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Tackling Difficult Problems in Women's Health: Conference Highlights

BY TAMAR JACOBSOHN, NICHD

Historically, many medical advances have come from studies of men because women were underrepresented as biomedical researchers and in clinical trials. Study findings were extrapolated to women without taking into consideration sex differences such as in metabolism and responses to medications. Even some animals and cells used in studies were male and assumptions were made about relevance to females.

Women's health research took center stage at the "Advancing NIH Research on the Health of Women" videoconference, hosted by NIH's Office of Research on Women's Health (ORWH) and held on October 20, 2021. The conference, which featured 44 speakers, was held in response to a congressional request to address three topics: rising maternal morbidity and mortality rates; increasing rates of chronic debilitating conditions in women; and stagnant cervical cancer survival rates.

ORWH Founded Out of Advocacy

Awareness of inequities in research and health care was percolating in the 1960s as the civil rights, women's rights, and women's health movements were in full swing. In the 1980s, the scientific, policy, and advocacy communities began to respond; NIH's **Ruth Kirschstein**, then director of the National

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Beyond the Books

A Dynamic NIH Library Inspires Innovation, Bolsters Discovery

BY MICHAEL TABASKO, OD

CREDIT: KATHLEEN MCGLAUGHLIN, NIH LIBRARY

NIH Librarians provide virtual support to the NIH Community through trainings, reference services, and more.

Senior radiologist Ahmed Gharib at the National Institute of Diabetes and Digestive and Kidney Diseases is a timepiece connoisseur. He had an idea: What if the popular NATO watch band—a clever nylon strap and buckle of military origin—could be adapted for use in magnetic resonance imaging (MRI)? He envisioned the utilitarian design could be used to secure coils (specialized pieces that help the MRI scanner gather images of a specific body part) to larger patients or to irregularly shaped testing devices called phantoms that act as a stand-in for human tissue. Gharib took his concept to the NIH Library, where the Tech Hub team used their 3D printer to build a supersized version of the NATO buckle. Gharib's group has continued to work with the library.

"They are an outstanding service," he said. "They go out of their way to be helpful."

His branch has since created custom paddings to optimize liver coils that are being used

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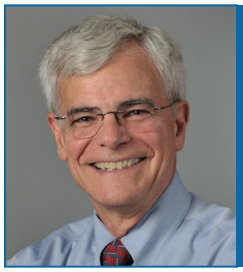


My Time as Deputy Director for Intramural Research: The Early Years

BY MICHAEL GOTTESMAN, DDIR

On July 15, 2021, NIH Director **Francis Collins** announced my decision that it was time to step aside as the deputy director for intramural research (DDIR) and make way for new leadership. This decision was made after considerable self-reflection and with the desire to do what I felt was best for the NIH intramural program (IRP), which I truly believe represents the epitome of biomedical research excellence. I will remain as DDIR until a new IRP leader is in place. Then I will return full time to the lab, where I will continue as the chief of the Laboratory of Cell Biology in the National Cancer Institute's Center for Cancer Research.

I've had a lot of time to think about the nearly 30 years that I've served as the DDIR. My philosophy of science management has led to important changes while preserving the IRP's basic conceptual underpinnings—that long-term, stable support of a diverse group of talented scientists is a formula for the extraordinary innovation and achievements of the IRP.

My willingness to take on responsibility for the IRP grew out of my involvement as co-chair of the NIH committee responding to a charge from Congress to review the "role, size, and cost" of the IRP. In 1992, Acting NIH Director **Ruth Kirschstein** asked me to take on this responsibility shortly after I had stepped down as acting director of the National Center for Human Genome Research (now known as the National Human Genome Research Institute). The NIH committee worked with an external committee chaired by Gail Cassell (University of Alabama at Birmingham) and Paul Marks (Memorial Sloan Kettering Cancer Center), which produced a report that has been a blueprint for the current architecture of the IRP. My reward for this involvement with the Marks-Cassell report was to be asked by then–NIH Director **Harold Varmus** to become acting DDIR in 1993. I became DDIR the following year after a search process.

The report expands on the congressional concerns that led to the review of the IRP. To quote: "The challenge of 'reinventing' the IRP requires that NIH rethink some of its practices regarding: 1) NIH-wide appointment and promotion of scientists; 2) recruitment and retention of outstanding scientists; 3) invigorating postdoctoral training programs that transcend institute lines; 4) use of patient and research facilities in the Clinical Center; 5) instituting efficient management and review practices that are more responsive to the needs of the research enterprise; and 6) exploring opportunities for increased collaboration with the extramural community, including industrial and academic laboratories."

An ideal research environment is a very delicate flower that must be cultivated and can easily be damaged. Successful research institutions are able to balance the needs of many different personalities and talents with regulatory considerations and a healthy interaction between local and central interests. The environment for creative science requires adequate resources, opportunities for collaboration, a shared mission, and a diversity of ideas, backgrounds, and scientific orientations made available to a group of talented, diverse scientists who are eager to take advantage of this nurturing environment. I have always viewed my job as encouraging the finer impulses of our scientists, discouraging the less productive inclinations, and exercising my power to convene various groups with shared interests. I have helped to make matches between scientists and between them and their research-resource needs. I have truly enjoyed serving as a convenor, matchmaker, and good listener, perhaps my most valuable "powers," since I do not have direct supervisory authority over most of the scientists at the NIH.

A major concern raised in the report was the need for NIH to continue to attract the most diverse and talented scientists and sustain their careers in the IRP. Very early on, we established a tenure-track system at the NIH and a process for recruiting, reviewing, and rewarding excellence (the Boards of Scientific Counselors review process and the tenure process). We had a legacy of outstanding scientists who collaborated with our PIs and were essential for support and progress in our laboratories. They became staff scientists who now make up the largest population of intramural professionals. A system has been developed for their recruitment and review.

For our trainees, I wanted to assure a continuity of opportunities—from high school students to postdoctoral fellows—in the IRP. Over the years we have built the Office of Intramural Training and Education (very ably led by **Sharon Milgram**), which works with training directors in each of our institutes and centers (ICs). In particular, I was directly involved in the formation of

the postbac program; the NIH Academy for postbacs interested in health-disparities research; the Undergraduate Scholarship Program for undergraduates from diverse backgrounds; the NIH Academy for postbacs interested in health-disparities research; the Graduate Partnership Program for graduate students; and various time-off programs for medical students to learn about biomedical research (the NIH-Howard Hughes Medical Institute program and its successors, the Clinical Research Training Program and the Medical Research Scholars Program). A student can enter this continuum at any point and leave and re-enter as career aspirations dictate. In fact, some of our current PIs started at NIH as high school and college students.

None of this could have been accomplished without a dedicated, scientifically adept senior staff in the Office of Intramural Research (OIR), including many volunteers from the ICs, talented and hard-working directors of OIR programs and their staffs, and the strong support of the scientific and clinical directors and leadership in the Office of the NIH Director and in each of our ICs. We are very fortunate at the NIH to have such capable leadership at all levels and in all institutes.

In the next installment of my ruminations on the past 30 years of the IRP's history, I will consider research resource requirements, the reinvigoration of the Clinical Center and clinical research programs at the NIH, technology transfer developments, more recent changes in our IRP program, and what the future may hold. ●

NEW SIG: Trans-NIH Gene Therapy Scientific Interest Group

The Trans-NIH Gene Therapy Scientific Interest Group (GRx SIG) was developed to strengthen cross-disciplinary gene-therapy research at NIH. The diversity of gene therapies dictated the need to establish the Gene Therapy SIG to promote synergy across the intramural research program (IRP). For example, the broad clinical areas of interest are rare diseases, pediatric diseases, neurological diseases, infectious diseases, metabolic diseases, and cancer. Approaches and technologies include antisense oligonucleotides; adeno-associated vectors and lentiviral vectors; small-interfering RNAs; and gene-, transcript-, and base-editing technologies. The translational and regulatory aspects of gene therapy span the following areas of interest: target identification, preclinical research and investigational-new-drugs-directed studies (including pharmacokinetics, pharmacodynamics, toxicology, and safety pharmacology), formulation and manufacturing, clinical trials, bioethics, and regulatory affairs.

The goals of the GRx SIG are to 1) provide leadership, vision, and support to promote gene-therapy research and development within the IRP; 2) share knowledge about gene-therapy research across institutions, disciplines, and NIH institutes and centers (ICs); 3) collect, evaluate, and disseminate resources and opportunities for gene-therapy research and development at NIH; 4) promote interactions, collaborations, and mentorship among intramural scientists and clinicians, and with extramural academic and industry researchers; and 5) establish and implement a cohesive roadmap for gene-therapy research at NIH.

The GRx SIG members include program officers, program directors, and intramural investigators from different ICs. SIG activities will be coordinated by a steering committee that oversees the organization of meetings and educational offerings on developing and applying gene therapy within NIH. Extramural academic and industry researchers may be invited to attend as guests. A combination of face-to-face meetings and remote webinars will be held, featuring guest speakers to provide perspective, comments, and expert feedback. The steering committee will communicate the Gene Therapy SIG recommendations and suggestions to the Gene Therapy Taskforce and vice versa. Meetings will be held monthly (days and times to be determined).

To receive e-mail notices of meetings and how to attend, please subscribe to the Gene Therapy LISTSERV at https://list.nih.gov/cgi-bin/wa.exe?A0=gene-therapy-sig and click on the "Subscribe or Unsubscribe" link in the right sidebar. For more information and a schedule of meetings, visit the Gene Therapy SIG web page (https://oir.nih.gov/sigs/gene-therapy-scientific-interest-group) or contact the chair of the Gene Therapy SIG, **Bryan Traynor** (bryan.traynor@nih.gov), or advisors **Avi Nath** (NINDS), **Donald Lo** (NCATS), and **Carsten Bönnemann** (NINDS). ●

For a full lists of scientific interest groups, go to https://oir.nih.gov/sigs/view-name.

From the Fellows Committee

Making Social Connections During COVID-19

BY ALISON JANE MARTINGANO, NHGRI

Like many others, I started my postdoctoral training at NIH during the COVID-19 pandemic. I arrived in August 2020, after almost all NIH employees, contractors, and trainees were assigned to mandatory telework (beginning in March 2020). In June 2020, those whose could not work remotely were allowed to return to the labs. But the return was limited. Capacity limitations to ensure safe distancing meant that most trainees worked only part-time or in shifts. Trainees like myself, who can telework effectively, are still working entirely remotely.

All of these changes, while necessary for ensuring employee and trainee safety, serve to make socializing with colleagues difficult. One trainee, who chose to remain anonymous, shared with me that "I quite literally haven't spoken to another postdoc" since starting in August 2020.

Most trainee events are held online nowadays including career and professional development activities, wellness webinars, and meetings of trainee groups as well as research symposiums and awards ceremonies. For many of these virtual venues, cameras-off has become the accepted norm so you often don't get to see the participants. In addition, there are few opportunities for the kind of informal chitchat that might naturally occur at in-person gatherings.

Zoom webinar formats usually do not allow for any audience interaction. Participants are held in virtual waiting rooms before events start and are unceremoniously kicked out when the presenter is finished. These types of arrangements severely limit the opportunities trainees have to socialize. **Mallory Smith**, a trainee in the National Institute of Child Health and Human Development, put it simply: "You could reach out via email afterwards, but frankly, you're not very likely to do that."

Having social support is, unsurprisingly, a predictor of happiness and productivity at work. A survey of 522 remote workers during COVID-19 found that more social support people have, the less likely they are to procrastinate and feel lonely (*Appl Psychol* **70:**16–59, 2020).

I asked several trainees to describe the successful social-connection strategies their institutes and centers (ICs) were using. They said that making connections was easier, and deeper conversations possible, when small virtual working groups shared a common interest and met regularly to write policy documents or organize events. Some ICs hosted outdoor activities such as hikes in which people break off naturally into conversational pairs. I personally found meaningful connections at a virtual weekly support group for women scientists run by the Office of Intramural Training and Education (OITE), where I found empathy and encouragement in abundance.

Dedicated social events held virtually were the least likely to generate meaningful connections. Trainees reported being more likely to find deep connections at events not deliberately designed for socializing, but where socializing was possible nonetheless.

One of the problems with dedicated social events is that they are often filled with small talk rather than substantial conversations. How many of us internally groan when asked to "go around and introduce ourselves"? To deepen social connections, psychologists recommend we avoid small talk. Instead, we can try some of the closeness-generating questions—such as, "Before making a call, do you ever rehearse what you're going to say? Why?", "What would constitute a perfect day for you?", or "For what in your life do you feel most grateful?"—designed by social psychologist Arthur Aron (*Pers Soc Psychol Bull* **23:**363–377, 1997). He found that asking and answering such questions with a stranger led to feelings of closeness that approached that of longtime friends.

To encourage these kinds of deeper conversations in virtual settings, it is vital that trainees have access to private meeting spaces so they can feel free to speak honestly and candidly. Trainees who work on campus must still attend virtual trainings, but they may not have any privacy. "Attending virtual meetings while in a shared office makes it difficult to make personal connections with those on the call," explained postdoctoral fellow **Tiffany Zarrella** (National Cancer Institute).

While COVID-19 continues to upend our lives, we may have to accept that the way we socialize is different, but that does not mean it has to be nonexistent. To find trainee events that might interest you, subscribe to the Fellow-L LISTSERV (https://list.nih.gov/cgi-bin/wa.exe?SUBED1=fellow-l&A=1) for official events, or contact the FELCOM social committee chair **Nicholas Madian** or the health and wellness committee chair **Tiffany Zarrella** for other suggestions. More info on getting involved with OITE groups can be found at https://www.training.nih.gov/wellness and https://www.training.nih.gov/resources/justarrived. ●

Alison Jane Martingan is a postdoctoral fellow in the Immersive Stimulation Research Program, at the National Human Genome Research Institute. Her research involves using virtual reality to evaluate how providers communicate genetic concepts and show empathy during physician–patient interactions.

Lawrence Tabak Named Acting Director of NIH

Will Continue to Carry Out NIH's Important Initiatives

FROM THE OFFICE OF THE NIH DIRECTOR

Acting NIH Director Lawrence Tabak.

On December 20, 2021, Lawrence A. Tabak, the principal deputy director of the National Institutes of Health (NIH), began serving as the acting director of NIH. The previous NIH director, **Francis S. Collins**, who stepped down from that position on December 19, was the longest-serving, presidentially appointed NIH director, having served three U.S. presidents over more than 12 years. Collins will continue to lead his research laboratory at the National Human Genome Research Institute.

Tabak had served as the NIH principal deputy director and the deputy ethics counselor since August 2010. He previously served as the NIH acting principal deputy director in 2009, and prior to that as director of the National Institute of Dental and Craniofacial Research (2000–2010).

Before joining NIH, Tabak was the senior associate dean for research and professor of dentistry and biochemistry and biophysics in the School of Medicine and Dentistry at the University of Rochester (Rochester, New York). Tabak's major research focus has been on the structure, biosynthesis, and function of glycoproteins. He continues work in this area, maintaining an active research laboratory within the NIH intramural program in addition to his administrative duties.

A native of Brooklyn, New York, Tabak received his undergraduate degree from City College of the City University of New York (New York), his D.D.S. from Columbia University (New York), and both a Ph.D. and certificate of proficiency in endodontics from the University of Buffalo (Buffalo, New York). A former NIH MERIT recipient, Tabak has received several honors and awards for his work including being an elected member the National Academy of Medicine (formerly the Institute of Medicine) of the National Academies.

"I am honored to assume the role of the acting director of the National Institutes of Health and lead the agency during this time of transition," Tabak wrote in an email message to NIH staff on December 20, 2021. "Having served at Dr. Collins' side as the principal deputy director since August 2010, I have been intimately involved in the science, policies, and operations of the agency and will continue to carry out the important initiatives that Dr. Collins and I have built and fostered together over the past 12 years…. Dr. Collins' singular focus has always been finding the best ways that NIH research can improve health, end suffering, and provide hope for all people. As acting director of NIH, I will try to sustain that legacy."

Other changes in the Office of the NIH Director:

Tara A. Schwetz, who has been the NIH associate deputy director and alternate deputy ethics counselor at NIH since 2019 and recently did a detail to the White House Office of Science and Technology Policy as the assistant director for biomedical science initiatives, will serve as acting NIH principal deputy director. **Courtney F. Aklin**, who was the senior advisor in the immediate Office of the Director, will resume her position as acting NIH associate deputy director. **John Burklow**, formerly the NIH associate director for communications and public liaison, will continue as the acting chief of staff. ●

To watch a farewell tribute to Francis Collins, held on December 16, 2021, go to https://www.nih.gov/farewell-dr-francis-collins.

Building for the Future

NIH Construction Updates Facilities, Affects Parking and Traffic

BY MICHAEL TABASKO, OD

CREDIT: OFFICE OF RESEARCH FACILITIES

Conceptual rendering of the Surgery, Radiology, and Laboratory Medicine addition to the Clinical Center from the northwest view at Center Drive and the Old Georgetown Road entrance.

Are you returning to the office or lab in 2022? Major construction projects may change how you navigate the day. A new multilevel parking (MLP) garage for patients and employees is emerging along Convent Drive in the northwest corner of the Bethesda campus. Across South Drive, an expansion promises to nearly double the size of the Vaccine Research Center (VRC). With funding recently appropriated by Congress, the long-awaited Surgery, Radiology, and Laboratory Medicine (SRLM) addition will begin to take shape on the west wing of the Clinical Center (CC). And out in Hamilton, Montana, a new facility will boost Rocky Mountain Laboratories (RML) square footage by nearly 30%.

During this biomedical infrastructure growth spurt, the Office of Research Facilities (ORF) has made easing the day-to-day impact on patients and employees a top priority. A comprehensive strategy of mitigation measures aims to keep the chessboard of parking as well as vehicle and pedestrian travel in motion. ORF, the Office of Research Services (ORS), and the CC are rolling out a collaborative communications campaign to keep the NIH community informed. Over the coming months, be on the lookout for emails as well as signage and posters that will direct movement throughout campus.

Patient Parking Garage and Utility Vault

Work on the new parking garage, MLP-14—located on the west side of Convent Drive parallel to the CC—has been underway since January 2021. The structure will shift parking from the aging garage located below the CC's Ambulatory Care Research Facility (ACRF), a nearly 40-year-old building that houses outpatient facilities and clinical laboratories. Beyond 2028, the old ACRF garage will eventually close. ORF is considering options to repurpose the space.

Adjacent to MLP-14, upgraded electrical equipment will be installed in a new utility vault to power the growing hospital complex once the new SRLM is completed. And protecting pedestrians from weather and traffic, a tunnel under Convent Drive will link to the CC.

Construction on MLP-14 will wrap up later this year, but you won't be able to park there just yet. Access will be restricted because workers will use the garage and surrounding area to stage materials for the SRLM project. The grand opening comes in summer 2028, when driveways off Center and South Drives will make all 750 spaces available to patients, visitors, and staff.

VRC expansion

Cranes and crews have begun preparing the VRC for Building 40A: A six-story, 80,000-square-foot addition that artfully integrates with the north side of the existing structure via a central corridor and new lobby. On the north elevation, workers are installing a temporary weather barrier wall behind the building's exterior skin to shield the interior and allow research activity to continue unabated during construction. The 20-year-old VRC is currently at capacity, and the new expansion will provide dedicated space for the future of critical vaccine research. Supported by funds from the Coronavirus Aid, Relief, and Economic Security (CARES) Act, ORF awarded the construction contract in November 2021. Completion is expected in the fall of 2024.

SRLM

A contemporary nine-story (with one basement level) addition to the west wing of the CC will total 547,290 square feet, ensuring a future home for many of the advanced services that make the CC a world-class research facility. New space will house the General Radiology and Imaging Services, Department of Perioperative Medicine, Department of Laboratory Medicine, National Cancer Institute labs, and other medical departments. The ambitious project will also renovate 82,150 square feet of the existing CC and close

150 parking spaces in the ACRF garage and its west side P1 entrance. Construction will commence in February 2022 and last until 2028. During this time, two roads will be closed: 1) Center Drive from the gate at Old Georgetown Road to the front of the Northwest Child Care Center (the parking lot to the child care center will still be accessible); and 2) Convent Drive north of the MLP-9 garage entrance.

RML Comparative Medicine Center (RCMC)

A sister project to the VRC addition, the RCMC is also supported by CARES Act funds and adds a three-story, 120,000-square-foot vivarium, or animal facility. Scientists at the National Institute of Allergy and Infectious Diseases' RML campus conduct vital research on emerging infectious diseases. They often use animal models to better understand pathogens and design therapeutic studies for treatment and prevention. The new centralized animal receiving and holding building replaces nearly 60-year-old facilities. It will support all biosafety levels of research throughout the RML campus and scores of wide-ranging research projects including work on SARS-CoV-2.

The RCMC will provide expanded capabilities for studies with exotic species (such as bats), state-of-the-art imaging systems, and a multispecies insectary to support the discovery of vector-borne diseases. Mosquitos and fleas could find a new home here, as well as ticks.

Newly emerging and re-emerging infectious diseases can trigger immediate needs to shift research plans. With this in mind, each holding suite in the RCMC was designed for quick adaptation to accommodate different species. Construction is already underway, and impacts to the scientific staff should be minimal. The project is scheduled to finish in spring 2024. ●

PARKING AND TRAFFIC MITIGATION MEASURES

Closures (dates are subject to change)

- **February 2022**: Center Drive will close from the gate at Old Georgetown Road to the front of the Northwest Child Care Center (its parking lot will still be accessible, however); Convent Drive alongside the CC (Building 10) will also be closed, but CC employees will still have access to the MLP-9 parking garage. Both roads will reopen in 2028 once the SRLM is complete.
- **February 2022:** The P1 entrance (on the west side) to the ACRF parking garage will close, but the P3 entrance (on the east side) will remain open for patients, visitors, and staff. To access the P3 entrance, employee vehicles are encouraged to enter campus on North Drive off Rockville Pike (where a new inspection station is being built), and CC patients and visitors will continue to use the West Drive entrance and inspection station. Remaining unchanged are designated parking levels for patients and visitors, general parking, and red-tag holders.

Changes (dates are subject to change)

- **Early 2022**: The North Drive entrance will be open in the evening for exiting traffic only to allow vehicles to exit right on Rockville Pike and access points east. ORF is currently working with the NIH police to finalize signage, details, and timing.
- **February 2022**: The MLP-9 garage, which is now used by any NIH staff, will be only for staff who work in the Clinical Center/Building 10 complex. Employees working in the surrounding buildings may park in the MLP-6 and MLP-8 garages. To minimize cross-campus traffic, all staff parking in MLP-6, -8, and -9 are encouraged to enter campus through the Lincoln Drive or South Drive gates. Staff who work in buildings near the middle of campus are encouraged to park in Lots 41 and 42.
- **February 2022:** The CC visitor and patient valet parking will move to lot 4A. Visitors and patients will still take their cars to the North Entrance of the CC for valet parking, and those self-parking in the ACRF will proceed to the P3 entrance.

Additions (dates are subject to change)

- **March 2022:** A second gate arm installed at the Lincoln Drive entrance will double the gate's capacity for vehicles to enter campus. The guard booth and exit lanes will be repositioned to improve pedestrian safety at the intersection of Old Georgetown Road.
- **March 2022**: A temporary road from South Drive (between Old Georgetown Road and Convent Drive) will access Building 60 and the Safra Family Lodge. The one-lane road is designed to minimize environmental impact and will include a small easement for oncoming vehicles to pull off.
- **March 2022:** Secured parking attendant booths installed at Lot 10H (on the south side of Building 10) will offer attendant-controlled general parking and recover 80 spaces lost from the ACRF garage.
- **July 2022:** Lot 18, a new visitor parking lot, will open on the south side of campus on the site of Temporary Buildings 32 and 18 (which are slated for demolition). Visitors who used to park in Lot 4A (which will become the new valet parking lot for patients) will be able to park in Lot 18. A campus shuttle will serve the new lot.
- **August 2022:** A remote inspection station will be set up along North Drive on parking lot 31B, replacing inspection capacity from the closed ACRF P1 entrance. Vehicles will receive a time-stamped ticket before proceeding to the ACRF P3 entrance on Memorial Drive.

You can also check the "Campus Traffic and Parking Changes" website for the latest on construction projects, timelines, an interactive map, and links to resources that will ease the effects of traffic on your daily commute (work schedule flexibilities, commuting alternatives, and more): https://traffic.nih.gov.

Intramural Research Briefs

CREDIT: NIH MEDICAL ARTS

NIBIB et.al.: Artist rendition of the triple-view line scanning confocal microscope obtaining an image of the roundworm, *C. elegans*, in conjunction with deep learning.

NIBIB, NHLBI, NICHD, NCI: ARTIFICIAL INTELLIGENCE AND HARDWARE INNOVATIONS ENHANCE MICROSCOPY

Confocal microscopy is a powerful tool in biomedical research. By using a focused beam of laser light, narrow slices of a biological sample are scanned and then digitally reconstructed to create 3D images. However, the technology has limitations: Images become blurry along the third dimension, and resolution diminishes in thicker samples. An NIBIB-led team of researchers and their collaborators recently developed an improved confocal microscope capable of generating higher-quality images. The scientists captured images of more than 20 biological structures and processes ranging from nanoscale dynamics of proteins within immune cells to developing nerve cells in roundworm embryos.

Using a technique called triple-view line-scanning confocal microscopy, the researchers sequentially scanned, in low light, slices of a sample from three directions with the new microscope. Computer software stitched together the images into a single super-resolution 3D image and applied a form of artificial intelligence called deep learning to process images. Low light scanning can avoid damaging biological structures but the images are blurry. Deep-learning algorithms were able to compensate and produce a higher-quality image than the original.

The authors hope these new approaches will deepen our understanding of how organisms develop. (NIH authors: Y. Wu, X. Han, Y. Su, J. Liu, R. Fischer, C. Combs, J. Sun, X. Wu, R. Christensen, L. Bao, Y. Sun, J. Chen, Y. Pommier, Y. Shi, E. Murphy, and H. Shroff, *Nature* **600**:279–284, 2021)

[BY JONATHAN CHU, NIAID]

NICHD, NHGRI, NIAMS: ALS DRUG MAY HELP TREAT RARE NEURODEGENERATIVE DISORDER

In a mouse model, NIH scientists have repurposed riluzole, a drug currently approved to treat amyotrophic lateral sclerosis (ALS), as a potential treatment for Niemann-Pick disease type C1 (NPC1). NPC1 is a rare genetic disorder typically affecting children and adolescents. The disorder is marked by the gradual loss of brain cells known as Purkinje neurons in the cerebellum and can cause uncoordinated movements, cognitive decline, and death.

An NICHD-led team first analyzed RNA sequencing data from mice with a form of NPC1 and observed decreased expression of a gene that encodes a protein that transports glutamate in the brain. High concentrations of glutamate can be toxic to neurons.

The investigators then treated the NPC1 mice with the FDA-approved drug riluzole, which reduces the release of glutamate, and found that treated mice survived 12% longer than untreated ones. The findings suggest that riluzole or similar glutamate-inhibiting drugs could be used as a new therapeutic to treat patients with NPC1. (NIH authors: A. Cougnoux, J.C. Yerger, M. Fellmeth, J. Serra-Vinardell, F. Navid, C.A. Wassif, N.X. Cawley, and F.D. Porter, *Mol Genet Metab* **134**:330–336, 2021; DOI:10.1016/j.ymgme.2021.11.008)

[BY RAGHURAM REDDY, NINDS]

NIA, NCI: CANCER DRUGS BEING TESTED TO FIGHT ALZHEIMER DISEASE

NIA researchers and their collaborators have discovered that young individuals who are genetically susceptible to Alzheimer disease (AD) may benefit from drugs currently used to treat cancer.

In a recent study, scientists analyzed post mortem brain samples from participants of two existing studies who carried *APOE4*, a known AD genetic-risk variant. The researchers identified protein changes associated with *APOE4* in the brains of participants with an average age at death of 39 years and compared them with the brains of those who died at an average age of 89 years, with and without AD. *APOE4*-associated changes observed in mouse models further confirmed their findings.

Using in vitro experiments, the investigators tested whether existing FDA-approved or experimental drugs targeted the identified proteins. They found that an experimental drug for liver cancer, and dasatinib (used to treat chronic myeloid leukemia), acted upon the AD-related proteins. NIA scientists are analyzing large real-world clinical datasets to test whether commonly used drugs like dasatinib may be effective Alzheimer treatments. (NIH authors: J. Roberts, V.R. Varma, Y. An, J. Candia, G. Fantoni, V. Tiwari, C. Anerillas, A. Williamson, R. Moaddel, M. Khadeer, J. Lovett, T. Tanaka, D.L. Croteau, S.M. Resnick, M. Gorospe, V.A. Bohr, L. Ferrucci, and M. Thambisetty, *Sci Adv* 7:eabi8178, 2021; DOI:10.1126/sciadv.abi8178)

[BY SUNITA CHOPRA, NCI]

NIAID: HIV-INFECTED INDIVIDUALS CONTROL THE VIRUS IN DIFFERENT WAYS

NIAID scientists have identified two distinct ways in which HIV-infected individuals were able to control the virus after stopping antiretroviral therapy (ART). ART is effective at suppressing HIV, but is a lifelong medication regimen that can have long-term side effects

and the potential for developing drug resistance.

In this study, two adult participants began ART soon after acquiring HIV and continued treatment for over six years, successfully suppressing the virus. They then joined an HIV clinical trial and stopped taking ART under medical supervision. The participants were monitored for viral rebounds every two to three weeks over the course of several years.

The first participant suppressed the virus with intermittent rebounds for nearly 3.5 years until drug testing revealed that he had begun taking undisclosed, suboptimal ART. The investigators found that this participant had high concentrations of HIV-specific immune cells called CD8+ T cells that may have contributed to his control of the virus.

For nearly four years, the second participant almost completely suppressed HIV and showed a very strong neutralizing antibody response not seen in the first participant. The authors suggest that this near-complete HIV suppression may have been facilitated by the neutralizing antibodies. This individual eventually experienced a dramatic viral rebound when he became infected with a different HIV strain.

Understanding the mechanisms of virus-suppression could provide insight into the development of new treatments for HIV. (NIH authors: J. Blazkova, J.S. Justement, V. Shi, E.J. Whitehead, R.F. Schneck, E.D. Huiting, K. Gittens, J. Lack, M.C. Sneller, S. Moir, A.S. Fauci, and T.W. Chun, *Nat Med* **27**:1893–1898, 2021; DOI:10.1038/s41591-021-01503-6)

[BY NATALIE HAGEN, NCATS]

NICHD: EARLY CHILDHOOD EATING PROBLEMS LINKED TO DEVELOPMENTAL DELAY

In a recent study, NICHD researchers found that frequent eating problems in the first three years of life could be used to identify children at risk for developmental delay. Scientists analyzed data from 3,597 children born between 2008 and 2010 in New York State whose mothers reported their children's feeding behavior and developmental progress as part of Upstate KIDS, a population-based birth cohort study. When the children were 18, 24, and 30 months old, each mother rated their child's eating problems in several categories including food refusal, mechanical (swallowing) issues, and distress such as crying during meals. Using the Ages and Stages Questionnaire, developmental milestones were assessed at the same three time points.

The results revealed that children with feeding problems were more likely to be scored as developmentally delayed, especially true as the frequency of eating problems increased. Compared with kids with no trouble eating, children with frequent feeding problems at one or two time points were more than twice as likely to miss developmental milestones, and those with frequent feeding problems at three time points were more than four times as likely to show developmental delay.

The authors noted that neurological, motor, or communication deficits associated with developmental delay may underlie feeding issues. (NIH authors: D.L. Putnick, S.L. Robinson, R. Sundaram, and E. Yeung, *J Pediatr* 2021; DOI:10.1016/j.jpeds.2021.11.010)

[BY TAMAR JACOBSOHN, NICHD]

NIEHS: AUGMENTING IMMUNE RESPONSE MAY EFFECTIVELY TREAT PNEUMONIA

Pneumonia, commonly caused by *Streptococcus pneumoniae* bacteria, is a leading cause of mortality in the United States. Treatment can be limited by antibiotic drug resistance, and a recent study led by NIEHS scientists has shown how targeting the body's own immune response may provide an alternative treatment option.

During lung infection caused by bacteria, a natural inflammatory response prompts macrophages to consume and remove the pathogens. To keep tissues healthy and control inflammation, signaling compounds known as epoxyeicosatrienoic acids (EETs) are also produced, but can inhibit macrophage activity.

CREDIT: NIAID

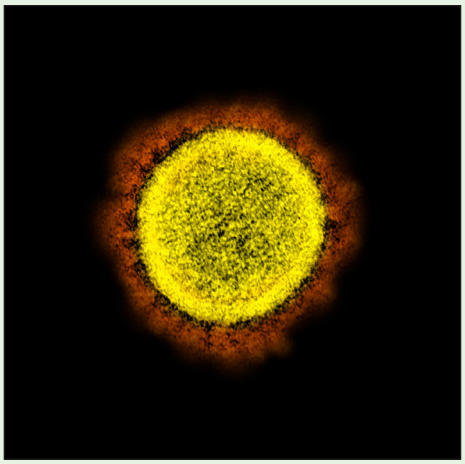
NIAID: Scanning electron micrograph of an HIV-infected (orange) H9 T cell.

The research team discovered that infection induced a protein called soluble epoxide hydrolase (sEH), which degraded EET and allowed macrophages to more effectively clear bacteria. When sEH was blocked in genetically modified mice, EET concentrations spiked, hampering the macrophages' ability to eat bacteria and resulting in more severe lung infections. In contrast, when EET was blocked using a synthetic molecule called EEZE, the scientists observed an increase in the eating capacity of the macrophages, leading to reduced numbers of bacteria in the lungs of mice. Identical results were seen when the authors studied the interaction between bacteria and human lung macrophages in vitro. (NIH authors: H. Li, J.A. Bradbury, M.L. Edin, J.P. Graves, A. Gruzdev, J. Cheng, S.L. Hoopes, L.M. DeGraff, M.B. Fessler, S. Garantziotis, S.H. Schurman, and D.C. Zeldin, *J Clin Invest* **131:** e129679, 2021; DOI:10.1172/JCI129679)

[BY SATABDI NANDI, NIA]

Read longer versions of these briefs at: https://irp.nih.gov/catalyst/v30i1/research-briefs.

COVID-19 Timeline at NIH (November–December 2021)



CREDIT: NIAID

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

November 2: NICHD supports a four-year follow-up study on the potential long-term effects of COVID-19 on women infected with SARS-CoV-2 during pregnancy.

November 3: NIH's Rapid Acceleration of Diagnostics initiative announces the launch of the When To Test Calculator for Individuals. By answering a few prompts, the online tool helps people determine whether they are at risk of getting or transmitting COVID-19 and make informed testing decisions.

November 4: The Department of Health and Human Services (HHS) announces its plan for a phased return to the physical workplace, replacing the NIH framework in place since June 2020. NIH Director **Francis Collins** follows up with an email to all staff that the NIH return to the physical workplace intranet page has been updated and that he expects workplace flexibilities to continue for most staff.

November 4: An NIH commentary published in *Pediatrics* highlights the need for research that involves community engagement in underserved or vulnerable areas of the United States for safe in-person school during the COVID-19 pandemic. (*Pediatrics* e2021054268B, 2021; DOI:10.1542/peds.2021-054268B)

November 4: HHS Secretary **Xavier Becerra** and Deputy Secretary **Andrea Palm** visit NIH to meet with top NIH leadership and get a tour of a Clinical Center lab and a lab demonstration at the Vaccine Research Center.

November 5: NIDCR researchers identify an enzyme process that may influence infectivity of SARS-CoV-2 variants and potentially boost the virus's ability to spread. (*PNAS* **118:**e2109905118, 2021; DOI:10.1073/pnas.2109905118)

November 9: The *New York Times* (*NYT*) reports that Moderna seeks to exclude U.S. government scientists from its COVID-19 vaccine patents. The vaccine was the result of a collaboration with NIH's Vaccine Research Center researchers who worked with Moderna to design the genetic sequence that prompts the mRNA vaccine to produce an immune response. Results from this collaboration played "a major role in the development of the vaccine," according to NIH Director **Francis Collins** who was quoted in a *Nature Biotechnology* article published in December. (*Nat Biotechnol* **39:**1481, 2021)

November 9: A study featured in the "NIH Director's Blog" shows waning COVID-19 immunity over time after vaccination. (*N Engl J Med* **385:**e85, 2021; DOI:10.1056/NEJMoa2114228)

November 12: In his weekly email, NIH Director **Francis Collins** reminds federal employees to report their vaccination status by the November 22 deadline, and that the deadline for contractors has been extended to January 18, 2022. He reports that asymptomatic testing will be offered on Mondays and Tuesdays through the end of the year.

November 15: HHS withdraws a policy established during the previous administration that limited FDA's ability to assess whether certain COVID-19 tests work as intended, ensuring that tests are accurate, reliable, and available.

November 15: NIAID launches a three-year study that will evaluate the physical and mental health of up to 1,000 children and young adults who previously tested positive for COVID-19.

November 16: On his blog, NIH Director **Francis Collins** features early clinical trial data from Pfizer that show that their new orally administered therapeutic drug may prevent severe illness and hospitalization in people with COVID-19. (*Science* **374:**1586–1593, 2021; DOI:10.1126/science.abl4784)

November 17: NIH scientists and their collaborators publish a study that shows how SARS-CoV-2 spreads in the lungs and prevents tissue repair, revealing trends that could help develop new COVID-19 treatments and fine-tune when to use existing therapeutics. (*Sci Transl Med* **13:**Issue 620, 2021; DOI:10.1126/scitranslmed.abj7790)

November 18: The "NIH Director's Blog" covers an NIH-funded study demonstrating how the SARS-CoV-2 delta variant packs more of its genetic material into an infected host cell and may help explain delta's increased transmissibility. (*Science* **374:**1626–1632, 2021; DOI:10.1126/science.abl6184)

November 24: A new variant of SARS-CoV-2, B.1.1.529 (omicron), is reported to the World Health Organization.

November 24: HHS Secretary announces to staff that more than 96% of HHS employees have been vaccinated against COVID-19.

November 28: Speaking to CNN about the newly detected omicron variant, NIH Director **Francis Collins** says, "We don't know yet how much of an impact this will have. It ought to redouble our efforts to use the tools that we have, which are vaccinations and boosters... [and] Imitigation strategies...like wearing masks while indoors with other people who might not be vaccinated and keeping that social distance issue."

December 1: The first case of COVID-19 attributed to omicron is reported in the U.S.

December 2: President Joseph Biden visits NIH for a live broadcast event and speaks about the White House's strategy for fighting COVID-19 this winter.

December 2: The Centers for Disease Control and Prevention (CDC) announces that it is revising the current Global Testing Order to shorten the timeline for required testing for all international air travelers to one day before departure to the United States.

December 6: HHS Secretary **Xavier Beccera** reports that Phase 2A employees in leadership positions and those supporting them will begin returning to the workplace this week. However, plans to return the approximately 11,000 employees in Phase 2B and 2C have been paused. NIH Director **Francis Collins** follows up on December 7 with an email to staff that the NIH Return to the Physical Workplace intranet page will be updated as more information becomes available.

December 10: **Francis Collins** sends his last biweekly Friday coronavirus update email to staff as NIH director before stepping down on December 19 and remarks on the privilege of hosting President Joseph Biden on campus December 2. He reports on the importance of boosters now that new SARS-CoV-2 infections in the United States are on the upswing and that the new omicron variant has been detected in more than 20 states. Collins concludes by expressing gratitude for the staff who keep NIH running.

December 13: The Gateway Vehicle Inspection Station (Building 66A) off Rockville Pike re-opens, on weekdays only, to alleviate morning congestion at the Commercial Vehicle Inspection Facility. The partial reopening of the building is due to the need to continue to operate a COVID-19 testing site for symptomatic or for-cause staff at this location.

December 14: On his "NIH Director's Blog," **Francis Collins** writes, "There has been great concern about the omicron variant of SARS-CoV-2....The main reason is that it has accumulated over 50 mutations, including about 30 in the spike protein....All of these genetic changes raise the possibility that omicron could cause breakthrough infections in people who've already received a Pfizer or Moderna mRNA vaccine."

December 15: The latest results from the NIDA-supported Monitoring the Future study show that the percentage of adolescents reporting substance use decreased significantly in 2021 as the COVID-19 pandemic went on. These findings represent the largest one-year decrease in overall illicit drug use reported since the survey began in 1975.

December 16: NIAID Director **Anthony Fauci**, and NIAID scientists **Jeffery Taubenberger** and **David Morens** publish a commentary in *The New England Journal of Medicine* urging the global scientific and medical research community to pursue a universal coronavirus vaccine to counter future outbreaks. (*N Engl J Med* 2021; DOI:10.1056/NEJMp2118468)

December 16: NIH hosts a virtual farewell tribute to NIH Director **Francis Collins** who will be stepping down as director on December 19.

December 17: The Office of Research Services (ORS) reports that they have vaccinated 16,082 staff at NIH and given boosters to over 3,434 employees this past year. ORS will no longer be scheduling appointments. New employees are required to be vaccinated prior to their start date and will need to be vaccinated in the community.

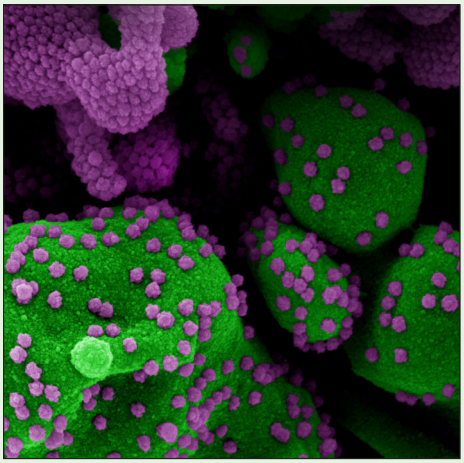
December 17: The *New York Times* reports that Moderna has backed down from its dispute with NIH over who deserves credit for a crucial component of its coronavirus vaccine.

December 19: NIH Director **Francis Collins** steps down as director and will continue to lead his lab in NHGRI.

December 20: **Lawrence A. Tabak** begins serving as the acting director of NIH.

December 22: HHS announces new guidance to boost accessibility and equity in COVID-19 vaccine programs to ensure nondiscrimination on the basis of race, color, and national origin.

December 27: CDC announces that it has updated and shortened the recommended isolation period (for people who test positive for COVID-19) and quarantine period (for people exposed to someone with COVID-19).



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.

December 28: The Clinical Center announces that beginning January 3, 2022, the asymptomatic COVID-19 testing clinic will expand its schedule to four days a week. Appointments are required (https://clinweb.cc.nih.gov/cct; access to website limited to NIH VPN, NIH IC CITRIX, or from NIH workstations).

December 29: HHS announces that the Biden-Harris Administration has brought two new over-the-counter, at-home COVID-19 tests to the U.S. market. The tests have received emergency use authorization by the FDA. These quick authorizations are thanks to collaboration between the FDA and NIH Rapid Acceleration of Diagnostics Technology (RADx) program. ●

Read a more detailed version of this timeline, complete with links, at https://irp.nih.gov/catalyst/v30i1/covid-19-timeline-at-nih-november-december-2021.

NIH Library

CONTINUED FROM PAGE 1

to further refine testing of MRI studies. The NIH Library is supporting many scientists on their research journeys in unexpected ways—and offers much more than people realize.

Located on the first floor of the Clinical Center, the NIH Library sits just across campus from the National Library of Medicine, the largest biomedical library in the world. Far from lying in the shadow of its bigger cousin, the NIH Library's presence is unique.

"We're explicitly serving the intramural workforce at NIH, and our collection and services are based on the needs and wants of that customer base," said NIH Library Acting Director **John Doyle**.

The NIH Library's collection holds over 28,000 print books and provides online access to more than 13,000 journals, 169,000 eBooks, and 10,000 educational videos. NIH staff can search 55 proprietary databases such as Scopus, Embase, and UpToDate as well as PubMed@NIH—a special version of PubMed that expedites full-text access to the NIH Library's collection. Not only does the library provide curated resources, training, and services to intramural researchers and administrators, but it also supports select offices across the Department of Health and Human Services (HHS).

Where to begin

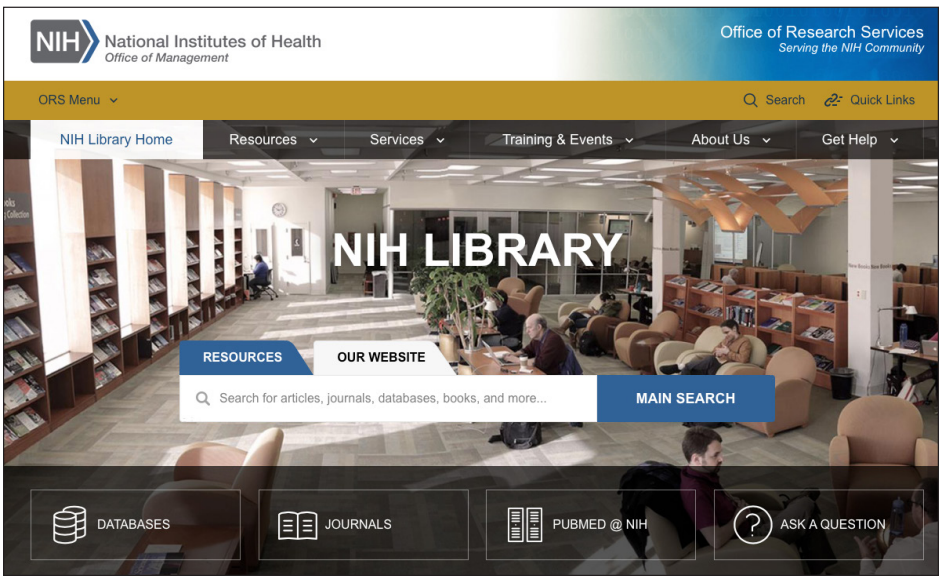
So where does an inquiring researcher begin? Reach out through the Point-of-Contact program. Each institute, center, or office (ICO) at NIH or HHS is assigned a dedicated librarian who understands that ICO's research portfolio and serves as a gateway to NIH Library resources. These subject-matter experts pride themselves on developing one-on-one individualized relationships with their customers and tailoring a wide range of services from systematic literature reviews and manuscript editing to customizing new training classes. And although the physical space has been closed during the COVID-19 pandemic, there's been a silver lining: These services and more continue to be accessible remotely, providing a wealth of resources to NIH employees not only in Maryland, but also in Montana, North Carolina, Arizona, and elsewhere.

Bioinformatics support

Bioinformatician **Li Jia** defines bioinformatics as a combination of computer science, biology, statistics, and mathematics. In the age of big data, identifying the best way to sift through reams of complex information is no easy task. "Many scientists and research or clinical fellows have a science background but need assistance with data analysis—and my team helps them with that," said Jia, who is one of seven NIH Library employees listed as co-authors on papers published during the past year. Her team consults with researchers on study design, suggests appropriate data-wrangling tools, and teaches classes to improve analytical skills. Team members also provide direct support to analyze genome-sequencing results and can even generate high-quality visuals such as charts and tables to help prepare manuscripts for publication. Users have direct access to much of the NIH Library's subscription-based software (such as CLC Genomics Workbench by Qiagen) by remotely logging into one of four high-performance workstations: Three are dedicated to bioinformatics while the other caters to data science and multimedia needs.

Workshops and training

Training classes for tools supported by the NIH Library have been growing in number and variety. From learning how to use EndNote to programming in R, the NIH Library has held more than 220 virtual training sessions this past year alone, with a spike in attendance seen at the beginning of the pandemic. Staff Scientist **Yixing Han** manages bioinformatics-related research at her lab in the National Human Genome Research Institute and uses genomic data to understand complex childhood diseases. She recognizes the importance of keeping on top of a rapidly progressing field. "I highly recommend the NIH Library workshops to the postdocs and postbacs in my lab,"



Check out the NIH Library website for access to journals, databases, resources, services, training and events, and more, at https://www.nihlibrary.nih.gov/agency/nih.

CREDIT: CHARLES KING, NIH LIBRARY

Skull model printed in 3D at the NIH Library.

said Han. "And [I] encourage them to join the bioinformatics symposium and other beneficial training." Most classes are led by in-house staff who stay abreast of the latest developments in information science. And when they can't teach a class, they'll bring in an NIH or industry expert to help.

Emerging technology and translation expertise

Need to record a podcast or produce a video for an upcoming conference? Or perhaps you'd like to learn 3D-modeling software to design (and print) a dental model to demonstrate a procedure. Emerging Technology Specialist **Alicia Lillich** is likely to assist. "I keep an eye on what's going on tech-wise that we should be preparing for," she said. Lillich oversees a suite of services called the Tech Hub that includes a digital production studio, 3D printers, a virtual reality headset, and even assistive hardware to allow people with visual or motor impairments to interact with the computer. Although many of these services are on hold until the physical library reopens, Lillich reports a burgeoning interest in video production, editing, and graphic design as people continue publishing and attend conferences virtually. Customers can remotely access software such as Adobe's Creative Cloud through two of the high-performance workstations. And the Tech Hub offers training sessions that cover everything from data visualization and video editing to an introduction to artificial intelligence and machine learning.

Supporting the multinational staff and scope of work at NIH is the talented Translation Team, interpreting over 2 million words per year. They have deciphered everything from an excerpt of a German book on birds' eyes at a microscopic level to scientific articles from Russia on the effects of nuclear radiation. In January 2020, they translated the first practice guidelines that China distributed for treating COVID-19 patients. More often, work involves medical records or journal articles and translators frequently process documents for administrative purposes and protocol consents. Spanish is the most translated language but the team can meet any request, either in-house or by sending documents to specialist contractors.

Customer service

The NIH Library is a customer service organization. "We need to make sure our strategic planning and decision making for major service areas is based on evidence from our users," said Communication Librarian **Kathleen McGlaughlin**, who recently hosted a focus group with clients representing several ICOs. The group echoed sentiments that people like virtual classes and the ability to take focused self-guided tutorials. Moreover, they found that customers are looking for more beginner and advanced-level training classes and appreciate a space to collaborate with colleagues online after class. And what resource did users find most valuable? That honor goes to the nearly 60 individuals who make up the NIH Library staff.

Limited on-site services through contactless pickup of physical literature are set to restart this year. Simultaneously, the NIH Library is streamlining its remote services. A cloud-based approach in which customers can access individual applications and software in a more seamless remote environment may be on the horizon. The list of training classes continues to grow, and McGlaughlin hopes to develop more classes that demystify the publishing process. Also happening, the Digital Production Studio (DPS) is piloting a project called "DPS on-the-go": People can check-out a camera, tripod, and lights and make a high-quality recording at their office or lab.

In 1901, NIH, then known as the Hygienic Laboratory, was moving from Staten Island, New York, to five acres at the old Naval Observatory in Washington, D.C. Hygienic Laboratory Director **Milton Rosenau** asked to incorporate a room for a scientific library that would be an integral part of the laboratory to "quickly and conveniently provide research scientists with the information necessary to their work." From these origins, the ways in which the NIH Library delivers information to the NIH community has evolved, but its primary mission remains unchanged. So when the physical doors reopen, step inside and pay the staff a visit. Maybe you'll search for a journal, record a podcast, or plan your next study design. Or perhaps just find a quiet sunny corner, and read a book. ●

For more information, links to resources, trainings, and more, go to https://www.nihlibrary.nih.gov/agency/nih.

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

Dissecting the Causes of Health Disparities

Michele Evans Delivers the Anita Roberts Lecture

BY JANETTE NORRINGTON, OD

CREDIT: NIA

Michele K. Evans

"As a daughter of the South Bronx who lived and worked there before coming to NIH, I had an indelible recollection of the broken promises, the false promises that never ameliorated poor health," said Senior Investigator **Michele K. Evans** during her Anita Roberts Lecture held on November 1, 2021. "I knew I had to become a physician to improve health in communities like this."

When Evans began her NIH career in 1986 as a medical oncology fellow and clinical associate in the National Cancer Institute (on the Bethesda, Maryland, campus), she was studying DNA repair in cancer-prone heritable syndromes associated with DNA damage hypersensitivity and deficient DNA repair. In 1992, she transferred to the National Institute on Aging (NIA) on the Baltimore campus and saw the poverty in the surrounding neighborhoods. "As I came to work every day in Baltimore, the scene was very much the same as I had experienced as a child," she said.

She soon redirected her research to focus on the risk factors and causes of health disparities among minority Americans and those of low socioeconomic status (SES). Now she's NIA's deputy scientific director and chief of its Health Disparities Research Section.

Multidisciplinary approach

Socially disadvantaged groups of people—such as racial or ethnic minorities, sex and gender minorities, socioeconomic disadvantaged populations, and those living in underserved rural areas—may lack access to good health care. Evans and other health-disparities researchers are trying to identify and understand the causes of adverse health outcomes in disadvantaged groups and to develop effective interventions to reduce and eliminate health disparities.

Health disparities are associated with biological and behavioral risk factors (poor diet, obesity, smoking, excess alcohol consumption, and physical inactivity). But social determinants of health play a role, too (education, economic stability, structural racism, occupational opportunities, neighborhood factors, social and community support, and access to good health care). Evans uses an interdisciplinary approach to dissect the interactions of all these factors and their relationship to disproportionate rates of age-related disease and disability in socially marginalized groups.

In 2004, Evans and NIA Senior Investigator **Alan B. Zonderman** established the Healthy Aging in Neighborhoods of Diversity across the Life Span Study (HANDLS) to explore the interaction of race and SES on the development of age-associated health disparities among African Americans and whites who reside in Baltimore.

Using HANDLS data, Evans and Zonderman conducted the first study that examined the associations between diabetes and cognitive performance as a function of both race and poverty status. They found that African Americans with diabetes who were living below the poverty level may have an increased risk of cognitive deficit at a younger age. (*Psychosom Med* **77:**643–652, 2015).

Evans, working with her colleagues, has also found that poverty and discrimination may be drivers in accelerated aging and adverse health outcomes and may operate through many biological pathways such as telomere length, brain matter volume, and oxidative stress. She believes that interventions and implementation science (the study of methods that facilitate the use of evidence-based practices and research) are the future of health-disparities research. ●

The "Anita B. Roberts Lecture Series: Distinguished Women Scientists at NIH" honors Roberts who was known for her groundbreaking work on transforming growth factor–beta. To watch a videocast of Evans' lecture, go to https://videocast.nih.gov/watch=41534.

Janette Norrington, a postdoc in the Office of Intramural Training and Education, is interested in pursuing a career in science communication.

Read a longer version of this article, complete with links, at https://irp.nih.gov/catalyst/v30i1/dissecting-the-causes-of-health-disparities.

Where Did All the Acne Go?

Gary Peck's Discovery Led to a Drug to Treat Severe Acne

BY E. GORDON MARGOLIN, OFFICE OF NIH HISTORY

Did you know that an NIH scientist's work on a vitamin A derivative (retinoid) led to the development of a drug that can treat, and even cure, severe acne? Acne affects up to 50 million Americans annually; 85% of people between the ages of 12 and 24 have experienced at least minor acne, according to the American Academy of Dermatology. Most cases are mild and may be controlled with topical therapy. But about 15% of cases are severe enough to cause scarring and won't respond to antibiotics and other conventional therapies. NIH's **Gary Peck** discovered, in the 1970s, that a powerful drug called isotretinoin (or 13-cis retinoic acid) was effective against treatment-resistant severe acne.

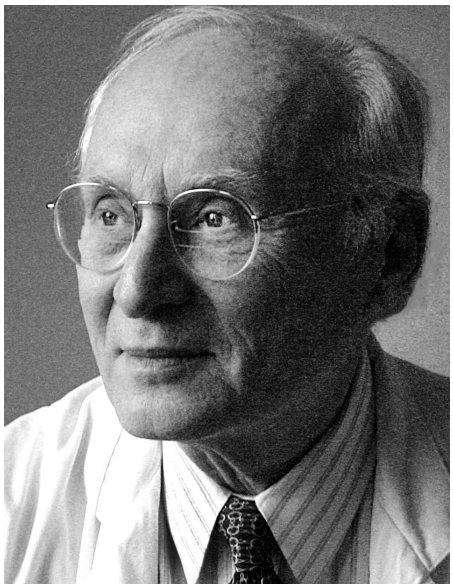
Isotretinoin, a retinoid synthesized by Hoffmann-LaRoche (Nutley, New Jersey) in the 1960s and patented in 1969, was initially intended to be a preventive agent for skin cancer. In the 1970s, Peck, who was a senior investigator in NIH's Dermatology Branch (then in the National Cancer Institute, NCI; now in the National Institute of Arthritis and Musculoskeletal and Skin Diseases), discovered that isotretinoin was an effective treatment for severe acne.

When Peck started his career at NCI in July 1969, he learned that the research he had expected to continue—on the isolation and characterization of epidermal keratohyaline granules in newborn rat skin—was being studied in fetal calf hooves by another senior investigator in the Dermatology Branch. Determined to find a different area of study, Peck spent six months reviewing medical literature in the NIH Library and became fascinated by Dame Honor Fell's (Cambridge University, in Cambridge, England) work on modifying the differentiation pathway of fetal chicken skin in culture by adding retinol to the medium. Instead of becoming keratin-producing, the embryonic chick epidermis became mucin-producing, a process called mucous metaplasia. Peck chose it as his research area and eventually started to study the effect of oral retinoids in treating skin disease. At the same time, then–NCI investigator **Michael Sporn** (now at Geisel School of Medicine at Dartmouth College in Hanover, New Hampshire) was studying isotretinoin as a possible lung-cancer preventive agent.

It had been known since 1940 that retinoids could be used to treat a variety of skin diseases. Some of the earliest articles were written in the 1940s by NIH investigator **Samuel Peck** (no relation), who used vitamin A to treat Darier disease, a skin condition characterized by wartlike blemishes on the body (*Arch Dermatol Syphilol* **43:**223–229, 1941). In 1975, Gary Peck contacted Hoffmann-LaRoche about testing isotretinoin in all dermatological diseases that had been treated with oral or topical retinoic acids—acne, psoriasis, and genetic disorders of the skin—and as a preventative for skin cancer.

In 1977, Peck began a four-month, placebo-controlled, double-blind clinical trial that tested isotretinoin in treatment-resistant acne. When some of the patients developed chapped lips, a sign that they were on the medication and not the placebo, the double-blind design was broken at the first four-week follow-up visit. Most of the patients were either eventually cured of severe acne or had long-term remissions without continuing therapy. (*New Engl J Med* **300:**329–333, 1979).

Peck's study was pivotal to FDA's approval, in 1982, of Hoffman-LaRoche's isotretinoin (trade name Accutane) as an oral prescription medication for treating severe acne. When the patent expired in 2002, generic versions of isotretinoin were produced and approved by the FDA and are now marketed under many different names.



COURTESY OF GARY PECK

In the 1970s, NCI Senior Investigator Gary Peck discovered a drug that was effective for treating severe acne.

Thanks to Peck's contributions, isotretinoin has been used by millions of people worldwide. The social and psychological benefits of treating potentially scarring, severe acne have been overwhelming. Universally recognized in the field of dermatology, Peck's many awards include the 2002 Discovery Award of the Dermatology Foundation, the highest award in dermatology. ●

More details can be found in Peck's full oral history at https://history.nih.gov/display/history/Peck%2C+Gary+2021.

E. Gordon Margolin, M.D., a retired internist and nephrologist, has been a volunteer in the Office of NIH History and Stetten Museum since 2011. He conducted the oral history interview with Gary Peck.

Difficult Problems in Women's Health

CONTINUED FROM PAGE 1

Institute of General Medical Sciences and later NIH principal deputy director, was appointed chair of HHS's Public Health Service Task Force on Women's Health Issues. And in 1990, legislators and NIH Acting Director **William Raub** established ORWH to develop a research agenda that would include more women in clinical studies. Kirschstein was appointed as the ORWH acting director. In 1991, **Vivian Pinn** took over as ORWH's first full-time director and led the office through 2011.

"The Office for Research on Women's Health was founded out of advocacy from the beginning," said ORWH Director **Janine Clayton**. "Since then, the reach of the program has expanded dramatically" and includes ORWH-supported research, policy innovations, and career programs that have helped to expand the field and produce better science.

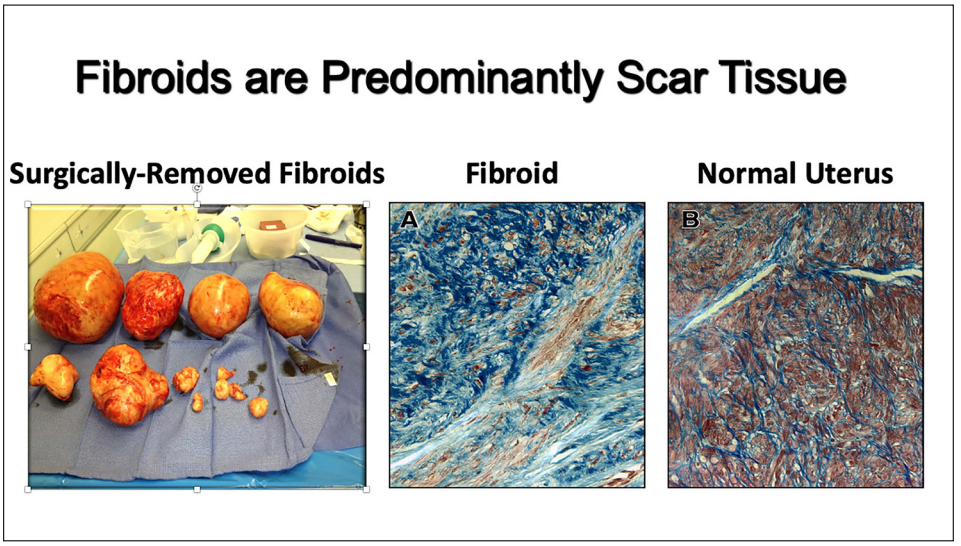
The ORWH led the development of sex as a biological variable (SABV) policy that went into effect at NIH in 2016. SABV policy requires scientists to factor sex into research designs, analyses, and reporting in vertebrate animal and human studies. In 2019, ORWH released the first of its Research Project Grants (RO1s) that focus on studying the intersection of sex- and gender-related variables in health and disease. And in May 2021, the topic of NIH's Fifth Annual Vivian Pinn Symposium (VPS) was "Integrating Sex and Gender Into Biomedical Research as a Path for Better Science and Innovation."

Current Policies Lack Teeth

"The current policies are making a difference, but they lack teeth," said senior sociologist at RAND Corporation **Chloe Bird**, a former senior advisor for ORWH and one of the speakers at the October conference as well as at the VPS held in May. At the October conference, Bird emphasized the need for more funding to test whether interdisciplinary research findings hold similarly for males and females. She pointed out that the SABV policy mainly requires a justification for how sex is or is not accounted for but does not require systematic analysis for sex and gender differences or assessments of the generalizability of findings.

"We still very much need women's health research policies that compel scientists to push against myopic scientific assumptions, algorithms, and prevailing beliefs and examine instead what has not been studied," she wrote in an email to *The NIH Catalyst* after the conference. "In addition, we need policies that require scoring that recognizes proposals that examine what has not been studied in women as both innovative and significant."

Following are highlights from a few of the other presentations.



CREDIT: WILLIAM CATHERINO, USUHS

A disproportionate number of women, compared with men, are affected by chronic debilitating diseases and conditions. In his presentation, William Catherino explained that there's a lack of accessible and effective treatments for a condition unique to women—uterine fibroids, which are painful, cause heavy menstrual bleeding, and increase the rate of miscarriages. Shown (from left): surgically removed fibroids; fibroid tissue; and normal uterine tissue.

Maternal Morbidity and Mortality

"Maternal morbidity" is defined as any short- or long-term health problems that result from being pregnant and giving birth; and "maternal mortality" is defined as the death of a person from complications of pregnancy or childbirth. According to the CDC, maternal mortality in the United States has increased in recent years (658 women in 2018 to 754 women in 2019). Although an estimated 50% of maternal deaths are preventable, the United States has poorer outcomes than peer countries. In addition, these outcomes are more pronounced among African American, American Indian, and Alaska Native women.

More maternal morbidity and mortality research is needed and it needs to be coordinated, said **Uma Reddy**, a former medical officer at the National Institute of Child Health and Human Development (NICHD) and current section chief of Maternal-Fetal Medicine at Yale School of Medicine (New Haven, Connecticut). She proposed the establishment of an NIH Obstetric Research Consortium (similar to the existing NIH Pediatric Research Consortium) that would coordinate maternal health research across NIH. She also suggested an initiative for pregnant

and lactating people equivalent to the Best Pharmaceuticals for Children Act that would encourage studies to improve therapeutics products for these groups.

The maternal mortality rate in the United States "is a symptom of a society that does not value women and does not value innovative research questions," said former NICHD postdoctoral fellow **Maeve Wallace**, who is now the associate director of the Mary Amelia Center for Women's Health Equity Research at Tulane University (New Orleans, Louisiana). In her presentation, she advocated for a holistic life-course approach for research on maternal mortality instead of just focusing on when a woman is pregnant. She urged conference attendees to implement policies rather than simply gathering information.

Chronic Debilitating Conditions

A disproportionate number of women, compared with men, are affected by chronic debilitating diseases and conditions. For example, more women than men suffer from rheumatoid arthritis, lupus, Alzheimer disease, depression, and migraines as well as from chronic conditions—such as uterine fibroids—that are unique to women. The conference presenters called for research that provides a deeper understanding of the role that sex and gender play.

One area that demands more research is uterine disorders and diseases. The "uterus is the most disrespected organ in the body," said former NICHD postdoc **William Catherino**, a professor at the Uniformed Services University of the Health Sciences (Bethesda, Maryland). He explained that there's a lack of accessible and effective treatments for uterine fibroids (benign growths in the uterus that often appear during childbearing years), which are painful, cause heavy menstrual bleeding, and increase the rate of miscarriages. They affect up to 70–80% of women during their lifetime and account for 18–30% of gynecologic visits and 50% of all hysterectomy procedures. Given that these fibroids have afflicted women for more than 5,000 years, Catherino believes there ought to be more research done to expand treatment options. Most current treatments—including surgical, minimally invasive, and medications—are suboptimal. An investment in this research, he explained, would result in a decrease in deaths, disability, and suffering and improvement in quality of life, productivity, care of children, and care for the elderly.

Stagnant Cervical Cancer Survival Rates

The incidence of and mortality rates for cervical cancer have remained about the same over the past 20 years despite prevention efforts through the human papilloma virus vaccines and cancer screening. According to the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results Program (SEER), there were an estimated 14,480 new cases of cervical cancer in 2021 and 4,290 deaths, with a survival rate of 66.3%. The burden of disease is highest among Black women who remain 30% more likely to be diagnosed with cervical cancer and 75% more likely to die of disease compared with white women.

Uterine and cervical cancer treatments must be a national priority both in terms of funding and research, argued **Charles Kunos**, a former NCI medical officer and currently a clinical research officer at the Markey Cancer Center at the University of Kentucky (Lexington, Kentucky). Cervical cancer survival rates have been stagnant for two decades. According to SEER data, death rates have decreased minimally in the past five years from 2.7 per 100,000 women in 2001 to 2.2 per 100,000 women per year; the five-year survival rates have decreased slightly from 70.7% in 2001 to 66.3% now. He discussed the variety of treatments for cervical cancer such as twice-weekly brachytherapy (an internal radiation therapy), weekly cisplatin therapy (a concurrent chemotherapy and radiation therapy regimen), and an NCI experimental treatment (currently in clinical trials) of monthly radiopharmaceutical therapy to deliver tumor-targeted radioactive agents. He noted that pretherapy F-fluorodeoxyglucose positron-emission tomography is being evaluated as an intervention to predict disease prognosis.

The conference successfully "identified gaps and potential opportunities for the future," said Clayton in an interview with *The NIH Catalyst*. The federal Advisory Committee on Research on Women's Health, which advises ORWH and met the day after the conference, will make official recommendations through a report to be submitted to Congress. Recommendations may include developing a research definition for chronic diseases that would be relevant for women's health, making sure inclusion criteria for clinical studies take into consideration biological sex and gender identity, and integrating sex and gender topics into curriculums and meeting sessions.

"How we do science leads to change," said Clayton. ●

For more on the ORWH, go to https://orwh.od.nih.gov. To watch a videocast of the conference, "Advancing NIH Research on the Health of Women," go to https://videocast.nih.gov/watch=42584.

Tamar Jacobsohn is a postbaccalaureate fellow in NICHD's Contraceptive Development Program. She is applying to medical school and is interested in the intersection of the women's health and mental health fields.

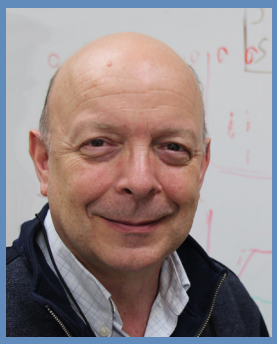
Recently Tenured

ANDREA B. APOLO, NCI-CCR

SUSAN HARBISON, NHLBI

BRANDON K. HARVEY, NIDA

ROSANDRA KAPLAN, NCI-CCR



CARLO PIERPAOLI, NIBIB

ANDREA B. APOLO, M.D., NCI-CCR

Senior Investigator and Chief, Bladder Cancer Section, Genitourinary Malignancies Branch, Center for Cancer Research, National Cancer Institute

Education: Lehman College, City University of New York (B.S. in chemistry and biochemistry); Albert Einstein College of Medicine, New York (M.D.)

Training: Residency in internal medicine at New York Presbyterian Hospital/ Weill Cornell Medical Center (New York); fellowship in medical oncology, Memorial Sloan Kettering Cancer Center (New York)

Before coming to NIH: During her medical oncology fellowship, she helped write and/or develop five therapeutic protocols for patients with bladder cancer.

Came to NIH: In 1996 as part of the NIH Undergraduate Scholars Program (1996–1998); returned in 2010 as assistant clinical investigator in NCI; in 2014 became a Lasker Clinical Research Scholar and chief of NCI's Bladder Cancer Section, Genitourinary Malignancies Branch

Outside interests: Loves to spend time with her husband and their two boys, including hiking and biking together

Website: https://irp.nih.gov/pi/andrea-apolo

Research interests: I am interested in improving the treatment and survival of patients with genitourinary tumors. My team and I design and implement clinical trials to test novel agents for the treatment of urologic cancers. My primary research interest is in bladder cancer (urothelial carcinoma). In particular, we are developing new bladder-cancer therapies that use targeted agents including anti-angiogenesis compounds and inhibitors of Met receptors, which are essential for organogenesis and wound healing but are deregulated in some cancers. I test these targeted compounds individually or in combination with immunotherapies. We are also developing predictive and prognostic biomarkers in muscle-invasive and metastatic disease.

I led the bladder cancer study of avelumab that resulted in its FDA approval for the treatment of advanced bladder cancer in people whose cancer has gotten worse when other therapies have failed (*J Clin Oncol* **35**:2117–2124, 2017). Avelumab is an immune checkpoint inhibitor and blocks proteins called checkpoints that keep the immune system from working properly. The drug prevents programmed cell death protein 1 (PD1) on the surface of T cells from interacting with PD1 ligand 1 proteins on cancer cells. The T cells are then able to attack the cancer cells.

I also led a clinical trial testing the combination of a targeted therapy, cabozantinib, plus the checkpoint inhibitor nivolumab with or without ipilimumab, which led to the development of a phase 3 trial and FDA approval of this combination for patients with advanced kidney cancer.

SUSAN HARBISON, PH.D., NHLBI

Senior Investigator and Head, Laboratory of Systems Genetics, National Heart, Lung, and Blood Institute

Education: North Carolina State University, Raleigh, North Carolina (B.S. in aerospace engineering; Ph.D. in genetics)

Training: Postdoctoral fellowships in neuroscience, University of Pennsylvania (Philadelphia); postdoctoral fellowship in genetics, North Carolina State University

Other positions: Worked as an aerospace engineer for the Naval Aviation Depot (Marine Corps Air Station, Cherry Point, North Carolina) for eight years before completing her Ph.D. in genetics

Came to NIH: In 2012 as an Earl Stadtman Investigator in NHLBI
Outside interests: Hiking with her husband and their two Basenji dogs; powerlifting; knitting.
Website: https://irp.nih.gov/pi/susan-harbison

Research interests: People aren't the only ones who sleep. Mammals, birds, fish, reptiles, amphibians, and invertebrates do, too. Poor sleep habits and sleep deprivation lead to ill effects on health and cognition. My lab and I are trying to better understand sleep and sleep disorders.

We are investigating the genetic networks underlying sleep and their interactions with the environment. We use *Drosophila melanogaster* as a model organism, because fly sleep is similar to mammalian sleep. We have identified more than 1,500 genes associated with natural variations in sleep, many of which function in nerve-cell development. We also found that 250 genes account for variability in the circadian clock, including three genes that each contribute 1–1.5 hours to circadian cycle timing (*J Biol Rhythms* **36:**239–253, 2021).

We are also studying how environmental changes—such as exposure to drugs, dietary changes, varying temperatures, and social isolation—can affect sleep in flies and humans. Daily sleep fluctuates in flies just as it does in humans. We identified genes that contribute to these intra-individual differences (*Sleep* **41:**zsx205, 2018).

If sleep has a common purpose, then genes and gene networks affecting sleep are likely to be conserved across species. We bred flies for extreme sleep duration, producing flies that sleep for as long as 18 hours and for as little as 3 hours per day (*PLoS Genet* **13:**e1007098, 2017). These populations enabled us to discover conserved genes for sleep duration and to develop community resources (*Sci Rep* **10:**20652, 2020; *G3* **8:**2865–2873, 2018). These genes may have similar functions in humans. For example, with colleagues at the University of Alabama at Birmingham, we found that a gene (*dSdc)* we uncovered in a Drosophila sleep study has a human homologue (*SDC4*) associated with sleep and resting metabolic rate in children (*PLoS One* **5:**e11286,2010).

We hope that one day our research will lead to an understanding of the purpose of sleep, its role in human health, and the identification of targets and treatments for sleep disorders.

BRANDON K. HARVEY, PH.D., NIDA
Senior Investigator and Chief, Molecular Mechanisms of Cellular Stress and Inflammation Section, Integrative Neuroscience Branch, National Institute on Drug Abuse
Education: University of Rochester, Rochester, New York (B.S. in molecular genetics, M.S. and Ph.D. in neurobiology and anatomy)
Training: Postdoctoral training in NIDA
Came to NIH: In 2002 for training; became a staff scientist in 2006 and associate scientist in 2010; director of the Optogenetics and Transgenic Technology Core (2011–2016); in 2016, became a tenure-track investigator and chief of the Molecular Mechanisms of Cellular Stress and Inflammation Unit
Outside interests: Biking; kayaking; woodworking; gardening; and beekeeping
Website: https://irp.nih.gov/pi/brandon-harvey

Research interests: The Integrative Neuroscience Branch conducts research at the cellular, molecular, and systems levels to identify the neural substrates upon which substances of abuse act to produce long-term alterations in behavior and brain function. I lead the Molecular Mechanisms of Cellular Stress and Inflammation Section, in which we study the role of endoplasmic reticulum (ER) stress and inflammation in neuronal dysfunction caused by substance abuse or neurodegenerative diseases. The ER is a continuous membrane system within the cytoplasm of eukaryotic cells and performs such functions as protein synthesis and folding, lipid metabolism, and calcium storage. Dysregulation of ER is associated with neurodegenerative, muscular, and diabetic conditions.

We also identify and study the biology of secreted ER calcium modulated proteins (SERCaMPs) and Lys-Asp-Glu-Leu endoplasmic reticulum protein retention (KDEL) receptors; examine the influence of drugs of abuse and SERCaMPs on microglial activation; and develop genetic and pharmacological tools to monitor and modulate ER calcium.

In one study, we described a mechanism of cellular pathology linked to ER calcium depletion termed "exodosis," which is observed in diabetes, stroke, Alzheimer disease, and cardiovascular diseases (*Cell Rep* **25:**1829–1840.e6, 2018). In another study we identified a collection of small molecules that may play a therapeutic role in diseases associated with ER calcium dysfunction and exodosis (*Cell Rep* **35:**109040, 2021).

We hope our work will lead to therapeutic strategies to restore ER function in a range of diseases.

CONTINUED ON PAGE 20

Recently Tenured

CONTINUED FROM PAGE 19

ROSANDRA KAPLAN, M.D., NCI-CCR

Senior Investigator, Head of Tumor Microenvironment Section, Pediatric Oncology Branch, Center for Cancer Research, National Cancer Institute

Education: Connecticut College, New London, Connecticut (B.A. psychology and biochemistry); Dartmouth Medical School, Hanover, New Hampshire (M.D.)

Training: Residency in pediatrics at Boston Children's Hospital (Harvard Medical School) and Boston Medical Center (Boston University School of Medicine, Boston)

Before coming to NIH: Assistant professor of pediatrics, Memorial Sloan Kettering Cancer Center and Weill Cornell Medical Center (New York)

Came to NIH: In 2010 as a tenure-track investigator

Outside interests: Loves staying active and spending time in nature with her family; loves to sing and before COVID enjoyed singing in an a cappella group

Website: https://irp.nih.gov/pi/rosandra-kaplan

Research interests: My lab and I are investigating how cancer spreads by avoiding immune detection and developing a structural matrix and its own blood supply that can support its metastasis to distant locations. Our work also aims to develop novel therapies that target a tumor's ability to grow blood vessels and spread to other sites. We are detailing the earliest microenvironmental events in the metastatic cascade in hopes of translating our findings to the clinical setting.

When I was at Memorial Sloan Kettering Cancer Center and Weill-Cornell Medical College (New York), I worked with my research mentor to develop the concept of the pre-metastatic niche. We demonstrated that even localized tumors can prepare distant tissue sites for metastasis (*Nature* **438:**820–827, 2005). We discovered that bone marrow–derived cells (such as immune cells known as myeloid cells) are recruited to future sites of metastasis and establish a receptive microenvironment for incoming circulating tumor cells. These specialized bone marrow–derived cells are present in circulating blood as well as in metastatic tissue of patients with pediatric and adult cancers. At NCI, my lab is focusing on the role of these cells in tumor progression, in neo-angiogenesis, in promoting immune evasion, and in regulating gene expression in the pre-metastatic niche.

Recently, we developed genetically engineered myeloid cells (GEMys) that deliver interleukin-12 (IL-12) to metastatic sites. We found that, in mouse models, chemotherapy with IL-12–GEMys reverses immune suppression and activates antitumor immunity (*Cell* **184:**2033–2052.e21, 2021). GEMys might also be used to deliver other therapies to metastatic sites and be a treatment for late-stage malignancies and possibly other types of diseases that involve inflammation.

We are performing several studies to determine the trafficking of GEMys to tissue sites and their survival; the changes that occur with chemotherapy, radiation, and surgery; as well as differences in these cells in circulation and in specific tissues. Our studies may lead to targeted therapies that can thwart the interaction of a tumor and its microenvironment as well as to myeloid-cell therapies that may be used to modulate this microenvironment to limit metastatic progression.

CARLO PIERPAOLI, M.D., PH.D., NIBIB

Senior Investigator, Laboratory of Quantitative Medical Imaging, National Institute of Biomedical Imaging and Bioengineering

Education: University of Milan, Milan, Italy (M.D. and Ph.D. in neuroscience)

Training: Visiting fellow (1991–1995) and visiting associate (1995–1997), Neuroimaging Branch, National Institute of Neurological Disorders and Stroke (NINDS)

Came to NIH: In 1991 for training; became a visiting scientist and chief of NINDS's Diffusion MRI Unit (1997–1999); became a staff scientist at the National Institute of Child Health and Human Development (1999–2016); in 2016 became a Stadtman Investigator in NIBIB

Outside interests: Sailing; hiking; cycling; cooking; stubbornly trying to give advice to his grown-up kids

Website: https://irp.nih.gov/pi/carlo-pierpaoli

Research interests: The goal of my research is to develop biomarkers that can characterize human anatomy and physiology across the lifespan and in disease using noninvasive imaging techniques, such as magnetic-resonance imaging (MRI). My lab and I aim to translate our research findings into effective clinical tools and to design a new role for radiology and imaging sciences in achieving noninvasive phenotyping with quantitative metrics that are ideally suited for inclusion in large, integrated databases.

We pioneered the clinical translation of diffusion tensor imaging (DTI), an MRI modality, that can noninvasively reveal information about tissue microstructures in the central nervous system. We performed the first DTI study of the human brain

(*Radiology* **201:**637–648, 1996). The MRI signatures we described in our early work are still used today by clinicians to interpret diffusion MRI changes in stroke.

In subsequent years, we worked consistently on making DTI metrics more biologically specific, reliable, and accurate. We proposed biomarkers that are informative of white-matter structure and organization, reversible brain ischemia, stroke, postnatal cortical maturation, and a type of nerve degeneration called Wallerian degeneration (*Neuroimage* **13:**1174–1185, 2001). We worked on validating the accuracy of diffusion MRI to study brain connectivity (*PNAS* **111:**16574–16579, 2014).

We have systematically addressed issues that make the use of potentially excellent biomarkers unreliable or even impossible in clinical applications. We investigated the effect of noise and artifacts such as subject motion, cardiac pulsation, or magnetic-field inhomogeneity on the computed metrics. We showed that these effects represent serious confounding factors in clinical applications, and we proposed a number of corrective strategies (*Magn Reson Med* **85:**2696–2708, 2021).

We also developed TORTOISE, a software package used for processing diffusion MRI software data, and we have made it publicly available to the scientific and clinical communities for quantitative image analyses.

NEWS BRIEF

President Biden's New Plans for COVID-19

CREDIT: CHIA-CHI "CHARLIE" CHANG

President Joe Biden visited NIH on December 2, 2021, to discuss the nation's winter strategy against the COVID-19 pandemic. (Left) NIH Director Francis Collins and the president greet one another with a fist bump. (Right) The president announces his plan—developed with the advice of top physicians, scientists, and public health experts—for dealing with COVID-19 and its variants: expanding the nation's booster campaign; launching new family vaccination clinics; expanding free, at-home COVID-19 testing that's covered by health insurance; increasing the number of surge response teams to help communities with rising caseloads and overwhelmed hospitals; speeding up efforts to vaccinate the rest of the world; and more.

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

Former NIH scientists and other NIH-affiliated people who died in 2021.

Milton Corn (died February 7, 2021, at 93), a former dean of the Georgetown University School of Medicine (Washington, D.C.) and an internationally known expert in research directions in biomedical informatics, joined the National Library of Medicine in 1990 and later was its acting scientific director.

Manuel Datiles (died February 12, 2021, at 69) was a senior investigator, eye physician–scientist, and medical officer at the National Eye Institute. He and a NASA physicist codeveloped a clinical device based on a dynamic light-scattering technique and used it to show that oxidation-caused loss of a lens protein called alpha-crystallin leads to the formation of human age-related cataracts. The finding helped hasten the development of nonsurgical anticataract drug treatments in places where cataract surgery is not available.

Roswell Eldridge (died June 3, 2021, at 87) was a neurogeneticist at the National Institute of Neurological and Communicative Disorders and Stroke from the mid-1960s until his retirement in the early 1990s. He studied neurofibromatosis, a genetic condition that causes benign tumors, and co-discovered the *NF2* gene. After he retired from NIH, he trained as a general practitioner and took over a medical practice in upstate New York.

Leonard Henry "Pug" Evans (died June 24, 2021, at 77) was a mouse retrovirus expert and chief of the retroviral molecular biology section at the National Institute of Allergy and Infectious Diseases' (NIAID's) Rocky Mountain Labs (Hamilton, Montana). At the onset of the pandemic, he devoted his full attention to developing a therapeutic for COVID-19.

Emil J. Freireich (died February 1, 2021, at 93) worked at the National Cancer Institute (NCI) from 1955 to 1965, where he introduced the idea of treating childhood leukemia—a disease once considered to be a death sentence—with combination chemotherapy and fresh platelets that kept children from bleeding to death. In 1965, he left NIH for the University of Texas MD Anderson Cancer Center (Houston), from which he retired in 2015.

Walter "Walt" Friauf (died October 5, 2021, at 93) was a former chief of the electrical and engineering section of the Biomedical Engineering and Instrumentation Program. He co-created an electro-optical device in 1971 for the continuous measurement of blood oxygen concentrations for use with the artificial lung.

Daniela Gerhard (died June 25, 2021, at 68), a pioneer in functional genomics research, had been the director of NCI's Office of Cancer Genomics since 2004 after she left a faculty position at Washington University School of Medicine (St. Louis, Missouri).

Barbara Faye Harkins (died July 25, 2021, at 65) was the archivist in the Office of NIH History and Stetten Museum (2008–2020). She helped researchers get the information they needed and made historical documents and photos available to the public. She managed NIH's oral history collection, oversaw the archiving of NIH websites, and undertook an overhaul of the office's archival collection.

H. James Hoffrichter (died August 5, 2021, at 77) was a longtime senior investigator and section chief in the National Institute of Diabetes and Digestive and Kidney Diseases. His innovative research contributions were in sickle-cell hemoglobin polymerization, time-resolved spectroscopy, and protein folding. In the sickle-cell arena, he helped develop the novel double-nucleation mechanism to explain sickle hemoglobin polymerization kinetics, a mechanism that is now used to explain the kinetics of fibril formation in Alzheimer disease.

Linda Maxsell Huss (died April 11, 2021, at 64) retired in 2015 after a 40-year career as a public affairs specialist at the National Eye Institute.

John Inman (died on February 25, 2021, at 93), who came to NIH in 1965, was head of NIAID's Bioorganic Chemistry Section until his retirement in 2005. His research in organic and medicinal chemistry laid the groundwork for many biomedical advances including drug development for cancer and HIV as well as methods for purifying some COVID-19 vaccines.

Miriam Kelty (died June 6, 2021, at 82), a psychologist and bioethics and behavioral researcher, held many leadership positions in her nearly 40 years at NIH. She was the former National Institute on Aging associate director and founder of the Bioethics Interest Group.

Bryan Kercher (died May 8, 2021, at 55) died in a climbing accident near Hamilton, Montana, where he worked as an engineering technician for NIAID's Rocky Mountain Labs for nearly 20 years. He was also an avid photographer and was responsible for practically every NIH photo over the last decade showing the Montana setting at the Rocky Mountain Labs.

Daniel Lednicer (died January 5, 2021, at 91), a volunteer at the Office of NIH History and Stetten Museum for the last 15 years, catalogued the office's library, identified museum objects, scanned hundreds of instrument manuals and photographs, and wrote biographies of prominent NIH scientists. He was an accomplished research chemist, worked in industry before coming to the NCI in 1989, and is best known for discovering the synthesis of bromadol, an opioid analgesic selective for the mu-opioid receptor with a potency between codeine and morphine.

Walter Thomas Lingenfelter (died March 2, 2021, at nearly 73) was born with a heart defect and not expected to live past the age of 18. In 1958, when he was 10 years old, he underwent open heart surgery at NIH and was one of the first people to be placed on a heart and lung machine.

Desmond McLearen (died August 15, 2021, at 89) was chief of the Grants Management Branch for the National Institute on Drug Abuse (approximately 1970–1985).

Mortimer Mishkin (died October 2, 2021, at 94) was one of NIH's preeminent cognitive neuroscientists whose foundational work spanned more than six decades and elucidated the pathways through which vision, hearing, and touch connect with brain structure to encode memory. He joined the National Institute of Mental Health in 1955 and became the chief of the Laboratory of Neuropsychology in 1985 and later chief of the lab's Section on Cognitive Neuroscience.

Churchman Louis Napper Sr. (died May 24, 2021, at 86), who retired in 1992, began his career at NIH in 1963 as a heart and lung technician. He later worked as a senior administrative duty officer at the Clinical Center before being appointed the first African American administrative officer in the National Eye Institute in 1970.

Phillip G. Nelson (died April 22, 2021, at 89) was a retired investigator and longtime scientist emeritus at the National Institute of Child Health and Human Development (NICHD). He was chief of NICHD's Laboratory of Developmental Neurobiology until his retirement in 2004, and much of his work focused on understanding how experience shapes the development of the nervous system and how synapses function. Among his many accomplishments, he was first to show, in collaboration with **Marshall Nirenberg** (who won the Nobel Prize in 1968), that clonal lines of nerve and muscle were capable of establishing competent synapses.

Arthur Nienhuis (died February 3, 2021, at 79) was a past chief of the Clinical Hematology Branch in the National Heart, Lung, and Blood Institute and the fourth director of St. Jude Children's Research Hospital in Memphis, Tennessee (1993–2004). His career at NIH (1970–1993) was marked by many clinical successes in the areas of treatment of hemoglobinopathies, such as sickle-cell anemia, and the development of gene therapies.

George Patterson (died June 20, 2021, at 50) was a senior investigator and chief of the Section on Biophotonics in the National Institute of Biomedical Imaging and Bioengineering (NIBIB). His work focused on the development of probes and techniques for diffraction-limited and sub-diffraction-limited fluorescence of imaging of cells and tissues. When he was a staff scientist in the lab of **Jennifer Lippincott-Schwartz** (NICHD), he worked with **Eric Betzig** in the development of the nanometer-level resolution techniques that earned Betzig a Nobel Prize in 2014. In 2009, Patterson accepted an investigator appointment at NIBIB, where he made major contributions to create both novel and improved genetically encoded fluorescent protein for use as markers and sensors.

Maxine Richardson (died October 19, 2021, at 85) was NCI's Equal Employment Opportunity (EEO) director from 1980 to 1996. Her office adopted an initiative created in the NHLBI EEO office to recycle medical textbooks and publications to historically Black colleges and universities and a community college on the Rosebud Indian Reservation in South Dakota.

John D. Termine (died June 3, 2021, at 82) spent more than 20 years as a research biochemist—focusing on diseases of bone and enamel—at the National Institute of Dental and Craniofacial Research, where he was chief of the Bone Research Branch. In 1991, he became vice president and executive director at Lilly Research Laboratories, Eli Lilly and Co., and led a team in the development of a breakthrough treatment for osteoporosis.

George Vande Woude (died April 13, 2021, at 86) is known for his groundbreaking contributions to the fields of virology and oncogenes, including the 1984 discovery of the MET oncogene, which has been successfully targeted by several drugs currently used in personalized therapies. He joined NCI in 1972 as head of the Human Tumor Studies and Virus Tumor Biochemistry section and was appointed chief of the Laboratory of Molecular Oncology in 1980. He left NIH in 1999 to become the founding research director of Van Andel Research Institute (Grand Rapids, Michigan), then returned to NCI in 2009 as distinguished scientific fellow, emeritus, retaining his role as head of the Laboratory of Molecular Oncology.

Thomas Alexander Waldmann (died September 25, 2021, at 91), who started working at NIH in 1956, was an NIH Distinguished Investigator and chief of the Lymphoid Malignancies Branch at NCI. As a renowned immunologist, his work led to many high-impact discoveries that advanced the field of organ transplantation, autoimmune diseases, and cancer. He was a leader in the study of cytokines and their receptors and of monoclonal antibodies, now a dominant form of cancer immunotherapy.

Samuel H. Wilson Jr. (died on April 23, 2021, at 82), a protein biochemist, did a two-year postdoctoral fellowship at the National Heart Institute, then moved to NCI in 1970, where he worked for 22 years. In 1992, the University of Texas Medical Branch (Galveston, Texas) recruited him to establish the Sealy Center for Molecular Science. In 1996, he returned to NIH as deputy director and then acting director of the National Institute of Environmental Health Sciences, where he maintained an active lab for the rest of his life. His lab made many scientific contributions toward the understanding of mechanisms of faithful replication and repair of DNA and how abnormalities in the genome are corrected by a process named base excision repair. ●

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

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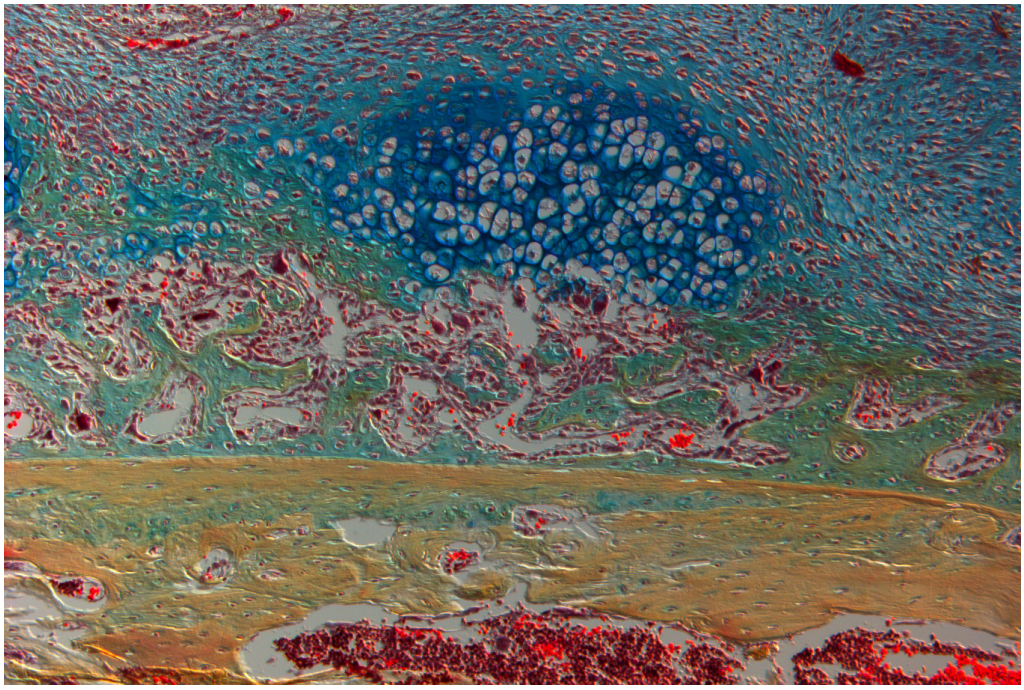
PHOTOGRAPHIC MOMENT

Bone Growth Near a Fracture



CREDIT: PHILIPP LEUCHT, NYU SCHOOL OF MEDICINE

This image, from the *National Institute of Arthritis and Musculoskeletal and Skin Disorders Update* (August 29, 2019) "Spotlight on Scientific Imagery," shows a section of mouse bone near a fracture, with marrow full of red blood cells at the bottom and healthy bone on top of that (tan). New bone (green) and cartilage (dark blue) are in the upper layer. Researchers suggest that chronic inflammation is the reason that bones do not heal as well as we age, as opposed to simply the passage of time.

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