseases, is studying protein–antibody interactions related to systemic capillary leak syndrome, or Clarkson disease.

GuLF Study

CONTINUED FROM PAGE 1

Researchers at the National Institute of Environmental Health Sciences (NIEHS) have been assessing the health effects of the oil spill ever since. In a recently released monograph, the scientists described the extraordinary work that went into developing inhalation and skin exposure estimates for people involved in the response and cleanup efforts (*Ann Work Expo Health* **66:**Supplement 1, i3–i249, 2022). The report underpins 10 years of research generated from the Gulf Long-term Follow-up study (GuLF study).

Shortly after the Deepwater Horizon disaster, NIEHS launched the GuLF study to follow response workers over time and examine the health effects associated with environmental exposures during the cleanup effort. Participants living in states along the Gulf completed home exams that collected biological samples and clinical data. Two follow-up efforts have been completed. Health histories were updated by telephone interviews and clinical exams; clinical data—including measures of lung and neurological function—were collected for a subset of the cohort. The study is the largest ever conducted on the potential health effects associated with an oil spill; it has enrolled about 33,000 participants and produced more than 40 publications.

Papers resulting from the GuLF study have reported that workers who participated in the cleanup effort experienced mental health problems, such as post-traumatic stress disorder and depression; decreased lung function; heart disease; and a range of symptoms consistent with the effects of neurological and respiratory diseases. Workers also experienced increased risk of developing high blood pressure (*JAMA Netw Open* **5:**e220108, 2022) and were 60% more likely to be diagnosed with asthma than those who did not work on the cleanup (*Environ Int* **167:**107433, 2022).

In the monograph, scientists described how the statistical and methodological underpinnings of the exposure estimates were developed. They highlighted approaches for dealing with large amounts of missing data, sources of data used to generate estimates, and theoretical models that were developed to describe exposures that could not be directly measured. Reports include exposure levels of six components of crude oil and fine particulate matter produced by the burning and flaring of oil and natural gas.

"No oil spill study has ever undertaken an exposure-assessment project as extensive as ours," said Senior Investigator **Dale Sandler**, who is chief of the NIEHS Epidemiology Branch and leads the study. "This [project] is a monumental accomplishment by our exposure-assessment team."

Workers exposed

The researchers found that workers on all vessels associated with the oil rig, fire control, research, and other water operations had exposure to the compound benzene—a known carcinogen.

"With information on which job roles may be most vulnerable, those responsible for oil-spill cleanup work can better plan how to protect workers from similar exposure scenarios," said **Kaitlyn Lawrence**, a staff scientist in the NIEHS Chronic Disease Epidemiology Group. She began working on the GuLF study in 2014 as a summer intern, and under the mentorship of Sandler. Lawrence used GuLF study data in completing her doctoral dissertation on the impact of oil-spill exposures on lung function.

Measuring exposures

The research team first created exposure groups, defined as workers performing similar tasks who likely had comparable exposures. Those groupings were based on information about both inhalation of and skin contact with oil components over varying time windows during the cleanup effort. Assessments took place over a broad geographic area in the Gulf of Mexico and along the coast of five Gulf of Mexico states. Workers' exposures varied with weather and location, and over time.

"The [oil-cleanup site] exposures on one day were not the exposures on another due to weathering of the oil, which changes the levels of volatile chemicals over time," said Sandler. Health effects also depended on responders' job tasks and the length of time worked.

Novel statistical methods were developed to assign exposure levels to all workers participating in the GuLF study. According to Sandler, the scientists combined air exposure measurements taken at the time of the spill, the team's modeling of exposures not measured at the time of the spill or afterward, and individuals' descriptions of their cleanup-related jobs.

CREDIT: STEVE MCCAW, NIEHS

NIEHS Senior Investigator **Dale Sandler** is leading the GuLF study, which is assessing the long-term health effects of the 2010 Deep Water Horizon oil spill.

CREDIT: STEVE MCCAW, NIEHS

NIEHS Staff Scientist **Kaitlyn Lawrence**, who began working on the GuLF study in 2014 as a summer intern, used the study's data in completing her doctoral dissertation on the impact of oil-spill exposures on lung function.

Oil spills around the world

With a continuing need for oil-cleanup operations around the globe as accidents occur, many people may be exposed to toxic substances in cleanup efforts. Data from the U.S. National Oceanic and Atmospheric Administration Office of Response and Restoration show that the office responded to 139 incidents in the first 10.5 months of 2021. Of those cases, 108 involved oil.

"One would be hard-pressed to find this level of detailed exposure assessment following occupationally related disaster exposures of any type," said Lawrence. "This monograph should be looked to as a model for any future similar industrial hygiene effort." ●

The exposure methods and findings are now accessible to researchers and policymakers in the journal *Annals of Work Exposures and Health* (*Ann Work Expo Health* 66:Supplement 1, i3–i249, 2022). More information can be found on the Gulf Study website: https://GuLFstudy.nih.gov/en/index.html.

Catherine Arnold is a writer for the NIEHS Office of Communications and Public Liaison.

NEW SIG: Long-read and Long-range Sequencing

The past decade has demonstrated the power of genomics to unravel the etiology of complex traits and diseases. The vast majority of genomic studies have been based on mostly short-read sequencing technologies (50–200 base-pair fragments). With the development of long-read sequencing, it is now possible to routinely sequence fragments of 10–100 kilobases and longer. At the same time, long-range linkage technologies such as Hi-C or Strand-Seq can be used to profile chromosome-scale interactions.

Many groups at NIH have already explored recent advances in long-read sequencing with technologies that make it feasible to sequence entire genomes, identify structural and complex variants, and sequence full-length transcriptomes of practically any imaginable sample. The Long-read and Long-range Sequencing SIG will build upon this new field's changing and innovative technology in a monthly seminar series that will feature both internal and outside experts in the field. Potential future events include a scientific symposium and workshops to discuss best practices of sample preparation, sequencing, and data analysis.

A kickoff meeting will be held 2:00–3:00 p.m. on Friday, September 9; after that, meetings will be held at 2:00–3:00 p.m. on the first Friday of each month. Meetings will be held virtually for now. For more information and instructions for joining the LONG-READ-SIG LISTSERV (to receive notices about meetings, etc.), please visit the SIG website at https://oir.nih.gov/sigs/long-read. You can also contact the SIG chairs with other questions: **Arang Rhie** (rhiea@nih.gov; NHGRI), **Cornelis Blauwendraat** (cornelis.blauwendraat@nih.gov; NIA), or **Mikhail Kolmogorov** (mikhail.kolmogorov@nih.gov; NCI).

Renamed SIG: Redox Biology Interest Group

The Free Radical Research Interest group has been renamed the NIH Redox Biology Interest Group. The Redox Biology SIG hosts seminars and workshops that promote all aspects of basic, translational, and clinical research in redox biology. The SIG brings together individuals from a wide range of fields.

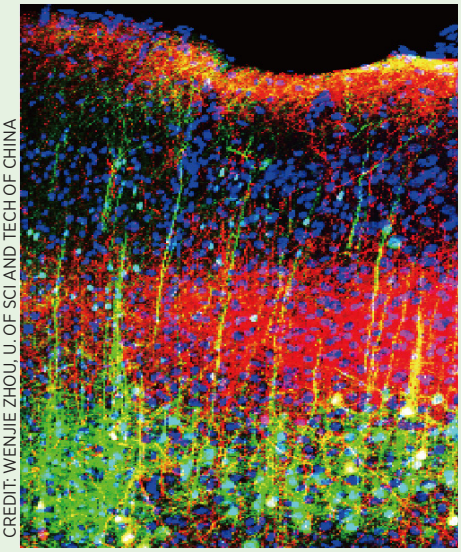
The Redox Biology SIG draws from its historic roots with the Oxygen Club of Greater Washington, D.C., founded in 1987, which along with the NIH Free Radical SIG was one the first interdisciplinary groups organized to enhance collaborations in the study and discussion of redox biology. The Redox Biology SIG is following in the footsteps of the Oxygen Club by fostering collaborations and promoting the dessemination of knowledge and research through seminars covering topics that span mechanisms of redox homeostasis and stress, mitochondrial functions and organelle signaling, immunobiology, DNA damage and repair, redox-based pharmacology and radiation treatments, redox analytical tools, the chemistry of free radicals, and more.

The group meets (virtually for now) 12:00–1:00 p.m. on the first Thursday of each month from September through June. Each meeting features a 50-minute talk (and 10-minute Q&A) by early-career and senior intramural or extramural investigators.

The first talk will be held on September 1 at the special time of 11:30 a.m.–12:30 p.m. and will feature Boyi Gan (MD Anderson Cancer Center in Houston), who has published groundbreaking studies on the molecular underpinnings of cancer metabolism, acquired resistance, and ferroptosis.

For more information, including how to join the Redox Biology Interest Group LISTSERV mailing list, visit https://oir.nih.gov/sigs/redox-biology-interest-group, or contact the chair, **Urbain Weyemi** (urbain.weyemi@nih.gov; NCI). ●

Intramural Research Briefs



CREDIT: WENJIE ZHOU, U. OF SCI AND TECH OF CHINA

NIDCR: Sound reduces pain in mice by lowering the activity of neurons in the brain's auditory cortex (green and magenta) that project to the thalamus.

NIDCR: YOUR BRAIN ON MUSIC; HOW SOUND REDUCES PAIN

Music has magical qualities: Studies have shown it can relieve stress, improve memory recall, and even blunt pain. Precisely how music-induced analgesia works has remained a mystery, and researchers at NIDCR have uncovered new clues about how the brain turns sound into an effective painkiller.

Previous functional MRI studies in humans have associated activity in certain brain areas with the pain-blunting effects of music. To find out which pathways are involved, the team used noninfectious viruses coupled with fluorescent proteins to identify and trace neural connections in the mouse brain. And to mimic music's impact on the brain, scientists turned those brain circuits on and off while testing the pain threshold of mice with inflamed paws.

NIDCR investigators and their collaborators at the University of Science and Technology of China (Hefei, China), pinpointed one route from the auditory cortex in the brain to the somatosensory thalamus, which relays sensory information including pain. When exposed to low-intensity white noise or classical music, the cells at the thalamus end of that pathway fired less often and the mice felt less pain.

Researchers were then able to mimic music's painkilling effects by turning off cells in this pathway without playing music. In contrast, activating the corticothalamic pathway blocked the sound-induced pain relief. Scientists may be able to determine whether the animal findings apply to humans and develop new, safer alternatives to opioids for treating pain. (NIH authors: T. Li, L. Hayashi, and Y. Liu, *Science* **377**:198–204, 2022)

[BY PETER MANZA, NIAAA]

NCI, NIAID: BACTERIAL POPULATIONS CONCENTRATE IN LUNG CANCER CELLS

Bacteria and other microbes within tumors influence how lung cancer progresses and responds to treatment. But the exact location and nature of interaction between the microbiome and its host tumor cells is unknown. In a recent study, researchers at NCI, NIAID, and their colleagues used an advanced technology to map the local microbiome of lung-tumor tissue in 12 patients with early-stage lung cancer. The scientists discovered that lung-cancer cells harbor more bacteria than any other cell type, such as immune cells. Furthermore, tumor cells with high concentrations of bacteria also had increased expression of the beta-catenin gene, which is associated with a tumor-promoting signaling pathway.

The investigators used a new technique called spatial meta-transcriptomics that measured thousands of RNA molecules within the intact tumor samples. Those molecules signaled the presence of human genes, bacteria, and other microbes.

This study provides the first spatial microbiome map in the intratumor landscape. Lung cancer is the leading cause of cancer-related death in the United States and the new findings support the idea that therapies aimed at reducing bacterial load in the lungs might be beneficial for patients with lung cancer. (NIH authors: A. Wong-Rolle, J. L. Hor, A. Rajan, R. N. Germain, and C. Zhao, *J Immunother Cancer* **10**:e004698, 2022)

[BY AMRITA MANDAL, NICHD]

NIDA: NOVEL BRAIN MECHANISM INFLUENCES COCAINE-SEEKING IN RATS

Inhibiting certain acetylcholine receptors in the lateral habenula (LHb), an area of the brain that balances reward and aversion, made it harder for rats to resist seeking cocaine, according to a recent study led by NIDA researchers. The discovery may inform future treatments for cocaine-use disorder, for which there are currently no approved medications.

Using a rat model of impulsive behavior, rats were trained to self-administer cocaine: Pressing a lever led to injection of the drug. Then, the rodents were trained that cocaine was available only when lights were on, but not when the lights were off. Animals quickly learned to inhibit responses to obtain cocaine when it was not available.

The scientists then injected an experimental drug called AFDX-116, which blocks a specific type of acetylcholine receptor, known as M2Rs, into the LHb of rats. When M2Rs in the LHb were blocked, the trained rodents continued to seek cocaine even when the lights were off and drug was unavailable. Further experiments measured electrical activity changes in the LHb in response to other acetylcholine-like drugs, which identified cellular mechanisms by which AFDX-116 worked and confirmed the neural circuit's role in enabling response inhibition for cocaine.

"While the immediate results of this study are related to cocaine seeking, there are also implications for impulsivity as it relates to other drugs as well as to psychiatric conditions like obsessive-compulsive disorder," said lead author **Carl Lupica**. (NIH authors: C.I.C. Wolfe, E. Hwang, E.C. Ijomor, A. Zapata, A.F. Hoffman and C.R. Lupica, *J Neurosci* **42**:5552–5563, 2022)

[BY SHIVALEE DUDUSKAR, NCI]

NEI: LOSS OF YOUTH PROTEIN MAY DRIVE AGING IN THE EYE

Scientists have called pigment epithelium-derived factor (PEDF) the youth protein: It's found in abundance in young retinas and

declines during aging. In a recent study, NEI researchers and their colleagues discovered that a loss of PEDF led to a host of genetic alterations that may accelerate age-related changes in the retina, the light-sensitive tissue at the back of the eye. Diseases of the retina include age-related macular degeneration (AMD), which can cause blindness.

PEDF is expressed by a monolayer of cells behind the retina called the retinal pigment epithelium (RPE), which nourishes and supports photosensitive photoreceptor cells. When PEDF binds to its receptor, PEDF-R, this stimulates the breakdown of lipid molecules—a critical step toward supporting photoreceptor function. Accumulation of lipid deposits is a distinctive feature of AMD.

In this study, investigators used genetically modified mice that lacked the gene *Serpin1*, which encodes the PEDF protein. Those mice were found to have an increased expression of aging-related genes in their RPE cells and fewer PEDF receptors. Compared with healthy controls, the modified mice's RPE cells also showed more accumulation of lipids. These findings highlight the protective role that PEDF plays in facilitating retinal homeostasis and preventing age-related changes. (NIH authors: I.T. Rebustini and S.P. Becerra, *Int J Mol Sci* **23:**7745, 2022)

[BY DEVIKA BOSE, NEI]

NIEHS: SCIENTISTS SOLVE FIRST-EVER 3D STRUCTURE OF TWINKLE PROTEIN

NIEHS scientists have characterized the first-ever three-dimensional structure of the human twinkle protein, an enzyme that unwinds DNA and is implicated in inherited mitochondrial diseases. Mitochondrial diseases can lead to conditions including neurological disorders and liver failure and currently have few treatments. The new model allows researchers to successfully map disease-causing mutations in twinkle, which was impossible using previously available models.

Mitochondria are responsible for energy production and are vulnerable to mutations. Along with the nucleus, they are the only cellular organelles that have their own DNA. When mutations in the twinkle helicase enzyme prevent the accurate separation of the mitochondrial DNA double helix, multiple disease conditions can result.

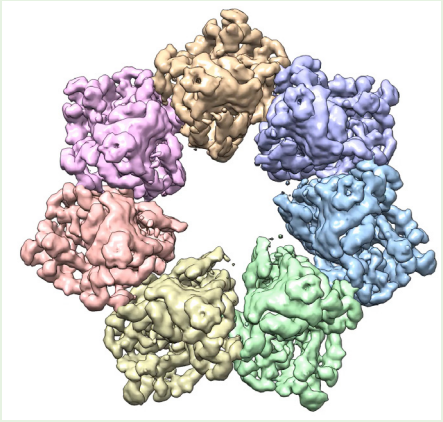
To build their model, the researchers used a disease variant of twinkle called W315L and were able to observe the intricate inner structure of the protein with an advanced imaging technique known as cryoelectron microscopy. Computer simulations then helped the team understand why mutations affect the function of the helicase and result in disease.

"The arrangement of twinkle is a lot like a puzzle," said lead author **Amanda A. Riccio**. "A clinical mutation can change the shape of the twinkle pieces, and they may no longer fit together properly to carry out the intended function." The authors hope that the new information could lead to the development of treatments for mitochondrial diseases and allow clinicians to pinpoint the causes of mutations and help families make choices, including decisions about having more children. (NIH authors: A.A. Riccio, J. Bouvette, L. Perera, M.J. Longley, J.M. Krahn, J.G. Williams, R. Dutcher, M.J. Borgnia, and W.C. Copeland, *PNAS* **119:**e2207459119, 2022)

[BY SATABDI NANDI, NIA]

NIAID: MONOCLONAL ANTIBODY PREVENTS MALARIA IN U.S. ADULTS

Prevention is the most effective strategy against malaria, the mosquito-borne disease caused by the Plasmodium parasite. Prophylaxis measures for the disease have long proved difficult, but scientists at NIAID's Vaccine Research Center have developed a new monoclonal antibody, known as L9LS, that was found to be safe and efficacious in preventing malaria with just one subcutaneous injection. This study provides data showing that it may be feasible and cost effective to use a monoclonal antibody to prevent malaria in infants, young children, and pregnant women in regions where malaria is endemic.



CREDIT: A.A. RICCIO, NIEHS

NIEHS: This image shows the 3D structure that NIEHS researchers created of the twinkle protein. Disease mutations on the protein can lead to mitochondrial diseases. To see a video of the rotating image, go to https://www.youtube.com/watch?v=RrQtk_n_J28.

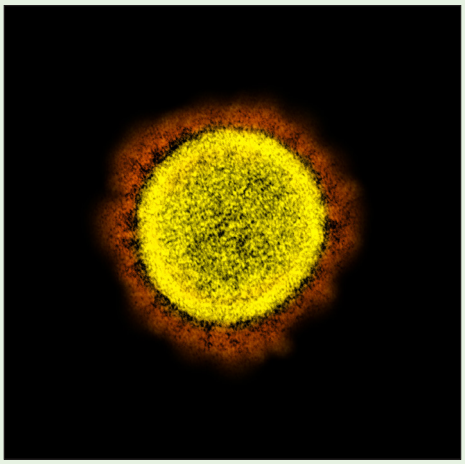
L9LS interrupts the Plasmodium's unique life cycle in humans. The antibody targets the parasite in the skin and blood before it has a chance to infect the liver, where it would normally reproduce prior to emerging in the blood to cause clinical symptoms.

In this phase I trial conducted at the NIH Clinical Center and Walter Reed Army Institute of Research (Silver Spring, Maryland), 18 participants received various does of L9LS. Two to six weeks after, participants were exposed to malaria in a carefully controlled setting known as controlled human malaria infection. L9LS protected against infection in 88% of participants, even in four of the five participants who received a single low subcutaneous dose. In contrast, all participants who did not receive L9LS developed Malaria. Ongoing trials are underway in Mali and Kenya in infants and children to establish safety and efficacy of L9LS against seasonal and perennial infection. (NIH authors: R.L. Wu and R.A. Seder for the Vaccine Research Center 614 Study Team, *N Engl J Med* **387**:397–407, 2022)

[BY JONATHAN CHU, NIAID]

Read longer versions of these briefs, including photos, at: https://irp.nih.gov/catalyst/v30i5/research-briefs.

COVID-19 Timeline at NIH (July–August 2022)



CREDIT: NIAID

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

July 1: The CDC updates its COVID-19 community levels. Bayview Research Center, Baltimore, Maryland, transitions from low to medium community level and Phoenix, Arizona, moves from medium to high. All other NIH locations remain at their current levels.

July 5: An analysis led by NCI researchers finds that COVID-19 was the third leading cause of death in the United States between March 2020 and October 2021 (*JAMA Intern Med* **182**:883–886, 2022).

July 5: An NINDS team of researchers led by **Avindra Nath** publishes a study describing an immune response triggered by COVID-19 infection that damages the brain's blood vessels and may lead to short- and long-term neurological symptoms (*Brain* awac151, 2022; DOI:10.1093/brain/awac151).

July 6: The FDA revises the Emergency Use Authorization for the antiviral pill Paxlovid (nirmatrelvir with ritonavir) to authorize state-licensed pharmacists to prescribe the drug to eligible patients, with certain limitations.

July 8: Acting NIH Director **Lawrence Tabak** emails staff to announce that NIH expects to start implementing the NIH COVID-19 Vaccination Policy for the Healthcare Workforce, as required by HHS policy. He mentions the previous week's FDA recommendation that advised manufacturers to develop a two-component booster vaccine to provide protection against circulating and emerging variants in the fall and winter months. Tabak also highlights NIH COVID-19 research updates released earlier this week.

July 9: The CDC moves Phoenix, Arizona, from high to medium COVID-19 community level. All other NIH locations remain at their current levels.

July 14: In a recent study, NCI researchers and their collaborators find that interferon treatment may reduce severity of COVID-19 in people with certain genetic factors (*Nat Genet* **54**:1103–1116, 2022).

July 15: The CDC moves Phoenix, Arizona, from medium back to high COVID-19 community level. All other NIH locations remain at their current levels.

July 19: A clinical trial sponsored by NIAID finds that neutralizing antibody concentrations against the omicron variant of SARS-CoV-2 decrease substantially in adults within three months of receiving a booster vaccination (*Cell Rep Med* **3**:100679, 2022).

July 19: The CDC recommends that Novavax's protein-based COVID-19 vaccine be used as another primary series option for adults in the United States ages 18 years and older. The vaccine was developed with support from NIAID. "This is the third COVID-19 vaccine available in the [United States] as a result of the unprecedented government research response to develop safe and effective COVID-19 vaccines, for which NIH spearheaded the clinical testing," says **Lawrence Tabak**, whose new title, effective July 17, is "Performing the Duties of the Director of NIH." Federal requirements limit the time anyone can serve as "acting" in a presidentially appointed position. Tabak's duties remain unchanged, and he will once again be "acting NIH director" when President Biden nominates a new NIH Director and until that new director is confirmed by the U.S. Senate.

July 19: A trans-NIH collaborative study supported by NIAMS, NIAID, NIDCR, and NCI finds that disruptions in neutrophil biology are associated with the pathogenesis and severity of COVID-19 in children and adults (*JCI Insight* 2022; DOI:10.1172/jci.insight.160332).

July 21: President Biden tests positive for COVID-19. He is fully vaccinated and twice boosted and experiencing very mild symptoms. He has begun taking Paxlovid. Consistent with CDC guidelines, he will isolate at the White House and will continue to carry out all his duties fully during that time.

July 22: Lawrence Tabak (Performing the Duties of the Director of NIH) emails staff with a coronavirus update. He continues to expect that NIH will implement the COVID-19 Vaccination Policy for Healthcare Workforce, as required by HHS policy, in the coming weeks. Tabak also highlights this week's CDC recommendation of Novavax's protein-based COVID-19 vaccine, which was developed with the support of NIAID scientists and their collaborators.

July 29: The CDC updates Detroit, Michigan, from low to high COVID-19 community level. All other NIH locations remain at their current levels.

August 5: The CDC updates its COVID-19 community levels. Montgomery County, Maryland, moves from medium to high, Rocky Mountain Labs in Hamilton, Montana, moves from medium to low, and Phoenix, Arizona, moves from high to low community level. All other NIH locations remain at their current levels.

August 5: In an email to all staff, **Lawrence Tabak** (Performing the Duties of the Director of NIH) remarks on the increase of COVID-19 community levels across the United States driven by the omicron subvariant BA.5. With Montgomery County, Maryland, moving to high community level, he reviews safety requirements when reporting onsite for all staff as laid out in the NIH Safety Plan. All staff are required to wear a mask; maintain 6 feet of physical distance; follow the guidance on density limits specified on the Physical

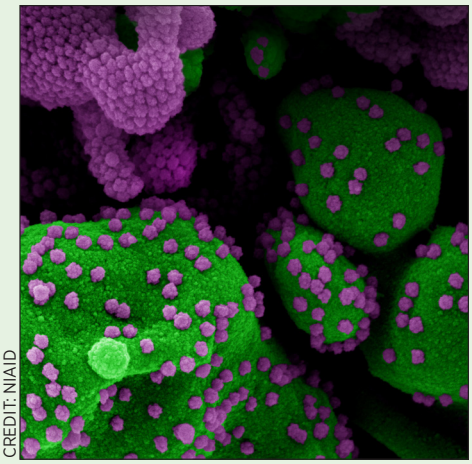
Distancing and Onsite Density Requirements webpage; test weekly if partially vaccinated, unvaccinated, or have not reported vaccination status; submit the NIH COVID-19 In-Person Meeting/Event Safety Plan for all in-person meetings and events regardless of size. The CDC COVID-19 community level reporting now gives NIH the information needed to inform workplace mitigation efforts, and the NIH staff COVID-19 surveillance charts will be removed from the Guidance for NIH Staff on Coronavirus intranet site.

August 12: The CDC updates its COVID-19 community levels. NICHD in Detroit, Michigan, moves from high to medium community level and Rocky Mountain Laboratories in Hamilton, Montana, moves from low to medium. All other locations remain at their current levels.

August 17: NIH updates its COVID-19 safety plan for meetings and testing requirements based on CDC updated recommendations. Employees and visitors entering NIH facilities or attending NIH-sponsored meetings will not be asked to disclose any information regarding vaccination status or be asked to present a negative COVID-19 test. Additionally, there is no longer a testing requirement for unvaccinated staff when the COVID-19 community level is at medium or high. Staff who have had a COVID-19 exposure and are not experiencing symptoms are permitted to come onsite but are required to wear a mask for 10 days after exposure and get tested on day 5. These updates do not apply to health care workers, who remain subject to more stringent requirements.

August 19: The CDC updates its COVID-19 community levels. Montgomery County, Maryland, moves from high risk to low and NICHD in Detroit, Michigan, moves from medium back to high. All other NIH locations remain at their current levels.

August 19: **Lawrence Tabak** (Performing the Duties of the Director of NIH) emails staff with a coronavirus update. He reviews NIH's updated COVID-19 safety plan announced on August 17. The new plan reflects the CDC's streamlined recommendations for non-health-care workers regarding quarantine requirements after exposure and no longer requires testing or reporting of vaccination status when entering NIH facilities or to participate in NIH-sponsored meetings.



CREDIT: NIAID

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

August 22: **Anthony Fauci** announces that, in December 2022, he will stepping down from the positions of NIAID director and chief of the NIAID Laboratory of Immunoregulation, as well as the position of Chief Medical Advisor to President Joe Biden.

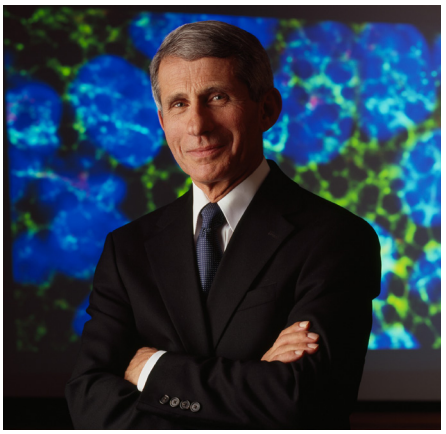
August 26: A study funded by NIH's Rapid Acceleration of Diagnostics Tech program found that with age-appropriate instructions, school-aged children can successfully use a nasal swab to obtain their own COVID-19 test specimen. The study provides data to support recommendations regarding self-swabbing that can be implemented by schools and in other settings where children undergo COVID-19 testing (*JAMA* 2022; doi:10.1001/jama.2022.14877).

Read a more detailed version of this timeline, complete with links, at https://irp.nih.gov/catalyst/v30i5/covid-19-timeline-at-nih-july-august-2022.

Anthony Fauci To Step Down by Year End

On August 22, 2022, Anthony **Fauci** announced that he will be stepping down in December 2022 as the director of the National Institute of Allergy and Infectious Diseases (NIAID), chief of the NIAID Laboratory of Immunoregulation, and Chief Medical Advisor to President Biden.

He stated that he is not retiring but plans to pursue the next phase of his career and use what he has learned as NIAID director to continue to advance science and public health and to inspire and mentor the next generation of scientific leaders as they help prepare the world to face future infectious disease threats. Fauci, who is 81 years old, has spent 54 years at NIH, 38 as the NIAID director, advising seven U.S. Presidents and reassuring the public as America's doctor during outbreaks of infectious diseases on newly emerging and re-emerging infectious disease threats including HIV/AIDS, West Nile virus, the anthrax attacks, pandemic influenza, various bird influenza threats, Ebola and Zika, among others, and, of course, most recently the COVID-19 pandemic. ●



CREDIT: NIAID

Anthony Fauci, M.D.

PIs Pursuing Their Passions

CONTINUED FROM PAGE 1

CREDIT: STEVEN HODAK

When she's not working in the lab, **Elodie Ghedin** enjoys drawing humorous cartoons.

The Cartoonist: Elodie Ghedin, Ph.D.

Senior Investigator and Chief, Systems Genomics Section, and Deputy Chief, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases

Elodie Ghedin's mother was a model and beautician, and her father owned a business designing and building beauty appliances. But in the cartoons Ghedin creates, her parents have alter egos: Her mom is a French spy who fixes the world's fashion faux pas; her dad is a secret agent, masquerading as a musician, protecting his designs. (He played the accordion in real life.) Ghedin's cartoons center on her family's inside jokes and the situations they get into. Inspiration can strike at any moment.

The funny stories that Ghedin's family members share about their lives have been the source of many of her cartoons. She keeps a running list of scenarios based on real-life events. When a family member's birthday approaches, she chooses a few of the scenarios to weave together into a short storyline. For example, her Jojo the spy cartoons were inspired by the time her mother, Joelle, wore a punk outfit, complete with a pink wig, nose ring, leather skirt, and Dr. Martens lace-up leather boots to meet Ghedin's husband for the first time. In the cartoons, Jojo is wearing that exact outfit with a complement of spy gadgets including an eyelash curler that doubles as a camera and a secret message receiver.

After figuring out a storyline, Ghedin drafts a cartoon with pencils and then traces the figures with a fine-point black marker. Then she adds pops of color, such as to eyes or pieces of clothing. Capturing the expressions of real people and distilling them into cartoon characters is one of the challenges of the process, since adding a few extra lines can drastically change how a character looks. Deciding the specific scenes to include in each panel is also tricky.

"The reader has to sort of guess what action happened between Panel A and Panel B," said Ghedin. "You don't want to have too many panels, and not too few either."

To Ghedin, what makes the hours that go into her creations worthwhile is seeing her family members' reactions when they look at her cartoons. Some people have even framed and hung her cartoons in their homes, and they often ask when she will draw them another one.

"When you make people laugh, when you see they're happy with it, that's the most rewarding," Ghedin said.

The Opera Singer: Sergi Ferré.M.D., Ph.D.

Senior Investigator and Chief, Integrative Neurobiology Section, National Institute on Drug Abuse (NIDA)

Opera has always been a part of Sergi Ferré's life. His mother was a piano teacher and his parents loved opera, fostering in him a special connection with music from a young age. Growing up in Barcelona, Spain, Ferré even saw the debut of the famous operatic tenor, and Barcelona native, José Carreras in the Gran Teatre del Liceu (Barcelona's Opera House). For years, however, opera singing remained at the back of Ferré's mind. It wasn't until he moved to the United States more than 20 years ago—to become a research fellow at NIDA—that he began to pursue the possibility of singing opera.

During his commute to work each morning, Ferré would listen to opera music and try to imitate what he heard. It was then that he realized he could hit the high notes required for the tenor register. Challenging himself to reach higher notes and improve his pitch, he was soon able to surprise his family and friends with his singing.

Then, in 2010, Ferré struck an informal deal with NIDA's scientific director, **Barry Hoffer**, who was an opera lover, too. One day, Ferré joked that he could sing the opera

COURTESY OF: SERGI FERRÉ, NIDA

Sergi Ferré, a tenor, enjoys singing opera at different venues, including at a colleague's retirement party.

music Hoffer played in his office. Hoffer responded that if Ferré could perform a particular aria from the opera *La Fille du Régiment*, which requires hitting five high-C notes, then he would promote Ferré to senior investigator (he was a tenure-track investigator at the time). Holding up his side of the deal, Ferré prepared three arias to perform at Hoffer's 70th birthday party, leaving the one that he had bet upon until the end. To Hoffer's surprise, Ferré performed the arias, reaching all the high notes. Ferré was promoted…based on his job performance…in 2012.

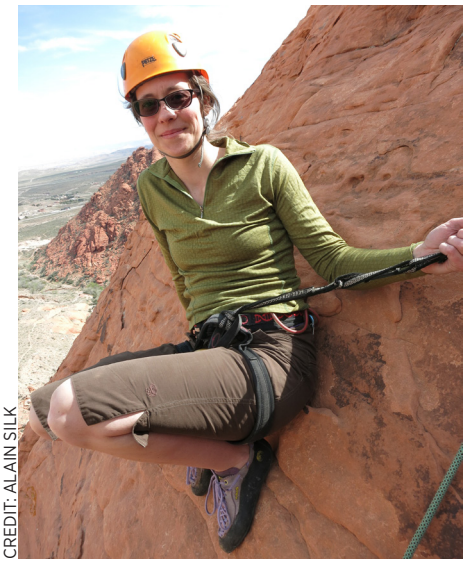
Ferré's talent led to love as well. NIDA senior investigator **Elliot Stein** watched Ferré's performance at Hoffer's birthday party and later told one of his postdocs, who was also an opera singer, about it: **Annabelle (Mimi) Belcher**. Belcher, a soprano, reached out to Ferré, and they began to perform duets with each other in 2010—their first gig was in December at a NIDA holiday party.

Bonding over their shared passion for music, Ferré and Belcher fell in love and were married in 2012. Belcher is now an assistant professor of psychiatry at the University of Maryland School of Medicine (Baltimore).

It's been more than 20 years since he first began to sing opera, but Ferré's love for it is still going strong. He and his wife used to host regular opera nights at a small Baltimore restaurant, where they tried to dispel the stiff and formal atmosphere that's often associated with opera and to convey the beauty of the music. The venue has since closed but they're still performing wherever they can.

"And then comes the big reward," said Ferré. "The applause, someone with tears in the eyes, or someone saying, 'I did not know I liked opera!'"

To hear a recording of Sergi Ferré singing an aria, go to https://youtu.be/ypvW9wQuLsA.



CREDIT: ALAIN SILK

Katie Kindt climbing in Red Rock Canyon near Las Vegas .

The Rock Climber: Katie Kindt, Ph.D.

Senior Investigator and Chief, Section on Sensory Cell Development and Function, National Institute on Deafness and Other Communication Disorders

Many people have an outlet for stress, in which they can channel their energy into a single task and tune out distractions. For some, this outlet might be running, journaling, dancing, or creating art. For **Katie Kindt**, it's rock climbing. When she climbs, she doesn't think about anything else—losing her concentration could result in a fall.

Kindt started rock climbing when she was a graduate student at the University of California at San Diego (San Diego). After trying out different activities, she found that the outdoor ones, such as rock climbing, camping, and mountain biking, appealed the most to her. With that in mind, Kindt and a few other students would meet every Wednesday with a local climbing group, who showed them how to climb and set up climbs safely. Nowadays, Kindt regularly climbs with other scientists at NIH, members of her lab, and her family. A few days a week, she'll head to the Movement Rockville indoor climbing gym (Rockville, Maryland). Weather permitting, she'll sometimes climb outside at Great Falls National Park (McLean, Virginia) or at Carderock Recreation Area (Potomac, Maryland), both of which are located along the Potomac River.

Kindt uses a style of climbing called top roping at these local climbing spots, making the climb rather straightforward. With top roping, the climber is attached to a rope running through an anchor that's already at the top of the route so they are always supported from above. But she often does lead climbing when she's out West: The lead person wears a harness attached to a rope, which in turn is connected to other climbers below. Lead climbing is more difficult and dangerous because the lead climber must set up their rope and place protection equipment—permanent bolts or removable nuts and cams—into the climbing wall as they are ascending.

In the spring, Kindt usually takes a climbing trip to Red Rock Canyon near Las Vegas or Joshua Tree National Park in southern California. Between taking in the desert scenery and focusing on the climb, she never forgets the gravity of the process she's undertaking.

"It's good to remind yourself that you're hundreds of feet up in the air," she said. "Like, you should be afraid [and] take this seriously."

A longer version of this article is at https://irp.nih.gov/catalyst/v30i5/pis-pursuing-their-passions

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PIs Pursuing Their Passions

CONTINUED FROM PAGE 13

CREDIT (BOTH): JOSEPH M. ZIEGELBAUER, NCI

Top: **Joseph M. Ziegelbauer**, an astrophotographer in his spare time, uses a camera connected to a telescope to capture dramatic photos of the night sky, like this one of the Orion Nebula (bottom).

The Astrophotographer: Joseph M. Ziegelbauer, Ph.D.

Senior Investigator, HIV and AIDS Malignancy Branch, National Cancer Institute

Five years ago, Joseph Ziegelbauer's wife bought him a telescope, thinking that astronomy would be something that would interest him. Her guess was right. Since that first telescope, Ziegelbauer has moved from observing objects in the night sky to capturing them with a camera, creating vivid, out-of-this-world photos.

It's been a constant learning process for Ziegelbauer. He first had to figure out the basics—how to connect a camera to the telescope, how to take sequences of images over long stretches of time, and how to stack images to produce sharper photos. With help from discussion forums, YouTube videos, and other online resources, Ziegelbauer has gradually optimized his photography process, such as by using a Raspberry Pi minicomputer to automate taking photos and upgrading his camera to one specifically designed to work with telescopes.

"A pleasant surprise has been the community of astrophotographers," he said. "You can just post a question, and people will take time to answer your superspecific questions."

From setting up the telescope to processing the images, it takes him roughly 30 hours to create a final image.

Among the photos he's taken, capturing the great conjunction of Jupiter and Saturn in December 2020, in which the two planets appeared the closest together in nearly 400 years, was the most difficult. Ziegelbauer needed to capture Jupiter, Saturn, and the moons of both planets in the same frame within a very short window of time, and because the objects differ in brightness, each required a different exposure. The images then needed to be layered on top of one another for each object to be seen clearly.

To Ziegelbauer, the biggest challenge in astrophotography is really a series of smaller ones. Is the sky cloudy? Is the moon visible? Are there trees or other objects blocking the view? These are among the variables that he must account for to produce the cleanest shot. Processing the raw image sequences requires lots of fine-tuning as well. Ultimately, however, what makes it all worth it to Ziegelbauer is seeing the cumulation of his effort.

"When you see that first image pop out of the computer after hours and hours of image processing, there have been multiple times when I've literally gasped looking at the screen," he said.

The Mountaineers Edward Giniger, Ph.D.

Senior Investigator, Axon Guidance and Neural Connectivity Section, National Institute of Neurological Disorders and Stroke

Adrian R. Ferré-D'Amaré, Ph.D.

Senior Investigator, Laboratory of RNA Biophysics and Cellular Physiology, National Heart, Lung, and Blood Institute

At 2:00 a.m., many of us are fast asleep in our beds, trying to get a good night's rest. But thousands of feet up in the mountains, the day is just beginning for **Edward Giniger** and **Adrian Ferré-D'Amaré**, who have summited mountains throughout Europe and North America. After scrambling to eat breakfast and double-checking that they have all the equipment they need, they head out in the dark to begin their climb.

Giniger and Ferré-D'Amaré discovered their mutual interest in climbing when they met as faculty members at the Fred Hutchinson Cancer Research Center in Seattle. Giniger had taken classes from local hiking clubs, gaining experience with ice climbing and rock climbing. Ferré-D'Amaré "inherited" his passion for mountaineering from his grandfather, who had emigrated from Catalonia (in northeastern Spain) to Mexico, where he loved to ascend the glacier-covered volcanoes scattered around Central Mexico.

For their first expedition together, Giniger and Ferré-D'Amaré summited Mount Hood, the highest mountain in Oregon. In the years since, the duo has climbed the European Alps, scaled the Canadian Rockies, and ascended mountains throughout the United States. They're hoping to take more mountaineering trips in the future.

An alpine mountaineering trip is a multiweek event. It takes several days for the body to acclimate to the high altitude and thinner air before the actual climb begins. In the United States, Giniger and Ferré-D'Amaré hike for a couple of days to get in shape before tackling a mountain. In Europe, however, cable cars can transport them to higher elevations to the edge of a glacier in just a few hours. Unlike most climbing areas in the United States where climbers must set up camp and carry their own their supplies, areas in Europe and Canada have well-organized mountain hut systems with basic amenities, like beds, central heating, and meals that make the climbing experience easier.

CREDIT (BOTH): ADRIAN R. FERRÉ-D'AMARÉ, NHLBI

Top: **Adrian R. Ferré-D'Amaré** sitting atop the Grand Teton Mountain in Jackson, Wyoming (2014); bottom: **Edward Giniger** standing on Mount Shuksan in North Cascades National Park in Washington state (2009).

When they are dealing with snow-covered mountains, Giniger and Ferré-D'Amaré prefer an "alpine start," which means leaving their camp or hut in the middle of the night when the ice and snow are still frozen. Once the sun rises and the air warms, the thin crust of ice on the surface melts causing the climbers to sink into the snow with every step. There's also more risk when melting ice dislodges snow (as avalanches), ice, and rocks. And getting an early start means that they'll return to camp when it's still light outside and won't be stumbling back—hungry and exhausted—in the dark.

For experienced climbers, mountaineering is not necessarily more dangerous than other sports, said Ferré-D'Amaré. It's up to the climbers to decide the level of risk they're comfortable with—based on the strength and abilities of the climbing party, weather conditions (and knowing that conditions may rapidly change), and other factors. Global warming adds another layer of complexity—many historically famous alpine climbing routes have already collapsed.

Despite the risks, Giniger and Ferré-D'Amaré find alpine mountaineering rewarding for a combination of reasons. There are the beautiful views and the physical exertion. There's the teamwork, as well as having to problem solve and constantly reassess a climb based on changing variables.

The Zenlike mindfulness that comes with having to concentrate on the present is also a draw for the pair, "especially for people like us who think way too much," Giniger said. ●

A longer version of this article is at https://irp.nih.gov/catalyst/v30i5/pis-pursuing-their-passions

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
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
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
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

Recently Tenured

JAMES A. BOURNE, NIMH and NINDS

HANS ELMLUND, NCI-CCR

SHAHINAZ GADALLA, NCI-DCEG

CHRISTOPHER HOURIGAN, NHLBI

ANDREW L. MAMMEN, NIAMS

JAMES A. BOURNE, PH.D., NIMH AND NINDS

Senior Investigator and Chief, Section on Cellular and Cognitive Neurodevelopment, National Institute of Mental Health; Adjunct Investigator, National Institute of Neurological Disorders and Stroke

Education: Imperial College of Science, Technology and Medicine, London (B.Sc. in biochemistry); King's College, London (Ph.D. in neuropharmacology)

Training: Postdoctoral fellowships in the Vision, Touch and Hearing Research Institute, University of Queensland (Brisbane, Australia); and in the Department of Physiology, Monash University, Australia (Clayton, Australia)

Before coming to NIH: Group leader and professor of neurobiology, Australian Regenerative Medicine Institute, Monash University

Came to NIH: In May 2022

Outside interests: Having recently arrived from Australia, he, his partner, and their Cavapoo Charlie (who rides in a backpack) enjoy exploring the Washington, D.C., metropolitan area via bicycle, courtesy of Capital Bikeshare; their favorite weekend activity is to cycle in the early morning along the Capital Crescent Trail to D.C. for brunch.

Website: https://www.nimh.nih.gov/research/research-conducted-at-nimh/principal-investigators/james-a-bourne-phd

Research interests: I am fascinated by how reliably and capably the brain develops so it can enable complex behaviors. Neurodevelopment, however, is an area of neuroscience that is often overlooked in terms of trying to define the substrate and cause of neurological and psychiatric disorders. Moreover, there is often considerable focus on a single species being representative of the evolution of specific processes. Therefore, my overarching research goal is to probe how the mammalian brain becomes interconnected. I am also exploring the neural substrate of certain diseases and conditions through the developmental lens.

We are interested in the pulvinar region (in the thalamus), which has expanded in size, complexity, and function throughout mammalian evolution; some pulvinar nuclei are specific to nonhuman primates. (The pulvinar is associated with the processing of visual information.) We are exploring the development of thalamocortical circuits and their plasticity into adulthood. This approach has the potential to identify the neural underpinnings of disorders, including schizophrenia, autism, and cortical blindness (total or partial loss of vision caused by damage to the brain's occipital lobe), as well as help us understand how the brain differentially operates at different stages of life.

Through a multidisciplinary cell-to-system approach, my group has influenced views on the developmental organization and plasticity of the primate visual system and how perturbations to specific areas of the brain during particular periods of development can have lifelong implications for visually guided behaviors (*Proc Nat Acad Sci U S A* **115:**1364–1369, 2018). I am pleased to be continuing that work at NIH.

HANS ELMLUND, PH.D., NCI-CCR

Senior Investigator and Head, Biological Computing Section, Center for Structural Biology, Center for Cancer Research, National Cancer Institute

Education: University of Southern Stockholm, Stockholm (B. Sc. in physical chemistry); Royal Institute of Technology, Stockholm (Ph.D. in structural biotechnology)

Training: Postdoctoral fellow, Gothenburg University (Gothenburg, Sweden); postdoctoral fellow, Department of Structural Biology, Stanford University School of Medicine (Palo Alto, California)

Before coming to NIH: Tenured Senior Research Fellow, Biomedicine Discovery Institute, Monash University (Clayton, Australia)

Came to NIH: In October 2021

Website: https://irp.nih.gov/pi/hans-elmlund

Research interests: I started my scientific career using a 300,000-volt helium-cooled electron microscope (EM) to image biological molecules operating as "machines" inside cells. I quickly realized that available computational methods were limiting progress and started to write my own specialized computer code—an open-source program package called SIMPLE—to transform 2D EM images into 3D structures of biomolecules at near-atomic resolution.

In 2014, I established an independent group at the Biomedicine Discovery Institute at Monash University. We began developing game-changing new technologies for 3D structure determination and time-series analysis of movies obtained with aberration-corrected transmission EM of individual nanoparticles tumbling in solution (*Science* **349:**290–295, 2015; *Science* **368:**60–67, 2020; *Science Adv* **7:**eabe6679, 2021). We also developed algorithms that allowed 3D reconstruction of biomolecules at near-atomic resolution in a matter of hours, using standard desktop computers (*Structure* **24:**988–996, 2016; *Protein Sci* **1:**51–61, 2017; *J Struc Biol* **204:**172–181, 2018; *Bioinformatics* **36:**2237–2243, 2019; *J Struc Biol* **4:**100040, 2020).

At NIH, my group is designing algorithms that make unsupervised decisions about how to collect the data and create "intelligent" microscopes via direct feedback between analysis and instrument. We are also developing algorithms for atomic-resolution structure identification of nanocrystals. Our work will allow the translation of structure into function at the cellular and organism levels, which could lead to conceptual advances in a range of biological research fields.

SHAHINAZ GADALLA, PH.D., NCI-DCEG

Senior Investigator, Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute

Education: Ain Shams University School of Medicine, Cairo, Egypt (M.D.); University of Maryland, Baltimore (M.S. in epidemiology and preventive medicine; Ph.D. in epidemiology)

Training: Cancer Prevention Fellow, NCI-DCEG

Came to NIH: In 2007 to complete Ph.D. dissertation; in 2008 joined NCI's Cancer Prevention Fellowship Program for postdoctoral training; promoted to staff scientist in 2011; became Earl Stadtman investigator in 2014

Outside interests: Spending time with the family; cooking

Website: https://irp.nih.gov/pi/shahinaz-gadalla

Research interests: Myotonic dystrophy (DM) is a slowly progressive multisystem genetic disorder that represents the most common type of adult-onset muscular dystrophy group of diseases. People with this disorder experience progressive muscle wasting and weakness, and, often, prolonged muscle contractions (myotonia)—such as being unable to release their grip on a doorknob, having slurred speech, or having temporary locking of their jaw.

I published the first epidemiological evidence that patients with DM are susceptible to colon, endometrium, ovary, brain, or possibly thyroid cancers (*JAMA* **306:**2480–2486, 2011). My research focuses on identifying individuals with DM who are at high risk for these cancers and discovering predictive and prognostic biomarkers that may guide therapeutic decisions.

I am also studying severe aplastic anemia (in which the body stops producing enough red blood cells) and myeloid neoplasms (bone-marrow cancers). Treatments for these diseases might include medications, blood transfusions, and in most cases hematopoietic-cell transplant (HCT), also known as a bone-marrow transplant.

In 2014, I discovered that after HCT, young patients with severe aplastic anemia had a higher chance of survival when the donor leukocytes had longer telomeres (*JAMA* **313:**594–602, 2015). In my current research, I am investigating markers of cellular aging, germline genetic variants, and somatic copy-number alterations.

I am also an adjunct assistant professor of epidemiology and public health at the University of Maryland School of Medicine (Baltimore).

CHRISTOPHER HOURIGAN, M.D., D.PHIL., NHLBI

Senior Investigator and Chief, Laboratory of Myeloid Malignancies, National Heart, Lung, and Blood Institute

Education: Swarthmore College, Swarthmore, Pennsylvania (B.A. in biology); Manchester University, Manchester, England (M.S. in immunology and immunogenetics); University of Oxford, Oxford, England (B.M., B.Ch., D.Phil., and D.M)

Training: Residency in medicine and surgery at Guy's and St. Thomas' Hospital (London); residency in internal medicine at Johns Hopkins Bayview Medical Center (Baltimore); clinical fellow in medical oncology and research fellow in cancer immunotherapy at Johns Hopkins Hospital (Baltimore); clinical fellow in hematology at NHLBI

Came to NIH: In 2012; became tenure-track investigator in 2015

Outside interests: Spending time with his wife, **Suchitra Hourigan** (a new Lasker Clinical Research Scholar at NIAID), and their two sons

Website: https://irp.nih.gov/pi/christopher-hourigan

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Recently Tenured

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Research interests: I was a scientist before I became a physician. I was amazed to find how often only limited and poor-quality information was available for even the most important of medical decisions. While we aspire to apply scientific insights for personalized and precision medicine, particularly when caring for those suffering from cancer, the reality is that we are often working with "best guesses, on average" rather than certainty for the person in front of us.

"Am I cured now, doc, or will this cancer come back?" is a question asked by my patients who have acute myeloid leukemia (AML), a rare, highly fatal blood cancer. AML is diagnosed in 21,000 Americans a year and only around 1 out of 3 survive it. While many have an apparently good response to initial treatment (a "complete" remission), that illusion is often shattered when the cancer becomes evident again ("relapse") within months despite the best available treatment. My research has focused on why remissions represent a cure only for some.

My team and I have studied patients with AML in clinical remission using highly sensitive and specific genomic tools to detect evidence of very low amounts of this blood cancer associated with higher risks of relapse. We were the first to show, using a NIH-funded randomized phase 3 trial, that early intervention in patients with AML with detectable "subclinical" measurable residual disease (MRD) could improve survival (*J Clin Oncol* **38:**1273–1284, 2019). This MRD concept is now the basis for a personalized medicine approach to AML in several new nationwide therapeutic and disease-monitoring initiatives that I lead.

In addition to predicting AML relapses, we also worked on preventing and treating them. I performed several immunotherapy clinical trials—including one using a novel combination regimen—at the NIH Clinical Center. I also remain a faculty member on the acute leukemia service of Johns Hopkins Hospital where I trained. I have found continuing to care for patients with this horrible disease is both motivating and helps keep the focus on what is most important.

Ultimately, I work at the NIH as a physician–scientist because I want to use science to make medicine better. My hope is that better information will allow us to provide evidence-based, personalized, and effective treatment for patients with cancer.

ANDREW L. MAMMEN, M.D., PH.D., NIAMS
Senior Investigator and Muscle Disease Unit Leader, National Institute of Arthritis and Musculoskeletal and Skin Diseases

Education: Reed College, Portland, Oregon (B.A.in biology); Johns Hopkins University School of Medicine, Baltimore (M.D. and Ph.D. in neuroscience)

Training: Residency in neurology, fellowships in neuromuscular medicine and in rheumatology at Johns Hopkins Hospital

Before coming to NIH: Associate professor of neurology and medicine, Johns Hopkins University School of Medicine

Came to NIH: In 2014

Outside interests: Hiking; reading; traveling

Website: https://irp.nih.gov/pi/andrew-mammen

Research interests: My research focuses on myositis, a rare family of autoimmune diseases in which the body's immune system attacks healthy muscle tissue, causing inflammation, weakness, fatigue, and pain in skeletal muscles. My team studies dermatomyositis, which can include a skin rash; the anti-synthetase syndrome, which can include rash, lung disease, and arthritis; inclusion body myositis, which typically affects the muscles of older adults; and immune-mediated necrotizing myopathy, which can cause especially severe weakness in children and adults alike.

When I was on the faculty at Johns Hopkins, I co-founded the Johns Hopkins Myositis Center in 2007. My Hopkins colleagues and I discovered a form of immune-mediated necrotizing myopathy that can be triggered by statins, a type of medication used to lower cholesterol concentrations (*Arthritis Rheum* **63:**713–721, 2011). This disease occurs in approximately 1 in 50,000 Black and white Americans who are exposed to statins. However, working with colleagues in New Mexico, I found that members of the Navajo Nation are much more likely to develop this disease (*Arthritis Rheum* 2022; DOI:10.1002/art.42126; online ahead of print). Indeed, approximately 1 in 300 of these American Indians may develop this form of myositis if exposed to statins. We are currently trying to understand why some people can safely use statins while others are at an increased risk of developing myositis and should avoid this type of cholesterol-lowering medication.

At NIH, my lab is 1) defining the different subtypes of autoimmune muscle disease based on muscle histology, autoantibodies, and other biomarkers; 2) elucidating the role of myositis autoantibodies in the pathogenesis of myositis; 3) developing animal models of myositis that are relevant to the human diseases; 4) understanding how environmental exposures, including medications such as statins and cancer immunotherapies, can trigger autoimmune muscle disease, and 5) using novel therapeutic strategies to treat myositis patients at the NIH Clinical Center.

I am also an adjunct professor of neurology and medicine at Hopkins, where I continue to see patients at the Myositis Center. ●

Radiation Exposure Among Early NIH Workers

Dosimetry Cards and the History of Radiation Safety

BY HALEY HIGINGBOTHAM, OD

The following is based on a historical overview provided by Michael Roberson, Deputy Director of the Division of Radiation Safety.

When we think of radiation exposure, large nuclear disasters may come to mind. But people who work with radioactive materials in medical settings can be exposed daily to small amounts of radiation that may accumulate over time, resulting in a small increase in cancer risk. NIH researchers, clinicians, and other staff have been working with radioactive materials and radiation-emitting devices since the 1940s, when it was routine to use radium needles for cancer therapy, run radium-radon generators that converted radium to radon for cancer treatments, or operate X-ray machines.

Today, radiation exposure is still a concern for many workers. To ensure exposure limits are not exceeded, some medical and research personnel wear dosimeters, devices that measure cumulative radiation exposure.

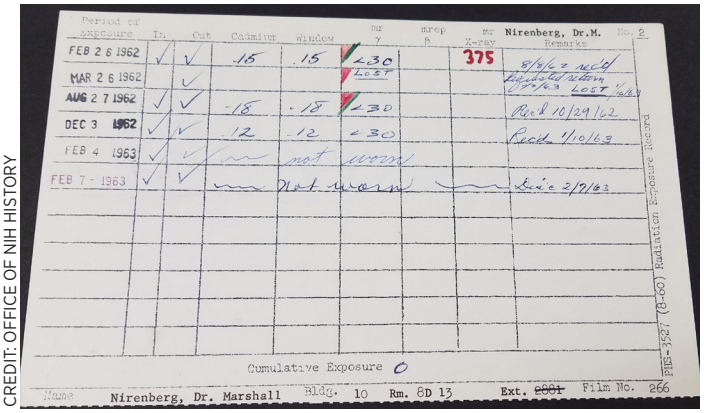
Early days of radiation safety

Radiation safety was formalized in 1947 at NIH when then–NIH Director **Rolla E. Dyer** issued the "Precautions for Protection from Radiation at the National Institute of Health." In 1948, he appointed a Radiation Safety Committee to conduct inspections and issue radiation-safety recommendations.

Methods to detect radiation exposure

Before 1950, NIH employees who worked with radioactive materials underwent blood draws semiannually that were analyzed to see whether significant decreases had occurred in white-blood-cell and platelet counts. This method was phased out by the mid-1950s and was replaced by film badges and personal dosimeters, which detect high-energy beta, gamma, or X-ray radiation. The results were recorded on index-card-sized dosimetry cards.

As part of an effort to preserve NIH's history of radiation safety, the NIH Division of Radiation Safety recently donated about 100 of its 27,000 record cards—including several with blood analysis results—to the Office of NIH History and Stetten Museum. The collection includes dosimetry cards from well-known NIHers: **Donald Frederickson** long before he became the director of NIH in 1975; **Isabelle Barr Ackerman**, the first woman radiation safety professional at NIH; and 1968 Nobel Laurate **Marshall Nirenberg**.



CREDIT: OFFICE OF NIH HISTORY

Marshall Nirenberg's dosimetry card. Nirenberg shared the Nobel Prize in Physiology or Medicine in 1968 for discovering the key to deciphering the genetic code.

CREDIT: LAURA S. CARTER, OD

Dosimeters come in all shapes and sizes. Clockwise from left: film badge holder that can fit on a wristband, badge to measure whole-body radiation exposure, two ring dosimeters, and pocket dosimeter.

The card system was used from the 1940s until 1979 when an early computer system took over. Dosimeters come in all shapes and sizes ranging: ring-sized dosimeters that fit on the finger; dosimeters worn on the wrist; small badges worn on the chest or waist to measure whole-body radiation exposure; and pocket dosimeters that could give a relatively good estimate of exposure in real time. The earliest film badges were not very sensitive, but have improved over time.

Radiation safety at NIH has evolved since its implementation in the 1940s. Today, NIH's Division of Radiation Safety ensures the safe use of all radioactive materials and sources of ionizing radiation throughout NIH, provides training courses for workers using radioactive materials, and requires the use of personal dosimeters in certain areas. ●

Haley Higingbotham is a Pathways intern in the Office of NIH History and Stetten Museum. She recently graduated from George Washington University with a master's in museum studies specializing in collections management.

Read more at: https://irp.nih.gov/catalyst/v30i5/from-the-annals-of-nih-history

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PHOTOGRAPHIC MOMENT

Changing the Conversation About Drug Addiction

CREDIT: THERESA CLOWER; COMPOSITE BY JOSIE ANDERSON, NIDA

The INTO LIGHT exhibit, on display at the NIH Clinical Center until October 1, 2022, aims to reduce the stigma that surrounds the tragedy of drug overdose. Read online article at https://irp.nih.gov/catalyst/v30i5/photographic-moment.

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