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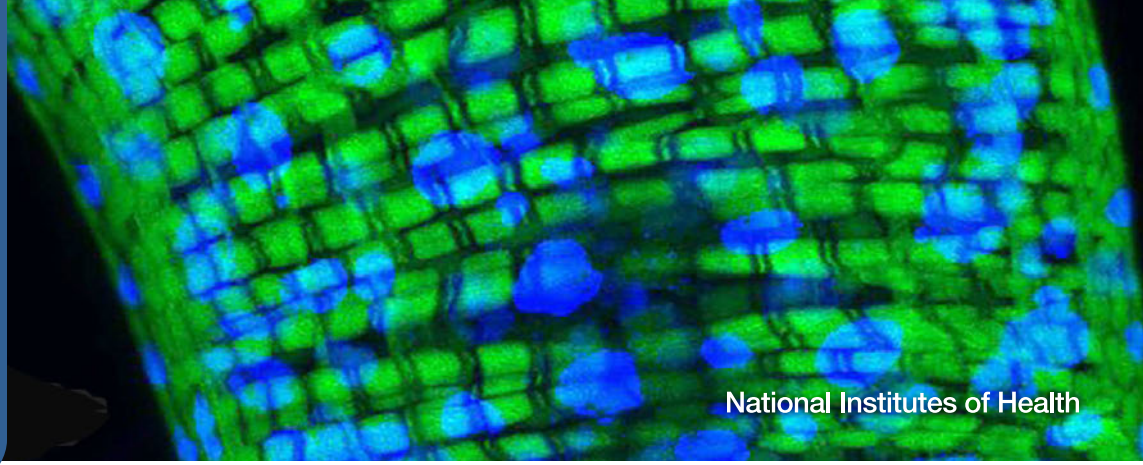


'STICKING CLOSE TO THE SCIENCE'

8th Town Hall on Coronavirus Provides Updates, Outlook

BY CARLA GARNETT

NIH director Dr. Francis Collins moderated an 8th virtual town hall on coronavirus on Sept. 10 to provide a status update on Covid-19 and its impact on NIH's community. Close to 14,500 people tuned in live, with nearly 1,000 viewing on demand via NIH VideoCast.

"I sincerely hoped the Covid-19 pandemic would have been mostly over by now," he said. "But as we at NIH know—all too well—we are not there yet. The Delta variant had other plans."

Joining him on screen were familiar

The NIH director updates employees at the Sept. 10 virtual town hall on coronavirus.

pandemic point person (and President Biden's chief medical advisor) NIAID director Dr. Anthony Fauci, NIH deputy director for management Dr. Alfred Johnson, Office of Research Services Director Colleen McGowan and Chief People Officer Julie Berko.

Presenters all wore the color yellow in recognition of National Suicide Prevention Day (Sept. 10), which Collins acknowledged as "another public health crisis." Promoting active maintenance of mental health, especially during the past several months of varying degrees of unusual social isolation worldwide, has been an important point of emphasis. In addition, the town hall occurred the day before the U.S. marked the 20th anniversary of the 9/11 terrorist attacks.

The hour-long meeting's agenda included briefings on the state of the pandemic, treatments and vaccines; new vaccination requirements for staff; and plans for eventual return to the physical workplace. NIH leadership also answered more than a dozen top frequently asked questions; more than 450 queries had been submitted in the weeks leading up to meeting day.

"Unfortunately, this is not where we thought we would be after the development of highly effective and safe vaccines," Collins said. "The highly contagious nature of

SEE **TOWN HALL**, PAGE 6

NSO performs again at the Clinical Center. See story, p. 12.

ALSO THIS ISSUE

REDIRECTING CALCULATIONS

Mathematical Biologist Takes Up Covid Modeling

BY AMBER SNYDER

Dr. Carson Chow

Like many NIH researchers faced with the devastating Covid-19 pandemic, Dr. Carson Chow shifted to mandatory telework, wondering how he could contribute to the world's understanding of the virus. To many, though, his pivot to Covid research might seem incongruous.

A mathematical biologist, Chow is a senior investigator in NIDDK's Laboratory

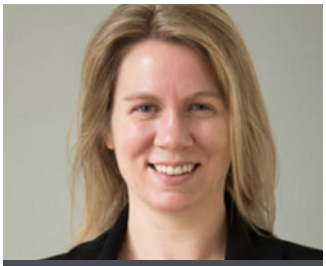
SEE **MATH**, PAGE 4

This is the fifth and final article in a series on intramural scientists who pivoted their research to pursue a pandemic-related topic.

Robinson Studies Genetic Variation and Autism

BY DANA TALESNIK

The diagnosis of autism spectrum disorder (ASD) includes a wide range of behavioral and cognitive symptoms and outcomes. Researchers are learning more about this variability thanks to genetic data.



Dr. Elise Robinson

"ASDs are not one thing; they are many different things," said Dr. Elise Robinson, at a recent NIMH Director's Innovation Speaker Series lecture. "We're starting to be able to use genetic data to understand variability within the diagnostic category of autism, as well

SEE **ROBINSON**, PAGE 8

NIAID's Dr. Michael Proschan will give ODP's next Mind the Gap webinar.

Proschan to Present Methods Webinar, Oct. 15

Join the Office of Disease Prevention for a Methods: Mind the Gap webinar with Dr. Michael Proschan on the use of randomization-based inference in prevention research. This webinar will take place on Friday, Oct. 15 at 11 a.m. ET.

Clinical trials are the gold standard of medical evidence and randomization is the cornerstone of clinical trials. In this presentation, Proschan will show how to conduct a test of an intervention effect using only the randomization.

This "randomization test" is valid with virtually no assumptions and can be applied regardless of the randomization method—simple, permuted block, even covariate- or response-adaptive randomization (but avoid response-adaptive randomization in clinical trials!). With the most standard randomization methods, the randomization test is nearly the same as a t-test if the sample sizes are large.

Randomization tests can also be used to construct confidence intervals. If your trial requires major unplanned changes and you have not yet broken the treatment blind, guess what approach can save you? That's right—the randomization test!

Proschan is a mathematical statistician at NIAID with 32 years of experience in clinical trials. He received his Ph.D. in statistics from Florida State University in 1989 and is a fellow of the American Statistical Association. He loves teaching and has been an adjunct professor at Johns Hopkins University and George Washington University. He is co-author of two books, *Statistical Monitoring of Clinical Trials: A Unified Approach* and *Essentials of Probability Theory for Statisticians*, and just completed a third book, *Statistical Thinking in Clinical Trials* (in press).

Registration is required. Register at prevention.nih.gov/education-training/methods-mind-gap/randomization-based-inference-prevention-research. The webinar will be recorded and available on the ODP website within approximately 1 week.

The webinar series explores research design, measurement, intervention, data analysis and other methods of interest in prevention science. For more information, visit prevention.nih.gov/MindTheGap.

Virtual Workshop on Telehealth in Rural Areas Set, Oct. 12-14

NIH's Office of Disease Prevention will host the Pathways to Prevention Workshop: Improving Rural Health Through Telehealth-Guided Provider-to-Provider Communication on Oct. 12–14. This virtual workshop is free and open to the public.

Telehealth-guided collaboration between care providers has the potential to increase access to services and improve health outcomes in rural areas. However, more research is needed to better understand how provider-to-provider telehealth affects rural patients, populations, health care providers and payers. Workshop speakers will identify those research gaps and explore barriers to and facilitators of successful and sustainable implementation of provider-to-provider telehealth in rural settings.

The workshop is co-sponsored by NCATS, NHLBI, the Health Resources & Services Administration and the Centers for Disease Control and Prevention.

Learn more or register for the workshop at prevention.nih.gov/P2P-RuralHealth.

CFC Hosts Virtual Halloween Event

Masks Due Oct. 6

NIH's 2021 Combined Federal Campaign will host a virtual Halloween Charity Fair and Mask Contest on Thursday, Oct. 28, from 11 a.m. to 1 p.m. Returning this year by popular demand, the event combines fun and CFC information. Three charities will discuss their mission and how important donors are to reaching their goals.

1st place winning mask from 2020, "Love Conquers All" by Lisa King of NCI

In the contest, participants create original masks with a special theme—"Superheroes." For details on entering your design, visit https://cfc.nih.gov/. All mask entries are due on Wednesday, Oct. 6.

The CFC is the federal government's largest workplace giving campaign. It provides an opportunity to support favorite causes easily and efficiently. Donors choose from more than 6,000 local, national and international organizations participating in the 2021 effort. The national CFC theme is "You Can Be the Face of Change." NIH has a $1M goal.

Ogunyemi To Give Next Lovelace Lecture

Dr. Omolola Ogunyemi will deliver the NLM Ada Lovelace Lecture on Tuesday, Oct. 12 from 3 to 4 p.m. ET via videocast. She will discuss "Tackling Diabetic Retinopathy in a Safety Net Healthcare Setting with Telehealth and Machine Learning."

Dr. Omolola Ogunyemi

The talk will describe the approach taken to address diabetic retinopathy in a medically underserved area (South Los Angeles) by researchers in the Center for Biomedical Informatics at Charles R. Drew University of Medicine and Science, using telehealth and machine learning on data from patient electronic health records.

Ogunyemi is director of Drew University's Center for Biomedical Informatics and a co-chair of the UCLA CTSI's biomedical informatics program. She is also an adjunct professor of radiological sciences in the David Geffen School of Medicine at UCLA with the medical and imaging informatics group. She was recently a principal investigator on a National Library of Medicine-funded R01 grant to develop a variety of machine learning approaches for identifying patients with latent/undiagnosed diabetic retinopathy from electronic health records or digital retinal images.

Her talk will be broadcast live and archived at https://videocast.nih.gov/watch=43839.

'Feds Feed Families' Ends for Summer

The 2021 Feds Feed Families Virtual Campaign has ended. This summer, NIH donated almost 175,000 pounds of food to our local communities to assist children, older adults, veterans and families who are in need. Across the federal workforce, more than 7 million pounds of food have been donated.

While the campaign is ending, the need, of course, continues. For those who want the opportunity to continue to assist, there are ways to give year-round to support those who face food insecurity:

• Find a food bank or pantry through the Ample Harvest website (https://ampleharvest.org/find-pantry/) or on your own. Give directly to that site and record your donations using the Feds Feed Families Record Donation Form (https://survey123.arcgis.com/share/10a5efa3de024beda91d4c61b0bc0a4f?portalUrl=https://usfs.maps.arcgis.com). You can record donations all year long.

• Make a Combined Federal Campaign "two-for-one" contribution. The CFC giving season takes place through Jan. 15, 2022. If you donate to a food bank or pantry through CFC, you can also record that donation on the Feds Feed Families Record Donation Form (https://survey123.arcgis.com/share/10a5efa3de024beda91d4c61b0bc0a4f?portalUrl=https://usfs.maps.arcgis.com).

MOSAIC scholars Dr. Cassandra Hayne and Dr. John Jimah

Intramural Postdocs Named MOSAIC Scholars

The final FY 2021 Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC) scholar awards were issued recently. Four were awarded to postdocs in NIH's Intramural Research Program:

Dr. Cassandra Hayne of NIEHS, Dr. John Jimah and Dr. Agnes Karasik of NIDDK and Dr. Velencia Witherspoon of NICHD. All are funded by NIGMS.

MOSAIC facilitates the transition of promising postdoctoral researchers from diverse backgrounds into independent faculty careers at research-intensive institutions. The program provides these scientists with up to 5 years of mentored career development and research support.

In addition, each scholar becomes part of a cohort-based career development program to expand their professional networks and gain additional skills and mentoring through programs administered by MOSAIC UE5 awardees—the American Society for Biochemistry and Molecular Biology, the American Society for Cell Biology and the Association of American Medical Colleges.

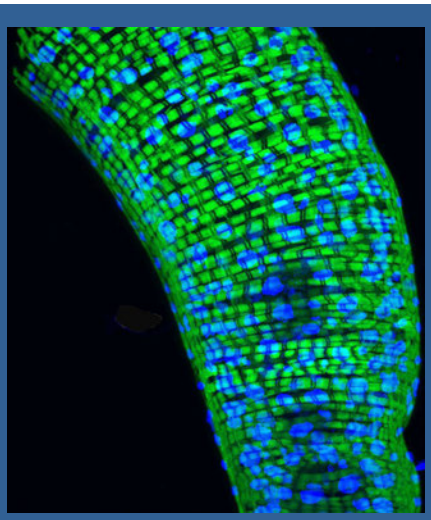
About 75 percent of MOSAIC scholars are from racial/ethnic groups that are underrepresented in the biomedical sciences. To see the complete list of 2021 scholars funded NIH-wide, visit: https://www.nigms.nih.gov/training/careerdev/Pages/mosaic-scholars.aspx.

An inaugural annual meeting for the scholars, featuring scientific sessions highlighting their research, will be held virtually Oct. 14-15 from 1 to 5 p.m. ET each day. NIH director Dr. Francis Collins, NIGMS director Dr. Jon Lorsch and NIH chief officer for scientific workforce diversity Dr. Marie Bernard are scheduled to address attendees. NIA director Dr. Richard Hodes, NIMHD director Dr. Eliseo Pérez-Stable, NIDCD director Dr. Debara Tucci and NIDA director Dr. Nora Volkow also will participate.

For more information about the meeting, visit: https://mregs.nih.gov/channels/Z142-A515.

NIH accepts applications for the MOSAIC K99/R00 award three times per year. Wednesday, Oct. 27 is the next application receipt date. Awards are limited to U.S. citizens and permanent residents.

MOSAIC scholars Dr. Agnes Karasik (l) and Dr. Velencia Witherspoon



ON THE COVER: *Drosophila fly gut, a key source of bacteria*

IMAGE: GINIGER LAB, NINDS

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

At a pre-Covid in-person lecture, Chow discusses how he deploys NIH Biowulf supercomputing resources in his math modeling research.

Math

CONTINUED FROM PAGE 1

of Biological Modeling. He has worked at NIH since 2004, using math to understand and model conditions such as obesity. Most recently, Chow has been employing mathematical modeling to develop a more complete understanding of DNA transcription. He acknowledges that it's a "super-complicated process" with many steps that scientists do not yet have the tools to observe and comprehend.

"Biology consists of a lot of data—gathering data—and it's a mostly experimental field," he explains. "But sometimes you need to make sense of the data; it's not immediately obvious what the data means, and that is where mathematical modeling can be helpful." Chow uses his modeling in concert with molecular biologists to help piece together data that is accumulated from studying DNA transcription.

Models can augment data supplied by physical research. "The data gives you a snapshot of what's going on, but it's a snapshot in time," Chow says. "You can fill in the gaps with a mathematical model." The data can be used to inform a prediction, such as in modeling asymptomatic Covid cases.

Supercomputer Biowulf uses a massive cooling system to maintain the appropriate temperature for its 99,000 cores.

PHOTO: BEN CHAMBERS

★★★

"The data gives you a snapshot of what's going on, but it's a snapshot in time. You can fill in the gaps with a mathematical model."

–DR. CARSON CHOW

★★★

He became interested in Covid modeling when NIH went virtual in March 2020. Suddenly relegated to his attic office for the foreseeable future, he began thinking about how he could contribute to the current understanding of Covid-19. He found himself drawn to asymptomatic cases, which no one knew much about at the time.

"It's a computational question," Chow says, "because at that moment people were taking data—the number of cases being reported—and the number of people that were dying from those cases, and the number of people recovering from cases. The question was, could you infer from that information the hidden number of people who are infected?"

The "hidden number" Chow referred to is the number of unreported cases, or people who are infected and shed the virus, but experience no or very mild symptoms. Current understanding is that roughly 1 out of every 5 Covid cases will be unreported.

Chow recruited several current and former fellows from his lab and got to work building models. They first had to familiarize themselves with the principles of epidemiology and the mathematical tools commonly used to understand disease spread. Then, he says, they "assembled some modern ideas from statistics," and "tried to put together a model to see if [they] could infer what the hidden number of cases [was]."

The team employed an SIR-type model for the spread of disease, which represented possible states of the members of a population affected by an infectious disease (Susceptible, Infected, Case, Recovered, and, added in some models as SIR[D], Death). Health agencies report the number of cases, recoveries and deaths but the total number of susceptible and infected individuals are unknown and are predicted by the model.

Chow utilizes latent-variable Bayesian statistical methods in concert with the SIR models. Bayesian modeling uses probability to represent uncertainty within a model, which, in Chow's research, can account for variables such as deaths unrelated to Covid, disease progression effects, population mixing and errors in classifying and reporting the data used in the research.

Using these models, he estimated that the number of unreported cases in April 2020 in the U.S. was 9 unreported for every 1 recorded. However, that number has dropped since.

Chow is currently collaborating with Dr. Kaitlyn Sadtler, another pivot scientist, in her work using antibody assays to detect asymptomatic Covid cases. Sadtler's data helps inform Chow's models, and Chow's models can simulate a larger population than Sadtler could ever sample.

He attributes his breadth of projects to the flexibility of his field.

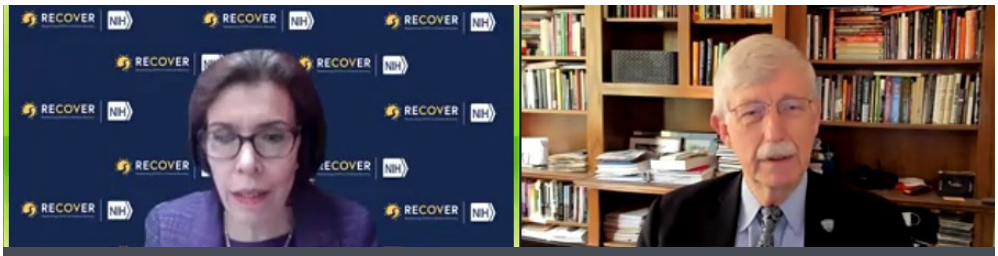
"There's very little cost compared to an experimental lab," he notes. "The only thing you lack in any pivot for a mathematician is knowledge." He learns the science associated with whatever topic he wants to pursue, and then develops models based on the science he has learned.

"The only cost to a mathematician is opportunity cost," he concludes.

Register Now for ODS Anniversary Symposium

Registration is open for the Office of Dietary Supplements 25th Anniversary Scientific Symposium that will take place virtually on Oct. 25–26. ODS was established in November 1995 in the Office of the Director with the congressionally mandated purposes "to promote scientific study of the benefits of dietary supplements in maintaining health and preventing chronic disease and other health-related conditions."

A symposium marking ODS's establishment will feature presentations by experts in the field, showcase ODS contributions to dietary supplement research and discuss the future of dietary supplement research. The event is open to the public and there is no cost to attend. To register, fill out the form at https://events-support.com/events/ODS_25th_Anniversary_Scientific_Symposium/page/3375.



NHLBI deputy director for clinical research and strategic initiatives Dr. Amy Patterson and NIH director Dr. Francis Collins speak during a Sept. 15 virtual telebriefing on RECOVER.

RECOVER Builds Large Nationwide Study Population for Research on 'Long Covid'

NIH awarded nearly $470 million to build a national study population of diverse research volunteers and support large-scale studies on the long-term effects of Covid-19. The Researching Covid to Enhance Recovery (RECOVER) Initiative made the parent award to New York University (NYU) Langone Health, which will make multiple sub-awards to more than 100 researchers at more than 30 institutions and serves as the RECOVER Clinical Science Core.

This major new award to NYU Langone supports new studies of Covid-19 survivors and leverages existing long-running large cohort studies with an expansion of their research focus. This combined population of research participants from new and existing cohorts, called a meta-cohort, will comprise the RECOVER Cohort. Funding was supported by the American Rescue Plan.

NIH director Dr. Francis Collins discussed the award Sept. 15 at a virtual telebriefing that also included NHLBI director Dr. Gary Gibbons, NYU Clinical Science Core principal investigator Dr. Stuart Katz and NHLBI deputy director for clinical research and strategic initiatives Dr. Amy Patterson.

NIH launched RECOVER to learn why some people have prolonged symptoms (referred to as "long Covid") or develop new or returning symptoms after the acute phase of infection from SARS-CoV-2, the virus that causes Covid-19. The most common symptoms include pain, headaches, fatigue, "brain fog," shortness of breath, anxiety, depression, fever, chronic cough and sleep problems.

"We know some people have had their lives completely upended by the major long-term effects of Covid-19," said Collins, announcing the award. "These studies will aim to determine the cause and find much needed answers to prevent this often-debilitating condition and help those who suffer move toward recovery."

Data from the RECOVER Cohort will include clinical information, laboratory tests and analyses of participants in various stages of recovery following SARS-CoV-2 infection. With immediate access to data from existing, diverse study populations, it is anticipated researchers will be able to accelerate the timeline for this important research.

"This scientifically rigorous approach puts into place a collaborative and multidisciplinary research community inclusive of diverse research participants that are critical to informing the treatment and prevention of the long-term effects of Covid-19," said Gibbons, who also co-chairs RECOVER.

Researchers, people affected by long Covid and representatives from advocacy organizations worked together to develop the RECOVER master protocols that use standardized trial designs and research methods to enable uniform evaluation of study populations across studies and the ability to quickly pivot the research focus depending on what findings show. This approach allows for data harmonization across research studies and study populations. Data harmonization allows data to be compared and analyzed, which will facilitate the research process and provide more robust findings.

Studies will include adult, pregnant and pediatric populations; enroll patients during the acute as well as post-acute phases of SARS-CoV-2 infection; evaluate tissue pathology; analyze data from millions of electronic health records; and use mobile health technologies, such as smartphone apps and wearable devices, which will gather real-world data in real time.

Together, the studies are expected to provide insights over the coming months into many important questions including the incidence and prevalence of long-term effects from SARS-CoV-2 infection, the range of symptoms, underlying causes, risk factors, outcomes and potential strategies for treatment and prevention.

Also on screen for the telebriefing were NICHD director Dr. Diana Bianchi, NIAID medical officer Dr. Andrea Lerner and NINDS associate director and director of the Division of Clinical Research Dr. Clinton Wright. R

NHLBI director Dr. Gary Gibbons (lower r) addresses the virtual telebriefing, as (clockwise from lower l) NICHD director Dr. Diana Bianchi, NIAID medical officer Dr. Andrea Lerner and NYU Clinical Science Core principal investigator Dr. Stuart Katz stand by to answer questions.

New Bioengineering Seminar Series Takes Flight

The newly established Biomedical Engineering Scientific Interest Group (BMESIG) is launching a seminar series, to start on Tuesday, Oct. 12 at 1 p.m. with a lecture by Dr. Gordana Vunjak-Novakovic, director of the Laboratory for Stem Cells and Tissue Engineering at Columbia University. View the remote lecture at https://videocast.nih.gov.

Columbia's Dr. Gordana Vunjak-Novakovic

BMESIG focuses on community-building and resource knowledge among engineers and scientists in the intramural research program. The group's creation was spearheaded by the National Institute of Biomedical Imaging and Bioengineering and the National Cancer Institute, with clinical advisors from the National Institute of Allergy and Infectious Diseases.

The inaugural speaker Vunjak-Novakovic has pioneered the use of stem cell engineering to grow tissue. Working primarily in the field of temporomandibular joint (TMJ) disorders, Vunjak-Novakovic's lab has successfully grown bone grafts that match a patient's original jawbone for facial reconstruction surgery to repair injuries, disease or birth defects.

This spectacular advancement in bone tissue engineering provides all the advantages of the body's original jawbone and uses real bone as a scaffold to grow a new TMJ graft. In related research, the Vunjak-Novakovic lab is engineering vascularized and electromechanically functional cardiac tissue by culturing stem cells.

The BMESIG seminar series is held during the second week of each month, for now remote-only. For more information and to view upcoming speakers through May 2022, visit https://oir.nih.gov/sigs/biomedical-engineering-scientific-interest-group.

On screen at the virtual town hall were (top, from l) NIAID director Dr. Anthony Fauci, NIH director Dr. Francis Collins and NIH Chief People Officer Julie Berko. Deputy director for management Dr. Alfred Johnson (bottom, l) and Office of Research Services Director Colleen McGowan also provided updates during the meeting. Also shown is ASL interpreter Jay Krieger.

Town Hall

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the Delta variant combined with—let's be honest—less-than-optimal vaccination rates have played havoc with our nation's efforts to return to normalcy, causing more cases, hospitalizations and deaths to reach now their highest level since winter. That means we still have a lot of hard work ahead of us."

More than 40 million cases of Covid-19 have now been confirmed in the United States, Collins reported. The number is almost certainly larger, though, because many cases probably were not diagnosed, especially last year.

"In recent weeks," Collins continued, "confirmed infections have averaged more than 150,000 a day. Even worse, deaths have been climbing up to about 1,500 a day and the daily average of hospitalized people is hovering around 100,000. That's the highest since most Americans were eligible for vaccinations back in January. On a positive note, vaccination rates have been trending upward, with about 800,000 doses on average being administered in the U.S. each day."

Still, he pointed out, about 80 million Americans have yet to get their first dose of any vaccine. "They are in real jeopardy from Delta," Collins said.

In response to those vaccination numbers, President Biden had announced just the day before a six-point plan to try to get everyone age 12 or older vaccinated. The plan includes mandates that apply to all federal employees and contractors; mandates will no longer allow an option to refuse vaccination and undergo regular testing. Only legitimate medical or religious exceptions will be considered.

"Freedom is not just about rights," Collins said, addressing a topic popular among people who have declined the shot(s). "It's also about responsibilities. Those who are unvaccinated are putting others around them at risk, including immunocompromised people."

• • •

"You have heard us say that this is now an outbreak or a pandemic of the unvaccinated. That is the reason the President emphasized so strongly why it is so important to get people vaccinated."

-DR. ANTHONY FAUCI

• • •

Fauci used his opening remarks to outline both encouraging findings and remaining challenges.

"Everything about the real world effectiveness of the vaccines underscores the fact that they do work very well in virtually all circumstances in the United States and in every country in which the vaccines we utilize in the United States have been used," he said. "I refer specifically and predominantly to the mRNA vaccines of Pfizer and Moderna as well, to a lesser degree, the [Johnson & Johnson] vaccine. You have heard us say that this is now an outbreak or a pandemic of the unvaccinated. That is the reason the President emphasized so strongly why it is so important to get people vaccinated...Some have interpreted that as an overreach, but it really is not. We have tried everything—from trusted messengers to making vaccines easily and readily available. [Vaccinations are] free, convenient, they work. Why not get it? That has really been the mantra that has guided us."

Johnson provided a snapshot of Covid-19 in the NIH community.

As of Sept. 9, NIH had tested 19,035 staff members and recorded 1,749 index cases from NIH testing and community reports combined.

"We have detected 259 positive tests through our asymptomatic testing program," he reported. "In terms of genomic analysis, our first Delta variant was detected on May 14. Since that time, 31 out of 53 samples analyzed have been the Delta variant. All samples analyzed after Aug. 31 have been the Delta variant."

NIH's vaccination rate has fluctuated between 67 percent and 70 percent, due to routine staff onboarding and off-boarding. In terms of positive tests after vaccination, there have been 174 cases. There have been 115 positive cases among staff who have been fully vaccinated.

McGowan talked about the vaccination requirements for employees, which had just shifted the previous day.

"President Biden's executive order released yesterday mandates Covid-19 vaccinations for all federal employees and contractors in the Executive Branch, which includes NIH," she explained. "This is a change from what we shared with you back in mid-August, as testing in lieu of vaccination is no longer an option unless you have a medical or religious exemption...

"There are a few things that haven't changed," McGowan said. "First, we continue to offer vaccines at our Occupational Medical Service clinic to all federal employees, contractors, fellows and tenants. We have plenty of appointments available. We also encourage you to take advantage of your community vaccination resources, if that's more convenient...Second, we are planning to set up a Covid-19 booster clinic once we get more guidance from the FDA on approvals. For some of you, we might be able to time boosters in conjunction with our annual 'Foil the Flu' campaign, but we need more information."

Berko briefly described deliberations involved in getting the majority of NIH'ers back to the physical workplace. Currently, most of the agency is functioning under maximum telework provisions. An HHS timeline suggests no sooner than November for full-staff returns.

"We do not currently know when we will be able to increase the number of staff working on site," she said, "but we are actively planning for both the near and long term. The NIH response and recovery team will continue to be cognizant of current public health conditions and the predominance of the [coronavirus] variants, making sure that we are sticking close to the science and the data as it emerges."

NIH has conducted and funded much of the science being relied upon during the pandemic. Collins reminded town hall viewers of NIH's role from the earliest days of the worldwide health crisis, from development of the incredible breadth and depth of Covid-19 diagnostics, vaccines and treatments to remarkable efforts to share resources and disseminate information related to the pandemic.

"All of this is very swift and impressive progress," he said. "And none of it would have been possible without decades of basic and clinical research, supported by NIH, preparing us for this kind of a challenge. So my thanks to all of you who have been all-hands-on-deck and must be pretty exhausted... But we have risen to the charge. We have delivered over and over again. You should be proud to be part of the National Institutes of Health—I know I am."

NIH'ers can view the entire town hall at https://videocast.nih.gov/watch=42710.

VRC TO GROW

Expanding Space for Vaccine Research

The pandemic put vaccines in the spotlight, though the plan to enlarge the Dale and Betty Bumpers Vaccine Research Center at NIH was in the works years earlier. Now, with congressional approval to build an extension of the VRC (Bldg. 40A), construction is expected to begin this winter.

Renderings show the forthcoming VRC expansion, Bldg. 40A. Construction will begin this winter and is expected to continue through August 2024.

Bldg. 40, completed in 2000, was originally designed to accommodate a future addition, and the time has now come, to support the growing need for vaccine research.

The 5-story, 65,000 square-foot expansion will house BSL-2 and BSL-3 laboratories and administrative space with design flexibility that can adapt to the changing needs of translational and computational science. The addition, which is slated to be completed by August 2024, will bring the building up to the edge of South Drive and Convent Drive.

NIAID responds annually to 4-5 emerging infectious diseases with medical countermeasures to treat, prevent or lessen the burden of disease. Bldg. 40A will facilitate and broaden this research into developing and testing vaccines for a range of global public health diseases including influenza, coronaviruses, Ebola, Zika and HIV/AIDS. Other research areas include vaccines for under-diagnosed syndromes and pediatric vaccines.

Robinson

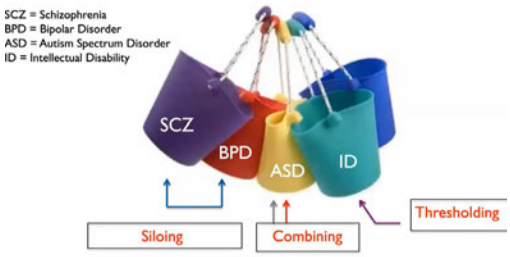
CONTINUED FROM PAGE 1

as more broadly variability in how human beings think and act."

Robinson, assistant professor of epidemiology at the Harvard T.H. Chan School of Public Health and an institute member of the Broad Institute of MIT and Harvard, framed the topic by depicting psychiatric disorder diagnoses as buckets. There can be overlap between genetic risk factors of different mental illnesses but also heterogeneity within a single illness.

Outcomes of an autism diagnosis can range from absence of speech to highly articulate, from the need for life-long full-time care to independent living and professional success in adulthood. "That's an enormous suite of possibilities to put into one bucket," said Robinson.

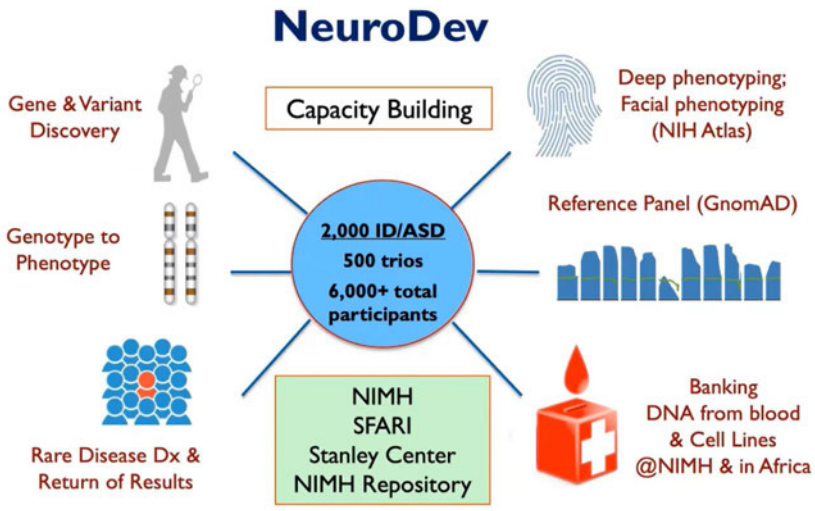
There's also heterogeneity within autism-associated genes. As sequencing data expands, said Robinson, "we're starting to see a gradient emerging in the extent to which a gene can create risk for autism without commonly also causing global developmental delay or intellectual disability."

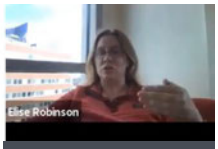


One approach investigators take to studying the spectrum of outcomes looks at de novo variants—changes that occur in the sperm or egg and are therefore seen only in the child, not in the parents. Most of these variants are well-tolerated, but some are not. Through de novo variation studies, scientists have identified genes that are not tolerant to loss-of-function variation, in which one copy of the gene is disrupted.

"It's estimated that about 10 percent of genes fall into this category," said Robinson, "and 71 of them at this point have been associated with ASD at a genome-wide significant level."

Of these 71 genes, 61 are also associated with intellectual disability. "In fact, most ASD-associated genes to this point have a stronger association with intellectual disability than they do with autism," she said.





Robinson discusses NeuroDev, a project that has identified some novel candidate genes for ASD and intellectual disability. Below left, Robinson depicts psychiatric disorder diagnoses as buckets.

It's been known for some time that strong-acting de novo variants that create risk for autism are more likely to be found in individuals with autism and intellectual disability and/or broader neurodevelopmental impairment.

More recently, investigators have learned that autism-associated genes related to intellectual disability and those associated with, say, schizophrenia are less overlapping than one would expect. "We're beginning to be able to differentiate ASD-associated genes in terms of their phenotypic properties," she said.

Another approach for studying ASD outcomes is looking at polygenic risk—the sum of many small effects from thousands of common variants across the genome. In people with ASD, higher polygenic risk score is associated with higher measured IQ, said Robinson.

"There's been an enormous shift in [the severity] of ASD diagnosed over the last 30 years," she said. The people who participated in ASD studies in the 1990s and 2000s generally had a very different behavioral and cognitive profile than people enrolled in current studies. "This shift is highly relevant to genetic studies, particularly [those] that are aggregating data over time."

For example, the longitudinal SPARK study—funded by the Simons Foundation with 30,000 families enrolled—reveals substantially greater educational attainment, higher IQ and independent living in individuals diagnosed with ASD now compared with 30 years ago, said Robinson, when 70 to 80 percent of those diagnosed with autism met criteria for intellectual disability. In the United States and parts of western Europe, that rate has fallen below 30 percent in recent years.

An ongoing data collection effort called NeuroDev has uncovered a different scenario in Africa.

"One of the unique things about NeuroDev [beyond] the genetic aspects," said Robinson, is learning that "in different communities and different cultures...in this case in Kenya and South Africa, the type of autism that's on average ascertained is much more similar to that which was ascertained in the U.S. about 30 years ago. On average, it's much more severe."

NeuroDev is collecting a range of cognitive, behavioral and medical data to study ASD and intellectual disability in Kenya and South Africa and will release the data publicly through NIMH at the study's conclusion. With data from nearly 2,000 people, the project has already identified some novel candidate genes.

Another program, Matchmaker Exchange, may also help yield some clues about autism and potentially a range of other conditions. The program is collecting genetic data from clinical geneticists globally aiming to match deleterious variants, find overlapping phenotypes and ultimately identify causative genes for a range of syndromes and conditions.

Robinson's lab so far has submitted 14 gene candidates to the exchange, variants they suspect may be causal for intellectual disability and/or autism. Through the exchange, she said, "We've already been matched with seven groups working on the description of novel genetic syndromes."

Winn To Give NCI CURE Seminar, Oct. 14

VCU Massey Cancer Center director Dr. Robert A. Winn will present the next lecture in the NCI Center to Reduce Cancer Health Disparities' (CRCHD) Continuing Umbrella of Research Experiences (CURE) Distinguished Scholars Seminars Series on Thursday, Oct. 14, from 1 to 2:30 p.m., via WebEx. Winn is the second-ever African-American director of an NCI-Designated Cancer Center. His talk is titled, "Structure, Trust and Science."

Dr. Robert A. Winn

A former CURE K22 and R21 scholar, Winn became director of VCU Massey Cancer Center in December 2019. In addition to directing 205 research members from 39 departments in 9 colleges and schools at VCU, he manages a research lab and is a pulmonologist, actively treating veterans each week at the nearby Hunter Holmes McGuire VA Medical Center.

Winn's current research centers on the translational aspects of the role that proliferation pathways and cellular senescence play in lung cancer. He brings a focus on cancer disparities, equity and community to his research and his cancer center leadership. He has published more than 60 authored or co-authored manuscripts in peer-reviewed academic journals.

Before coming to Richmond, Winn served as director of the University of Illinois Cancer Center and spent more than a decade at the University of Colorado Health Sciences Center and School of Medicine. He completed his bachelor's degree at the University of Notre Dame, his medical degree at the University of Michigan Medical School in Ann Arbor, his internship and residency in internal medicine at Rush-Presbyterian-St. Luke's Medical Center in Chicago and a fellowship in pulmonary and critical care medicine at the University of Colorado Health Sciences Center in Denver.

Among the many awards and honors he has earned, Winn received the NCI CRCHD CURE Program Lifetime Achievement Award and was recently named vice president and president-elect of the Association of American Cancer Institutes. In February 2021, he hosted First Lady Dr. Jill Biden during her visit to VCU Massey Cancer Center.

The CURE series recognizes former CURE scholars and champions who are making seminal contributions to the fields of cancer and cancer health disparities research. Begun in 2017, the lectures are held semi-annually.

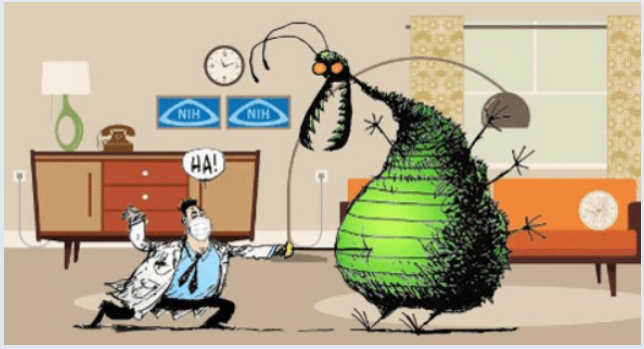
To register, visit: https://cbiit.webex.com/cbiit/onstage/g.php?MTID=ef97ec-c02576069883796c3449ac1cd4d. Those who need reasonable accommodation to participate should contact Victoria Coan at (240) 276-7659 and/or the Federal Relay Service (1-800-877-8339) at least 2 days before the meeting. R

2021 PROGRAM CHANGES

'Foil the Flu' Underway

Foil the Flu, the annual seasonal influenza immunization program for NIH employees and contractors, has begun and will end Nov. 5. The yearly clinic has significant changes this year. The vaccine will be given by appointment only through an online registration system. Walk-in immunization will not be available. The on-campus location is Bldg. 10 FAES Terrace.

All federal employees and contractors with a valid NIH identification badge are eligible to receive flu vaccine for free and are encouraged to be immunized. The best way to reduce the risk of getting the flu is to get the vaccine every year. All staff who have patient contact, including both employees and contractors, are required to get immunized each year.



All teleworking employees in the Washington, D.C., area are encouraged to schedule an appointment at the Shady Grove, Fisher's Lane or Rockledge locations. Visit https://ors.od.nih.gov/flu/pages/default.aspx for more information.

NINDS's Koroshetz, Nath Lauded by ANA

The American Neurological Association (ANA) recently honored NINDS director Dr. Walter Koroshetz and clinical director Dr. Avindra Nath for their outstanding accomplishments in academic neurology and neuroscience. The awards—which recognize leaders in academic leadership and neuroscience who have exemplified excellence in research, teaching and clinical practice across the scope of clinical neurology and neuroscience—will be presented virtually at ANA's 146th annual meeting Oct. 17-19.

Dr. Avindra Nath

Nath received the Soriano Lectureship, which was established in 1987 and acknowledges a brilliant lecture delivered by an outstanding scientist, for his presentation "Neurobiology of Covid-19."

Koroshetz received the ANA Award of Excellence for Outstanding Contribution in a Senior Administrative Role. The honor, which is new this year, recognizes outstanding, innumerable contributions to the field of neurology and neuroscience as a senior administrator over a sustained period.

Dr. Walter Koroshetz

"The individuals recognized this year are conducting exciting work that is transforming our understanding of the brain and helping move treatment forward," said ANA President Justin C. McArthur in a press release announcing the awards.

"We hope this recognition will inspire the awardees to even greater achievements and encourage a new generation of physician-scientists to pursue careers that bring research and teaching together with clinical practice," said McArthur, who also serves as director of Johns Hopkins's department of neurology and a professor of neurology.

The annual ANA meeting brings together the world's leading academic neurologists and neuroscientists to share groundbreaking research and updates on the diseases and conditions that affect more than 100 million Americans.

ANA is a professional society devoted to advancing the goals of academic neurology, teaching and educating neurologists and other physicians in the neurologic sciences, and expanding both the understanding of diseases of the nervous system and the ability to treat them.—**Shannon E. Garnett**

Can Brain Functions Improve with Age?

Computer tests of attention and focus revealed that older adults declined in 1 one out of 3 key brain functions. The other functions actually improved during aging, at least until the mid-to-late 70s. The results of the NIA-funded study were published in *Nature Human Behaviour.*

Study finds not all brain functions may decline with age.

MONKEY BUSINESS IMAGES/SHUTTERSTOCK

Cognitive changes such as mild forgetfulness are often a normal part of aging. Older adults may find it takes longer to remember a fact or learn a new skill. At the extreme end, the risk of dementia rises with aging. In fact, the number of people with Alzheimer's disease doubles about every 5 years beyond age 65.

But not all brain functions may decline with age. Cognitive skills that need constant practice, such as understanding and using language, are usually well preserved.

To further explore whether some cognitive skills improve with age, a research team studied more than 700 adults ages 58 to 98. Study participants took computerized tests of three aspects of attention: readiness to respond to incoming information (alerting); moving attention to a particular location (orienting); and executive control—the ability to ignore distractions and focus on the task at hand.

Increasing age was associated with slower response times and less alertness to incoming information, but the other two aspects of attention improved with age. Older participants could more efficiently orient attention toward different objects and were better at ignoring distractions than younger participants.

These two preserved brain functions showed different trajectories over time. Attention orienting ability increased steadily from middle age into older adulthood. Executive control increased into the mid-to-late 70s, then declined. Yet the gains from earlier old age were large enough so that even the oldest adults were no worse at ignoring distractions than the youngest.

The improvements found in brain functions may have benefits for higher-level cognitive abilities, such as decision-making and long-term memory. More research is needed to see if targeting such skills could help protect against overall cognitive decline during aging. —adapted from *NIH Research Matters*

Scientists Build Cellular Blueprint of MS Lesions

A new study lays the groundwork for potential new therapies for progressive multiple sclerosis. Chronic lesions with inflamed rims, or "smoldering" plaques, in the brains of people with MS have been linked to more aggressive and disabling forms of the disease. Using brain tissue from humans, NINDS researchers built a detailed cellular map of chronic MS lesions, identifying genes that play a critical role in lesion repair. The study was published in *Nature.*

"We identified a set of cells that appear to be driving some of the chronic inflammation seen in progressive MS," said NINDS senior investigator Dr. Daniel Reich. "These results give us a way to test new therapies that might speed up the brain's healing process and prevent brain damage that occurs over time."

Chronic active lesions are characterized by a slow, expanding rim of immune cells called microglia. Normally, microglia help protect the brain. But in MS and other neurodegenerative diseases, microglia can become overactive and secrete toxic molecules that damage nerve cells.

To better understand MS lesions, Reich and colleagues used single-cell RNA sequencing to examine post-mortem brain tissue of 5 MS patients and 3 healthy controls. Samples were provided by the Netherlands Brain Bank and the NINDS Neuroimmunology Clinic.

By analyzing the gene activity profiles of over 66,000 cells from human brain tissue, researchers created the first comprehensive map of cell types involved in chronic lesions, as well as their gene expression patterns and interactions.

More detailed analyses revealed that the gene for complement component 1q (C1q), an important and evolutionarily ancient protein of the immune system, was expressed mainly by a subgroup of microglia responsible for driving inflammation, suggesting that it may contribute to lesion progression.

In mouse models, knocking out the C1q gene led to significantly decreased tissue inflammation. Study authors contend it's possible that targeting C1q in human microglia could halt MS lesions in their tracks.

For progressive MS, anti-inflammatory medications help patients manage their symptoms, but treatments are not as effective for patients with chronic lesions who experience ongoing brain tissue inflammation. By gaining a deeper understanding of lesion features, this study may help pave the way toward early clinical trials to test new therapies for this aspect of the disease.

New Robotic Cane Offers New Direction

Equipped with a color 3-D camera, an inertial measurement sensor and its own onboard computer, a newly improved robotic cane could offer blind and visually impaired users a new way to navigate indoors. When paired with a building's architectural drawing, the device can accurately guide a user to a desired location with sensory and auditory cues, while simultaneously helping the user avoid obstacles like boxes, furniture and overhangs.

Study author Lingqiu Jin tests the robotic cane.

PHOTO: CANG YE, VCU

NEI and NIBIB co-funded the cane's development. Design details were published in *IEEE/CAA Journal of Automatica Sinica*.

While there are cell phone-based applications to help blind users stay within crosswalks, for example, large spaces inside buildings are a major challenge. Earlier versions of this robotic cane began tackling the problem by incorporating building floorplans. Users could tell the cane where they wished to go, and the cane—through auditory cues and a robotic rolling tip—could guide users to their destination. But when used over long distances, the inaccuracies could build up, eventually leaving the user at an incorrect location.

To help correct this issue, the cane's developers added a color depth camera to the system. Using infrared light, the system can determine the distance between the cane and other physical objects, including the floor, doorways and walls, as well as furniture and other obstacles. Employing this information, along with data from an inertial sensor, the cane's onboard computer can map the

user's precise location to the existing architectural drawing or floorplan, while also alerting the user to obstacles in their path.

There are still a few kinks to be worked out before the system will be market-ready—it's still too heavy for regular use, for example. Nevertheless, with the ability to switch easily between its automated mode and a simpler, non-robotic "white cane mode," this device could provide a key independence tool for the blind and visually impaired, without losing the characteristics of the white cane that have stood the test of time.

HEALing Communities Disparities in Opioid Overdose Deaths Continue to Worsen

The opioid overdose death rate was significantly higher for non-Hispanic Black individuals in four U.S. states from 2018 to 2019, while the rates for other race and ethnicity groups held steady or decreased. These findings appeared in a new NIH study, published in the *American Journal of Public Health.*

Recent data reveals significantly higher opioid overdose death rates for Black individuals in four U.S. states.

PHOTO: 5D MEDIA/SHUTTERSTOCK

This alarming data is in line with other research documenting a widening of disparities in overdose deaths in Black communities in recent years, largely driven by heroin and illicit fentanyl. The research emphasizes the need for equitable, data-driven, community-based interventions that address these disparities.

The research was conducted as part of the HEALing Communities Study, which aims to significantly reduce opioid-related overdose deaths by helping communities implement evidence-based practices to treat opioid use disorder and reduce other harms associated with opioid use in New York, Massachusetts, Kentucky and Ohio. It's the largest addiction implementation study ever conducted and is administered in partnership by NIDA and HHS's SAMHSA through the Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative.

For this study, researchers collected death certificates for 2018 and 2019 across 67 communities with a total population of more than 8.3 million people in the 4 states participating in the HEALing Communities Study. The researchers calculated rates and trends of opioid overdose deaths overall and for each state, and then further analyzed trends by race and ethnicity.

Overall, no change was observed in the opioid overdose death rate in these states from 2018-2019 but researchers found a staggering 38 percent increase in the opioid overdose death rate for non-Hispanic Black individuals.

Trends varied at the state level. Among non-Hispanic Black individuals, increases were highest in Kentucky (a 46 percent increase) and Ohio (a 45 percent increase). No significant increase was observed in Massachusetts. In New York, the rate was unchanged for non-Hispanic Black individuals and, in fact, there was an 18 percent decline among non-Hispanic White individuals, suggesting that non-Hispanic Black individuals have not benefited equally from prevention and treatment efforts.

The study authors note these increasing disparities in opioid use deaths highlight the importance of access to timely, local data to inform effective community-tailored strategies to reduce these deaths. Numerous evidence-based prevention and treatment interventions exist for addressing the opioid overdose crisis: overdose education, naloxone distribution, medications for opioid use disorder, behavioral therapies and recovery support services. Unfortunately, these interventions have largely failed to gain widespread implementation in community settings including addiction treatment, general medical care, social support services, schools and the justice system.

To address this challenge, the HEALing Communities Study is working with local, state, and federal partners to gain access to data on opioid-related overdose fatalities, treatment, other related health concerns and demographic data in a timelier fashion.

"We must explicitly examine and address how structural racism affects health and leads to drug use and overdose deaths," said NIDA director Dr. Nora Volkow. "Systemic racism fuels the opioid crisis, just as it contributes mightily to other areas of health disparities and inequity, especially for Black people. We must ensure that evidence-based interventions, tailored to communities, are able to cut through the economic and social factors that drive disparities in substance use and addiction, to reach all people in need of services."

Dengue Virus Study Recruits NIH'ers

NIAID researchers are conducting a study to better understand long-lived protection against the dengue virus. The study is enrolling NIH employees who have lived in Latin America, the Caribbean, Africa, the Middle East, South Asia, Southeast Asia or Oceania. Compensation is provided. Join by contacting the Clinical Center Office of Patient Recruitment (866) 444-2214 or PRPL@cc.nih.gov and ask for study #11-I-0109. Online: https://go.usa.gov/xHQyg.

Volunteers with Food Allergy Sought

NIAID researchers are seeking volunteers ages 2 and older who have at least one food allergy to participate in a study to better understand how food allergies affect health. Participants receive a comprehensive nutritional evaluation and meet with a dietitian for individualized counseling. Compensation for participation is provided. For more information, call the Office of Patient Recruitment at (866) 444-2214 (800-877-8339 TTY/ASCII) or email prpl@cc.nih.gov. Refer to NIH study #15-I-0162, https://go.usa.gov/xQYw9.

Healthy Volunteers Wanted

Researchers at the National Heart, Lung, and Blood Institute are enrolling healthy volunteers or volunteers diagnosed with moderate or severe psoriasis in an observational study to determine how chronic inflammation caused by psoriasis affects blood flow to the heart. In this study, all tests, treatments and procedures are provided at no cost. Compensation and travel assistance may be available. Contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY/ASCII 800-877-8339) or prpl@cc.nih.gov. Refer to study 0000136. Read more online at https://go.usa.gov/xFBC2.

Remote Study Seeks Volunteers

Neurofibromatosis type 1 (NF1) is a condition that can cause changes in skin color and growth of tumors (called plexiform neurofibromas or PNs) under the skin. NCI is conducting a new study to see if NF1 patients who are treated with Selumetinib have a noticeable improvement in the appearance of their tumors.

Researchers at NCI are looking for volunteers to help rate changes in the appearance of PN tumors viewed in patient photos before and after treatment. This is a remote study using a smartphone or computer to complete an online questionnaire in one or two 1-hour sessions to review photographs of patients with or without treatment and score the appearance of visible tumors.

To learn more, contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY: 800-877-8339) or email prpl@cc.nih.gov and refer to study 000173-C, or visit https://go.usa.gov/x6Qqb.

Top (from l): Clinical Center CEO Dr. James Gilman introduces the performance; NSO chamber group guest conductor Lina Gonzalez-Granados leads the group; (r and below) members of the string section entertain patients and staff.

NSO Chamber Group Performs at CRC

PHOTOS: CHIA-CHI CHARLIE CHANG

How sweet the sound when the National Symphony Orchestra performed in the Clinical Research Center atrium on Sep. 2. The repertoire included *Amazing Grace*, Mozart's *Allegro* from movement 1 of *Eine Kleine Nachtmusik*a and several other classical selections.

Led by Lina Gonzalez-Granados, an internationally acclaimed young conductor, the NSO's chamber group comprises strings and percussion. It was no surprise that the Colombian-American conductor—dedicated to highlighting works by Latin-American composers—included a Peruvian composition in the mix, the lively *Coqueteos* from Gabriela Lena Frank's *Leyenda: an Andean Walkabout.*

The concert marks the start of the 9th year of the NIH-Kennedy Center Sound Health partnership.

ABOVE: Gonzalez-Granados conducts a lively Peruvian piece that reflects her Latin American heritage. At right, a socially distanced audience on the atrium's ground floor enjoy the music, which wafts up to doctors, staff and patients in the hallways and patient rooms above.