THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

NATIONAL INSTITUTES OF HEALTH • OFFICE OF THE DIRECTOR | VOLUME 30 ISSUE 4 • JULY–AUGUST 2022

ARPA-H Established Within NIH

FROM HHS NEWS RELEASE AND OTHER SOURCES

Health and Human Services (HHS) Secretary **Xavier Becerra** announced, on May 25, 2022, the formal establishment of the Advanced Research Project Agency for Health (ARPA-H) as an independent entity within NIH and the appointment of **Adam H. Russell** as acting deputy director.

Russell was the chief scientist at the University of Maryland's Applied Research Laboratory for Intelligence and Security (College Park, Maryland). He spent more than a decade as a program manager, first at the Intelligence Advanced Research Projects Activity, which invests in high-risk, high-payoff research programs to tackle some of the most difficult challenges of the agencies and disciplines in the Intelligence Community; and then at the Defense Advanced Research Projects Agency, which invests in breakthrough technologies for national security.

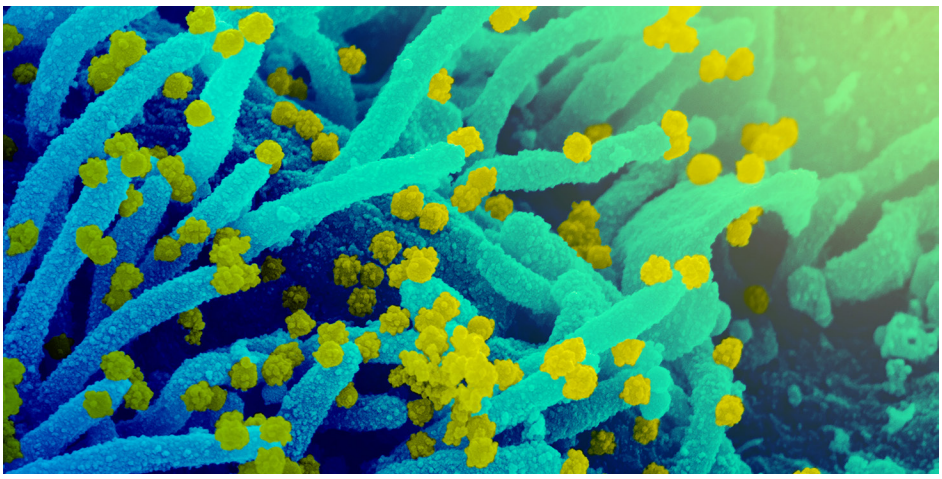
"We are ecstatic that Dr. Adam Russell has accepted the challenge to help launch ARPA-H," said Secretary Becerra in a recent news release. "ARPA-H will have a singular purpose: to drive breakthroughs in health, including the prevention, detection and treatment of diseases such as cancer, Alzheimer's, and diabetes."

Russell began his new role in June. President Biden will appoint an ARPA-H director who will report to the HHS Secretary. It has not yet been determined where ARPA-H will be physically located. ●

Why Some Stay Sick

Unraveling Long COVID Alongside Other Post-viral Illnesses

BY MICHAEL TABASKO, OD



CREDIT: NIAID

This scanning electron microscope image shows SARS-CoV-2 (round yellow particles) emerging from the surface of a cell cultured in the lab. SARS-CoV-2, also known as 2019-nCoV, is the virus that causes COVID-19.

Well before the term long COVID was coined, scientists at NIH's intramural research program (IRP) and elsewhere began preparing for the likelihood that some people would not fully recover after infection from the novel coronavirus. Also known as post-acute sequelae of SARS-CoV-2, or PASC, long COVID is still being defined but is often described as a constellation of symptoms that persist or appear one to three months or more after an acute infection. People experiencing PASC report a markedly lower quality of life and increased rates of anxiety and depression compared with before their illness. The most common complaints include fatigue, shortness of breath, musculoskeletal pain, and a host of neurological problems such as difficulty with memory and concentration, sleep disturbances, dizziness, and changes in the senses of smell and taste.

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CRISPI and the Evolution of Clinical Informatics at NIH

BY ANDY BAXEVANIS, YANG FANN, AND JANICE LEE

Data is as essential to research as water is to life. Its flow nourishes our thirst for knowledge; its purity invigorates. Similarly, research vitality is jeopardized in the face of floods, reservoir breaches, poor data quality, and overtly restricted use. How, then, can we best enable the flow of data in a changing and challenging climate characterized by new regulations on data use, ever-present security threats, and an unprecedented deluge of information made available through advanced technologies and raw computational power?

Such is the key question addressed by the Clinical Research Informatics Strategic Planning Initiative, or CRISPI, launched in November 2021. CRISPI is our vision for clinical informatics (CI) at the NIH to enable more consistent and efficient clinical research practices and to more fully translate the scientific discoveries made in our laboratories into new approaches for diagnosing, treating, and preventing disease. This essay describes our efforts here to you, the distributors and consumers of clinical data.

The NIH has long been a leader in informatics. In the early 1980s, well before the nationwide adoption of electronic health records (EHR) systems, the NIH Clinical Center introduced the first CI systems. By 2004, the Clinical Center launched the innovative Clinical Research Information System, followed five years later by the Biomedical Translational Research Information System, the latter of which bridged clinical research data from the Clinical Center and other NIH institutes and centers. Both systems are still being used today. But to return to our water analogy, these data reservoirs are showing their age and cannot fully meet our modern demands.

We do envision data management as a harmonious ecosystem, a cycle in which streams and rivers of data are pooled and rise into clouds and are deposited in lakes for all to explore, given the necessary safeguards to avoid any poisoning of the wells. This may sound like a lofty goal, but we believe CRISPI has the potential to foster such a data ecosystem.

The challenges

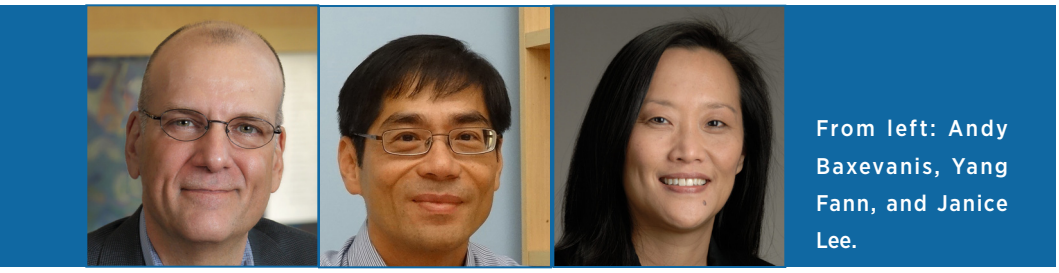
As in other areas of biomedical research, clinical research is becoming more data intensive. Clinical data gathered from a single patient visit may include genomics, images, chemistry and laboratory tests, specialty-specific tests, patient surveys, and clinical notes. Additionally, the many sources and capture methods for collecting data add another dimension of complexity: the inclusion of electronic data capture using tablets, paper surveys, wearable sensors, and even mobile devices. There is an increasing need to ensure that the intramural research program's (IRP's) clinical informatics landscape evolves to meet the growing and ever-changing requirements and needs of clinical investigators' efforts to collect—as well as share—data with collaborators around the world.

Not only do clinical investigators have to deal with voluminous and diverse data, but they also face a variety of policy and regulatory compliance requirements covering areas such as human-subject oversight, consenting, data sharing, and mandatory reporting. In turn, investigators must navigate a multitude of information systems that these data enter and pass through. Within the IRP, there are more than 100 information systems, which fall into four categories: EHR systems; clinical trials management systems and databases; regulatory and clinical-research administration systems; and data-sharing platforms registered with the NIH BioMedical Informatics Coordinating Committee. Unfortunately, many of the systems have limited interface with one another, making it difficult for investigators to enter, extract, and share data.

Enter CRISPI

CRISPI is a broad-based effort to address our current clinical informatics needs while preparing for the future of comprehensive data sharing. This strategic planning initiative aims to connect key components of the existing clinical research infrastructure through secure standards-based electronic data capture and data exchange. CRISPI also seeks to streamline regulatory compliance and reporting, improve data workflows, reduce operational barriers for collaboration, and respond to emerging research that may address public health—including the ongoing COVID-19 pandemic—through data sharing.

The CRISPI team completed the first phase of its assessment in June 2022. To thoroughly understand our current and future clinical informatics needs, the team conducted in-depth interviews with clinical



From left: Andy Baxevanis, Yang Fann, and Janice Lee.

investigators and technical staff to make sure that the vision for any new clinical informatics infrastructure would address current challenges and support the visionary biomedical science for which the IRP is known.

Commonly cited concerns included too many disconnected clinical systems in which data must be entered; a lack of CI support resources, tools, and information technology infrastructure; and investigators having to rely on support teams associated with the systems. In addition, a lack of standards in how IRP clinical research data are represented, and the absence of data dictionaries or common identifiers, make it extremely difficult to link various data types together. These challenges make the analysis of data across multiple studies difficult and highlight an opportunity to implement data standards that will support data sharing and downstream analyses.

The assessment lays the groundwork for the next phase of CRISPI: the development of a long-term strategic plan that will produce recommendations to guide the evolution of the infrastructure (both systems and services) that will be needed to support clinical research across the IRP. Critical factors will include strong policies on data sharing and governance, interoperability of the clinical-research ecosystem, and adequate funding for support and maintenance of the systems and services for clinical investigators.

We expect that our robust strategic plan for clinical-research informatics will be completed by the end of 2022 and that pilot projects to test the recommendations will begin soon after. We will then develop an implementation plan and budget to ensure that our clinical investigators have access to the tools and systems they need to perform impactful research. Ultimately, the CRISPI effort will result in the development of shared, innovative clinical informatics practices that are adaptive, and will enable the use of cutting-edge approaches such as machine-learning, deep-learning, and remote-sensing technologies. This effort must be in conjunction with methods that enable the storage, data management, and analysis of highly diverse study datasets, using both established and exploratory scientific practices.

Our hope is that CRISPI, with rigor of design, will make rich data available with all the important and necessary protections, while quenching all communities in need, creating a multitude of research oases. ●

Andy Baxevanis, Yang Fann, and Janice Lee are leading the CRISPI team. Baxevanis is the director of computational biology in the Office of Intramural Research (OIR) and a senior scientist in the National Human Genome Research Institute; Fann is OIR's director of clinical informatics and the information-technology director in the National Institute of Neurological Disorders and Stroke; Lee is OIR's deputy director for intramural clinical research and is a senior clinician and clinical director in the National Institute of Dental and Craniofacial Research.

Renovated Pharmacy Begins Phased Reopening

BY DONOVAN KUEHN, CC (AND OTHERS)

Who says you can't go home again? After years of construction and operating out of temporary locations, the Clinical Center's Pharmacy reopened in a renovated space in the southeast wing on the first floor of the Clinical Research Center within the Building 10 complex.

The 10,000-square-foot facility incorporates the pharmacy's outpatient, unit-dose, and intravenous admixture unit (IVAU) operations into a single location. The outpatient section opened in early May 2022, followed by the unit-dose section opening in the new space at the end of May and the IVAU coming online this fall.

While many things changed behind the scenes, the impact on the patient experience was minimal. Patients meet with a facilitator during the check-in process and continue to check in at a kiosk, and the waiting area in front of the travel office remains the same.

A new outpatient medication pick-up area features three transaction windows with several features to help with patient privacy: frosted glass dividers and acoustic wall coverings and sound absorbing ceiling panels.

Behind the scenes, there will be several new procedures that will be invisible to patients but will improve the patient experience and safety. A new system will automate the storage and retrieval of prescriptions making pick-up faster, more accurate, and more efficient.

At the core of the Pharmacy is the XR-2 Automated Central Pharmacy System, a robotic medication management system that stores and dispenses medications. ●

Read more online at https://go.usa.gov/xJ7dn.

From the Fellows Committee

What Community Can Do for You

BY MAÏSHA KASOLE, NIAID

Over a year ago, I secured a postbaccalaureate research training position at the National Institute of Allergy and Infectious Diseases (NIAID). I had been accepted to the Intramural NIAID Research Opportunities (INRO) Program, and I felt overjoyed at the prospect of conducting research at the nexus of biomedical research and learning more about science. At the same time, I was plagued with worries about housing, potential roommates, taxes, transportation, climate, and leaving the community I had at the University of Wisconsin at Madison (Madison, Wisconsin). NIH was new, unfamiliar territory.

There is never just one answer for every anxiety, and many things must be figured out slowly as you acclimate. However, I must admit that having an INRO research cohort made all the difference and made my journey that much more fulfilling. Through the INRO Program, I had the opportunity to meet frequently with other research trainees in my institute. Through them, I had the support of a community of people who had either already gone through a similar transition or were about to go through one. My cohort members were people with whom I could discuss my evolving career goals. They became trusted sounding boards, increased my resilience, kept me accountable, and helped me make the most of my experience. They also expanded my perspectives and my network beyond my own lab, exposing me to the multitude of research projects being conducted at NIH, which is both humbling and inspiring.

My program cohort was my community. As more and more trainees return to the workplace, I encourage you to seek out new communities, connecting with others who are at a similar training stage or who share your social or research interests. An opportunity to learn from the people you meet at NIH can transform your career in more ways than any laboratory techniques that may quickly become outdated. Science moves fast. As research trainees, we not only learn to keep up with it, but to continue advancing it beyond what we have inherited from those who came before us and trained us. Building your community or cohort can expand your support network and access to diverse perspectives and create tangible connections with people in fields outside of your own. This can in turn increase collaborations, scientific networks, and interdisciplinary mindsets, which are key to scientific progress and positive impacts on human health.

There are many communities available to you at NIH. Scientific Interest Groups welcome investigators and trainees at all levels to build on shared research interests. The Office of Intramural Training and Education (OITE) facilitates affinity groups through which you can find people with similar backgrounds to yours. Finally, there are many leadership and involvement opportunities: Summer interns can join a summer journal club; postbacs can connect through the Postbac Committee; and graduate students can participate in the Graduate Student Council, which includes a social committee option. Postdoctoral fellows can get involved with the Fellows Committee (FelCom), which includes a Visiting Fellows Subcommittee. Trainees at all levels can join a variety of other activities and workshops listed on the OITE website.

Joining a new community during your time at the NIH can be a game changer, as it was for me. Whatever your training or career stage, I encourage you to find and build your own community and experience the many benefits that are sure to follow. ●

Where to find groups mentioned in this article:

- **Scientific Interest Groups: https://sigs.nih.gov**
- **Affinity Groups: https://www.training.nih.gov/you_are_not_alone**
- **OITE: https://www.training.nih.gov/programs**
- **Summer intern journal club: https://www.training.nih.gov/summer_intern_journal_clubs**
- **Postbac Committee: https://www.training.nih.gov/trainees/postbacs**
- **Graduate Student Council: https://www.training.nih.gov/gsc**
- **Visiting Fellows Subcommittee: https://www.training.nih.gov/felcom/visitingfellows2**

Maïsha Kasole joined NIH in 2021 as a postbac in the Neuroimmunological Diseases Unit of the National Institute of Allergy and Infectious Diseases. Her research included investigating the phenotypes of multiple sclerosis using machine-learning tools and validating patient autonomous disability measurements via smartphones. She completed her training in 2022 and is headed to graduate school. Outside of work, she enjoys baking and learning languages.

Special to the Training Page

The NIH Academy on Health Disparities: Improving Health Equity

BY JALEN BROWN, NCI

Recent events have widened our understanding of health disparities and the social determinants of health that exacerbate them. The COVID-19 pandemic has put a spotlight on health disparities: The pandemic has adversely affected many disadvantaged populations, putting them at greater risk of infection, hospitalization, and death. These populations include, but are not limited to, racial and ethnic minorities, socioeconomically disadvantaged groups, underserved rural populations, and sexual and gender minorities (people in the LGBTQ+ community).

The NIH Academy on Health Disparities offers postbac trainees the opportunity to learn about health disparities and investigate what is being done to address them. I joined the program myself in 2021 because I wanted to pursue a career in this field and increase my knowledge of the kinds of marginalized communities that exist.

The NIH Academy began with just 10 students in 2000 to train future researchers, physicians, physician–scientists, and other health care workers to lead change in addressing health disparities. The students each investigated health-disparity topics with an academic preceptor, volunteered their time and service to marginalized communities, and submitted summaries about their learning experiences.

"Around 2010, I started thinking about a model that would allow more postbacs to join," said **Sharon Milgram**, director of the Office of Intramural Training and Education (OITE). "I set a goal that I wanted 10 times the number of postbacs to learn about health disparities." The program has grown considerably since then—the 2021–2022 cohort included 210 trainees.

One way that OITE increased the number of postbacs in the program was to collaborate with various institutes and centers (ICs) and invite NIH Academy members to attend IC-hosted lectures and seminars on a variety of health-disparity topics. Postbacs then participated in speaker-led discussions as a community.

Each NIH Academy member must fulfill criteria that include attending lectures, seminars, panels, and discussions; completing an OITE diversity course; and developing and presenting a health-disparity-centered project. Milgram also expects that, after the COVID-19 pandemic, volunteering in communities affected by health disparities will return as a requirement.

My group, comprising seven individuals, centered our proposal on mandating the reporting of the number of sexual and gender minorities in NIH clinical trials and providing competency trainings to researchers on LGBTQ+ health. We explained how our proposal would help to reduce researcher prejudice and discrimination against people in the LGBTQ+ community and build inclusive clinical trials. We presented our ideas to the Sexual and Gender Minority Research Office at NIH. The experience has allowed me to connect with like-minded postbacs across the ICs and understand their passions for work in health disparities.

"We talk to many participants who say the Academy was a formative experience," said Milgram. "I think the Academy has helped people shape their applications and helped diverse individuals get into good [graduate and medical school] programs."

Tracking long-term outcomes for NIH Academy alumni is an important next step. "We have some serious work to evaluate outcomes from the program," said Milgram. "We want to know if this experience influenced career decision-making. We also want to understand how participation in our five-week diversity course, which can be challenging for participants, makes you more likely to lean into the beauty of diversity instead of the discomfort of the discussions."

Growing the next generation of health-equity researchers has become even more important today. "I think being aware of health disparities no matter what career path you choose is very important," said **Andrea Naranjo Erazo**, who has been one of the co-directors of the NIH Academy since 2021. "You can contribute in multiple ways."

Thanks to the NIH Academy program, my interest in health disparities has grown considerably. In particular, I have developed new research interests for investigating sexual and gender minority populations. When I enter medical school this year, I will be more prepared to participate in discussions of health equity that require forward-thinking on better treatment of minoritized communities and the dismantling of systemic barriers to accessing health care.

Applications for the next cycle of the NIH Academy on Health Disparities will open in August 2022. "The main component we look for is a letter of interest indicating a strong desire to learn about health disparities," said Naranjo Erazo. Applicants will also need approval from their mentor.

For more information, go to https://www.training.nih.gov/programs/academy. ●

Jalen Brown, a postbac in the National Cancer Institute's Division of Cancer Epidemiology and Genetics, is investigating health disparities affecting sexual and gender minority populations. Later this year, Jalen will begin pursuing an M.D./M.P.H. degree at Northwestern University's Feinberg School of Medicine (Chicago).

Elucidating Brain Structure and Architecture

Peter Basser: Inventor of Diffusion Tensor Magnetic-Resonance Imaging

BY RAGHURAM REDDY, NINDS

CREDIT: NICHD

Peter Basser, Ph.D.

Advanced imaging technologies have revolutionized the fields of neuroscience and neurosurgery by revealing the complex architecture of the human brain. Two of those technologies—diffusion tensor magnetic-resonance imaging (DTI) and DTI streamline tractography—were invented at NIH in the 1990s by National Academy of Engineering member **Peter Basser** when he was in the Biomedical Engineering and Instrumentation Program (BEIP, the forerunner of the National Institute of Biomedical Imaging and Bioengineering, NIBIB).

Today, neurosurgeons everywhere use planning software informed by DTI data to highlight critical brain regions that need to be avoided when excising tumors and performing other brain procedures. Basser holds several patents related to DTI technology which his lab uses to noninvasively study the microstructure of living tissues.

Basser, who's now a senior investigator at the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, described his inventions recently at the 15th annual Philip S. Chen Jr. Distinguished Lecture on Innovation and Technology Transfer in a presentation titled "Using Water Migration to Probe Brain Structure and Architecture."

Diffusion is a mechanism by which water molecules move or migrate throughout tissue in response to thermal energy. That water migration can be detected with a magnetic-resonance imaging (MRI) technology called diffusion imaging. One complication is that tissue-water-diffusion properties are influenced by the fiber architecture, which was not adequately described by diffusion imaging methods. Basser and his colleagues developed and applied a new mathematical model to measure and map diffusion properties to characterize the microstructure of fibrous tissues, such as brain white matter.

It was at the 1991 NIH Research Festival that Basser stumbled across a poster presented by French physician **Philippe Douek** (a medical resident at NIH at the time) and his colleagues. The poster displayed MRI images of different parts of the brain, color-coded according to what the authors thought was the preferred orientation of diffusion in white-matter pathways. Basser had a eureka moment—there was a proper way to analyze those images. Previous methods had analyzed MRI data using mathematical constructs known as scalar diffusivities. He believed that using a different type of model known as a diffusion tensor could more accurately capture how molecules moved throughout tissue in specific directions, a property referred to as diffusion anisotropy. Using such a model would also allow for complex 3D mapping of axons in the brain, a technique that would later become known as streamline tractography. However, there was a problem: No one had ever measured a diffusion tensor before.

Basser painstakingly combed the literature. He was drawn to earlier work by John Tanner and Edward Stejskal, a pair of scientists at the University of Wisconsin-Madison (Madison, Wisconsin). They had first proposed the idea of using pulsed-field magnetic gradients to measure molecular diffusion and had theorized formulas to measure a tensor. In 1991, Basser began collaborating with **James Mattiello** at BEIP and **Denis Le Bihans** at the NIH Clinical Center. Basser and Mattiello became the first to measure a diffusion tensor within water and then later in a pork loin specimen.

They presented their novel method at the International Society for Magnetic Resonance in Medicine conference in 1992. According to Basser only about five people visited his poster, but in his Chen lecture, he emphasized the importance of persistence. In 1993, the group demonstrated diffusion tensor MRI, giving rise to DTI.

Basser went on to propose a family of tensor-derived quantities that have become widely used quantitative-imaging biomarkers. Throughout the 1990s, NIBIB's Senior Investigator **Carlo Pierpaoli** and Basser worked together to define diffusion properties throughout the brain and bring the new technology to the clinic. In 1999, Pierpaoli and **Sinisa Pajevic** at NIH's Center for Information Technology would also pioneer direction-encoded color (DEC) maps. DEC superimposes color on tissue to generate vivid maps of its structure and orientation. Today, clinical applications of DTI include stroke visualization, brain tumor assessment, and even the study of neuropsychiatric disorders by examining how the brain is wired.

DTI data have been critical to the

inspiration of the NIH-supported Human Connectome Project, which provides an unparalleled compilation of neural data, and NIH's BRAIN Initiative, which aims to revolutionize our understanding of the human brain. The DTI technology has even made its way into popular culture as seen in the science-fiction book Cerebranauts: In Search of the Human Experience by Seth Sherman and on t-shirts depicting brain maps.

As for what has yet to be discovered using DTI technology, Basser thinks we are just at the tip of the iceberg. "Spinal cord, peripheral nerves, cardiac muscle [are] just becoming imageable with DTI," he said. "And there are a lot of possibilities for whole-body imaging that I think still can be and will be explored." ●

The annual Philip S. Chen Jr. Distinguished Lecture on Innovation and Technology Transfer Lecture was established in 2006 by the NIH deputy director for intramural research and the NIH Office of Technology Transfer (OTT) on the occasion of Chen's retirement after more than 40 years of service to the NIH. Chen established the OTT and formulated the guiding principles upon which technology transfer functions today, including the creation of the Cooperative Research and Development Agreement, known as the CRADA. To watch a videocast of Basser's presentation (April 29, 202), go to https://videocast.nih.gov/watch=44974.

Raghuram Reddy was a postbaccalaureate fellow in Desmond Brown's lab in the National Institute of Neurological Disorders and Stroke, where he helped analyze the role of primary cilia in Parkinson disease and glioblastoma. In June 2022, he left NIH to attend medical school at Florida International University (Miami).

NIH Issues Licenses to WHO for 11 COVID-19-related Technologies

BY LARISA GEARHART-SERNA, NCI

NIH HAS ISSUED LICENSES FOR 11 COVID-19 technologies to the World Health Organization (WHO) so that global manufacturers may develop COVID-19 vaccines, treatments, and diagnostics for low- and middle-income countries, where access to essential medicines is severely lacking.

The licenses are issued to and managed by the Medicines Patent Pool (MPP) through WHO's COVID-19 Technology Access Pool (C-TAP). WHO has called on institutions around the world to share their COVID-19 intellectual property, knowledge, and data through voluntary, nonexclusive, and transparent licenses.

More than a few NIH labs are invested in COVID-19-targeted research, and C-TAP presented a perfect opportunity to share their scientific advances to benefit public health. On May 12, 2022, at the Second Global COVID-19 Summit, United States President Joe Biden announced that NIH has licensed 11 technologies to C-TAP: three vaccine candidates; three diagnostic candidates; and five research tools for drug, vaccine, or diagnostic development.

"NIH's contributions to C-TAP provide a piece of the technology puzzle to help global manufacturers advance development of COVID-19 diagnostics, vaccines, and treatments," said Acting NIH Director **Lawrence Tabak** in a U.S. Department of Health and Human Services press release.

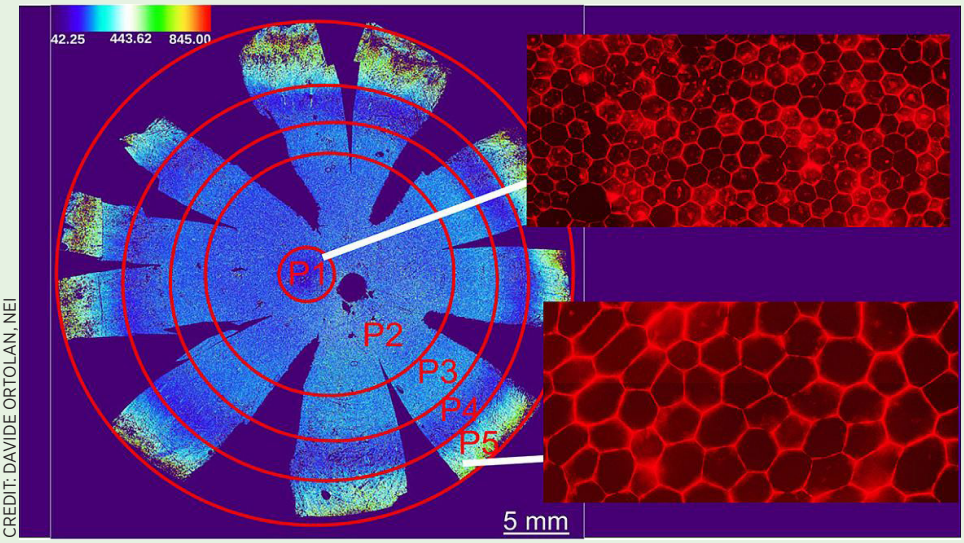
Licensed NIH technologies include patents on the SARS-CoV-2 stabilized spike protein, which is the backbone of current COVID-19 RNA vaccines; new rapid diagnostic methods; and a library of llama nanobodies, some of which have shown COVID-19 neutralizing capabilities. Through C-TAP, MPP will connect NIH technologies with quality-assured manufacturers that have the capacity to develop the technology, scale up production, and distribute their COVID-19 products in low- and middle-income countries.

Sharing NIH technologies and scientific knowledge is a crucial step in the global fight against COVID-19. The C-TAP licenses are made available through the hard work of many NIH technology transfer and licensing professionals in the National Institute of Allergy and Infectious Diseases, National Cancer Institute, National Center for Advancing Translational Sciences, National Institute of Environmental Health Sciences, National Eye Institute, and the Offices of Technology Transfer and Science Policy (both in the Office of the NIH Director).

"NIH provided the first licensed technology to MPP when it was founded in 2010," said NIH Special Advisor for Technology Transfer **Mark Rohrbaugh**. Then and now, NIH "demonstrates the U.S. Government's commitment to assisting [low- and middle-income countries] in the wake of the COVID-19 pandemic and encourages other patent holders [to make] their own voluntary contributions to C-TAP." ●

Larisa Gearhart-Serna, a postdoctoral fellow in the National Cancer Institute's Technology Transfer Center, is a member of The NIH Catalyst *Editorial Board. Outside of work, she enjoys flamenco dancing, baking, annoying her pet rabbit, and finding the best spots for ice cream and/or hiking in the area.*

Intramural Research Briefs



CREDIT: DAVIDE ORTOLAN, NEI

NEI: Investigators identified five subpopulations of retinal pigment epithelium (RPE) based on cell area, aspect ratio, hexagonality, and number of neighbors. Foveal RPE (P1) are tightly packed hexagons. Peripheral RPE (P5) are spread out.

NEI, NCATS: RETINAL CELL MAP COULD ADVANCE PRECISE THERAPIES FOR BLINDING DISEASES

A recent discovery by NIH researchers has shed light on tissue targeted by age-related macular degeneration (AMD) and other diseases. NEI scientists identified distinct differences among the cells comprising a tissue in the retina that is vital to human visual perception. They discovered five subpopulations of retinal pigment epithelium (RPE)—a layer of tissue that nourishes and supports the retina's light-sensing photoreceptors. Using artificial intelligence, the researchers analyzed images of RPE at single-cell resolution to create a reference map that locates each subpopulation within the eye.

Age and disease can cause metabolic changes in RPE cells that can lead to photoreceptor degeneration. The impact on vision from these RPE changes varies dramatically by severity and where the RPE cells reside within the retina. For example, late-onset retinal degeneration affects mostly the peripheral retina and, therefore, peripheral vision. AMD, a leading cause of vision loss, primarily affects RPE cells in the macula, which is crucial for central vision.

"The findings will help us develop more precise cell and gene therapies for specific degenerative eye diseases," said the study's lead investigator, **Kapil Bharti**. (NIH authors: D. Ortolan, R. Sharma, A. Volkov, A. Maminishkis, N.A. Hotaling, L.A. Huryn, C. Cukras, and K. Bharti, *Proc Natl Acad Sci U S A* **119:** e2117553119, 2022)

[BY KATHRYN DEMOTT, NEI]

NCI: UTERINE CANCER DEATHS ON THE RISE IN THE U.S. ESPECIALLY AMONG BLACK WOMEN

An NCI-led team of investigators found that mortality rates due to uterine cancer are rising in the United States and are highest among non-Hispanic Black women. The death rates among all women has risen 1.8% annually from 2010 to 2017.

Uterine cancer is among the most common types of cancer affecting women. The subtype endometrioid carcinoma, which accounts for nearly 75% of all cases, is often diagnosed early and has a good prognosis. Non-endometrioid uterine cancers account for approximately 15% to 20% of cases and are typically diagnosed in later stages with a poor prognosis.

The scientists analyzed data from 208,587 women diagnosed with uterine cancer, from 2000 to 2017, across different races and ethnicities. The results revealed that Black women experienced the highest mortality rates at twice that of women in other racial and ethnic groups. Deaths from the more aggressive non-endometrioid subtype increased 2.7% annually for all women. In contrast, mortality rates for endometrioid cancers remained stable.

The authors noted that these findings suggest limited progress in the treatment of uterine cancers. Moreover, the mechanisms behind the substantial disparities of mortality rates among Black women require more investigation. (NIH authors: M.A. Clarke, S.S. Devesa, and N. Wentzensen, *JAMA Oncol* **8:**895–903, 2022)

[BY SATABDI NANDI, NIA]

NIMH: IDENTIFYING VETERANS WITH HIGHEST RISK OF SUICIDE

Suicide rates among veterans are higher than those of other adults in the United States. Scientists at the Department of Veterans Affairs and their NIMH collaborator, **Michael Schoenbaum**, found that a Veterans Health Administration (VHA) program that uses an algorithm to identify suicide risk has reduced the number of suicides and suicide attempts.

The research team assessed the impact of the Recovery Engagement and Coordination for Health–Veterans Enhanced Treatment (REACH-VET) program. REACH VET, which was rolled out in 2017, is the nation's first clinical use of a validated algorithm to help predict suicide risk. Patients in the top 0.1% level of risk died from suicide at a rate 30-fold higher than the overall VHA patient population.

The authors compared the six-month changes in outcomes of more than 170,000 individuals with the highest predicted suicide risk who used VHA services before and after the implementation of the REACH VET program. The program was associated with patients having more outpatient appointments and fewer inpatient mental health admissions and emergency-department visits. REACH

VET was also associated with a 5% reduction in suicide attempts. These findings suggest that the program is a promising intervention. (NIH author: M. Schoenbaum, *JAMA Netw Open* **10**:e2129900, 2022)

[BY VICTORIA TONG, OD]

NICHD, NIAAA, NINR: GENES THAT REGULATE BIRTHWEIGHT IDENTIFIED IN THE PLACENTA

A fetus develops and grows in the womb for nearly 10 months, and the environment in which that occurs can set the stage for a person's future health. Although this concept of fetal programming is not new, scientists are still uncovering precisely how it happens. A baby's birthweight is important—low birthweight affects survival during the newborn period, and high birthweight can elevate a person's future risk for cardiovascular and metabolic diseases.

In a study led by Earl Stadtman Investigator **Fasil Tekola-Ayele**, NICHD researchers and their colleagues discovered that, in the placenta, 23 genetic regions associated with birthweight were a target for gene-expression and epigenetic processes such as DNA methylation—a mechanism by which genetic expression for certain traits can be influenced by the environment. The target genes shared common functions in influencing cardiometabolic, immune response, and hormonal pathways. Follow-up studies, particularly those examining the maternal-placenta-fetal interface, could help identify therapeutic targets to improve fetal-growth outcomes and future health. (NIH authors: F. Tekola-Ayele, X. Zeng, S. Chatterjee, M. Ouidir, and M. Tesfaye, *Nat Commun* **13**:2384, 2022)

[BY LINDA HUYNH, NICHD]

NIAID: VACCINE AGAINST MOSQUITO-TRANSMITTED VIRUSES SHOWS PROMISE

In a study published in *The Lancet Infectious Diseases*, scientists at NIAID's Vaccine Research Center and their colleagues found that a new viruslike particle vaccine intended to protect against western, eastern (EEEV), and Venezuelan equine encephalitis viruses was safe and immunogenic. Although these mosquito-transmitted viruses are rare, they have been linked to several outbreaks, including a 2019 EEEV outbreak across the northeastern United States that resulted in 38 confirmed cases and 19 deaths.

In a phase 1 clinical trial of the vaccine, 30 healthy adult volunteers between the ages of 18 and 50 years received a 6-, 30-, or 60-microgram dose of the vaccine with or without an adjuvant, which is an ingredient that helps create a stronger immune response. Participants then received a booster dose eight weeks later.

Neutralizing antibodies were detected in all study groups at 12 weeks after initial vaccination, and the strongest immune responses were observed in those receiving the 30-microgram dose with adjuvant and the 60-microgram dose without adjuvant. Immune response was found to be durable to 32 weeks. The vaccine was delivered by intramuscular injection and well-tolerated with only two adverse events, both of which resolved. Although further research is needed to establish dosing and administration of the vaccine, NIAID has executed a commercialization license for development of the vaccine to Emergent BioSolutions in Gaithersburg, Maryland. (NIH authors: E.E. Coates, and others including J.R. Mascola, J.E. Ledgerwood, and the VRC 313 Study Team, *Lancet Infect Dis* 2022; DOI:10.1016/S1473-3099(22)00052-4)

[BY JALEN BROWN, NCI-DCEG]

NCI, CC: VIRTUAL CT SCANS REDUCE RADIATION EXPOSURE

When being diagnosed for cancer and throughout treatment, patients undergo several PET-CT scans as well as other imaging studies that expose them to radiation. But some of that radiation may be unnecessary. NCI and CC researchers have developed an artificial intelligence (AI) method that produces high-quality images and significantly reduces radiation during PET-CT scan studies. The method and findings were presented at the Society of Nuclear Medicine and Molecular Imaging's (SNMMI 's) annual meeting in June.

CREDIT: NIAID

NIAID: Vaccine Research Center scientists have developed a vaccine that protects against rare mosquito-transmitted viruses. Shown: The Aedes mosquito, which can transmit diseases such as chikungunya, dengue, and Zika.

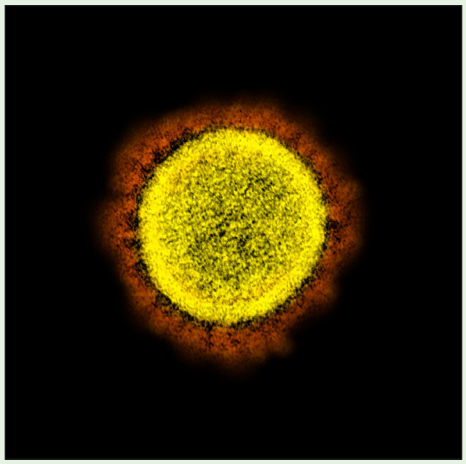
To develop the AI model, researchers included more than 300 PET-CT studies, each containing three scans: non-attenuation-corrected PET, attenuation-corrected PET, and low-dose CT. A machine-learning model was used to generate new images from the original non-attenuation-corrected PET scans, to create synthetic attenuation-corrected PET scans (gen-PET).

Two nuclear medicine physicians, working independently, reviewed 40 of the PET-CT studies and were able to successfully detect lesions on the gen-PET images 70% of the time. (NIH authors: K. Ma, E. Mena, L. Lindenberg, D. Citrin, P.A. Pinto, B.J. Wood, W. Dahut, J.L. Gulley, R.A. Madan, P.L. Choyke, B. Turkbey, and S. Harmon; abstract presentation at SNMMI Annual Meeting in 2022)

[BY VICTORIA TONG, OD]

Read more briefs and longer versions of these at: https://irp.nih.gov/catalyst/v30i4/research-briefs.

COVID-19 Timeline at NIH (May–June 2022)



CREDIT: NIAID

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

May 5: The FDA limits the authorized use of the Janssen COVID-19 vaccine to certain individuals, citing an elevated risk of thrombosis with thrombocytopenia syndrome.

May 11: An NICHD-led study finds that, unlike other SARS-CoV-2 variants, the delta variant can attach to copies of itself, forming larger clumps of viral particles. The researchers theorize that this linking property may have played a role in the ability of the delta variant to spread more rapidly than the variants that preceded it. (*Viruses* **14**:1024, 2022; DOI:10.3390/v14051024)

May 11: An NIH-funded study finds that proteins designed to confer resistance to new SARS-CoV-2 variants protected mice against infection when given through the nose. The researchers developed synthetic miniproteins that block all three binding domains of SARS-CoV-2's spike protein. With further testing, the antiviral proteins might be used as a nasal spray to prevent or treat COVID-19. (*Sci Transl Med* 2022; DOI:10.1126/scitranslmed.abn1252)

May 13: Acting NIH Director **Lawrence Tabak** emails staff with a coronavirus update and notes that the United States has surpassed one million deaths from COVID-19. Montgomery County and Baltimore, Maryland, move from the low to the medium COVID-19 community transmission level as evaluated by the CDC. Beginning May 16, NIH will implement mitigation measures, including requiring 6 feet of physical distancing in all buildings and testing for NIH personnel who are not fully vaccinated and will be entering an NIH facility.

May 16: An NIH-supported research team identifies characteristics of people with long COVID and those likely to have it by using machine-learning techniques on a large database of electronic health records available for COVID-19 research. (*Lancet Digital Health* **4**:E532–E541, 2022)

May 18: NIAID awards approximately $577 million to establish nine Antiviral Drug Discovery (AViDD) Centers. The AViDD Centers will conduct innovative, multidisciplinary research to develop candidate COVID-19 antivirals, especially those that can be taken in an outpatient setting, as well as antivirals targeting specific viral families with high potential to cause a pandemic in the future.

May 19: An NIH-funded study finds that people who reported feeling worried, depressed, or lonely had a greater chance of being hospitalized after a COVID-19 diagnosis. The findings suggest that psychological risk factors may increase hospitalization risk as much as physical risk factors. (*Psychol Med* 2022; DOI:10.1017/S0033291722000691)

May 20: The CDC updates the COVID-19 community levels on which NIH mitigation strategies are based. Research Triangle Park, North Carolina, changes from low to medium community level. Framingham, Massachusetts, and Detroit, Michigan, remain at high. Both Montgomery County and Baltimore, Maryland, remain at medium. All other counties with NIH facilities remain low.

May 23: The NIH Gateway Vehicle Inspection Station for visitors resumes normal operations. The COVID-19 car-line testing, which is by appointment only, will be relocated to the B-3 lower level of the MLP-7 parking garage. The B-3 level only will not be available for parking until further notice.

May 24: Baseline data from an ongoing NIAID-led longitudinal study at the NIH Clinical Center shows that people with post-acute sequelae of SARS-CoV-2 infection (PASC) experience a high burden of persistent symptoms compared with a control group. In most cases, extensive diagnostic evaluation revealed no specific cause for reported symptoms. Female gender and self-reported history of anxiety disorder were significantly associated with an increased risk for PASC. (*Ann Intern Med* 2022; DOI:10.7326/M21-4905)

May 24: The CDC updates its definition of what is considered up to date on COVID-19 vaccination as someone who has received all doses in the primary series and all boosters recommended for that individual, when eligible.

May 27: Acting NIH Director **Lawrence Tabak** emails staff with a coronavirus update. He reports this week's CDC recommendation that children ages 5–17 years should get one booster after completing their COVID-19 vaccine primary series. COVID-19 cases and hospitalizations continue to rise nationwide; however, there has been a subtle decrease in deaths. Another NIH location, Frederick, Maryland, moves from low into the medium COVID-19 community risk level. Baltimore City, Maryland, and Durham County, North Carolina, move from medium into high.

May 30: NIH announces an additional opportunity for staff working onsite to participate in the voluntary At-Home Antigen Testing Pilot Program. A limited quantity of rapid COVID-19 tests will be available for eligible staff to order online. To date, more than 350 NIH staff have tested positive using the at-home antigen test kits prior and stayed home, helping to keep the workplace safer for others.

June 1: An NIH-funded study finds that people with food allergies are less likely to become infected with SARS-CoV-2 than people without them. The new study also identifies obesity and high body mass index as associated with

increased risk for SARS-CoV-2 infection and determined that asthma does not increase risk for infection. (*J Allergy Clin Immunol* 2022; DOI:10.1016/j.jaci.2022.05.014)

June 1: NIH leadership hosts a Return to the Physical Workplace and Workplace Flexibilities Town Hall. More than 2,000 staff attend virtually to discuss the latest on workplace flexibilities, safety in the workplace, and updates on key initiatives.

June 2: Preliminary results from an NIH-led study show that treating adults hospitalized with COVID-19 with infliximab or abatacept—drugs widely used to treat certain autoimmune diseases—substantially improved clinical status and reduced deaths. The full report on these data is expected to be published in a peer-reviewed scientific journal later this year.

June 3: The CDC moves Frederick County, Maryland, from the medium COVID-19 community risk level back to low. All other NIH locations remain unchanged.

June 3: The Safer Federal Workforce Taskforce and the CDC updates their travel guidance and requirements. All staff, regardless of their vaccination status, are eligible for official government travel, both domestically and internationally.

June 10: Acting NIH Director **Lawrence Tabak** emails staff with a coronavirus update. He directs staff to the CDC's new online tool to help individuals determine whether they are up to date on COVID-19 vaccination. Tabak notes that Phoenix, Arizona, and Hamilton, Montana, moved from low to medium COVID-19 community level. The remainder of NIH locations held steady at their community level from the previous week. He reviews promising research results from one of the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) clinical trials as well as the preliminary results of the ACTIV-1 Immune Modulators clinical trial released on June 2.

June 12: The CDC no longer requires air passengers traveling from a foreign country to the United States to show a negative COVID-19 viral test or documentation of recovery from COVID-19 before they board their flight.

June 13: NIND's **Avindra Nath** co-authors a paper released as a preprint in *Cell*. The investigators show a neuroinflammatory mechanism in humans and mice that occurs after mild respiratory SARS CoV-2 infection that may contribute to the neurocognitive symptoms experienced in patients with long COVID. These findings share similarities to cancer therapy-related cognitive impairment, a neuroinflammatory condition that patients often experience after radiation or chemotherapy. (journal preproof: *Cell* 2022; DOI:10.1016/j.cell.2022.06.020)

June 15: NIAID Director **Anthony Fauci,** who is up to date on his vaccinations, tests positive for COVID-19. He is experiencing mild symptoms and will isolate and continue to work from home.

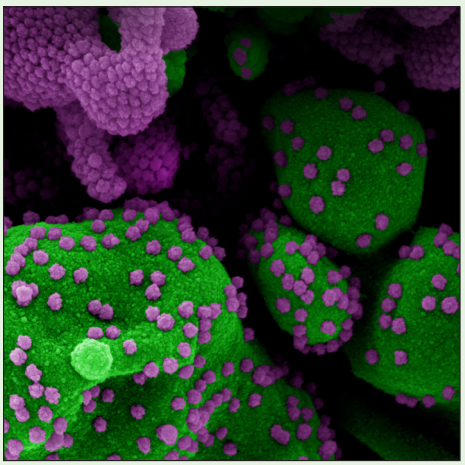
June 15: An FDA panel recommends the emergency use authorization of Moderna's and Pfizer's COVID-19 vaccines for children between the ages of 6 months and 5 years old. Both companies have reported that their vaccines are safe and produce a good immune response in this age group.

June 17: The CDC moves Baltimore's Bayview Research Center, Framingham, Massachusetts, and Detroit, Michigan, from high to low COVID-19 community risk level. The remainder of NIH locations remain at their community level from the previous week.

June 17: The FDA authorizes Pfizer's three-dose vaccine for children 6 months to 4 years old, and Moderna's two-dose vaccine for children 6 months to 5 years old.

June 18: The CDC recommends that all children aged 6 months through 5 years of age should receive a COVID-19 vaccine. This expands eligibility for vaccination to nearly 20 million additional children and means that all Americans ages 6 months and older are now eligible for vaccination.

June 24: Acting NIH Director **Lawrence Tabak** emails staff to announce that NIH expects to implement the NIH COVID-19 Vaccination Policy for Healthcare Workers as required by HHS policy in the coming weeks. He reviews travel guidance updates announced by the CDC earlier this month, as well as last week's authorization of COVID-19 vaccines for young children. Additionally, contact tracing at NIH will now be limited to staff who work in Building 10 or serve critical functions.



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.

June 29: An NIH-funded research team reports that it has developed a fast, cost-effective method to detect the circulation of SARS-CoV-2 variants. The team's customizable genotyping approach can augment current surveillance methods that use comprehensive next-generation sequencing of virus samples, helping to focus sequencing efforts on samples representing unknown and emerging variants. (*J Clin Microbiol* 2022; ; DOI:10.1128/jcm.00342-22)

Read a more detailed version of this timeline, complete with links, at https://irp.nih.gov/catalyst/v30i4/covid-19-timeline-at-nih-may-june-2022.

Long COVID

CONTINUED FROM PAGE 1

PASC's symptoms overlap with other post-viral syndromes that have mysterious physiological underpinnings. Ongoing complications have been documented in some survivors of two other coronaviruses—severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). And IRP researchers have investigated similar unexplained medical issues associated with Ebola outbreaks in West Africa. Unlike with MERS, SARS, and Ebola, the risk of developing PASC doesn't seem to correlate with disease severity. Even initially asymptomatic individuals can turn up with long COVID symptoms months later.

Several NIH scientists are studying long COVID in an attempt to better understand what's happening and how it might be treated.

Similar to chronic fatigue syndrome

At the National Institute of Neurological Disorders and Stroke (NINDS), Senior Investigator **Avindra Nath**, who's known for his work on how infections affect the brain, and his colleague **Brian Walitt**, have repurposed their observational study on myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS)—yet another unexplained condition associated with a previous history of infection that looks a lot like PASC. (Results from the ME/CFS study are expected to be published in 2023.)

Nath and Walitt began their long COVID study in 2020 and have engaged the help of several institutes and centers. They aim to recruit 240 individuals.

First, the investigators are ruling out what PASC isn't. For example, stroke is a known complication of COVID-19. A "silent stroke" could explain cognitive difficulties reported for some people. Others who developed a chronic cough and pulmonary issues while sick might also have trouble exercising and sleeping, experiencing fatigue as a result. Viruses can also unmask or exacerbate preexisting conditions. And some patients hospitalized with severe COVID-19 will develop post-ICU syndrome, an altogether different condition in which being on a ventilator or having pneumonia can damage the lungs, heart, or kidneys.

After excluding those patients with symptoms explained by something else, Nath thinks the true prevalence of patients with lifelong PASC will likely end up being approximately 5% to 10% of the unvaccinated population. Vaccination against COVID-19 also appears to decrease the risk of developing PASC. A long-term goal of the project is to create a data-driven definition of PASC.

The protocol's utility has also caught the attention of the U.S. Department of Veterans Affairs, which has been seeking answers for Gulf War Syndrome (GWS), another unexplained disorder with symptoms similar to ME/CFS and PASC. GWS affects approximately 30% of military veterans who served in the 1990–1991 Persian Gulf War. The NINDS team is planning to enroll patients with GWS into another trial that is similar to their PASC protocol.

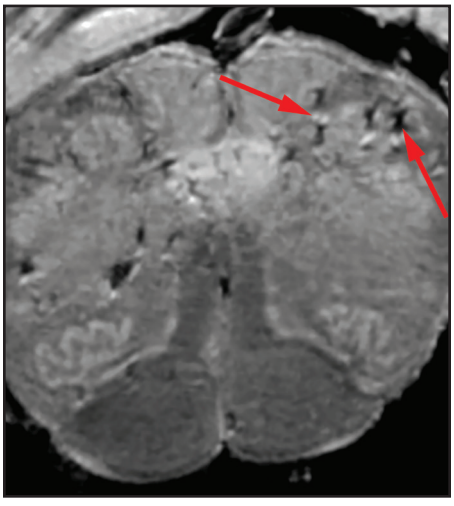
Treatments for neurological symptoms

Nath's group has found evidence of capillary damage in the brains of deceased patients who had COVID-19. He thinks that antibodies produced in response to SARS-CoV-2 infection may bind to endothelial cells in a way that damages the vessels. Blood proteins such as fibrinogen can then leak into the brain and trigger an immune reaction, causing lasting damage that could remain even if the immune system resets. NIH-funded studies have suggested similar mechanisms (*Ann Neurol* **91:**issue 6, 2022). This type of immune-mediated damage is usually associated with strokes and neuroinflammatory diseases, and the NINDS team is continuing to characterize the autopsied brain tissue to learn more (*N Engl J Med* **284:**481–483, 2021).

In a separate study set to begin soon, Nath and NINDS clinical fellow **Yair Mina** plan to test corticosteroids and intravenous immunoglobulin (IVIg) treatments for neurological symptoms in people with PASC. Both medications have been used to treat other autoimmune and neurological disorders.

"If it's an antibody-mediated phenomenon, the IVIg should probably work," said Nath. But "if the antibody is causing damage to the endothelial cells, then the corticosteroid should probably work."

Nath's lab is also developing therapeutic compounds to target viral RNA. This type of treatment could be



CREDIT: NINDS

A team of researchers led by **Avindra Nath** consistently found blood-vessel damage in the brains of COVID-19 patients but no signs of SARS-CoV-2 infections. Arrows point to light and dark spots that are indicative of blood vessel damage observed in the study.

CREDIT: NIAAA

Paule Joseph studies the biological underpinnings that lead to variations in taste and smell perception.

effective if PASC turns out to be caused by persistent viral replication. There is currently no conclusive evidence that coronaviruses persist in the body for months or years, but scientists continue to look. Tenure Track Investigator **Daniel Chertow** at the NIH Clinical Center has been leading a study to find SARS-CoV-2 RNA in an extensive list of body tissues, including the brain (preprint: *Biol Sci*, 2022; DOI.org/10.21203/rs.3.rs-1139035/v1).

No evidence of immune system dysfunction

Much of the data characterizing PASC thus far has been collected by survey or questionnaire. But since June 2020, a study led by **Michael Sneller** at the National Institute of Allergy and Infectious Diseases has been one of the first to conduct extensive in-person diagnostic evaluations comparing people with and without persistent symptoms.

Preliminary data on 189 post-COVID patients with (55%) and without (45%) PASC, compared with data for 120 control patients with no history of infection, showed almost no biochemical or physiological differences among the three groups that could explain PASC. There was no evidence of persistent viral infection or immune system dysfunction—two of the leading hypotheses that some scientists think could explain PASC. Increased risk for PASC, however, was noted in women and in people with a history of anxiety disorder. Sneller thinks that obesity might also turn out to be another risk factor. The study is continuing to enroll participants (*Ann Intern Med* 2022; DOI:10.7326/M21-4905).

"There is just a striking discoordination between the number of symptoms and the paucity of abnormal findings," said Sneller.

Long COVID affects smell and taste

Lasker Clinical Research Scholar **Paule Joseph**, at the National Institute on Alcohol Abuse and Alcoholism and the National Institute of Nursing Research, is working with the NINDS-led PASC protocol team to understand how SARS-CoV-2 affects the chemical senses of taste and smell. A meta-analysis by Joseph and colleagues established taste loss as a bona fide symptom in 39% of nearly 139,000 patients with COVID-19 (*Chem Senses* 47:bjac001, 2022). Altered chemosensation often accompanies other neurological symptoms; while most patients recover in three to four months, some do not.

Joseph plans to launch her own deep-phenotyping study of chemosensory dysfunction in patients with PASC in an attempt to understand COVID-19-induced phantosmia (detecting smells that aren't there), parosmia (a change in the normal perception of odors such as when the smell of something familiar is distorted), and dysgeusia (a condition in which all foods taste sour, sweet, bitter, or metallic).

She anticipates that studying the SARS-CoV-2 virome and the host's immune reaction might yield some mechanistic insights about the lingering chemosensory symptoms. A recent non-NIH study described how the virus can initiate an immune cascade that disrupts the genetic architecture and function of olfactory neurons (*Cell* **185:**1052–1064, 2022).

At the National Institute on Aging, Senior Investigator **Josephine Egan** studied cadaver tongue tissue and found that oral infection with SARS-CoV-2 occurred in taste buds. The finding suggests that the infection can disrupt stem-cell activity in taste receptors and provide a potential pathway for ongoing taste dysfunction (*Am J Pathol* **9:**1511–1519, 2022).

More questions than answers

Research into PASC continues to generate more questions than answers. Extramurally, NIH's Researching COVID to Enhance Recovery (RECOVER) initiative is funding hundreds of clinical trials across the country to understand, prevent, and treat long-term health effects related to COVID-19. Many intramural investigators contribute to the effort by reviewing manuscripts or serving on the steering committees at RECOVER sites. ●

NIH intramural scientists are eligible to apply for some funding opportunities through RECOVER. Updated research opportunity announcements will be posted at https://recovercovid.org/funding.

Learn more: For an interesting talk, "Long COVID: A Brief Overview," presented on June 2, 2022, by Ziyad Al-Aly (VA St. Louis Health Care System), go to https://videocast.nih.gov/watch=45629.

NIH Security and Emergency Response Office

Ensuring Everyone's Safety

BY MICHAEL TABASKO, OD

Before the COVID-19 pandemic, we had 27,000 people on NIH's campus in Bethesda, Maryland, each day. We are expecting a return to these levels at some point. This, coupled with the construction and potential hazards of offices left empty for so long, makes it important to review safety.

Entrusted with maintaining public safety on the scale of a small city is the Security and Emergency Response (SER) Office, which is in the Office of Research Services. SER's six divisions include Police; Emergency Management; Fire and Rescue Services (DFRS); Fire Marshal; Physical Security Management; and Personnel Security and Access Control (DPSAC). DPSAC operates badging facilities at the Bethesda campus and several NIH properties. SER also coordinates a Counterintelligence and Insider Threat Program for the NIH.

Read on to learn more about Emergency Management, Police, and Fire and Rescue Services and when to contact them in the event of an emergency.

Emergency Communications Center

For any police, fire, or medical emergency at NIH-owned facilities, call the 911 Emergency Call Center, also known as the Emergency Communications Center (ECC). (See numbers on facing page).

Division of Emergency Management

NIH's Division of Emergency Management coordinates the response to large-scale incidents, such as the derecho (a damaging windstorm) that knocked out power to much of campus in June 2012. During such events, limiting 911 calls to concerns that require immediate fire or police action helps keep the lines open and ensures first responders are available when needed. Only pull a fire alarm if there is a fire.

To stay informed during an emergency, sign up for AlertNIH, which will send emails or text notifications to announce emergencies and campus closures and give instructions on immediate actions. To receive alerts on your personal devices, you must provide accurate information in the NIH Enterprise Directory portal. Instructions can be found at https://go.usa.gov/xJP3A.

Division of Police

About 90 NIH police officers serve the Bethesda campus, 12 protect Rocky Mountain Laboratories (RML in Hamilton, Montana), and six officers patrol the National Cancer Institute portion of the campus at Fort Detrick (Frederick, Maryland). Other off-campus facilities leased by NIH have their own federally-operated security services and coordinate security protocols with NIH's Division of Physical Security Management. All NIH law enforcement officers train for a minimum of 480 hours at a certified federal training academy before they are authorized to carry a weapon and can respond to situations from routine traffic stops and criminal arrests up to a potential active shooter. In Bethesda, RML, and Fort Detrick, canine units assist with searching for explosives and firearms at campus entry points, respond to calls for suspicious packages, and conduct area sweeps before special events.

Officers attend more than 40 hours of annual in-service training to stay current on the latest law enforcement tactics as well as court cases and legislation relevant to policing operations. The department prides itself on staying in touch with the community and is involved with NIH's UNITE initiative to end structural racism.

In addition to regular foot and vehicle patrols, NIH police conduct security screenings at patient, visitor, employee, and commercial vehicle entrance gates. NIH security guards assist at these checkpoints; they are unarmed contractors who receive training with an emphasis on NIH security policy, procedures, and techniques.

Since the beginning of the pandemic, all nonpatient visitors are being asked whether they are visiting NIH in an official capacity. Depending on the COVID-19 community risk level, nonpatient visitors may be required to attest to their vaccination status; nonpatient visitors as well as employees who are not fully vaccinated or decline to report their status may need to show proof of a negative COVID-19 test within the past 72 hours to enter NIH property. Home test results are not accepted.

Officers also work with the NIH Clinical Center, the Children's Inn, and the Safra Lodge to ensure the safety and comfort of patients, as well as respond to more than 350 incidents throughout campus in a typical year. Most are minor, such as a traffic violation or loud arguments. "We try to resolve issues with minimal police intervention and always on a positive note," said Chief Security Officer **William "Bill" Cullen**, who oversees all NIH security operations. "The [officer's] job is to protect and serve, to be a guardian, not an enforcer."

If you witness a crime, discover a suspicious object, feel threatened, or fear for your safety, immediately call the appropriate emergency number. And always report suspicious activity—such as unrecognized individuals wandering through offices or repeatedly looking up at security cameras—to the NIH police at its nonemergency number. (See list on facing page).

Distributed throughout the Bethesda

Read more online at https://irp.nih.gov/catalyst/v30i4/news-you-can-use-safety

campus walkways and parking structures are 105 blue light phones (BLP), with most units featuring a closely mounted blue light. For immediate emergency assistance, each BLP will dial the ECC automatically after a person presses the call button. Some BLPs are also equipped with a strobe feature that activates when the call button is depressed.

Police help with nonemergency requests, too, such as unlocking offices or labs for employees who have lost or misplaced their keys. They also provide escorts for anyone who feels unsafe walking across campus at any hour. A supervisor can request police presence if an employee is being given a letter of reprimand or termination.

As more cars and pedestrians return to campus amid new construction projects, traffic safety will be a top priority. Note that moving violations committed on NIH property are cited under state law and will result in points applied to your driver's license. Motorists and pedestrians alike need to remain alert and obey all traffic rules. In addition, pedestrians should always use crosswalks and motorists should always yield to pedestrians in crosswalks.

Division of Fire and Rescue Services

The Division of Fire and Rescue Services (DFRS) personnel are on call for 72-hour shifts in which they live and sleep at the NIH firehouse. The 30 firefighters include those trained from the entry-level firefighter up to the more advanced fire officer. They administer emergency medical services, perform rescues, and mitigate fires, floods, and hazardous material (hazmat) spills.

Stuck in an elevator? Press the alarm button and use the emergency phone to alert the fire department.

If you have a medical emergency, you're in good hands. More than half of the department's calls are medically related. If additional medical care or advanced life support is needed, a pair of ambulances are standing by to transport patients to Suburban Hospital down the street.

You might even spot an NIH ladder truck or hazmat vehicle out in the community because the department has a mutual aid agreement with Montgomery County and Walter Reed National Military Medical Center. The fire and rescue team have advanced training and sophisticated testing equipment to identify and safely mitigate toxic chemical spills in a lab, as well as biohazardous and radioactive materials.

The DFRS conducts its own in-service training. A recent exercise in the NIH Clinical Center involved a simulation in which a fire hose had to be snaked through a nursing unit and firefighters had to navigate through people moving around and blocking an access stairwell. DFRS also participates in quarterly Montgomery County Fire Department–led battalion trainings, which allow for real-life scenarios to be actively trained on and promotes vital coordination with the surrounding community.

In addition to fires and hazardous material spills, all strange or burning odors should be immediately reported to the fire department. You should never assume someone else has reported it or the that source of the odor is nonhazardous. To report, call the appropriate emergency number (see list at end of this article).

Being safety savvy is everyone's responsibility. The foundation of NIH's multilayered security lies with its police and fire and rescue first responders. "Their dedication to the NIH is based on what they can do to enhance public safety and serve the community," said Cullen. "And they do it 24/7." ●

Emergency and non-emergency numbers

- **From landlines:** For fire, police, and medical emergencies: 911 (Bethesda campus), 9-911 (other NIH facilities); 0 (Rocky Mountain Laboratories).

- **From cell phones:** For fire, police, and medical emergencies: 301-496-9911 (Bethesda campus); 911 (other NIH facilities).

- **For nonemergency** police requests and to report a criminal act not in progress, a theft of personal property, or a non-injury accident: 301-496-5685 (Bethesda); 311 (Baltimore); 301-619-7114 (Fort Detrick); 406-363-2100 (Rocky Mountain Labs).

Websites for more information:

- **Emergency Communications Center:** https://ors.od.nih.gov/ser/dp/Pages/911-Call-Center.aspx

- **Division of Police** (includes safety tips and education videos): https://ors.od.nih.gov/ser/dp/Pages/default.aspx

- **Division of Emergency Management:** https://ors.od.nih.gov/ser/dem/Pages/default.aspx

- **Division of the Fire Marshal:** https://ors.od.nih.gov/ser/dfm/Pages/default.aspx

- **Division of Fire and Rescue Services:** https://ors.od.nih.gov/ser/dfrs/Pages/default.aspx

- **Division of Physical Security Management:** https://ors.od.nih.gov/ser/dpsm/Pages/default.aspx

- **Division of Personnel Security and Access Control:** https://ors.od.nih.gov/ser/dpsac/Pages/Home.aspx

In NIDDK Labs, It IS Easy Being Green

NIDDK Focuses on Environmental Sustainability

BY KATIE CLARK, NIDDK

CREDIT: VICTORIA TONG

NIDDK Technical Lab Manager **Minoo Shakoury-Elizeh** is one of the pioneers who started the NIH green labs movement.

At the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), even small changes made lab by lab are making a big impact in environmental sustainability in the scientific workplace. In NIH-certified Green Labs in NIDDK, changes prompted by a desire to improve the environment and human health have ended up saving energy, space, and even money in the process.

In one "green" example, the Genetics and Metabolism Section of NIDDK's Liver Diseases Branch traded in traditional X-ray imaging for digital-imaging systems, eliminating the need for costly X-ray films and hazardous waste, and freeing up laboratory space previously used for dark rooms and film equipment. This change led to a savings of more than $11,000 in one year alone.

"Improving environmental practices in the lab doesn't require drastic changes," said **Minoo Shakoury-Elizeh**, a recipient of the FY2020 Health and Human Services (HHS) Green Champion Award and a technical lab manager in NIDDK's Laboratory of Cellular and Developmental Biology (which has also won several HHS Green Champion awards). "Small changes add up, leading to improved conservation of energy and water, less waste, and safer, more effective lab practices."

NIDDK has been at the forefront of the NIH's green lab movement. Its Genetics and Metabolism Section is where iron and its role in diseases within NIDDK's mission are studied. It's also where Shakoury-Elizeh championed sustainability efforts as one of NIDDK's four NIH-certified green labs, following practices like replacing wet-blotting instruments used to detect proteins with safer dry-blotting versions, eliminating toxic methanol waste. An additional perk—the dry machine can detect proteins four times as fast as wet-blotting methods.

Although there is often an upfront cost with purchasing new equipment, long-term benefits, such as reduced energy, time, and maintenance and associated costs, can be substantial. To help offset costs of new equipment, Shakoury-Elizeh suggests sharing equipment with another lab or office.

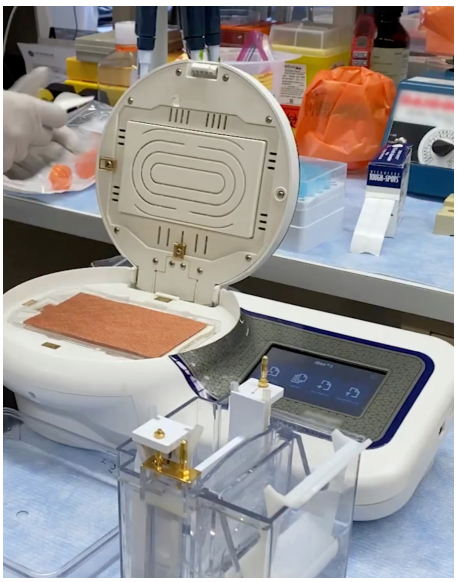
The NIH Green Labs Program was developed in 2018 to increase awareness and participation in sustainable practices without sacrificing research. Shakoury-Elizeh and colleagues across NIH have since worked to implement and expand NIH's sustainability efforts.

"Minoo is one of the pioneers who started the NIH green labs movement to educate researchers and promote the use of safer lab products," said **Bani Bhattacharya**, NIH Green Labs Program manager. "It is remarkable to see how her passion and dedication has grown over the years in increasing awareness and communicating sustainability efforts across the NIH."

In one effort, Shakoury-Elizeh and **Daman Kumari**, staff scientist in NIDDK's Laboratory of Cell and Molecular Biology, expanded NIH's Styrofoam Take-Back program in which Styrofoam shipping containers are returned for reuse, resulting in a reduction of solid waste. Between 2010 and 2021, the quantity of NIH-recycled Styrofoam coolers diverted from landfill disposal increased 27-fold—from 513 pounds to 13,900 pounds.

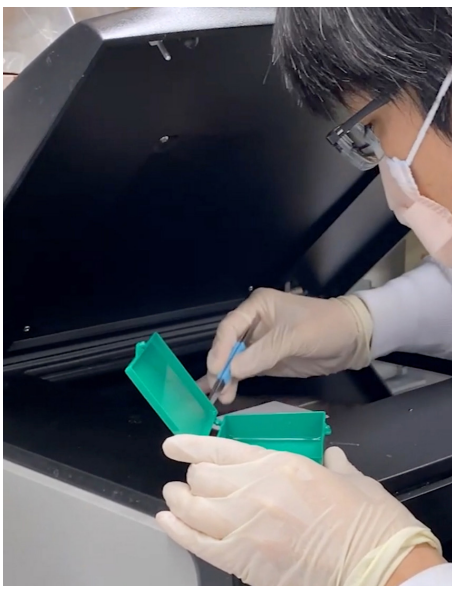
Shakoury-Elizeh and Kumari, among others, were recognized as Change Agents in the 2019 Department of Health and Human Services Green Champion Awards for leading sustainability by example at the NIH. This group serves as the voice of the NIH scientific community to senior-level management and has been intimately involved with green efforts within their own teams and the NIH Sustainable Lab Practices Working Group. Because of their efforts, for example, ethidium bromide, a toxic chemical dye used to detect DNA and RNA, was replaced with a nontoxic alternative in many labs across NIH.

"In line with our mission to improve health and quality of life for all, NIDDK is committed to conserving resources and reducing our environmental footprint," said NIDDK Director **Griffin P. Rodgers**. "Making sustainability practices a priority is important for



CREDIT: NIDDK

Practices like replacing wet-blotting instruments used to detect proteins with safer dry-blotting machines (shown here), eliminates toxic methanol waste, and can detect proteins four times as fast as wet-blotting methods.



CREDIT: NIDDK

Digital-imaging systems, eliminate the need for costly X-ray films and hazardous waste, and free up laboratory space previously used for dark rooms and film equipment.

every organization and is part of our responsibility to the communities we serve."

Shakoury-Elizeh concurs. "Going green is a win for everyone, for our research, and for our planet—and it doesn't have to be hard," she said. "From purchasing energy-efficient equipment, to swapping out toxic chemicals, to placing 'turn off' stickers on light switches, once you start looking, there are paths to a greener lab everywhere."

How can you go green? To learn more about the Green Labs Program or application process, visit the NIH Green Labs Program website at https://go.usa.gov/xJsrY. ●

This article was adapted from one that appeared as an NIDDK Director's Update in Spring 2022. For a behind-the-scenes look at an NIH-certified green lab, check out a video tour of the NIDDK Genetics and Metabolism Section: https://www.youtube.com/watch?v=-CzyZiR0BHQ&t=8s.

Katie Clark, who is a press officer in NIDDK, has been at NIH since 2018. In her spare time, she likes to go hiking, play with her dogs, and gather with friends and family.

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

Sex and Gender in Health and Disease (SGHD) SIG Panel Discussion

"Incorporating Sex and Gender in NIH Research"

BY ELIZABETH BARR AND ELENA GORODETSKY, OD

The Office of Research on Women's Health (ORWH) sponsored this SGHD SIG webinar, which featured three presentations followed by a panel discussion. NIH Associate Director for Research on Women's Health and Director of NIH Office of Research on Women's Health **Janine Austin Clayton** opened the panel discussion by providing an overview of the ORWH mission and the NIH vision for women's health research. Her presentation covered the establishment of ORWH in 1990, the landmark 2016 Sex as a Biological Variable (SABV) policy, and the establishment of the SGHD SIG in 2017.

Sex Differences in Taste and Smell

Paule Joseph (Lasker Clinical Research Scholar at the National Institute on Alcohol Abuse and Alcoholism and the National Institute of Nursing Research) discussed what is known about sex differences in taste and smell perception and future research. The question of whether men and women vary in their ability to taste and smell has been investigated for many years. Sex differences have been reported in taste preference, detection thresholds, and reactivity to taste stimuli. While there is heterogeneity in the literature, some studies suggest that for specific odorants, women seem to have a better sense of odor detection, identification, discrimination, and memory compared with men.

Sex-Based Differences in Cancer

Jill Barnholtz-Sloan (associate director for Informatics and Data Science, Center for Biomedical Informatics and Information Technology; senior investigator, Trans-Divisional Research Program; National Cancer Institute) talked about the importance of elucidating the mechanisms by which sex-based differences affect cancer development, prognosis, and treatment response. Recent guidance from NIH now requires all grants to outline how they will address SABV. However, sex-based differences in cancer are typically not accounted for in the study design for laboratory, clinic, or community-based studies in cancer. There are significant sex differences in cancer incidence and prognosis of many tumors that arise in both sexes. Little is known about the biological basis for these sex differences. Barnholtz-Sloan's group and others have demonstrated that males have a higher incidence of cancer. In addition, she and her colleagues have started to describe molecular mechanisms that could underlie sex differences in brain tumors. Recent studies have demonstrated that females with cancer have increased adverse events when compared to males and might not respond to targeted therapy and/or immunotherapy as well as males.

Working Group Update

Koyeli Banerjee (scientific program analyst, National Heart, Lung, and Blood Institute) and **Nina F. Schor** (deputy director and acting scientific director of the National Institute of Neurological Disorders and Stroke) reported that the Coordinating Committee for Research on Women's Health COVID-19 Working Group performed a portfolio analysis at the intersection of women's health and COVID-19. The portfolio analysis included awarded grants for FY2021 and was performed using research, condition, and disease categorization keywords related to disorders and conditions that preferentially affect women, followed by a manual curation of this list. It is intended to form the basis for the ongoing gap analysis to enable NIH institutes and centers to identify potential areas for the enrichment of their COVID-19 and women's health grant opportunities. ●

To view the video recording of the April 12, 2022, webinar, visit https://www.youtube.com/watch?v=cDsvPzlaIFM. For more info on this SIG visit https://oir.nih.gov/sigs/sex-gender-health-disease.

NEW SIG: QIS and Quantum Sensing in Biology

Studies in quantum information sciences (QIS) and quantum sensing in biology (QSB) are rapidly advancing for biomedical applications. Many cellular and subcellular phenomena such as photosynthesis, neurotransmission and cognition, enzyme tunneling, and mitochondrial electron transfer involve quantum physicochemical components. Advances in artificial intelligence, machine learning, and quantum computer designs have made it possible for applications in biomedical sciences such as sensing weak electromagnetic signals in neurons and tissues, in vivo imaging, biomolecular modeling, data encryption, privacy, and storage to become fruitful areas of exploration. These developments will affect the understanding of complex disease biology and enable new modalities for drug and biomarker discovery in the next decade.

The QIS and QSB SIG, initiated by NIMH and NCATS with participation from several other institutes, will be a resource for NIH intramural scientists, fellows, graduate students, and interns. Data and information scientists, bioengineers, chemists, biologists, physicists, and clinicians may be interested in this SIG's activities, too.

The SIG will hold seminars and workshops featuring invited national and international experts in QIS or QSB, and identify opportunities for learning, training, and workforce development for fellows and trainees in coordination with academia, industry, and government agencies. For more information, go to https://oir.nih.gov/sigs/QIS-Quantum-Sensing or contact **Geetha Senthil**, NIMH (geetha.senthil2@nih.gov); **Paige Derr**, NCATS (paige.derr@nih.gov); or **G. Sitta Sittampalam**, NCATS (gurusingham.sittampalam@nih.gov).

NEW SIG: Science of Science Communication

Effectively communicating research results to a broad range of audiences is integral to the scientific process. The ability to tell rigorous and compelling stories of science can elevate a researcher's profile, facilitate interdisciplinary collaborations, and increase the impact of their scholarly publications within the scientific community. Perhaps more importantly, strong communication can also enhance public engagement with science, allowing researchers to build bridges of trust with nontechnical audiences and instill a sense of curiosity and wonder among inquiring minds.

Although artistry is no doubt critical to communications, there exists an underlying body of literature that draws from fields including psychology, sociology, and political science that provides a theoretical foundation for scientific communications. The NIH Science of Science Communication Interest Group (ScioSciComm-SIG) plans to focus specifically on the scientific design and evaluation of science communication, with seminars and journal clubs highlighting measures of effectiveness and methods to increase general success or target efforts to respond to specific goals. A combination of face-to-face meetings and remote webinars will be held monthly (days and times to be determined).

The ScioSciComm-SIG is chaired by **Chris Gunter** (NHGRI) and **Maryam Zaringhalam** (NLM). Membership in the SIG is open to all interested individuals within NIH. Join the LISTSERV newsletter at https://list.nih.gov/cgi-bin/wa.exe?A0=SCIOSCICOMM. For more information, go to https://go.usa.gov/xJsrw or contact chris.gunter@nih.gov or maryam.zaringhalam@nih.gov.

Renamed SIG: Patent Law, Industry, & Technology Transfer

The Patent Law & Technology Transfer Interest Group has been expanded and renamed to include the biotechnology industry. The goal of the PLITT SIG is to provide educational and networking opportunities for NIH scientists interested in patent law, industry, and technology transfer. The SIG will include members of the NIH Office of Technology Transfer, technology development coordinators from NIH institutes, and bench scientists with interests in intellectual property and the biotechnology industry, as well as past fellows who have transitioned into applicable careers in local institutions or companies.

The SIG will hold seminars with invited representatives from the U.S. Patent and Trademark Office, law firms, and biotechnology and pharmaceutical companies; host mini symposia (at the NIH Research Festival) featuring former intramural investigators who have successful careers in patent law, technology transfer, or in the biotechnical industry; host poster sessions on careers in technology transfer and business development; and provide opportunities and support for trainees interested in industry through job fairs, networking events, technology demonstrations, and field trips to local companies and facilities. The SIG will also support the annual Philip S. Chen Lecture on Technology Transfer and Innovation. Meetings and activities will be coordinated with local chapters of the Technology Transfer Society, the Licensing Executives Society, and the Federal Laboratory Consortium for Technology Transfer.

Steven Ferguson (OD) and **Ulisses Santamaria** (NIAID) are co-chairs. For more information and instructions for joining the LISTSERV newsletter, go to https://oir.nih.gov/sigs/patent. ●

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Publication No. 22-6250

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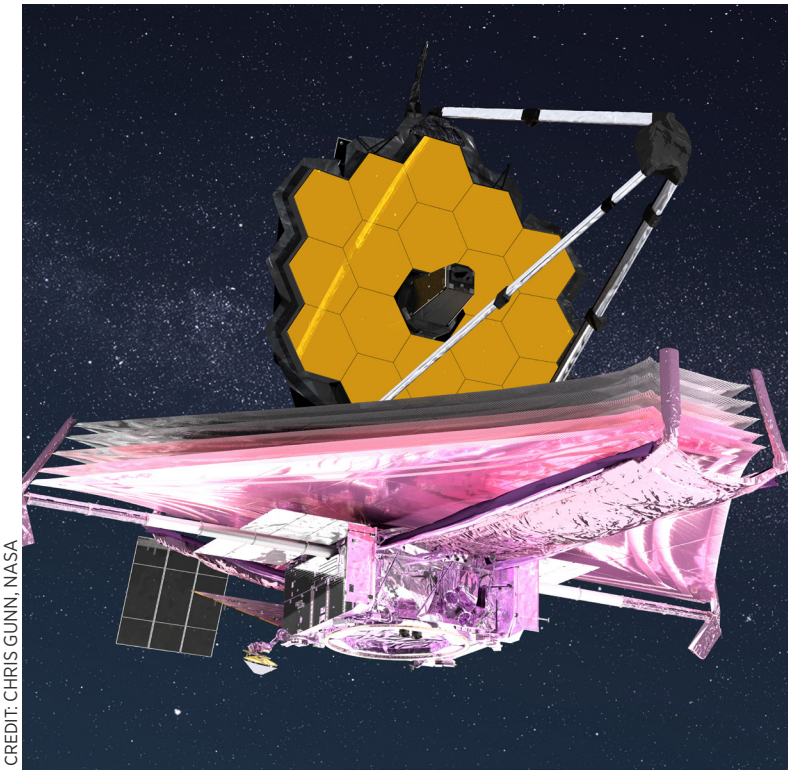
Also, we welcome "letters to the editor" for publication and your reactions to anything on the *Catalyst* pages.

READ MORE ARTICLES, AND EXPANDED VERSIONS OF THE ONES IN THIS ISSUE, ONLINE AT https://irp.nih.gov/catalyst/v30i4.

PHOTOGRAPHIC MOMENT

Searching for Signs of Life Beyond Our Solar System



CREDIT: CHRIS GUNN, NASA

NASA's James Webb Space Telescope, which is 100 times as powerful as the Hubble Space Telescope, was launched in December 2021 and will start sending images back to Earth in July. A recent Demystifying Medicine lecture featured Nobel laureate John Mather—NASA senior astrophysicist and senior project scientist for the Webb—who spoke about how the telescope will search for signs of life beyond our solar system. ●

Read feature at https://go.usa.gov/xJ7qZ.

The NIH Catalyst is published bimonthly for and by the intramural scientists at NIH.

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