NIH RECORD

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INTERNING DURING A PANDEMIC

Two Summer Programs Adapt to Virtual Workplaces

BY AMBER SNYDER

Every summer, student interns descend on the NIH campuses to get some first-hand experience conducting biomedical research or learn about the administration that supports that research. The summers of 2020 and 2021 were very different.

When the majority of NIH switched to remote work in March 2020, the summer programs had only a few short months to adapt. The NIH Summer Internship Program (SIP) typically hosts 1,200 to 1,300 STEM students in its research groups, and the Pathways program places about 150 students in NIH administrative offices. With in-person work prohibited, program organizers had to scramble to bring students online.

Dr. Sharon Milgram, director of the NIH Office of Intramural Training & Education (OITE), which organizes SIP, recalled the difficult decisions NIH faced in those early months. "We had to cancel [SIP] entirely in 2020 due to the nature of the program," she said, "which in normal years pairs each intern with a scientific mentor in a research lab." More than 800 students had already been offered positions by March, which made cancellation of the program particularly disappointing. Instead, OITE created a Virtual Summer Enrichment Program and made it available to all interested high school and college students.

The enrichment program returned for 2021. It is divided into two separate

SEE **INTERNS**, PAGE 4

Pathways intern Shelandria Williams

NIH'ers create faster Covid tests. See story, p. 9.

ALSO THIS ISSUE

Pulmonologist Develops Test To Predict Covid-19 Severity

BY DANA TALESNIK

Dr. Sean Agbor-Enoh

Of the various hurdles Dr. Sean Agbor-Enoh faced during the pandemic, one of the biggest was personal. For 2 months, he couldn't go home.

An NIH principal investigator, Agbor-Enoh is also a pulmonologist. When everything shut down in spring 2020, he still headed to work at the Johns Hopkins Hospital in Baltimore and at NIH, where he's on a pulmonary consult clinical team. His wife Juul is a pharmacist who also couldn't work from home.

SEE **PIVOT**, PAGE 6

3rd in Series | Pivots to Pandemic Science

'NO ALGORITHM FOR EMPATHY'

Topol Charts AI Path to More Accuracy in Medicine

BY CARLA GARNETT

Artificial intelligence (AI) is smart at assessing patterns in medicine, and getting smarter all the time. In some fields, it might already be as or more accurate than your typical seasoned practitioner. Truth is, someday, many years from now, machines may out-detect and out-diagnose physicians, but AI will never out-care human doctors. That caring is the "secret sauce" of the medical profession, emphasized Dr. Eric Topol at a virtual NIH Director's Wednesday Afternoon Lecture.

Renowned as a cardiologist and award-winning scientist whose forward thinking often challenges the traditional medical community's status quo, Topol founded Scripps Research Translational Institute at The Scripps Research Institute.

In 2016, NIH awarded him a $207 million

SEE **TOPOL**, PAGE 8

Annual Salzman Award Applications Due Sept. 30

The Salzman organizing committee, the Foundation for the National Institutes of Health and the NIH virology interest group announce the 23rd Annual Norman P. Salzman Memorial Awards in Basic and Clinical Virology for young investigators. The awards have been established to recognize outstanding research in the field of basic and/or clinical virology at NIH, FDA, Ft. Detrick Laboratories, LEIDOS, USDA or the Uniformed Services University of the Health Sciences. Awards honor the 40-year career of Salzman in virology research and his accomplishments in mentoring of young scientists.

The annual awards pay tribute to Dr. Norman P. Salzman, his 40-year career in virology research and his accomplishments in mentoring young scientists.

Two awards will be given: one to a postdoctoral fellow and one to a graduate student/postbaccalaureate trainee. The winning postdoctoral fellow receives a plaque and $2,500. The winning graduate student/postbaccalaureate trainee receives a plaque and $1,000. Mentors of awardees will receive plaques.

Winners will give talks during the 23rd Annual Norman P. Salzman Memorial Symposium in Basic and Clinical Virology being held virtually in November.

Applications for the award are due by Thursday, Sept. 30. Find forms and details at https://fnih.org/salzmansymposium. Applications must be submitted by email to SalzmanSymposium@mail.nih.gov.

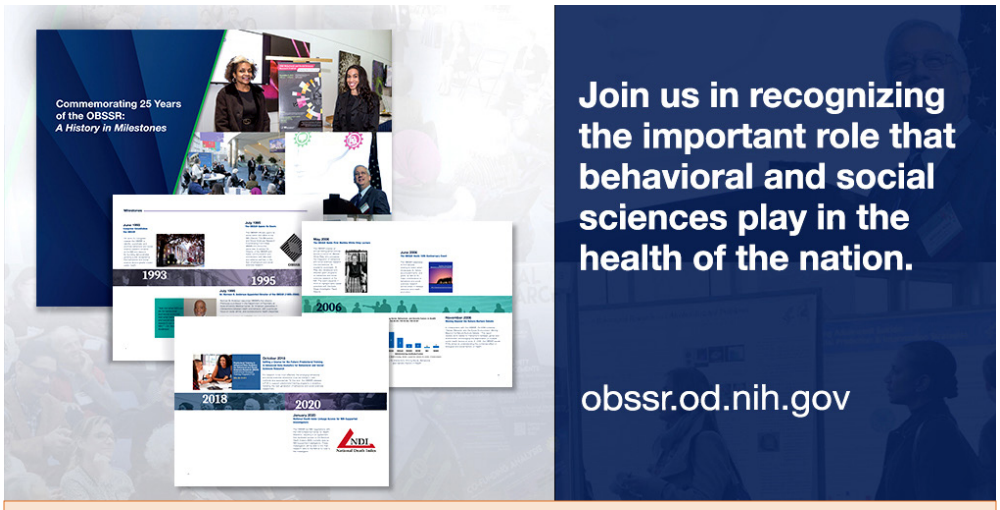
Employee Asymptomatic Testing Clinic Updates Hours

The Employee Asymptomatic Testing Clinic on the 5th floor of the CRC has changed its days of operation.

On Aug. 16, employee asymptomatic testing increased to 3 days a week on Monday, Tuesday and Friday. Previously, employee asymptomatic testing was available only on Tuesday and Friday.

Testing for SARS-CoV-2 involves a traditional nasopharyngeal swab, which looks like a 6-inch Q-tip. The swab is inserted through the nose to the back of the throat, rotated several times and left in place for 10-15 seconds. The hospital also offers Covid-19 saliva tests.

To sign up for asymptomatic testing, NIH'ers can visit https://clinweb.cc.nih.gov/cct.



OBSSR Launches History Timeline Online

Behavioral and social sciences were part of NIH's mission long before the Office of Behavioral and Social Sciences Research (OBSSR) was established. But OBSSR, during the past 26 years, has been instrumental in accelerating the behavioral and social sciences relevant to health, coordinating these sciences within the NIH research enterprise and increasing integration of these sciences at NIH.

Last year, to help commemorate its 25th anniversary, OBSSR developed a historical record of key events, accomplishments and leadership. An online resource, "Commemorating 25 Years of the OBSSR: A History in Milestones," recently launched to share the record. Viewers can click through OBSSR history according to such event categories as Directors, Training and Research, and by decade.

Soon, OBSSR will add recent accomplishments and activities such as work in firearms violence prevention, Covid-19 impacts and behavioral ontologies. Visit the timeline at https://obssr.od.nih.gov/about/obssr-timeline.

Latest Health Disparities Interest Group Lecture Available Online

NIMHD's Division of Intramural Research recently held its latest health disparities interest group lecture, "Structural Racism: The Roots and Relations of Inequality" by Dr. Gilbert Gee, professor in the department of community health sciences at the Fielding School of Public Health at UCLA. The virtual seminar was viewed by a capacity audience of 500 attendees. A robust question and answer session followed. Details about the interest group and recordings of the seminar series are available at https://www.nimhd.nih.gov/programs/intramural/hdig/index.html.

Dr. Gilbert Gee

New Additions to Food Service on the Bethesda Main Campus

The Office of Research Services is pleased to announce some new food service additions and a return of a favorite to NIH.

The Eurest food trailer located in the 10H Parking Lot (south side of Bldg. 10) now serves daily breakfast from 7:30 a.m. to 9 a.m. Menu items include a daily special, made-to-order sandwiches (including vegetarian options), hash browns and hot or iced coffee.

Chef's Table in Bldg. 35 now offers made-to-order lunch specials of your favorite dishes on Tuesdays, Wednesdays and Thursdays from 11:30 a.m. to 1:30 p.m.

The Outdoor BBQ has returned to the South Lawn of Bldg. 10 every other Wednesday. The BBQs will feature themed outdoor dining inspired by a traditional BBQ menu. For more information, see: https://ors.od.nih.gov/pes/dats/food/Pages/index.aspx.

Additionally, the CRC Atrium Coffee Bar and the FAES Bookstore Café, both located inside Bldg. 10, are open.

As more people return to the physical workplace, ORS will continue to evaluate the return to work levels of staff and determine what services can and should be provided.

Direct comments and concerns to the Food Services Team at (301) 827-3248 or ORSWEPB@ors.od.nih.gov.

Summit Focuses on Anti-SARS-CoV-2 Antibody Treatment, Prevention

BY AMBER SNYDER

What is the current state of Covid-19 antibody treatment and prevention strategies? What have we learned since the start of the Covid-19 pandemic, and what are future directions for further anti-SARS-CoV-2 antibody research? The recent Summit on Anti-SARS-CoV-2 Antibodies for Treatment and Prevention of Covid-19—Lessons Learned and Remaining Questions—identified key unanswered scientific questions to catalyze antibody clinical development and implementation. It was sponsored by the Office of the Director and NIAID.

The virtual summit was sponsored by OD and NIAID.

There are several antibody therapies in use or under study—convalescent plasma, monoclonal and polyclonal antibody products and hyperimmune globulin—but several monoclonal antibodies (mAbs) have proven so far to be the most successful in certain clinical scenarios.

Drug companies including Lilly, VIR/GSK and Regeneron have developed mAb treatments such as bamlanivimab, etesevimab and others. Some of these mAbs were tested in human clinical trials as early as May 2020.

Recently, viral variants have started to develop resistance to certain monoclonals (such as bamlanivimab), but other monoclonals, as well as combinations of several monoclonals are still effective. FDA recently revoked the emergency use authorization (EUA) for bamlanivimab and it is no longer distributed in the U.S.

Dr. Myron S. Cohen of UNC-Chapel Hill presented an overview of the mAbs used for Covid-19 prevention as they could offer immediate protection for unvaccinated individuals exposed to the virus or in high-risk settings. There are currently mAbs in every phase of development, and, because they are most beneficial when administered within 7 days of symptom onset, there is particular emphasis on ones that may be used in outpatient settings.

Drs. Ralph Baric (l) and Myron Cohen participate in the summit.

There are multiple animal models currently used for testing Covid-19 therapeutic and prevention candidates. These models are used to investigate how SARS-CoV-2, the virus that causes Covid-19, initiates infection, replicates and causes disease in the host. Dr. Ralph Baric of UNC-Chapel Hill provided a summary of studies using a variety of animal models that have been developed since the pandemic was initially reported, as well as proposed questions that researchers will target next. Animal models could be useful in modeling long Covid and other conditions that linger after acute infection.

"We know a lot more than we did at this time last year," commented Dr. Connie Schmaljohn, director of the NIAID Integrated Research Facility at Fort Detrick, "but we still have a long way to go" in our understanding of SARS-CoV-2 and Covid-19.

Dr. Katharine Bar of the University of Pennsylvania and a panel of experts discussed some of the challenges associated with antibody administration. One major challenge for mAb use, Bar says, is "the timely identification of eligible Covid-19 patients and linkage of them to a facility that can either refer or prescribe these antibodies."

Clinicians and researchers on the panel recommended linking testing to treatment by providing both in the same facilities so that patients and health care providers could readily find antibody therapies. Monoclonals may also be a viable alternative to vaccination for immunocompromised or immunosuppressed individuals, who may be unable to be vaccinated or did not have a sufficient immune response to Covid-19 vaccination.

Among take-home summit conclusions:

• Several anti-SARS-CoV-2 mAbs have been authorized by the FDA under EUA, as safe and effective in preventing hospitalizations and deaths.

• Anti-SARS-CoV-2 mAbs are most effective when administered early in the course of the disease but are vulnerable to virus mutation (variants) and may be more effective when combined with other mAbs.

• Further research on anti-SARS-CoV-2 antibodies also may be useful for developing treatments for other SARS coronaviruses.

As Dr. Skip Virgin of Vir Biotechnology Inc. reminded viewers, "We should look at this pandemic with an eye to the future, because it may not be the last one."

NIH director Dr. Francis Collins noted that presentations and discussions at the summit will inform future directions in this important field.

The entire summit can be viewed at https://videocast.nih.gov/watch=42078.

ON THE COVER: *3-D print of a SARS-CoV-2—the virus that causes Covid-19—particle. The virus surface (blue) is covered with spike proteins (red) that enable the virus to enter and infect human cells. The spikes on the surface of coronaviruses give this virus family its name—corona, which is Latin for "crown." Most any coronavirus will have a crown-like appearance.*

IMAGE: NIH

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Pathways intern Kelly Glass works in the Administrative Resource Center of NCI's Center for Cancer Research.

★★★

The current virtual SIP is no substitute for an in-person experience, but organizers "have learned that lots of educational programs work virtually and will help provide information to a larger audience."

-DR. SHARON MILGRAM

★★★

Interns

CONTINUED FROM PAGE 1

programs—one that focuses on high school students and the other reserved for students in college, graduate and professional schools.

In parallel with the enrichment program, OITE in collaboration with the Center for Information Technology, created a Virtual Summer Internship. As in prior years, students applied online and were selected for positions by NIH researchers. However, in summer 2021, the internships were once again entirely virtual.

Using a virtual desktop infrastructure implemented rapidly by CIT, interns spent the summer at locations throughout the U.S., analyzing data, learning data science and computational skills, writing review papers and participating in journal clubs, in addition to attending scientific and career development workshops. The summer ended with Summer Presentation Week, during which 650 of the more than 800 summer interns presented their research virtually in either poster or oral format.

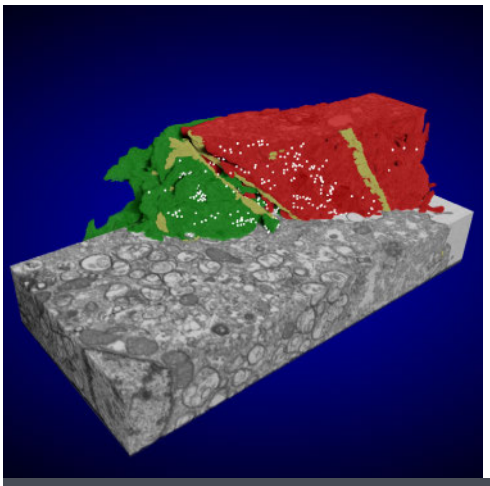
Ella Fitzgerald, a SIP student in the Werner H. Kirsten section at NCI, had no reason to expect a remote internship when she applied to the program pre-pandemic, but found her experience to be rewarding nonetheless. She interned in the Center for Molecular Microscopy, examining cellular images taken with a focused ion-beam scanning electron microscope and extracting features of interest. Like many remote workers, she faced technical difficulties and isolation from her coworkers, but she "wouldn't have traded this experience for anything in the world."

Pathways organizer Saimantha Kinsella was able to offer remote work to 73 new students in 2020. That number edged up to a little over 100 in 2021.

"Not all offices were in a place to offer remote work to an intern while they were still figuring out the logistics of long-term telework for their full-time employees," she said, but the students who did participate spoke highly of their experiences. Pathways students come from a variety of academic interests and work in an assortment of administrative settings to support the research conducted at NIH.

Shelandria Williams, an intern in Kinsella's office, said her time in the Pathways program "has been an overall positive learning experience." She had some difficulties adapting to the NIH organizational culture, but she believes that her struggles "created additional opportunities for training and have led to productive discussions within the division." Williams is grateful for the personal growth and resilience she has gained from her remote internship, and to her office for their flexibility.

Kelly Glass, another Pathways intern who works in the Administrative Resource Center of NCI's Center for Cancer Research, was referred to the program by a family friend. She applied in March 2020, not



SIP student Ella Fitzgerald interned in the Center for Molecular Microscopy, working with cellular images like the one at left. The rendering shows images Fitzgerald would receive (grayscale) and her end product (red and green shapes). The red and green shapes represent two individual cells; the white dots are SARS-CoV-2, the coronavirus that causes Covid-19.

CELL IMAGE: CENTER FOR MOLECULAR MICROSCOPY

Pathways organizer Saimantha Kinsella was able to offer remote work to 73 new students in 2020. That number edged up to a little over 100 in 2021.

expecting a remote internship, but was surprised at the ease of the newly online onboarding process. She said it has been challenging to learn a new job while being completely remote, but that "everyone has been extremely helpful and amazing to work with." She added that, while she has enjoyed her telework experience, she would like to eventually be able to meet her team members in person.

Summer program organizers hope programs will be in-person in summer 2022. The current virtual SIP, Milgram said, is no substitute for an in-person experience, but organizers "have learned that lots of educational programs work virtually and will help provide information to a larger audience." Organizers are hopeful for a return to at least some in-person work by next summer but have the resources to provide a rewarding virtual experience again if necessary.

Pathways has adapted well to virtual work and is currently hosting pre-pandemic numbers of students. As interns Williams and Glass demonstrated, offices can have great success with student workers even in fully remote settings. The program will continue to deliver career-building experiences regardless of work status.

No matter the program, organizers and participants seem to agree: Offices and especially students have demonstrated remarkable adaptability and creativity in these unprecedented times. R

8TH TOWN HALL ANNOUNCED

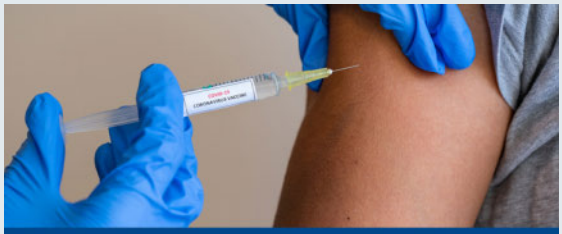
Covid-19 Vaccinations Required for All HHS Health Care Workforce

The Department of Health and Human Services announced Aug. 12 that it will require members of its health care workforce to be vaccinated against Covid-19.

The directive says all NIH staff who come into contact, or have the potential to come into contact with patients, must be vaccinated against Covid-19 in order to report to work. Covid testing will not be an option in place of vaccination for these staff members.

The mandatory vaccine requirement will be a primary topic for the 8th Virtual Town Hall on Friday, Sept. 10 at 10:30 a.m. ET: https://employees.nih.gov/pages/coronavirus/events.aspx.

"NIH's mission is to advance health and lengthen life," said NIH director Dr. Francis Collins, in a staff-wide email announcing the requirement. "We operate the largest hospital in the world dedicated entirely to clinical research. First and foremost, we must 'do no harm' and ensure patient and workforce safety. This includes minimizing the risk of transmission of illness to our patients and workforce."



Vaccine Requirements for Staff

With more than 4.54 billion Covid-19 vaccine doses administered worldwide, there is enough data to know the vaccines are highly safe and effective in protecting against severe disease and hospitalization.

The new directive applies to all people working at NIH facilities, including but not limited to employees, contractors, trainees and volunteers, whose duties put them in contact or potential contact with patients at an NIH facility. This includes all staff, whether or not they are considered a health care worker, who work in any part of the Bldg. 10 complex.

The directive also applies to health care practitioners, emergency medical responders, health care support staff (such as facilities, housekeeping, laundry, food services, waste management) and research staff who have contact or potential contact with patients at all other NIH facilities; those working in the carline Covid-19 test facility; and the NIH Fire Department, when emergency health services are provided.

NIH already requires personnel in health care settings to receive the seasonal influenza vaccine and other routine vaccinations, with processes for medical and religious exemptions. NIH will implement this new Covid-19 vaccination requirement using the same processes that are already in place for these other vaccines.

If your job puts you in contact or potential contact with patients and you have not yet been vaccinated, you can schedule your vaccination appointment today at NIH by visiting https://clinweb.cc.nih.gov/cct.

You can also get vaccinated in your community by going to vaccines.gov or texting your zip code to 438829, which will return the 3 closest vaccination sites near you.

NIH is working on a plan to implement this new requirement. The timetable is not yet worked out. Additionally, the Office of Research Services is in the process of updating the online tool to report vaccination in the community to allow all NIH staff to attest to their vaccination status. Those who do not attest will be considered unvaccinated.

As implementation planning progresses, regular updates and information will be posted to the Guidance for NIH Staff on Coronavirus intranet page: https://employees.nih.gov/pages/coronavirus/vaccination-requirements.aspx.

"In health care, in a pandemic, all of us have to pull up our boots together and just jump in," said Agbor-Enoh.

With 4 kids at home between ages 3 and 18, he didn't want to risk potentially exposing them to Covid, so he stayed at a hotel for 6 weeks, then quarantined for 2 more. "It was a trying experience for my family," he recounted.

Originally from Cameroon in central Africa, Agbor-Enoh first came to NIH on a fellowship. His mentor, former NHLBI investigator Dr. Hannah Valantine, soon invited him to join her team studying transplant rejection.

In 2015, newly hired as an NHLBI staff clinician, Agbor-Enoh set out to adapt a technology Valantine co-developed with a Stanford colleague to diagnose lung transplant rejection. That technology is a blood test called cell-free DNA, which—since dying cells release their content, including DNA—can measure cell death and injury.

But NIH doesn't have a lung transplant program, so Agbor-Enoh established GRAFT, the Genomic Research Alliance for Transplantation. By partnering with five local extramural hospitals, he could obtain patient samples to develop and validate this test.

Since getting his own lab in 2019, "[Our team] developed a method which, with a patient's blood sample, we can measure what tissues or organs are affected in any disease, not just in transplant," he said. "You can almost draw a whole-body injury map with this test."

When the pandemic struck, he wondered whether they could adapt this same testing to predict the trajectory of Covid-19 infections. But this was beyond the scope of their approved project and they needed resources. "We don't just have money sitting somewhere when you want to study [something new]."

With funding from ITAC (intramural targeted anti-Covid award), he obtained Covid-positive samples from GRAFT collaborators. Then, he and Drs. Moon Kong and Hyesik Kong, along with colleagues in Dr. Mehdi Pirooznia's and Dr. Robert Star's lab, made remarkable discoveries. They hypothesized that cell-free DNA analysis, which measures tissue damage, would identify Covid-19 patients at high risk of poor outcomes.

"We concurrently worked to develop the test and apply it to the Covid-19 samples and, boom, we found our hypothesis was correct," Agbor-Enoh said. "This virus is bad!"

The team saw injury in blood vessels, multiple organs and different tissue types. "It causes more injury than other viruses that we know," he observed.

Looking at their data in summer 2020, the team was stunned at the amount of injury they found. "Our tests showed the virus was causing tissue injury 100 times higher than in a healthy person," Agbor-Enoh said.

In fact, he was so astounded that he halted his lab's research to recheck their experiments. Several months later, they confirmed their initial results. "The strangeness of the virus made us unable to accept the results that we were seeing in front of us, because we'd never seen anything like this."

Agbor-Enoh wondered if the test also could predict which Covid patients would become hospitalized. "If we could use this test to identify patients who would need the ICU," he said, "we could really help with health care resource adjudication for this pandemic."

• • •

"In health care, in a pandemic, all of us have to pull up our boots together and just jump in."

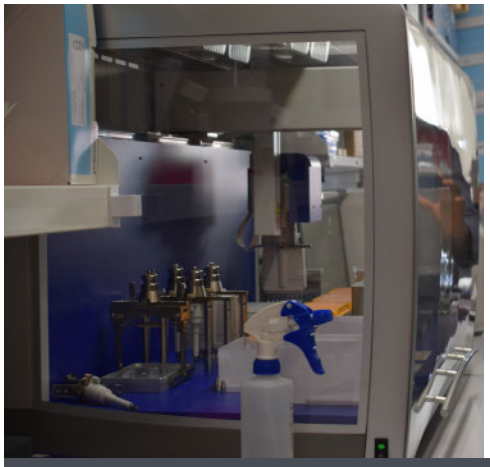
-DR. SEAN AGBOR-ENOH

• • •

Sure enough, the test also allowed them to stratify patients who would need critical care versus those who had milder cases. They found far greater injury among hospitalized patients, even more so among those who needed the ICU.

Meanwhile, the pandemic created an unexpected opportunity to further his original research project.

Normally, to prevent organ rejection, patients get biopsies—removing tissue samples for inspection. When the pandemic



Inside Dr. Sean Agbor-Enoh's lab at NIH (photos taken before the pandemic)

PHOTOS: NHLBI

Agbor-Enoh welcomes colleagues during a pre-pandemic tour of his lab.

hit, patients especially didn't want to come in for these invasive, costly tests.

With a company already on board to produce the transplant test, Agbor-Enoh teamed up with his clinical fellow Dr. Michael Keller to set up the ALARM [Analysis of Lung Allograph Remote Monitoring] study to bring cell-free DNA blood tests to patients' homes. Only patients who tested positive for cell-free DNA would come into the hospital for a confirmatory biopsy.

"With this approach and with FDA compassionate-use authorization," said Agbor-Enoh, "a company produced the tests, which turned out to be 90 percent accurate. And, we were able to avoid 85 percent of [unnecessary] biopsies."

What's more, these tests can detect whether a patient will develop transplant rejection 2-3 months before they show any signs of rejection.

"This experience really gives us hope," he said. "There seem to be NIH processes in place and companies ready to take these technologies and make them become clinically available very quickly."

While Agbor-Enoh is staying involved in Covid-19 research, his focus has returned to lung transplantation.

"I think I owe it to my lung transplant patients to continue that work," he concluded.

ANNUAL EARLY-CAREER SERIES

Cornell's Johnson To Give Greenberg Lecture, Sept. 29

Dr. Elizabeth Johnson

Dr. Elizabeth Johnson, an assistant professor in the division of nutritional sciences at Cornell University, will present the Judith H. Greenberg Early-Career Investigator Lecture on Wednesday, Sept. 29, at 1 p.m. via Zoom and NIH videocast. The lecture is open to everyone in the scientific community.

During her talk, titled "Looking for Lipids in All the Right Places: Host-Microbiome Interactions," Johnson will describe her research on how bacterial sphingolipids affect host signaling pathways. She believes that understanding how sphingolipids influence host-microbe interactions may ultimately enable precise control over microbiome makeup and host health.

After a 30-minute lecture, Johnson will answer questions from participants on Zoom about her research and career path.

This annual series highlights the achievements of NIGMS's early-career grantees. It is designed to introduce students and other early-career scientists to cutting-edge research and inspire them to pursue careers in the biomedical sciences.

Established in 2016 and originally called the NIGMS Director's Early-Career Investigator Lecture, the series was renamed in 2021 to honor former NIGMS deputy director Greenberg, who retired in 2020 after 45 years of service to NIH.

Anyone interested in viewing the event can attend via NIH videocast. Students and trainees are encouraged to register in Zoom so they can participate in the live Q&A following the lecture.

For details, visit https://www.nigms.nih.gov/News/meetings/Pages/2021-nigms-directors-early-career-investigator-lecture-aspx.aspx.

SAVE THE DATE

Virtual Seminar on Grants Administration Set, Nov. 1-4

Plan to participate in NIH's Virtual Seminar on Grants Administration and Program Funding, which is scheduled for Monday, Nov. 1 to Thursday, Nov. 4. The annual event is intended to help demystify the application and review process, clarify federal regulations and policies and highlight current areas of special interest or concern.

If you are an administrator, researcher, early-stage investigator, graduate student or anyone new to working with the NIH grants process, then this seminar is designed specifically for you. Visit https://grants.nih.gov/2021-nih-virtual-seminar.htm#registration to be notified when registration opens. Email questions about the seminar to NIHRegionalSeminars@nih.gov.

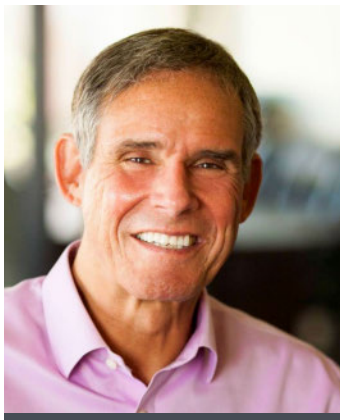
Topol

CONTINUED FROM PAGE 1

grant to help lead the Precision Medicine Initiative Cohort Program (now known as All of Us Research). However, it may be another pursuit for which he is best known—"world-class Twitter meister."

That's how NIH director Dr. Francis Collins described Topol, who has attracted more than 440,000 followers on social media.

"His tweets are probably the most information-rich of any in biomedicine," Collins remarked, describing how Topol "with all kinds of creativity is always trying to push the limits of what's possible into an even more exciting technological space, while retaining this critical aspect of keeping medicine about people and maintaining that compassion and that human focus."



Dr. Eric Topol

Topol used his WALS lecture, "Deep Medicine: How Artificial Intelligence Can Make Medicine Human Again," to point out ways that doctors who combine their expertise with machine learning are in fact exemplifying the care in health care.

Noting a recent National Academy of Medicine report that more than 12 million significant medical diagnostic mistakes are made every year and that every person will experience at least one such error during their lifetime, Topol talked first about precision medicine.

"That's where AI will have its biggest early impact," he said. "Precision medicine has become an important objective and a buzz word, but what we really want is not just precision medicine—that is, making the same mistakes consistently—but also we want accurate medicine. That's the end goal, and that's where AI can make a big difference."

Topol said we achieve medical accuracy by plumbing the depths of "deep neural networks," a subtype of AI.

Contrasting illustrations of actual neurons with artificial neurons, he described the system of connections, relationships and associations that machines establish using inputs of data—images, speech, text. Deep neural networks can be "trained" with hundreds of thousands, even millions more data points than human diagnosticians.

More training, more experience with similar information—"augmentation of interpretation"—leads to greater accuracy, Topol said, showing results from studies of chest x-rays and mammography where more tumors were detected routinely by machines using deep neural networks than by their human counterparts.

Topol pointed to images of human retinas from a study on predicting sex. Human retina experts viewing the photos were correct about half the time. The deep neural network had a 97 percent accuracy rate.

"There are better ways to predict sex than by looking at retinas," Topol acknowledged, "but I think it conveys that we can have machines see things better than humans and certainly the best is a fusion of efforts."

That growing collaboration between human care providers and well-coded computers or algorithms can revolutionize every aspect of the field, Topol said.

"Deep learning is going to have its effects across the board," he said. "There is no specialty or domain in medicine or health care—extending to pharmacists, paramedics and nurses—that will not benefit from some machine support."

Sharing a forecast by internationally acclaimed neurosurgeon Dr. Antonio Di Leva, Topol said, "Machines will not replace physicians, but physicians using AI will soon replace those not using it."

With an illustration that the future is now, Topol also described "momentous AI in the real world"—work that is helping critically ill infants today.

At Rady's Children's Institute in San Diego (and across the nation), physicians are using deep learning algorithms to progress from blood DNA sample of the ailing child to accurate diagnosis and management of the condition within 18 hours.

The practical result has been that even neonatologists and pediatricians without rare disease experience or expertise can have the best advice for managing very sick newborns.

Topol also acknowledged several of the cons involved with employing AI medicine, including concerns about privacy, accountability, safety and security, fairness, non-discrimination and bias. Many negative effects and results may not be due to algorithm error, he explained, but to problems with data input.

Basically, if the data points entered into the deep neural network are not from diverse populations, then the results AI derives will be neither accurate nor applicable to the widely diverse patients they're meant to serve.

Another growing trend to be mindful of, Topol suggested, are AI devices—smartwatches, biosensors and other wearables. These popular instruments empower people with their own health data, but that knowledge can have unexpected consequences if not also paired with physician guidance and advice.

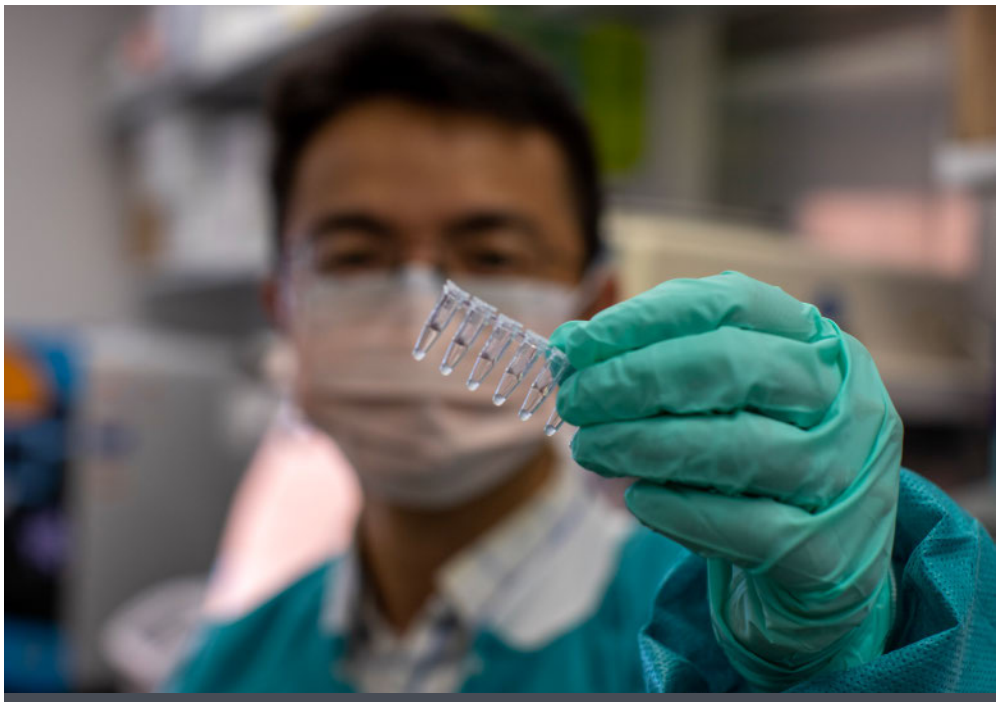
Ultimately, Topol concluded, AI returns to doctors the "gift of time." By allowing machines to carry out some labor-intensive and redundant tasks—synthesis of patient data, keyboarding medical records, primary/screening review of dozens of images and diagnosis of routine non-serious conditions, for instance—doctors can resume what they do best: providing care.

"I think we can all agree there isn't any algorithm for empathy," he said. "This is what we are for—the human connection. We aren't suddenly going to become more intelligent. But machines are. Our charge is to get more humane."

Topol said a physician's primary purpose was expressed succinctly by celebrated Harvard professor Dr. Francis Peabody nearly a century ago in a 1927 *JAMA* article that closed with this line: "'One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.' If we do this right, AI can help us with this most vital goal."

Topol's full lecture is archived at https://videocast.nih.gov/watch=41589.

WALS kicks off its 2021-2022 season on Sept. 29 with Dr. Sherita Hill Golden, vice president and chief diversity officer at Johns Hopkins Medicine. For a preview of the schedule, visit https://oir.nih.gov/wals/2020-2021/sneak-peek-2021-2022-season-click-here.



Dr. Bin Guan, a fellow in NEI's Ophthalmic Genomics Laboratory, holds samples prepared with the chelating agent that preserves SARS-CoV-2 RNA for detection by RT-qPCR.

PHOTO: DUSTIN HAYS, NEI

INTRAMURAL COLLABORATION

Faster Covid-19 Test Developed by NIH'ers

BY CLAUDIA COSTABILE

NIH scientists developed a new sample preparation method to detect SARS-Cov-2, the virus that causes Covid-19. The method bypasses extraction of the virus's genetic RNA material, simplifying sample purification and potentially reducing test time and cost. The method is the result of a collaboration among researchers at the National Eye Institute, the Clinical Center and the National Institute of Dental and Craniofacial Research.

Diagnostic testing remains a crucial tool in the fight against the Covid-19 pandemic. Standard tests for detection of SARS-CoV-2 involve amplifying viral RNA to detectable levels using a technique called quantitative reverse transcription PCR (RT-qPCR). But first, the RNA must be extracted from the sample. Manufacturers of RNA extraction kits have had difficulty keeping up with demand during the pandemic, hindering testing capacity worldwide. With new virus variants emerging, the need for better, faster tests is greater than ever.

A team led by Dr. Robert Hufnagel, chief of NEI's medical genetics and ophthalmic genomics unit, and Dr. Bin Guan, a fellow in NEI's Ophthalmic Genomics Laboratory, used a chelating agent called Chelex 100 resin to preserve SARS-CoV-2 RNA in samples for detection by RT-qPCR. Lab supply company Bio-Rad made the agent.

"We used nasopharyngeal and saliva samples with various virion concentrations to evaluate whether they could be used for direct RNA detection," said Guan, lead author of a report on the technique published in *iScience*. "The answer was yes, with markedly high sensitivity. Also, this preparation inactivated the virus, making it safer for lab personnel to handle positive samples."

Hufnagel's team made their discovery by testing a variety of chemicals using synthetic and human samples to identify those that could preserve the RNA in samples with minimal degradation while allowing direct detection of the virus by RT-qPCR.

To validate the test, NIDCR's Dr. Blake M. Warner and his team collected patient samples and stored them in either viral transport media or the newly developed chelating-resin-buffer at the NIH Symptomatic Testing Facility.

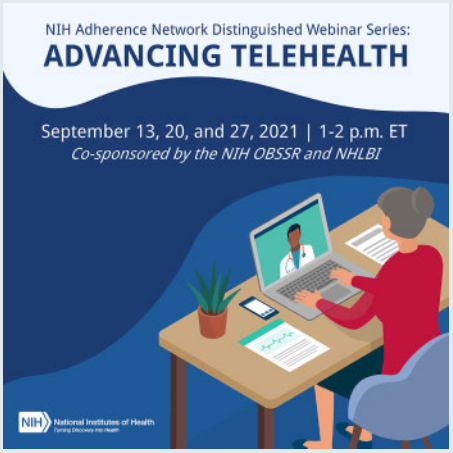
The samples in viral transport media were tested by CC's Covid testing team led by Dr. Karen M. Frank, using conventional RNA extraction and RT-qPCR testing. The samples in the chelating-resin-buffer were heated and the viral RNA was, then, tested by RT-qPCR. The new preparation significantly increased the RNA yield available for testing, compared to the standard method.

"We think this novel methodology has clear benefits of increasing sensitivity, cost and time savings for testing," said Hufnagel. "The method stabilizes the RNA at room temperature for easier transport, storage and handling in clinical settings." R

3-PART SERIES

NIH To Host Webinars on Advancing Telehealth

Telehealth has rapidly expanded during the Covid-19 pandemic. A three-part webinar series will explore opportunities, challenges and research needs in using telehealth approaches to keep patients engaged and committed to health care regimens. Join the NIH Adherence Network and cosponsors—the Office of Behavioral and Social Sciences Research and



the National Heart, Lung, and Blood Institute—for these online, public events:

- **Telemedicine/Telehealth: Promoting Wellness in Underserved Communities Using Technology**
  Monday, Sept. 13, 1-2 p.m. ET
  Michael Ray Murphree, Medical Advocacy and Outreach
  https://videocast.nih.gov/watch=42505

- **Covid and the Telehealth Transformation of Mental Health Treatment and Services: Navigating New Opportunities and Challenges**
  Monday, Sept. 20, 1-2 p.m. ET
  Dr. Jay Shore, University of Colorado
  https://videocast.nih.gov/watch=42549

- **Telemedicine and Pediatric Outpatient Care During Covid-19**
  Monday, Sept. 27, 1-2 p.m. ET
  Dr. Kirstin Ray, University of Pittsburgh School of Medicine
  https://videocast.nih.gov/watch=42551

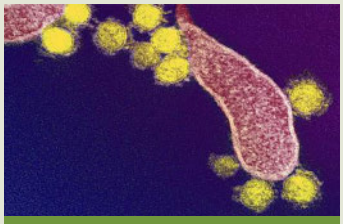
Registration is not required. All staff, colleagues, family and friends are encouraged to join.

Intranasal Covid-19 Vaccine Effective in Animal Studies

A nasal spray of the Oxford/AstraZeneca Covid-19 vaccine protected hamsters and monkeys against serious disease and reduced the amount of virus in the nose. Less virus in the nasal passages could reduce the risk that vaccinated individuals spread the virus. The findings appeared in *Science Translational Medicine.*

All Covid-19 vaccines now in use are injected into the muscle. This produces antibodies that circulate in the blood to recognize the virus. But intramuscular injection might not produce antibodies in the nose and nasal passage, which has raised the possibility that vaccinated people could still catch and spread the virus, even when they don't know they're infected. Vaccines given through the nose may be able to block SARS-CoV-2 in the nasal passages and bloodstream.

In the study, both intranasal and intramuscular administration of the Oxford/AstraZeneca vaccine produced high levels of antibodies against SARS-CoV-2, the virus that causes Covid-19, in the blood of hamsters after a single dose.



SARS-CoV-2 virus particles emerge from the surface of a cell cultured in the lab.

IMAGE: NIAID

When vaccinated and unvaccinated hamsters were then exposed to SARS-CoV-2, both vaccine administration routes protected hamsters from serious disease. Unvaccinated hamsters lost weight and showed signs of lung damage, but vaccinated hamsters did not. Those that received intranasal vaccination also had substantially less infectious virus in their nasal passages than unvaccinated animals.

The researchers next tested two doses of the intranasal vaccine in monkeys. Antibodies were found in the blood after the second dose, at levels resembling those seen in people who have recovered from Covid-19.

When the monkeys were then exposed to SARS-CoV-2, those that received the intranasal vaccine had less virus in their noses and lung tissue. And, 3 of 4 unvaccinated monkeys developed symptoms of pneumonia, while none of the vaccinated ones did.

More work is needed to understand the different immune response between the two routes of administration. A clinical trial is underway to test intranasal vaccination in people.—Brian Doctrow, *NIH Research Matters*

PHOTO: WAYHOME STUDIO/SHUTTERSTOCK

Pain Management Class Packs a Punch

A new study suggests a single 2-hour session of a pain management skills class could offer as much benefit as 8 sessions of cognitive behavioral therapy (CBT) for patients experiencing chronic low-back pain (CLBP). Supported by NCCIH and NIDA, the study—published in *JAMA Network Open*—explored whether a compressed intervention could lead to the same benefits as a longer course of CBT.

There's an increase in the use of surgery and medications to manage CLBP—the most common source of chronic pain worldwide—though growing evidence has led to pain education and CBT being recommended as first-line treatments.

The research team at Stanford University recruited 263 adults who had experienced CLBP for at least 6 months. The 87 patients randomized to the empowered relief group participated in a single, 2-hour pain relief skill-building class that incorporated pain education, mindfulness principles and such self-regulatory skills as relaxation, cognitive reframing and self-soothing. The 88 patients in the CBT group participated in eight 2-hour classes in pain management education and active cognitive behavioral skill-building. Within the health education group, 88 patients participated in a single 2-hour class about back health.

In the study, the primary outcome was measured in differences in the Pain Catastrophizing Score using a scale that evaluates 13 cognitive and emotional responses to pain. Pain catastrophizing can lead to increased attention to pain and feelings of helplessness or loss of control, which can prompt neural circuits in the brain to amplify pain signals.

When comparing Pain Catastrophizing Scale scores at 3 months after intervention, outcomes in the empowered relief group were on par with the CBT group, while researchers found that both CBT and empowered relief were superior to the health education session.

"CBT delivered in groups can offer important elements like contact with a therapist and peer support," said NCCIH director Dr. Helene Langevin. "But we realize that 16 hours of treatment time and the associated costs could be out of reach for some patients, so this research could expand treatment options and make nonsurgical and nonpharmaceutical pain management accessible to more patients."

Monoclonal Antibody Prevents Malaria in Small Trial

One dose of a new monoclonal antibody discovered and developed at NIH safely prevented malaria for up to 9 months in people exposed to the malaria parasite. The small clinical trial is the first to demonstrate that a monoclonal antibody can prevent malaria in people.

Findings from the trial, conducted by scientists from the Vaccine Research Center at NIAID, were published in the *New England Journal of Medicine.*

So far, no licensed or experimental malaria vaccine that has completed Phase 3 testing provides more than 50 percent protection from the disease over the course of a year or longer.

Malaria—a major cause of illness and death worldwide—is caused by *Plasmodium* parasites transmitted by the bite of an infected mosquito. The mosquito injects the parasites in a form called sporozoites that enter a person's skin and bloodstream. *P. falciparum* is the *Plasmodium* species most likely to result in severe malaria infections which, if not promptly treated, can be fatal.

Researchers led by Dr. Robert Seder, chief of VRC's cellular immunology section, found that a naturally occurring neutralizing antibody called CIS43 binds to a unique site on a parasite surface protein that facilitates malaria infection and is the same on all variants of *P. falciparum* sporozoites worldwide. The researchers subsequently modified this antibody, creating CIS43LS.

During the first half of the Phase 1 clinical trial, the study team gave half the participants one dose of CIS43LS. All participants in the second half of the trial consented to be exposed to *P. falciparum* in a controlled human malaria infection (CHMI), through bites of infected mosquitos in a carefully controlled setting.

Nine participants who had received CIS43LS voluntarily underwent CHMI and were closely monitored for 21 days. None of them developed malaria, but 5 of the 6 controls did. Further study indicated that 1 dose of the experimental antibody can prevent malaria for 1 to 9 months after infusion.

To build on this finding, a larger NIAID-sponsored Phase 2 clinical trial is underway in Mali during a 6-month malaria season.

"Monoclonal antibodies may represent a new approach for preventing malaria in travelers, military personnel and health care workers traveling to malaria-endemic regions," said Seder. "Further research will determine whether monoclonal antibodies can also be used…ultimately for malaria-elimination campaigns."

Dr. Bernard Talbot

Talbot Retires After 5-Decade Tenure at NIH

BY AMANDA CENNAME

Dr. Bernard Talbot retired in July 2021, marking the closure of a 51-year NIH career. He most recently served as a medical officer in the NCATS Division of Clinical Innovation (DCI), where he oversaw a portfolio of multimillion-dollar Clinical and Translational Science Awards Program grants.

He joined NIH in 1970 as a grants associate in the Division of Research Grants (now CSR) and served in numerous roles across NIH. These positions included special assistant to the NIH director (1978–1981), NIAID deputy director (1981–1987) and acting director (1984) and NCRR (National Center for Research Resources) program officer (1987). Talbot joined NCATS in 2011.

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"In the textbook entry for institutional memory, a photo of Bernie is the visual representation of this concept, and it is this aspect which will be most acutely felt."

–DR. MICHAEL KURILLA

• • •

Talbot earned an M.D. from Columbia University and a Ph.D. from Massachusetts Institute of Technology. He completed postdoctoral fellowships there and at the University of Rome.

Talbot shared his knowledge of recombinant DNA with members of the research community and key policymakers. He was awarded a U.S. Public Health Service Commendation Medal in 1977 for his outstanding dedication and superior performance in support of NIH recombinant DNA research activities.

Additionally, Talbot was called to testify before Congress on numerous occasions. His recombinant DNA expertise and advice were crucial in the development of the NIH Guidelines for Recombinant DNA Research through the Federal Register.

Talbot also contributed his experience and expertise on numerous government-wide interagency committees. He served as executive secretary of the industrial practices subcommittee of the federal interagency advisory committee on recombinant DNA research. Talbot was a member of the Public Health Service steering committee for the protection of human subjects, the Office of Science and Technology Policy interagency working group on biotechnology, the HHS Secretary's Task Force on Alzheimer's Disease and the Cabinet Council working group on biotechnology.

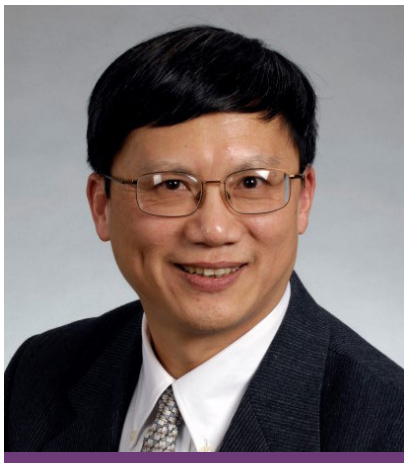
"In the textbook entry for institutional memory, a photo of Bernie is the visual representation of this concept, and it is this aspect which will be most acutely felt," reflected Dr. Michael Kurilla, DCI director. "Dr. Talbot's many years of service and outstanding contributions to the NIH, the broader scientific community and the general public set the standards for a truly impactful career."

Talbot planned to begin his retirement by traveling to Denmark with his wife for the summer. He hopes that some of those whose paths he has crossed in all his years at NIH might email him at berntalbot@gmail.com.

IRG Chief Ni Retires from CSR

BY PAULA T. WHITACRE

Language propelled Dr. Weijia Ni from his childhood in Shanghai, China, through a decade-long ordeal on a state farm during the Cultural Revolution, to education and a career in the United States. After 20 years at NIH, he retired Aug. 31 as chief of the Risk Prevention and Health Behavior Integrated Review Group in the Center for Scientific Review.



Dr. Weijia Ni

In the early 1960s, Ni was chosen to attend an English-language elementary school. That association, combined with his parents' careers as professors, contributed to hardship when China's political winds changed. His family was separated, his schooling ceased and he labored at a remote camp near the Sino-Siberian border.

When universities re-opened in 1978, he was determined to earn one of the coveted spots. Studying alone at night, he regained his English-language skills and graduated with a bachelor's degree in English in 1981 from Heilongjiang University in Harbin.

Ni went on to graduate studies in linguistics at Fudan University in Shanghai. Through the Open Door Policy, President Ronald Reagan visited Shanghai in 1984. His speech at Fudan inspired Ni and other students to seek advanced education in America. With the assistance of a U.S. Fulbright professor, Ni obtained a scholarship to study linguistics at the University of Connecticut. In 1985, he boarded a plane for the first time, with $40 in his pocket.

Ni earned his doctorate from UConn in 1991. After postdoctoral work at Haskins Laboratories at Yale, he conducted NIH-funded research on language disabilities at Haskins and other locations. He came to CSR in 2001.

"People were surprised that a Ph.D. linguist would work at NIH," he said, but explained that CSR sought expertise in his fields of psycholinguistics and neurolinguistics. The two study sections he helped launch after he came to CSR remain strong. In addition to serving as scientific review officer for 12 years, he worked as a referral officer for 9 of those years.

With encouragement from mentors and colleagues, Ni became IRG chief in 2013, managing a strong team of SROs. They, in turn, value his guidance and exemplar.

"He is an extraordinary mentor who epitomizes the role of servant-leader," said Dr. Miriam Mintzer, an SRO who nominated Ni for HHS's Dr. Francisco Sy Award for Mentorship. "He's in the trenches working side by side with us and at the same time he motivates us and gives us lots of autonomy."

One of Ni's NIH legacies is a database tool he developed called Review Management (RM) that tracks the multiple aspects of peer review and is used by more than 100 review officers in CSR and various institutes and centers. Mintzer noted Ni has continually improved RM and trained review officers to use it. He needed to prepare six SROs to maintain RM after his retirement.

Dr. Samuel Edwards, chief of the Brain Disorders and Clinical Neuroscience IRG, came to know Ni through participation in leadership training and experiences shared as fellow IRG chiefs. "Weijia is renowned as being hands-on, fair and honorable," Edwards said. "He is dedicated to the review process."

With his daughter completing her medical residency at Mount Sinai and beginning a fellowship at Montefiore Medical Center, Ni said, "I feel I can retire now."

Atop his agenda when possible after Covid-19: a visit to his and his wife's parents in China.

NINDS Nonprofit Forum Highlights Early Diagnosis, Patient Advocate Passion

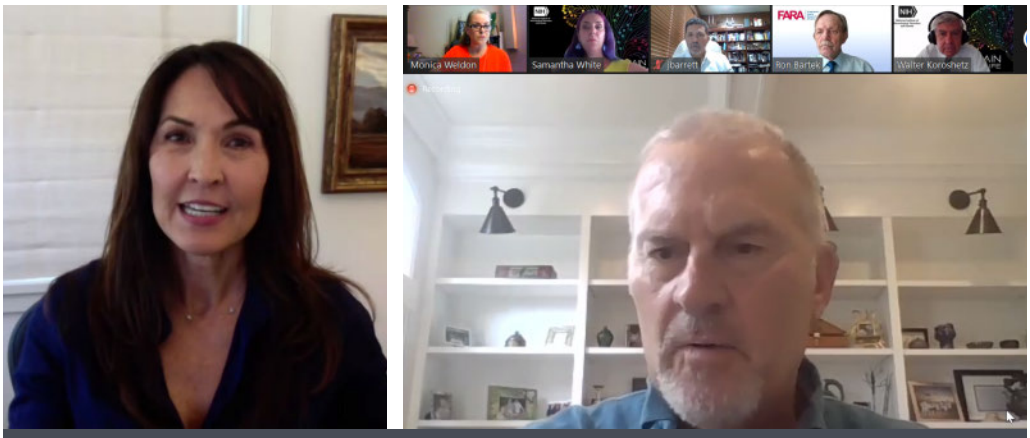
BY SHANNON E. GARNETT

NINDS's 15th nonprofit forum, "Progress through Partnership," drew its largest crowd to date with more than 260 participants. Representatives from more than 100 patient advocacy organizations across the country gathered virtually on July 7-8 to network with colleagues, learn about NIH and NINDS and engage with NINDS staff.

"Over the last year, all of us have been working remotely from these little rectangular boxes," said NINDS director Dr. Walter Koroshetz. "And in terms of advancing our mission, it's clearly been harder to connect with what it's all about, which is the patients and how to develop better treatments, figure out ways to better diagnose conditions, and reduce the burden of illness. By connecting with the people at this forum, we become reinvigorated."

NINDS director Dr. Walter Koroshetz welcomes participants to the recent virtual nonprofit forum.

Before the meeting, registrants were treated to a private showing of the movie *SPARK: Robin Williams and His Battle with Lewy Body Dementia (LBD)*. The 45-minute documentary—adapted from the feature film *Robin's Wish* that was released last fall—promotes awareness of LBD and was commissioned by the Lewy Body Dementia Association.



Susan Schneider, wife of the late Robin Williams, shared her journey to becoming a biomedical research advocate. Dr. David Cella of the Northwestern University Feinberg School of Medicine spoke about resources available to patient advocates and researchers.

The documentary served as preparation for the forum keynote speaker Susan Schneider Williams, wife of the late performer. She talked about the background of both films, the struggle she and her husband faced in finding a diagnosis and her journey to becoming a biomedical research advocate.

"Our story, what we went through, is an example of what you don't want to have happen," said Schneider. "Our story is not unique either. There are over a million and a half people dealing with this [LBD] in the United States alone."

Schneider emphasized the importance of getting a diagnosis and underscored one of the overall themes of the forum—the value of an early diagnosis.

"Diagnosis is everything, not only with this disease but with so many diseases. For someone with a LBD diagnosis, at least you would know you could stop chasing the unknown foe," she explained. "Diagnosis gives you your power back. When you have a proper diagnosis, you have more of a chance of getting the correct help. And that's key, particularly for a disease like Lewy body dementia."

The meeting also featured three timely panel discussions. "Clinical Solutions Following Covid" focused on ways researchers and clinicians were able to adapt in the wake of the pandemic and how they hope increased flexibility and accessibility will inform trial design in the future. Panelists explored health equity during the "Patient Engagement: Co-Producing Clinical Success" discussion as moderators emphasized NINDS efforts to address the needs of diverse stakeholders across the research landscape.

At the "Nonprofit Tools and Resources of Note" session, presenters shared several tools available including the NIH Toolbox (a comprehensive set of neuro-behavioral measurements to assess cognitive, emotional, sensory and motor functions) and PROMIS (Patient-Reported Outcomes Measurement Information System).

The forum provided several opportunities for nonprofit representatives to engage with NINDS staff including pre-scheduled one-on-one discussions and the Meet the Program Directors session.

The meeting concluded with success stories from three advocate scientists and mothers—Dr. Allyson Berent of the Foundation for Angelman Syndrome Therapeutics, Dr. Nathalie Maitre of NICU Developmental Therapies at Nationwide Children's Hospital and Dr. Dominique Pichard of the International Rett Syndrome Foundation (IRSF).

In each presentation a common thread was woven through all patient advocacy groups and throughout the meeting—passion.

"Passion drives this work. It was a passion of those original families that started our two legacy foundations," Pichard said. "And it's the passion of the individuals that continues to work in the IRSF. And that helps to make a difference every single day. A small, yet ambitious group can really make a significant impact."

Panelists encouraged the group to connect with pharmaceutical companies, reach out to the Food and Drug Administration early to talk about natural history studies and engage with industry especially regarding regulatory information and registries.

Speakers also shared information on clinical trial readiness and the importance of early diagnosis. "The earlier the better," said Berent. "The earlier the diagnosis, the earlier the intervention and potentially the better the outcome."

In closing, Koroshetz explained how the passion of patient advocates can drive scientists to develop treatments.

"From the scientist's point of view," he said, "science is mostly motivated—at least early on—by curiosity, but that doesn't necessarily get you to treatments. What gets you to the treatments is the passion. It's really something that should not be underestimated because it's the passion of the people we heard talking today who are in the nonprofits, many of whom have kids with disorders, that really drives the treatments. The passion that you have is contagious and what you want to do is infect the right people with your passion. You want to spread the passion that you have to the people who can help you get to your goal and that's the scientists, and sometimes, it's people like the FDA and sometimes it's the people at NIH."

For more information on NINDS nonprofit forums, visit https://www.ninds.nih.gov/About-NINDS/Who-We-Are/Nonprofit-Forum.