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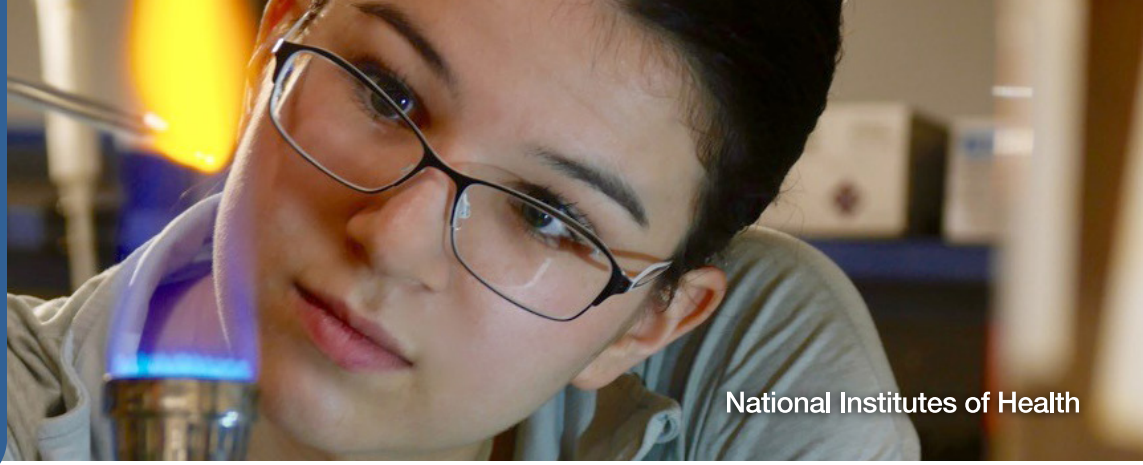


PUT TO THE TEST

Agencies, Researchers Plan for Safe In-Person School

BY DANA TALESNIK

Parents across the country are sending their children back to classrooms, likely with a mix of excitement and apprehension, as the coronavirus pandemic rages on. Even in areas better protected by higher vaccination rates, children younger than 12 are not yet eligible to get immunized. The situation is compounded by the more virulent Delta variant that's increasingly infecting kids and some vaccinated adults.

Getting students and school staff safely back to an in-person environment requires ongoing surveillance and mitigation strategies, an even greater challenge for communities hardest hit by the pandemic.

Earlier this year, NIH launched a Safe Return to School Diagnostic Testing Initiative, part of Rapid Acceleration of Diagnostics-Underrepresented Populations (RADx-UP). The initiative is a series of projects designed to scale up Covid testing in vulnerable, underserved communities that have been afflicted by disproportionately high infection and mortality rates, and to analyze data toward reducing these disparities.

Kids return to in-person school amid the ongoing Covid-19 pandemic.

PHOTO: ANDY DEAN PHOTOGRAPHY/SHUTTERSTOCK

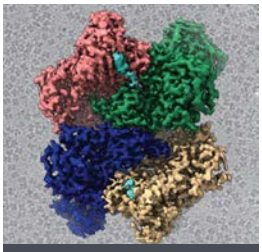
"This is the largest single disparities-related project NIH has ever funded," said NIMHD director Dr. Eliseo Pérez-Stable of the $500 million RADx-UP.

The Return to School component so far has invested more than $50 million to fund projects at 16 institutions across the country to build evidence on the efficacy of sustained Covid-testing and other mitigation efforts in schools. The projects focus on vulnerable populations including racial and ethnic

SEE **SCHOOLS**, PAGE 6

NIEHS Scientists Redirect Efforts to Fight Covid-19

BY ERIC BOCK



Nsp15, a protein found in coronavirus

IMAGE: MEREDITH FRAZIER

At the beginning of the Covid-19 pandemic, NIEHS scientists Dr. Mario Borgnia and Dr. Robin Stanley began contributing to NIH's research efforts against SARS-CoV-2. They used their experience in structural biology to learn more about the proteins involved in the essential function of the virus that causes Covid-19.

SEE **COLLABORATION**, PAGE 4

4th article in a series on intramural NIH scientists who pivoted their research project to pursue a pandemic-related issue

'GRATITUDE TOUR' GOES VIRTUAL

Collins Expresses Appreciation to Covid Response Teams

The NIH director's "Gratitude Tour" is continuing.

On Aug. 11, Dr. Francis Collins joined in a conference call to thank the NIH Covid Response Teams, i.e., the Call Center, Contact Investigations and OMS Return-to-Work Teams, as well as the IT specialists who helped to integrate the necessary processes. These are the more than 200 folks known to most they serve by voice alone, via phone. So this part of the Gratitude Tour had to be virtual.

Covid response workers, divided into several teams, established and maintained an essential "Covid hotline" for NIH, streamlined the case intake process, interviewed thousands of people who had been in contact with the more than 1,600 employees diagnosed with Covid-19, assessed risk for the

SEE **GRATITUDE**, PAGE 8

RML is set to get new center. See story, p. 12.

ALSO THIS ISSUE

40th Annual Immunohematology Symposium Set for Sept. 23

The Clinical Center's department of transfusion medicine and the American Red Cross will host the 40th annual Immunohematology and Blood Transfusion Symposium on Thursday, Sept. 23.

Dr. Kathleen Conry-Cantilena will deliver the annual Dr. Richard J. Davey Lectureship.

This year's symposium focuses on several current topics including various component therapies for patients with Covid, sickle cell disease or hyperleukocytosis as well as patients requiring massive amounts of blood products in a very short time period.

The annual Dr. Richard J. Davey Lectureship will be awarded to a longstanding transfusion medicine program fellowship director, Dr. Kathleen Conry-Cantilena, who will present "Physician Fellow Training in BB/TM: A Saga of 26 Years as a Program Director."

The symposium will end with a session featuring Dr. Harvey J. Alter, recipient of the 2020 Nobel Prize in Physiology or Medicine for his contributions to the discovery of the hepatitis C virus.

A session with 2020 Nobel laureate Dr. Harvey J. Alter will close the symposium.

PHOTO: CHIA-CHI CHARLIE CHANG

The symposium will be conducted via WebEx and is open to the public. Registration is required. Find the agenda and registration link at: https://www.cc.nih.gov/dtm/research/symposium.html.

Individuals with disabilities who need reasonable accommodation to participate in this event should contact Karen Byrne at Karen.Byrne@nih.gov or (301) 451-8645.

Applications to NIH Loan Repayment Programs Accepted through Nov. 18

The fiscal year 2022 NIH Loan Repayment Programs application cycle is officially open.

Awards are now up to $100,000 over a 2-year period and the NEW REACH LRP is available for extramural applicants. The deadline is Nov. 18.

If you are a qualified health professional who agrees to engage in NIH mission-relevant research for at least 20 hours per week at a nonprofit or government institution, you may be eligible to apply to 1 of the 6 extramural LRPs.

The objective of the Loan Repayment Programs is to recruit and retain highly qualified health professionals to careers in biomedical or biobehavioral research.

To apply visit: https://go.usa.gov/xMgCN.

Ma Featured at Inaugural Seminar on AAPI Health Disparities, Sept. 23

On Thursday, Sept. 23, the NIH Asian Pacific Islander health scientific interest group (AAPI-HSIG) will host its inaugural seminar, "Health Disparities Research: Addressing Multilevel Social Determinants of Health in Asian American and Pacific Islander Populations," at 11 a.m. ET.

The virtual seminar will feature a lecture by Dr. Grace X. Ma, founding director of the Center for Asian Health (CAH). NIMHD director Dr. Eliseo J. Pérez-Stable will open the seminar, which is co-sponsored by NCI's integrative medicine cancer health disparities working group. Dr. Dan Xi, program director at NCI who led efforts to establish AAPI-HSIG, will give a brief introduction of the mission, goals and vision of the group.

Dr. Grace X. Ma of Temple University will speak at AAPI-HSIG's inaugural seminar.

A pioneer in cancer and health disparities research, Ma has extensive experience conducting health system and population- and community-health research. She has made critical contributions toward reducing health disparities and improving health equity for underserved and racial/ethnic minority populations. She serves as associate dean for health disparities and Laura H. Carnell professor at Lewis Katz School of Medicine and Fox Chase Cancer Center at Temple University.

In establishing CAH in 2000, Ma founded one of the nation's first centers dedicated to reducing health disparities in underserved AAPI populations.

To attend the webinar, register at https://cbiit.webex.com/cbiit/onstage/g.php?MTID=e66f9e8bd429a1c90c078345fc9d12ae5. The event is open to the public.

AAPI-HSIG, newly established in 2021, is open to all participants in the intramural and extramural community, as well as HHS staff, who have an interest in research relating to the health of Asian Americans and Pacific Islanders, including Native Hawaiian populations. The group provides a forum to foster scientific communication, share and disseminate information, facilitate collaborations, provide education and training, assess the AAPI-health research funding portfolio and make recommendations to advance the NIH mission and improve the health and well-being of AAPI populations.

For more information, visit https://oir.nih.gov/sigs/AAPI-HSIG. Questions? Contact Xi at xida@mail.nih.gov.

Combined Federal Campaign Kicks Off 2021 Season

The 2021 Combined Federal Campaign started on Sept. 1, with the Fogarty International Center leading the NIH effort. The campaign will be virtual again this year and is set to end on Jan. 15, 2022.

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

Mark your calendars for these virtual events:

- **CFC Kickoff**, Thursday, Sept. 23, from 11 to 11:30 a.m. https://videocast.nih.gov/watch=42576
- **Halloween Virtual Charity Fair and Mask Contest**, Thursday, Oct. 28, from 11 a.m. to 1 p.m. Back by popular demand, the event will combine fun and CFC information. Three charities will talk about their mission and how donations make a difference.

The contest is an opportunity to design an original mask. This year's event has a special theme—"Superheroes." For details, visit https://cfc.nih.gov/. All mask entries due on Wednesday, Oct. 6.

Nominations Open for 'Mission First Safety Always Award'

Due Dec. 31

The Division of Occupational Health and Safety is seeking nominees for the "NIH Mission First Safety Always Award" for 2021. The award will recognize those who demonstrate leadership, innovation and involvement in their component's safety culture. Nominations will close on Dec. 31 at 11:59 p.m. ET.

The nominee must be an NIH employee, contractor or special government employee and nominations must come from an individual other than the person being considered.

To nominate a colleague, visit: https://ors.od.nih.gov/sr/dohs/Events/SafetyAwards/Pages/NIH-Mission-First%2c-Safety-Always.aspx.

If you have questions, contact DOHS at (301) 496-2960 or glassjac@nih.gov.

The Canyon Creek Schoolhouse became a laboratory investigating RMSF in September 1921.

PHOTOS: OFFICE OF NIH HISTORY AND STETTEN MUSEUM

ROCKY MOUNTAIN RESEARCH ORIGINS

New Website Celebrates 100th Year of NIAID's Montana Labs

BY MICHELE LYONS

A new disease, people dying needlessly and scientists racing to discover what causes it and how to stop it—sound familiar? But it was the early 20th century, not the early 21st century, when scientists from the Hygienic Laboratory (precursor to NIH) and the state of Montana did what seemed impossible at the time: They described a new disease and developed a vaccine for it in only 22 years. The 100th anniversary of the establishment of the Canyon Creek Schoolhouse Laboratory, where the Rocky Mountain spotted fever (RMSF) vaccine was developed in Hamilton, Mont., is being celebrated in a new website by the Office of NIH History and Stetten Museum (ONHM) and Rocky Mountain Laboratories (RML).

RMSF was often fatal. By 1921, researchers had discovered that *Rickettsia rickettsii*, a bacteria carried by infected ticks, caused the disease. But could it be prevented? At a time when a binocular microscope was advanced technology and molecular biology was unknown, the answer to that question was anything but assured.

In September 1921, everything from a small laboratory housed in a woodshed was loaded onto one truck and moved to the laboratory's new home—the empty Canyon Creek Schoolhouse. It was an auspicious move: Dr. Ralph Parker, an entomologist for Montana, was joining forces with physician Dr. Roscoe Spencer of the Hygienic Laboratory at a new Public Health Service field station.

The ONHM website uses many of the wonderful collection of photographs taken of the laboratory and its staff during the years of 1921 to 1928, when the laboratory was located in the schoolhouse, including photographs of the steps used to make a vaccine for RMSF out of ticks. The website includes a page with RMSF basics and the previous RMSF research that began in 1902.

In 1929, LeRoy Jones, Harley G. Sargent, Harry L. Sargent, and James Kerlee posed at the top of Blodgett Canyon in the Bitterroot Range in Montana. Each holds several white cloth bundles tied to a stick for collecting ticks. James Kerlee's brother, Arthur LeRoy Kerlee, had died the year before of RMSF that he had acquired in the laboratory.

PHOTO: OFFICE OF NIH HISTORY AND STETTEN MUSEUM

Another section of the website pays homage to those people who died while researching the disease at the Canyon Creek Laboratory—William Gittinger, Henry Cowan and Arthur Kerlee.

A lighter section explores how the story of the research and Spencer's experiments upon himself were interpreted in popular culture. For example, in 1936, a highly romanticized tale of RMSF vaccine research starring swashbuckling star Errol Flynn even became a high-grossing movie called *Green Light.*

Investigating a new disease and trying to prevent or treat it is nothing new for NIH scientists—it's why the Hygienic Laboratory was created. The RMSF work begun at the Canyon Creek Laboratory 100 years ago this month was particularly important because it jumpstarted research into tick-borne diseases, resulted in a life-saving vaccine and eventually led to the development of RML, now part of NIAID.

For more history, visit https://history.nih.gov/display/history/Canyon+Creek+Schoolhouse+Laboratory+100th+Anniversary+Intro.

For a glimpse at what's in RML's future, turn to Seen on p. 12. R

ON THE COVER: *Sarah Florig works in the lab during her first year as a BUILD EXITO trainee at Portland State University. EXITO, which stands for Enhancing Cross-Disciplinary Infrastructure and Training at Oregon, is the university's Building Infrastructure Leading to Diversity (BUILD) program, which is part of the NIH Common Fund's diversity consortium.*

IMAGE: BUILD EXITO

The NIH Record

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Collaboration

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Giving Serendipity a Boost

Borgnia said he had a choice: he could sit on his hands or do something to increase the probability of serendipitously finding something that would help researchers learn about SARS-CoV-2.

"I wasn't going to sit at home and be depressed," said Borgnia, director of the Molecular Microscopy Consortium at NIEHS. "I participated in the Covid-19 scientific interest group and helped organize talks so people had something constructive to do."

The consortium allows scientists to use single-particle cryogenic-electron microscopy (cryo-EM) and other tools employing high-tech microscopes to decipher macromolecular structures at the atomic level.

Cryo-EM is an advanced microscopy methodology to image complex biological molecules like proteins.

To obtain the images, molecules are frozen in a thin layer of ice on a grid. Then, they are bombarded with a beam of electrons to produce projection images. Next, images are combined to construct a 3-D map of molecules. The resulting images are like CAT scans for molecules.

The week before most NIH employees and trainees began teleworking full-time, Borgnia's team began to study the protein spikes conferring the corona-like appearance to the SARS-CoV-2 virus. These spikes bind to the surface of cells, the first step before the virus can invade a host cell.

"We concentrated our efforts on one particular set of proteins rather than a wider range of proteins," he said. "We were well positioned to get started and just put all of our firepower on the spike of the coronavirus."

Once he had the spike protein's structure, he began collaborating with researchers who were developing antibodies that would neutralize the spike. Essentially, his consortium created a pipeline so researchers could study how the spike behaves when exposed to different molecules.

★ ★ ★

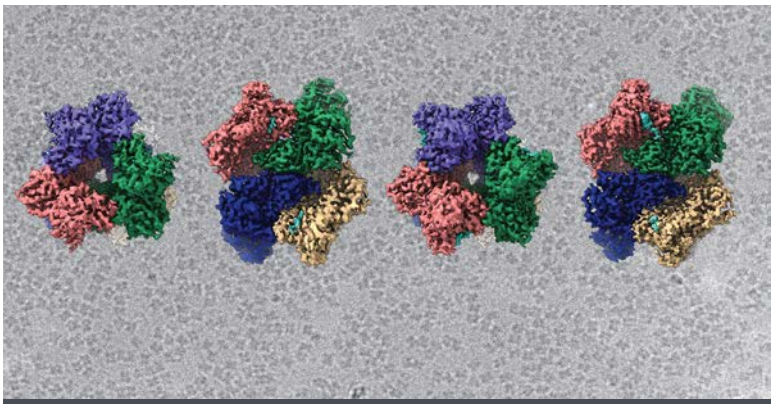
"We were well positioned to get started and just put all of our firepower on the spike of the coronavirus."

-DR. MARIO BORGNIA

★ ★ ★

Studying the SARS-Cov-2 virus wasn't a hard transition for him. Earlier in his career, Borgnia studied a protein, Env, the envelope glycoprotein, found on the surface of the HIV virus. Env allows the virus to target and attach to specific cell types.

Borgnia has done most of his work remotely from home. His team gathers via Zoom twice each day for check-in and check-out meetings that give structure to a remote work day. They have accelerated the transition to remote operation of the microscope, which allowed them to increase productivity both on-site and away from the workplace. During this period, a member of his team would go into the lab to prepare a sample to be imaged and then leave. Team members could then control the microscope from the sheltered environments of their homes.



The background represents an actual micrograph of Nsp15 particles, with the structure shown on top. The structure of Nsp15 is a hexamer so each subunit is shown as a different color with the bound RNA in cyan.

IMAGE: MEREDITH FRAZIER

Dr. Mario Borgnia

PHOTO: STEVE MCCAW

While the pandemic has been terrible, it has given Borgnia the opportunity to collaborate with researchers around the world who are studying the virus.

"My ability to communicate has increased dramatically," he said. "I can now sit in the same virtual room with people who are all over the world. I don't have to travel and can spend time talking to people."

'I Need to Be in a Lab'

Stanley never planned on studying the virus that causes Covid-19 because she didn't know much about viruses. Since she started her lab in 2014, Stanley has studied RNA processing enzymes involved in ribosome assembly and tRNA maturation. Shortly after she began teleworking full time, she realized she didn't like it. She decided to pivot from studying pre-rRNA processing to viral RNA processing because scientists working on Covid-19 research are allowed in labs.

"I don't like working at home. I need to be in the lab," said Stanley, Earl Stadtman investigator and head of the NIEHS nucleolar

Dr. Robin Stanley
PHOTO: STEVE MCCAW

integrity group. "I gave myself a crash course in the coronavirus and studied the different viral proteins. There was 1 viral protein that actually shared an awful lot of similarities with 2 RNA processing enzymes that we work on in our lab."

In addition, she thought the experience would be a great learning opportunity for her trainees. "It gave the lab something to focus on during that crazy period of time when we didn't know what was going on," she said.

Stanley applied to the Intramural Targeted Anti-Covid-19 funding program, which provided $12 million to intramural investigators for research into understanding and/or combatting the virus. She was awarded funding to study nonstructural protein 15 (Nsp15), which is an RNA processing enzyme found in all coronaviruses. Without Nsp15, the virus becomes vulnerable to the host's immune system. It's thought that the protein helps the virus evade detection.

Although Nsps do not become part of the mature virus, they "are really, really important for the virus," she explained. They are involved in virus replication, virus assembly and the evasion of host viral sensors.

Nsp15 is an endoribonuclease. It's an enzyme that cuts RNA in two—like a pair of molecular scissors. Some nucleases cut anything; others look only for a very specific sequence. Nsp15 only cuts after uridines, one specific nucleotide of RNA.

She collaborated with Borgnia to use cryo-EM to visualize the protein at a molecular level. These images have provided lots of information about why Nsp15 behaves the way it does.

"The big question we wanted to answer: how does it recognize and cut viral RNA targets?" she said. "Thankfully, through a combination of biochemistry, cryo-EM and some other techniques, we've been sort of able to answer that question. There are always more questions that arise from research, but we've been able to visualize the protein bound to some RNA, which has provided an abundance of information."

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"The ability to pivot is one of the awesome things about working at NIH."

–DR. ROBIN STANLEY

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At the beginning of her research, she thought making the protein would be easy. It turned out to be an unexpected challenge. The method Stanley typically uses to express proteins didn't work. Normally, her lab hijacks a bacteria's ability to make protein.

"But it turns out that bacteria don't like that protein, because likely it's toxic. When you express the nuclease in bacteria, it's probably chewing up all the bacteria's RNA and it's very unhappy," she explained.

After a month of trial and error, her group overcame this limitation and figured out another way to make the protein. Hopefully, these findings can be used to provide a structural framework for the development of new therapeutics.

Right now, her lab has begun to focus attention back on projects predating the pandemic. Two members are still working on NSP15.

"The ability to pivot is one of the awesome things about working at NIH," she concluded. "Hopefully, a pandemic won't happen again, but, if it does happen in the future, researchers at NIH can do it again."

REMOTE-ONLY FOR NOW

WALS Returns Sept. 29

The NIH Director's Wednesday Afternoon Lecture Series (WALS) for the 2021–2022 season will begin on Sept. 29 with a 3 p.m. lecture by Dr. Sherita Hill Golden, the Hugh P. McCormick Family professor of endocrinology and metabolism at Johns Hopkins Medicine. Her talk is titled "Diabetes Health Disparities: Biology, Race or Racism."

Dr. Sherita Hill Golden kicks off the 2021-2022 Wednesday Afternoon Lecture Series season.

Golden's epidemiological research interests focus on two areas: endogenous sex hormones as risk factors for heart disease, type 2 diabetes and insulin resistance in post-menopausal women; and mental health complications of diabetes and the biological, hormonal and behavioral factors that might explain these associations.

Her health services research focuses on understanding and eliminating diabetes health disparities and implementing and evaluating systems interventions to improve patient safety and quality of care in hospitalized patients with diabetes.

Golden also is vice president and chief diversity officer for Johns Hopkins Medicine, collaborating with leaders across the institution to further advance its diversity and inclusion efforts.

WALS is the highest-profile lecture program at NIH. Lectures occur on most Wednesdays from September through June, from 3 to 4 p.m. From September through December, lectures will be held remote-only via NIH VideoCast. We hope to resume in-person lectures in 2022, depending on the status of the Covid pandemic.

For the full WALS schedule, visit https://oir.nih.gov/wals.

Schools

CONTINUED FROM PAGE 1

minorities, underserved rural communities, people of low socioeconomic status and children with medical complexities—from Los Angeles to Miami, from Lincoln, Neb., to Baltimore.

On Aug. 9, partnering agencies and investigators shared ideas and plans for return-to-school projects during an NICHD-led virtual workshop. Several HHS and CDC program leads discussed nationwide testing efforts working directly with schools, health departments, laboratories and pharmacies.

HHS has made significant investments "to ramp up screening and testing to help schools reopen and keep them open," said Angelica O'Connor, CDC's program coordinator for Epidemiology and Laboratory Capacity for the Prevention and Control of Emerging Infectious Diseases (ELC).

O'Connor noted that the $10 billion from HHS, granted via the ELC Reopening Schools award, provides schools with critical resources to implement testing and prevention measures as they institute other pandemic safety protocols.

ELC-funded health departments will work with school districts to boost screening and diagnostic testing in K-12 schools and fund prevention and mitigation efforts such as personal protective equipment and portable high-efficiency particulate air filters through the current school year.

"The biggest focus moving forward is going to be continuing to work with our jurisdictions," said O'Connor. "Some jurisdictions have lacked parent or community buy-in for screening, although we may see that shift a bit now with [concern over] the Delta variant."

Another HHS-funded initiative, Operation Expanded Testing, is a $650 million public-private partnership with laboratories to provide no-cost Covid testing to K-12 schools and underserved settings such as shelters. Three companies serve as hubs to cover the entirety of the United States. So far, about 1,000 sites are enrolled and the program is rapidly expanding.

With the anticipated additional enrollment of more than 2,000 schools, "we're expecting by mid-September 1.5 million tests total per week being conducted in the program," said Dr. Matthew Humbard of HHS's testing and diagnostics work group.

A young girl gets swabbed using a rapid Covid-19 test kit.

PHOTO: CHATCHAI.WA/SHUTTERSTOCK

Further expanding national testing capacity, the Increasing Community Access to Testing in Schools (ICATT) has partnerships with pharmacy chains to facilitate school screenings.

Implementing this program requires "having a really clear plan for how testing is going to be executed and not just testing but what you're going to do when you get a positive test," said Dr. Joseph Miller, ICATT program lead. "[We're] also making sure [schools] are partnering with their local public health department to ensure consistency between the schools...[Also key is] early communication between school staff and leaders and making sure you're getting very, very quick results back to parents and schools."

During the workshop, Dr. Shamez Ladhani, a pediatric infectious diseases consultant at St. George's University in England, shared insights from the U.K., where in-person school resumed a year ago and schools have remained open even during successive national lockdowns.

Based on U.K. and U.S. data, "the risk of SARS-CoV-2 in children is not that different [than in] adults," said Ladhani. "The earlier narrative that children are less likely to get infected is probably not true and we've verified that in multiple antibody studies."

However, he contends, schools are not hubs of infection. "The evidence for in-school transmission—given all the mitigations in place, however well they're being done and managed given the circumstances—is sufficient to maintain an infection rate that's at least no higher than the community infection rates, and generally lower."

• • •

"Some jurisdictions have lacked parent or community buy-in for screening, although we may see that shift a bit now with [concern over] the Delta variant."

~ANGELICA O'CONNOR

• • •

PHOTO: SEVENTYFOUR/SHUTTERSTOCK

At left, Dr. Shamez Ladhani, pediatric infectious diseases consultant at St. George's Hospital in London; above, Dr. Sonia Lee, acting chief of NICHD's Maternal and Pediatric Infectious Disease Branch, moderated the workshop.

In the U.K., Covid outbreak risks have varied. In primary schools, Covid more commonly inflicts staff; in secondary schools, students are more likely to be infected.

"What's really interesting is the attack rate between students has remained very, very low, between 0.8 and 1.2 percent in primary and secondary schools," said Ladhani, "and this compares to almost 10-fold higher attack rates in primary schools and 4-fold higher attack rates in secondary schools [among staff]."

One U.K. study last year collected blood samples from 3,000 staff and students at nearly 50 primary schools across England over 6 months. In December, after a full term of in-person schooling, about 5 percent of staff and students went from being antibody negative at the start of the surveillance to antibody positive by December 2020, indicating that only a small proportion of students and staff developed symptomatic or asymptomatic infections despite full in-person teaching. Secondary schools had a higher antibody-positivity rate but nowhere near the community rate at the time.

"If [schools] were genuinely hubs of infection," said Ladhani, "we would've expected 4- or 5- times higher antibody rates after in-person teaching for 12 weeks."

What's more, the latest data offers good news about antibody protection in children.

"What we're finding now is that 6 months after infection, the antibody persistence in children appears to be as good as, if not better than, in adults," likely persisting for at least 12 months, he said. Children "do seem to develop very robust antibody responses even after asymptomatic infection."

But in January, another national lockdown closed U.K. schools for 2 months, as the more contagious Alpha variant wreaked havoc. Ladhani noted a small infection peak among 10- to 19-year-olds when schools fully reopened, despite mandatory testing of all secondary students before they returned. However, there was no increase in hospitalization or ICU admissions in that age group.

Kids in class elbow bump, a popular pandemic-era greeting.

PHOTO: PROSTOCK STUDIO/SHUTTERSTOCK

Experts continue to urge vaccinating all who are eligible because worldwide evidence shows that immunizing adults protects children.

"If we can control community infection rates," Ladhani said, "we probably will be able to do a better job of controlling infections in schools."

BACK TO SCHOOL

What We're Learning So Far

Since launching its Safe Return to School Diagnostic Testing Initiative in April, NIH has released some initial findings from its studies across the country:

• Testing in schools is feasible and can be implemented with strong, continuing community and school support, engagement and outreach.

• Low positivity rates and low secondary transmission can be achieved in schools when mitigation strategies are in place.

• Asymptomatic testing uptake by parents is challenging due to misconceptions about tests and/or Covid-19, distrust in Covid test results, concerns about quarantining and the perception of low risk due to other mitigation strategies at school.

• Access to testing after possible Covid-19 exposure is associated with increased uptake.

• It is important to disseminate information and results, provide access to the science and scientists, and rapidly respond to community requests for support.

• It's still unknown what impact increases in other respiratory viruses, as well as the virulent Covid-19 Delta variant will have on return to school.

—Dr. Alison Cernich, NICHD deputy director

In a conference video call, NIH director Dr. Francis Collins, with wife Diane Baker (top l), thanked the Covid Response Teams, which consisted of the Call Center, Contact Investigations and OMS Return-to-Work Teams, as well as the IT specialists who helped set it up and keep it all going. Teams consisted of more than 200 people known to most they served by voice alone, via phone. Many were retirees who volunteered to return to work.

Gratitude

CONTINUED FROM PAGE 1

workplace with in-depth interviews of those diagnosed with Covid-19 and their workplace contacts, and developed critical databases and IT tools to manage documentation and data analysis.

Set up in two FAES classrooms on the B1 level in March 2020, the teams' operations converted fully to virtual mode by October 2020. The Contact Investigations Team communicated with the thousands of workers who called to talk about the implications of testing positive for Covid-19 or having contact with a co-worker while they may have been contagious.

The "Negative" and "Positive" Resulting Teams worked quickly to pave the way for a safe and sound return to work for workers who were tested—whether virus was detected or not—or reported Covid-related health concerns such as signs of illness or a possible exposure to the novel coronavirus.

As Dr. Heike Bailin of the Occupational Medical Service said to introduce the virtual meeting, everyone working for the Covid response "took care of business and people."

As acting OMS director, Bailin oversaw the program that consisted of 200-plus NIH'ers who, pre-pandemic, worked in other roles all across the agency, but volunteered to serve as knowledgeable and sympathetic ears and messengers when the Covid crisis evolved.

"I'm amazed at how quickly and efficiently the call center was set up," said Collins, in the virtual meeting that added faces to the voices of more than 100 response workers who joined in the video call that day.

Diane Baker, Collins's wife and self-identified "invisible and silent fan" of the program, also appeared on camera to congratulate staffers. Over dinner many evenings, she'd heard from Collins about the incredible diligence and heroic efforts of response team employees and wanted to add her appreciation to the growing chorus of congratulations.

Several individuals in the meeting shared personal and deeply emotional testimonies about calls they had taken, employees and their family members who had been counseled and consoled, and the camaraderie the teams had built.

More than one life-saving situation had been handled deftly with extraordinary follow-up.

In addition, several calls with bad, even heartbreaking news had been delivered with empathy and compassion.

Overall, response crews—with their "upbeat attitudes and patient-centered guidance"—put caring first, "answering unprecedented need with unparalleled energy," according to Bailin.

"I'm fond of thinking of NIH not as an institution but as a family," Collins said. "I can't remember a time I've felt more like that than this afternoon hearing these stories. You all just stepped in and did what had to be done. I am deeply grateful that you have kept the NIH family safe."

Since March 2020, more than 1,600 NIH employees with Covid-19 were assessed by 3 contact-tracing teams. The week of Dec. 27, 2020, to Jan. 2, 2021, had the highest number of cases, with 109 cases in 1 week. April 2020 was the center's highest month of calls, with more than 3,700 calls.

As of the beginning of August 2021, the call center had handled about 42,000 calls; approximately 24,000 of those were incoming calls and about 18,000 were outgoing. Call teams also handled an impressive number of OMS Covid questionnaires, with almost 17,000 surveys received as of early August 2021.

Covid Vaccines Prevented Nearly 140,000 Deaths by May

An NIA-supported study estimated that Covid-19 vaccinations prevented nearly 140,000 deaths in the U.S. by May 2021. The study is one of the first to assess the impact of state-level vaccination campaigns. Results appeared in the journal *Health Affairs.*

PHOTO: HALFPOINT/SHUTTERSTOCK

"This study brings into focus the dramatic success of the early months of the nation's coronavirus vaccine rollout," said co-lead author Dr. Christopher Whaley, a policy researcher at the RAND Corp.

About half of the U.S. population had been fully vaccinated as of August 2021. But vaccination rates have varied across the country, with some states proceeding much faster than others.

Researchers collected data on state vaccine administrations from government websites and official statements. They determined how long each state took to reach a series of milestones—starting with 5 vaccine doses per 100 adults, up to 120 doses per 100 adults. They also calculated the number of vaccine doses per 100 adults at the end of each week.

The team used the data to create a statistical model. They then examined the relationship between state vaccination intensity and Covid-19 deaths.

Based on the model, Covid-19 vaccines prevented more than 139,000 deaths during the first 5 months they were available. About 570,000 Covid-19 deaths had occurred in the U.S. by May 9; the model projected about 709,000 deaths would have occurred without the vaccines. The researchers estimated the economic value of preventing these deaths was between $625 billion and $1.4 trillion.

The estimated reduction in deaths varied among states. In New York, vaccinations led to an estimated 11.7 fewer Covid-19 deaths per 10,000. Hawaii had the smallest estimated reduction, with 1.1 fewer deaths per 10,000.

The study had certain limitations that may have affected these estimates. Even so, the results highlight the crucial role of vaccinations in saving lives during the pandemic. The findings support policies that further expand vaccine administration, particularly to low-income and minority populations.—adapted from *NIH Research Matters*

Blood Test May Detect Cancer Earlier in People with NF1

People with an inherited condition known as neurofibromatosis type 1, or NF1, often develop benign tumors that grow along nerves and can sometimes turn into aggressive cancers.

Researchers from NCI and Washington University School of Medicine have developed a blood test that, they believe, could one day offer a highly sensitive and inexpensive approach to detect cancer early in people with NF1 as well as help doctors monitor how well patients are responding to their treatment. The findings are published in *PLOS Medicine.*

NF1 is the most common cancer predisposition syndrome, affecting 1 in 3,000 people worldwide. The condition, caused by a mutation in the *NF1* gene, is almost always diagnosed in childhood. Roughly half of people with NF1 will develop large but benign tumors on nerves, called plexiform neurofibromas.

In up to 15 percent of people with plexiform neurofibromas, noncancerous tumors turn into an aggressive form of cancer known as malignant peripheral nerve sheath tumor, or MPNST. Patients with MPNST have a poor prognosis because the cancer can quickly spread and often becomes resistant to both chemotherapy and radiation. Among people diagnosed with MPNST, 80 percent die within 5 years.

Currently, to determine whether plexiform neurofibromas have turned cancerous, doctors use imaging scans, which are costly, or biopsies, which are invasive. Both can be inaccurate.

Investigators collected blood samples from 23 people with plexiform neurofibromas, 14 patients with MPNST who had not yet been treated and 16 healthy people without NF1. Most study participants were adolescents and young adults, the age group in which MPNST most often develops.

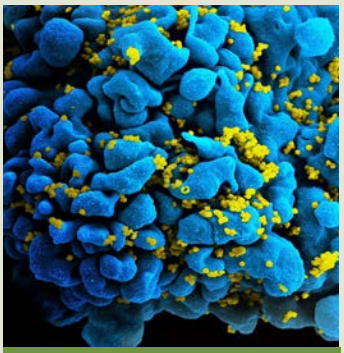
The researchers isolated cell-free DNA—that is, DNA shed from cells into the blood—from the blood samples and used whole-genome sequencing technology to look for differences in the genetic material among the three groups. Differences in cell-free DNA among the 3 groups allowed the researchers to differentiate, with 86 percent accuracy, between patients with plexiform neurofibromas and those with MPNST.

Blood tests of this type also have applications in early detection and monitoring of patients with other cancer-predisposing genetic disorders.

HIV Vaccine Candidate Doesn't Sufficiently Protect Women

An investigational HIV vaccine tested in sub-Saharan Africa posed no safety concerns but did not sufficiently protect against HIV infection, according to a primary analysis of data from the Imbokodo clinical trial. The Phase 2b proof-of-concept study, which began in November 2017, enrolled 2,637 women ages 18 to 35 from 5 countries.

The Imbokodo primary analysis was conducted 2 years after participants received their first vaccinations. The study's primary endpoint was based on the difference in the number of new HIV infections between the placebo and vaccine groups from month 7 (1 month after the third vaccination timepoint) through month 24.



Scanning electromicrograph of an HIV-infected T cell

IMAGE: NIAID

When comparing the number of new HIV infections between study participants, statisticians found that 63 participants who received the placebo and 51 participants who received the experimental vaccine acquired HIV infection. Therefore, the investigational vaccine's efficacy was 25.2 percent. The women who acquired HIV infection were directed to medical care and offered antiretroviral treatment.

The investigational vaccine is based on "mosaic" immunogens—vaccine components designed to induce immune responses against a wide variety of global HIV strains. The vaccine candidate used a strain of common-cold virus (adenovirus serotype 26, or Ad26), engineered to not cause illness, to deliver four mosaic antigens to spur an immune response. Earlier research indicated the vaccine could induce an anti-HIV immune response. Imbokodo participants received 4 vaccinations during a 1-year period. The primary analysis occurred 1 year after the last study participant's final vaccination.

Further analysis will continue. A different investigational HIV vaccine is in testing among a different patient population than this study (men who have sex with men and transgender populations in the Americas and Europe). That trial, a phase 3 study called Mosaico, is estimated to be completed in March 2024.

NIDDK's Knowler Retires After 46 Years

BY LISA YUAN

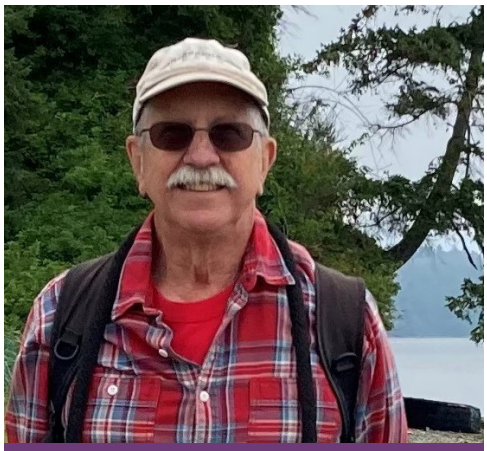
With September marking his official retirement after nearly 50 years at NIH, Dr. William Knowler leaves behind an extraordinary legacy. Since 1979, he has served as chief of NIDDK's diabetes epidemiology and clinical research section in the Phoenix Epidemiology and Clinical Research Branch (PECRB), where he has devoted decades of practice-changing research into diabetes and its complications, particularly among Southwest American Indian populations.

"Dr. Knowler is widely recognized as the leading researcher furthering our understanding of the causes, prevention and treatment of type 2 diabetes and related complications," said NIDDK scientific director Dr. Michael Krause. "His research has consistently driven clinical practice to prevent and treat this prevalent disease."

Knowler, who received his M.D., M.P.H. and Dr.P.H. degrees from Harvard University, joined NIDDK's PECRB in 1975. His research programs have included a 43-year longitudinal study that uncovered risk factors for type 2 diabetes and its complications, and several groundbreaking, multi-center studies, such as the Diabetes Prevention Program (DPP), the DPP Outcomes Study (DPPOS) and Action for Health in Diabetes (Look AHEAD) clinical trials.

DPP and DPPOS showed that weight loss through moderate physical activity and healthy eating or the medicine metformin can help prevent or delay type 2 diabetes—changing how people approach prevention of this disease worldwide. The Look AHEAD clinical trial showed that a lifestyle intervention in adults with type 2 diabetes reduced the risk of many, but not all, diabetes complications.

"In my opinion, Dr. Knowler has contributed more to improve the health of people with type 2 diabetes mellitus than any other physician/scientist, especially for Native Americans of the Southwest," said PECRB chief Dr. Clifton Bogardus II.



Dr. William Knowler enjoys retirement in Vashon, Wash.

For decades, Knowler and other PECRB scientists have worked closely with Southwest American Indian communities to gain valuable insight into the disease's risk factors and development. These communities have a high prevalence of type 2 diabetes. Knowler played a pivotal role in making sure American Indians were well-represented in the DPP's and Look AHEAD's diverse participant pools, which helped ensure the study results could be applied in the communities at highest risk for the disease.

Of all accomplishments, "I am most proud of our collaborations with the American Indian partners in research," said Knowler. "They volunteered to be in studies because they believed participation might benefit their own health, but also that of others in the future."

American Indian Center DPP and Look AHEAD research team members hike. Knowler's research programs have included several groundbreaking, multi-center studies, such as DPP, the DPP Outcomes Study and Look AHEAD.

PHOTO: DPPOS RESEARCH GROUP

His other achievements include more than 800 publications, over 100 major conference presentations and numerous awards, including the NIH Director's Award and the Tribal Leaders Diabetes Committee Award for "research in treatment and prevention of diabetes in American Indians."

Knowler has also dedicated much time to mentoring students, postdoctoral fellows and associate physicians, most of whom have gone on to successful positions at institutions worldwide. For example, former PECRB fellow Dr. Stephanie Tanamas, now an epidemiologist at Monash University, Australia, acknowledged the lasting impact Knowler had on her.

"He possesses a unique way of thinking and in-depth knowledge about a vast range of topics and I continue to benefit from his mentorship even now, years after I left NIDDK," Tanamas said.

Dr. Dana Dabelea, a PECRB fellow from 1997 to 1999, described Knowler's mentorship as "a life-changing experience and the impetus for a lifelong, successful career in academic research." Dabelea is director of the Lifecourse Epidemiology of Adiposity & Diabetes Center at the Colorado School of Public Health.

Several of Knowler's mentees have gone on to become leaders themselves at NIDDK, including Dr. Robert Hanson, chief of PECRB's diabetes genetic epidemiology section.

"I have learned a tremendous amount of epidemiology from Dr. Knowler," Hanson said. "His commitments to scientific excellence, to the well-being of research participants and to people affected by diabetes are inspiring, as is his welcoming attitude towards members of his research group."

Knowler plans to remain active scientifically, while enjoying retired life on Vashon Island in Washington. He looks forward to exploring mountain trails of the Pacific Northwest and spending time with his family.

"We wish him all the best, we applaud his accomplishments and we thank him for his extraordinary dedication," said Krause. "His career has been truly remarkable."

NIDDK director Dr. Griffin P. Rodgers echoed the thoughts. "Dr. Knowler has made

immeasurable contributions over nearly half a century," he said. "His pioneering research has led to changes in clinical practice that have improved the lives of people at risk for type 2 diabetes, including American Indian communities, and he has truly embodied the NIH spirit of improving health for *all* people. He's had an enormous impact on those who've been lucky enough to work with him, as well as those who have benefitted from his groundbreaking research."

CSR's Politis Retires

BY PAULA T. WHITACRE

Dr. Alex Politis, chief of the infectious diseases and microbiology integrated review group (IRG) at the Center for Scientific Review (CSR), retired in June. He served as IRG chief for 19 of his 23 years at NIH. Politis likened parts of the job as chief to his days of coaching basketball, baseball and soccer teams.

Dr. Alex Politis

"I operated the IRG like a team," he said. "There were circumstances where we had to scramble to get things done despite obstacles. The unit needed to act together. Motivation was a major issue. Respect for one another was another major issue. It all happens in athletics as well as administrative-type situations like an IRG."

Politis grew up playing sports, especially soccer, north of New York City. He credits good teachers in high school and the State University of New York in Cortland for cultivating his interest in biology.

He discovered his love of teaching while in graduate school at Florida State University. Politis continued teaching during his doctoral and postdoctoral research and training at the University of Maryland and the Uniformed Services University of the Health Sciences (USUHS). He was a research fellow, associate and assistant professor at USUHS from 1988 to 1994.

While at USUHS, Politis served as an ad hoc reviewer for the *Journal of Immunology*. In 1994, he joined the journal staff as assistant editor.

"That job introduced me to peer review and science administration," he noted. "When I applied to CSR as a review officer, it seemed a natural fit." He joined CSR as a scientific review officer of the immunological science study section in 1998, then became IRG Chief in 2002. Although he had little previous management experience, and some colleagues cautioned he may not like it, "my absolute favorite part of the job became building the team," he said.

"He has always been a wonderful, supportive, uplifting colleague," said Dr. Sally Amero, who also joined CSR in 1998. After leaving CSR to become the NIH review policy officer in OER, Amero would regularly ask Politis for help in training new extramural staff and in peer review policies and procedures.

"Review staff are tightly connected," she said. "He was cognizant of that and promoted cooperation and respect across NIH. He also has a knack for using humor to make a point or communicate complicated messages."

From 2015 to 2020, Politis teamed with CSR scientific review officer Dr. Gagan Pandya and Dr. Robert Eisinger, senior scientific advisor in the OD, to work on the $20-million Antimicrobial Resistance Diagnostic Challenge Prize, a project co-sponsored by NIH and the Biomedical Advanced Research and Development Authority (BARDA).

"Alex was important in developing the criteria in how the proposals would be reviewed," Eisinger said. "He also ensured that reviewers had relevant technical and scientific expertise to evaluate this novel competition." On this and other initiatives, Eisinger added, "Alex has been on the cutting edge of how to keep the NIH review process aligned with where the science is and to ensure that peer review is a level playing field."

For Politis, retirement so far has included travel to visit family, woodworking and golfing with his son. "I showed him how to play when he was 3 or 4 years old," he said. "Now he's giving me lessons."

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 effects 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. PNs can form anywhere in the body and based on their size or location, the tumors can become visible and cause unwelcome changes in appearance. 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.

Have Food Allergy?

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.

These two 1960s era ARMCO buildings were removed to clear the site for the new center.

NIAID Rocky Mountain Labs To Get Comparative Medicine Center

NIH will construct a Comparative Medicine Center at its Rocky Mountain Laboratories facilities in Montana. The new building previously known as "Bldg. B" during the planning phase, will alleviate stress on other buildings for NIAID, as facilities now do not have adequate animal holding space. Current accommodations limit research that scientists are conducting on the RML campus.

The new building will allow NIAID to expand its research response to future infectious disease outbreaks. Funding for the new construction was made available through the CARES Act, which enables increases in Covid-19 research capabilities. The new structure will replace RML's Armco I and II Bldgs., which were constructed in the 1960s. The Office of Research Facilities hopes to award a construction contract as early as this fall. The new center is estimated to be completed by spring 2024.

Artist's renderings of the new Comparative Medicine Center at NIAID's Rocky Mountain Laboratories in Montana show views east (above), south (below) and west (bottom).