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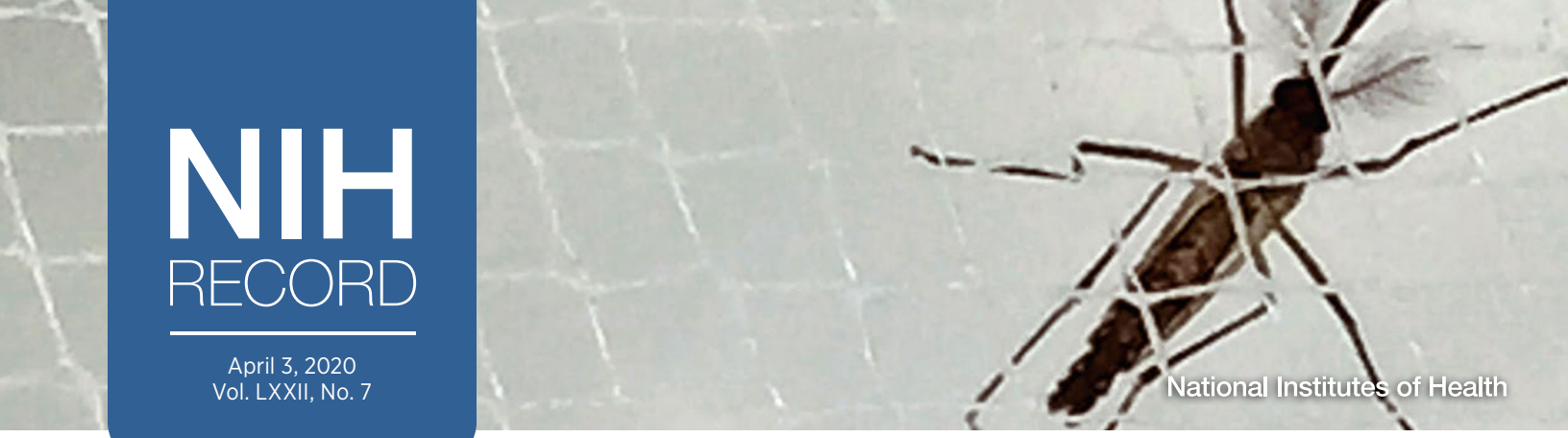


VIEW FROM OUTBREAK ORIGINS

NIAID's Lane Discusses WHO COVID-19 Mission to China

BY CARLA GARNETT

Dr. Cliff Lane was at Dulles International Airport waiting in line to board a flight to Tokyo when he got an urgent email. A World Health Organization mission to China—where the novel coronavirus outbreak was first discovered—had just been approved and Lane's appointment as a member of the WHO team needed to start immediately. How soon could he get to Beijing?

It was Feb. 13, a little more than 6 weeks since coronavirus infection in Wuhan, China, had led to the first cases of a serious respiratory illness now called COVID-19. Lane was already headed to a coronavirus

Masks were standard uniform for WHO mission participants.

trouble spot—a cruise ship docked at a port in Yokohama, Japan's second largest city. Rates of infection and illness were rising fast on board and a call had gone out to the international medical community. Was there anything NIH could do to accelerate a research response in the area of therapeutics? Remdesivir, a novel antiviral drug that had been studied in the recent Ebola outbreak in the Democratic Republic of the Congo (DRC), was being floated as a potential treatment. That's where Lane's head was too, even as he heard the boarding announcement for his flight.

"It wasn't even on my radar that I would be selected [for China]," he recalled, "because I knew that there were only a few people going."

Of course, after 41 years at NIH, Lane, NIAID's deputy director for clinical research and special projects, is no stranger to deadly pathogens. About 6 years ago, he was among the beaming NIH'ers waving a very public farewell to Nina Pham, a nurse and patient with Ebola successfully treated in the Clinical Research Center's new special clinical studies unit, which was established to conduct research on an emerging infectious disease.

"This goes back to SARS [severe acute respiratory syndrome]," said Lane, detailing

SEE **OUTBREAK**, PAGE 6

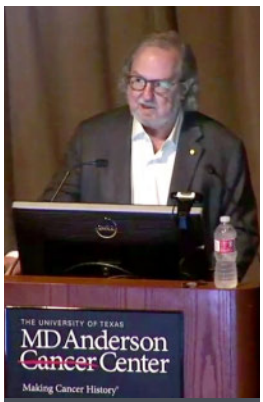
New reality, new look for CRC. See story, p. 7

ALSO THIS ISSUE

EMPTY HALL, FULL TALK

Nobelist Allison Pushes Deeper into Cancer Immunology

BY RICH MCMANUS



Dr. Jim Allison

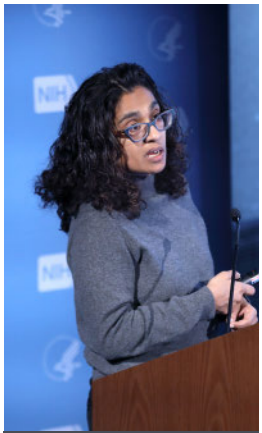
Never before in the history of the Wednesday Afternoon Lecture Series has a speaker in one empty room 1,400 miles from Masur Auditorium given a lecture to another empty room in Bldg. 1.

But such was the case Mar. 11 when, owing to public health concerns over the spread of COVID-19 disease, Nobel laureate (2018)

SEE **ALLISON**, PAGE 4

Algorithm Sifts Through 'Sea of Mutations'

BY ERIC BOCK



Dr. Mona Singh

An algorithm can search through a "sea of mutations" in cancer genomes to find those that play a role driving cancer initiation and progression, said Dr. Mona Singh at an NIH Director's Lecture held recently in Lipsett Amphitheater.

"There are lots of mutations per cancer genome, and yet only a few of these mutations within an individual are relevant for his or her cancer," said Singh, professor of

SEE **SINGH**, PAGE 8

Webinar on Improving Efficiency of Prevention Research, Apr. 15

The Office of Disease Prevention (ODP) will hold a Methods: Mind the Gap webinar with Dr. James Wagner on Wednesday, Apr. 15 at 2 p.m. His topic is "Improving the Efficiency of Prevention Research Using Responsive and Adaptive Survey Design Techniques."

Dr. James Wagner

Wagner is a research associate professor at the University of Michigan's Survey Research Center. His work is in the area of survey non-response, including indicators for the risk of non-response bias and adaptive/responsive survey design. He is the co-author of a new book (2017) titled *Adaptive Survey Design*. Wagner is also associate director of the Michigan Program in Survey Methodology.

Registration is required at prevention.nih.gov/education-training/methods-mind-gap/improving-efficiency-prevention-research-using-responsive-and-adaptive-survey-design-techniques.

The webinar will be recorded and available on the ODP website within about a week.

Annual EDI Awards Open for Nominations

The Office of Equity, Diversity and Inclusion (EDI) is accepting nominations for the annual Harvey J. Bullock Jr. Award, the Yvonne Thompson Maddox Award and EDI Award of the Year.

These awards recognize NIH employees who champion the ideals of equity, diversity and/or inclusion. Nominations must be submitted no later than Friday, Apr. 17 and may be emailed to Ijeoma Ofoha, ijeoma.ofoha@nih.gov.

The Bullock award honors a non-supervisory employee or group of employees at grade 12 and below or equivalent. The Maddox Award recognizes a non-supervisory employee or group of employees at grade 13 and above or equivalent. The EDI award honors executives, managers or supervisors who have made significant contributions toward furthering NIH's EDI efforts.

Awardees will be recognized during the 2020 NIH Director's Awards Ceremony, Aug. 19.

For more information, visit www.edi.nih.gov/consulting/outreach/edi-awards. To nominate, visit https://www.edi.nih.gov/sites/default/files/downloads/outreach/edi-award-nomination-form-2020.pdf. You may also contact your institute/center awards coordinator for details.

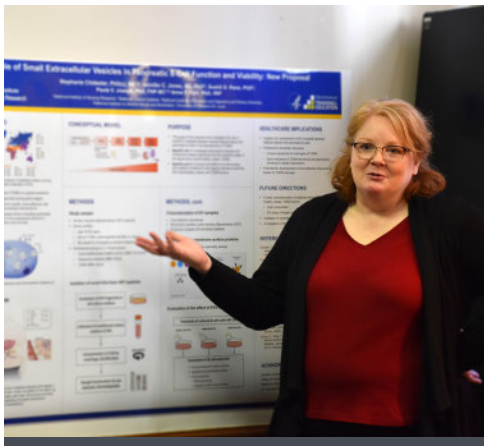
NINR staff celebrate American Heart Month in front of Bldg. 1.

PHOTOS: ANDREW LIANG

NINR Walk Promotes Heart Healthy Activities

In recognition of American Heart Month, the Division of Intramural Research at the National Institute of Nursing Research recently organized a walk for NINR staff.

The event encouraged staff to nourish both their hearts and their minds, starting with poster presentations from Graduate Partnerships Program (GPP) pre-doctoral fellows Delia Sass and Stephanie Chidester. Following the presentations, the group took a brisk walk across campus to Bldg. 1 where they enjoyed heart-healthy snacks. Colleagues encouraged each other to be heart-healthy and raised awareness for the health observance by wearing red.



Stephanie Chidester presents her GPP poster "Role of Small Extracellular Vesicles in Pancreatic ß-Cell Function and Viability: New Proposal."

NINR staff walk across campus while wearing red. It was also American Heart Month.

NINR staff hold apples in front of Bldg. 1.

Workshop Addresses Youth Vaping Epidemic

BY COLLEEN LABBE

Workshop attendees learn about the roots of the vaping epidemic among U.S. youth from Dr. Brian King, deputy director of CDC's Office of Smoking and Health.

PHOTO: JEN HESSION

There's a vaping epidemic among our youth, and we need to prioritize research that identifies and deploys the most effective prevention strategies, while helping those already addicted to stop using. These are the conclusions of a multidisciplinary workshop held Mar. 2-3 and organized by NHLBI, ODP, NCI, NIDA, OBSSR and others.

Long before the recent e-cigarette, or vaping, product use-associated lung injury outbreak that mobilized public health officials, young people were getting hooked. Dr. Brian King of the CDC's Office on Smoking and Health noted in the workshop's opening session that e-cigarette use among youth in the last 10 years has skyrocketed among both middle and high schoolers.

This rate hike has been driven by multiple factors such as targeted advertising, the use of enticing flavors and the development of extremely addictive products. And because new products are emerging all the time, "We must modernize and adapt our approach to researching the issue and establishing policies to stay current," he said.

Reducing e-cigarette use among youth may seem daunting, but we can potentially apply lessons learned from earlier tobacco control research and policy decisions, attendees learned.

For instance, peer leader models have been used successfully in teen cigarette smoking prevention. And research on vaping shows that kids with fewer peer bonds and fewer positive adult connections are more likely to vape.

"Researchers need to leverage peer influence in prevention and promote accurate perceptions of risk. We should also consider the influence of older adolescents" on younger kids, said Dr. Peter Wyman of the University of Rochester.

Data has already shown that the basic "vaccine" against smoking—a combination of smoke-free policies, price increases, access to cessation methods or treatments and media campaigns—can successfully curb tobacco use. In fact, youth use of tobacco products decreased significantly between 1990 and 2018 due in no small part to policy shifts and restrictions. But as Dr. Tesfa Alexander of FDA's Center for Tobacco Products noted, the e-cigarette industry's volatility and constantly shifting product landscape may call for a different approach.

Existing tobacco cessation campaigns that have been tweaked to address e-cigarettes show promise. For example, FDA's Real Cost Campaign, first conceived to divert teens from cigarette smoking, has widened its scope to include e-cigarettes. Initial testing of vaping prevention ads suggest they resonate with youth just as well as anti-cigarette ads, but it remains to be seen if they can influence behavior and prompt users to quit.

Dr. Donna Vallone of the Truth Initiative called for the research community "to improve our understanding of the digital landscape where youth spend so much of their time," so we can effectively leverage it. Recognizing that the vaping industry had already "lit the tech trend" by placing its ads and influencer endorsements on the social media apps most used by youth, the Truth Initiative aims to counteract the industry's messaging with its "This Is Quitting" or TIQ campaign. TIQ includes a texting support program—with 130,000 young people signing up in just 1 year—and the #thisisquitting campaign on TikTok, a wildly popular app among the 16- to 24-year-old demographic.

In 2019, some states began to implement policy changes designed to restrict e-cigarette use, and federal efforts also are underway, but many gaps remain. In addition, workshop participants cited concerns about unintended consequences of e-cigarette policy restrictions. For instance, if and when more restrictive policies are enacted, how well will they align with existing cessation resources? Will restrictions on e-cigarettes inadvertently tilt teens back toward using combustible tobacco products?

As the workshop participants brainstormed a list of clinical and policy-oriented research topics, there was general agreement that we need to develop and test tailored interventions, implementation strategies and prevention efforts, as well as link channels of influence to ensure cross-disciplinary engagement. R

ON THE COVER: Aedes Aegypti *mosquitoes. Female (l) and male* Aedes aegypti *mosquitoes can transmit the Zika virus.*

IMAGE: NIAID

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Allison

CONTINUED FROM PAGE 1

Dr. Jim Allison's lecture on "Immune Checkpoint Blockade in Cancer Therapy: Historical Perspective, New Opportunities and Prospects for Cures" became a videocast only.

"I am speaking to you from a very empty Wilson Hall," said NIH director Dr. Francis Collins, who introduced the lecture, seen live by more than 800 online viewers. "This is an historic lecture in two ways: Our speaker, Jim Allison, is a remarkable role model of a passionate, determined, inquisitive scientist. And, we've never done it like this before—a virtual presentation, due to concerns about this virus."

Collins called Allison "an interesting character, an iconoclast. One of his colleagues once observed, 'Jim's lab has the feel of a pirate ship.'"

Collins also divulged, "I once had the pleasure of performing a duet with [Allison], in a bar east of the Capitol." Collins, on guitar, accompanied Allison, whose skill on the mouth harp has put him on stage with country music star Willie Nelson in the past.

"I'm sitting in an empty room," began Allison, who is chair of the department of immunology at MD Anderson Cancer Center. He apologized for missing an opportunity to mingle with old friends at NIH. "I miss you guys."

He then reviewed in detail the history of checkpoint blockade, focusing on two molecules, CTLA-4 and PD-1. Surprisingly, he said, they work against some tumors very well in combination, "but not just as the sum of the two."

Importantly, the new therapies do not attack the tumor itself, but free the immune system to go after the tumor, Allison explained.

In the case of the anti-CTLA-4 antibody known as ipilimumab—which was developed from Allison's research—the blockade of a single molecule is enough to produce "an astounding result...It is sufficient to create long-lived immunity," Allison said.

One patient, treated 16 years ago with the antibody, is still doing fine, despite having once had melanoma with metastases to the lungs and brain.

"Another patient is 19 years out, so this is a very durable response," said Allison.

In an empty Hickey Auditorium at MD Anderson, Allison presents a talk to a small Wilson Hall audience that can be seen on the screen in the background.

"I think these patients can be considered cured."

But only about 20 percent of patients get this kind of response, so Allison and his colleagues are doubling down on finding other checkpoints. They are now using nivolumab for patients who fail ipilimumab, and vice versa.

"Combining these agents is at least additive," he said. Researchers report a survival rate of about 55 percent using combination therapy at the 5-year point. "We consider this a very durable response. We believe the 10-year survival may exceed 50 percent."

For perspective, prior to these therapies, life expectancy for patients with metastatic melanoma was only 7 months after diagnosis, Allison noted.

A common feature of the cancers for which checkpoint blockade is effective is the process of DNA defect repair, observed Allison. Anti-CTLA-4 antibodies target the CD 28 pathway, whereas anti-PD-1 antibodies affect only CD 8 cells. Monotherapy with either agent has "overlapping but quite distinct effects," he said. "They expand different cell types."

NIH director Dr. Francis Collins (l) and NCI Surgery Branch chief Dr. Steve Rosenberg chat virtually with Allison from NIH.

Allison believes there are other inhibitory molecules that may serve as potential targets in immunotherapy. In the future, he predicts more combinations of PD-1 and CTLA-4.

"Increases in median survival are what indicates efficacy," he said. "We hope to see this in as many different cancers as we can. With diligence and rational use of data, we are expecting more curative combinations."

One of some five people on hand for the lecture in Wilson Hall was Dr. Steve Rosenberg, chief of NCI's Surgery Branch, another pioneer in cancer immunotherapy. After a brief Q&A with questions submitted online, Rosenberg told Allison, "I always learn something when I hear you talk. You keep going, you keep learning and you keep teaching us new things."

T may be for Texas, according to Willie Nelson, but to Nobel laureate Allison, T is for T cells.

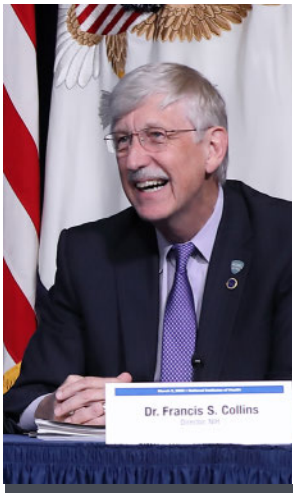
Inasmuch as coffee and cookies commonly follow WALS lectures, Collins held up samples of both, inviting onlookers to enjoy virtual refreshment.

"Thank you for being the first-ever virtual WALS lecturer," he told Allison. "I look forward to the end of this crazy pandemic and hope that you can come here again someday. Then maybe we can go off to a bar somewhere afterward and play music."

The full talk is archived at https://videocast.nih.gov/summary.asp?live=36081&bhcp=1.

EDI Names Collins Women's History Month 'Game Changer'

In recognition of Women's History Month, the Office of Equity, Diversity and Inclusion (EDI) has honored NIH director Dr. Francis Collins for being a catalyst for change by challenging structures that disadvantage women while continuing his commitment to the success of NIH.



NIH director Dr. Francis Collins
PHOTO: CHIA-CHI CHARLIE CHANG

"Dr. Collins is an example of how men can proactively and routinely advocate for women's rights, changes to culture and prevent gender discrimination," EDI said in a statement. Collins has said, "It is not enough to give lip service to equality; leaders must demonstrate their commitment through their actions."

Last year, he directed an advisory committee to the NIH director working group to develop strategies and system-wide changes to culture and climate, for the prevention of harassment and gender discrimination. He created the working group after learning of several high-profile sexual harassment cases involving federally funded investigators.

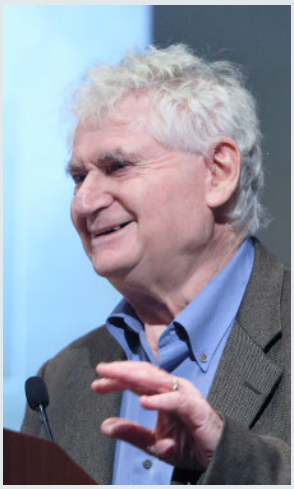
Collins has also spoken out against all-male panels. "Starting now," he said, "when I consider speaking invitations, I will expect a level playing field, where scientists of all backgrounds are evaluated fairly for speaking opportunities. If that attention to inclusiveness is not evident in the agenda, I will decline to take part. I challenge other scientific leaders across the biomedical enterprise to do the same."

EDI commended Collins for his stance on gender equality. "It is our honor to select him as the organizational Game Changer for Women's History Month," the office stated.

KUDOS

HHS Honors Seven from NIH

Seven NIH'ers are among winners of the 2019 HHS Departmental Awards, the highest awards issued by the department. They were scheduled to be honored May 6 in the Great Hall of the Hubert H. Humphrey Bldg.



Clockwise from upper left are Drs. David Henderson, Ira Pastan, W. Marston Linehan and Laura M. Lee. Below are (from l) Melissa Bronez and Drs. Henry Masur and William Gahl. All won HHS departmental awards for 2019.

Winning the Secretary's Award for Distinguished Service were: Dr. David Henderson, deputy director for clinical care at the Clinical Center and associate director for hospital epidemiology and quality improvement; and Dr. Ira Pastan, NIH distinguished investigator in the Laboratory of Molecular Biology, NCI.

Winning the Secretary's Award for Meritorious Service were: Dr. Laura M. Lee, director, Office of Patient Safety and Clinical Quality at the Clinical Center; and Dr. W. Marston Linehan, senior investigator in NCI's Urologic Oncology Branch.

Winning the HHS Award for Excellence in Management was Melissa Bronez, associate director for research operations and planning at NCI's Center for Cancer Research.

Winning the Hubert H. Humphrey Award for Service to America was Dr. Henry Masur, senior investigator in the Clinical Center's critical care medicine department.

And the Career Achievement Award went to Dr. William Gahl, NHGRI clinical director, senior investigator in NHGRI's Medical Genetics Branch and founder, in 2008, of the NIH Undiagnosed Diseases Program.

The WHO-China Joint Mission on COVID-19

Outbreak

CONTINUED FROM PAGE 1

some of NIH's recent history with novel infections. "SARS was the first outbreak for which we developed a Clinical Center protocol. There's a coronavirus that causes SARS and a coronavirus that causes MERS [Middle East respiratory syndrome]. There are also coronaviruses that cause the common cold. Ever since SARS [in 2003], NIAID has had a clinical research program on coronaviruses. We have been able to jumpstart some of the current research from that basis."

Over the past decade, Lane's group has conducted several clinical trials on Ebola virus here and in parts of West Africa such as Guinea, Sierra Leone and Liberia. Currently, a study is underway in the DRC. He was also on the front lines of HIV research back in the early days of the AIDS epidemic. The WHO summons to China, too, represented an incredible opportunity to experience and learn virtually at a disease's Ground Zero. But first, there was Tokyo.

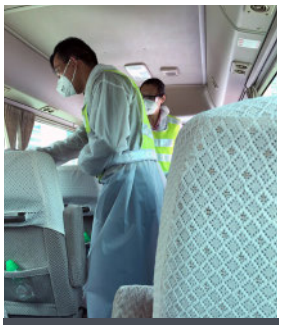
"I really felt I had an obligation to the Japanese government," Lane said. "Our relationships with other governments are important and we needed to honor that... So I'm basically [during] the entire flight to Tokyo working through all the different time zones trying to line up all the things that needed to be done.

"Getting a visa to China is a challenge in calm, usual situations," he continued. "Doing something like that in an emergency takes an enormous amount of coordination. It was WHO pitching in. It was NIH pitching in. It was the State Department, including the U.S. embassies in China and Japan, the WHO and the Ministry of Foreign Affairs in China all helping. It was an amazing number of entities working together. By the time I landed in Japan, I headed straight to the Chinese Embassy in Japan to get a visa to China. That was remarkable in itself."

The WHO-China Joint Mission on COVID-19 had one overall goal: "To rapidly inform national (China) and international planning on next steps in the response to the ongoing outbreak of the novel coronavirus disease (COVID-19) and on next steps in readiness and preparedness for geographic areas not yet affected," according to the mission's report.

Twenty-five members formed the group—half from China and half representing WHO. The WHO group included experts from several countries including Canada, Germany, Japan, Nigeria, Russia, Singapore and South Korea. Lane, on his first official WHO assignment, was one of two Americans.

"It was a really good group of people to work with," he said. "[WHO] tried to select people from different geographic areas as well as a diversity of skill sets. I was there representing the research response. Others represented epidemiology, infection control and diagnostics. The diagnostics person was from Russia."



A bus trip is interrupted for temperature checks.

The mission took about 9 days (tack on 3 extra for Lane, who rerouted himself from Japan prior to his WHO role). The WHO delegation traveled from Beijing to Shenzhen, Guangdong, and from there to Guangzhou. The group had briefings by political leaders, hospitals, community centers and China's equivalent of the U.S. Centers for Disease Control and Prevention at the national, provincial and municipal levels.

A smaller mission contingent that didn't include Lane visited Wuhan, epicenter of COVID-19. He was temperature-screened at each airport in Japan and China, and for safety's sake, he self-quarantined for 2 weeks after coming home.

He shared notable observations from his travels.

"The first thing I noticed at the boarding gate to the flight to China is that everybody's wearing a mask except me," he said. He noted the same thing on the bus from the airport to the hotel and was not allowed into his hotel without one. He was given a mask at the hotel entry's fever checkpoint before being allowed to go to the reception desk to check in.

"The Chinese were managing this in a very structured, organized way," he explained. "When we got there, the outbreak was already coming under control in China. The measures they put in place appeared to be working—I think they felt there were lessons learned they wanted to share with the rest of the world. It demonstrated their successful response and I think they felt a fair degree of pride in what they had done... From what I saw in China, we may have to go to as extreme a degree of social distancing to help bring our outbreak under control."

The world has experienced and endured pandemics before, so what makes COVID-19 unique?

For one thing, Lane explained, it is caused by a new virus and thus we are not entirely sure what to expect. "Typically, when we think of a respiratory virus, we think common cold, flu, MERS and SARS. The clinical syndrome of [COVID-19] is somewhere in that spectrum, but where it fits—in terms of its transmissibility, its pathogenicity or lethality—that's all being learned on the fly," he said. "It is a brand new virus—that's the thing about it...While you can guess a bit from the past, you really have to learn from the present."

Dexterity, agility and flexibility are all key in infectious diseases research, Lane said.

"The tools we developed to rapidly respond to Ebola outbreaks have been used to rapidly respond to this outbreak. We have staff throughout the institute who are very skilled at adapting assays to new pathogens and establishing clinical trials in austere environments...Also one of the great virtues of the Intramural Research Program and its elements is the ability to turn on a dime and respond in an instant."

In fact, Lane noted, through an international clinical study that the NIAID Division of Microbiology and Infectious Diseases is conducting, NIH is playing an important role

in the clinical research response to COVID-19.

"We have an active protocol to test the efficacy of the investigational antiviral agent remdesivir," he said, "and I anticipate as this outbreak unfolds, we will admit patients to the CC to participate in that protocol [see sidebar below]."

Does the risk of getting infected himself ever concern Lane as he rushes into various disease zones?

"It's what we do," he said. "That's part of our mission. We study infectious diseases, so we go to where the infectious diseases are. We know about infection control. I did not have any direct contact with patients. We were in hospitals, but in areas where they were doing fever checks before anyone entered the areas. There's some risk to anything that one does, but this is what you sign up for when you go into this career path. I worry as much about seeing a patient in the Clinical Center with drug-resistant TB as I do about going to China to look at COVID-19."

Health care worker infections in China occurred early in the outbreak, he continued, "before they had a sense of what was evolving. Health care worker infections are now rare in China, and these are the people directly taking care of the patients. The same has been the case with Ebola. When you take the proper precautions and pay attention to detail, you can substantially minimize the risk to the health care worker."

Still, he said, coronavirus is not to be taken lightly. "China adopted extreme social- distancing policies and the Chinese scientific community has been contributing substantially as well—including rapidly identifying and sequencing the virus and making the sequences publicly available.

"If there were more opportunities for collaboration between the Chinese research community as a whole and the U.S. research community as a whole, that could be of benefit," Lane concluded. "The cities, hospitals and laboratories in China are state-of-the-art. There's so much going on there that I think they could be a valued scientific partner, if one can get over the political hurdles."

China demonstrated that rapid implementation of extreme social distancing led to fairly rapid control of the outbreak, Lane observed. "That's a good lesson. There are probably lessons that everyone could take for influenza as well. People coming in to work when they're even a little bit sick is not in the best interest of public health and puts the health of other individuals at risk.

"The lesson going forward is that there are ways you can prevent the spread of a respiratory disease," he said, "but everyone has to take personal responsibility. It's not an issue of the individual being tough enough to work through the illness. That's not the issue. The issue is, you go to work and you infect your coworkers. It's a matter of whether you care enough about your coworkers to minimize their risk of infection."

Clinical Center Prepared to Deal With Coronavirus Patients, Gilman Says

BY DANA TALESNIK

As cases continue to surge nationwide, the Clinical Center is well equipped to take care of coronavirus patients, said Clinical Center CEO Dr. James Gilman.

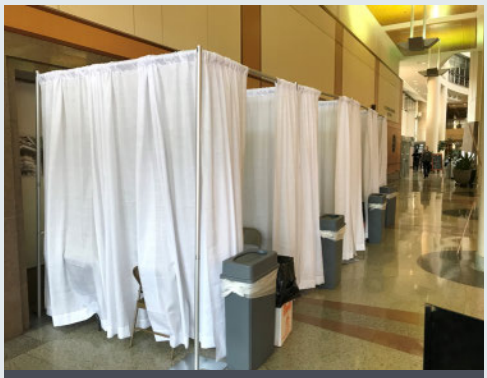
"We have the facilities to take care of the patients, but our fundamental mission is research so that's the backdrop for anything else that happens here," he said.

Supporting NIH researchers as they work toward bringing treatments and a vaccine from bench to bedside, the Clinical Center is currently one site of a multi-center clinical trial of a potential drug for coronavirus patients. The hospital began accepting such patients on Mar. 24, when two research participants began a randomized, controlled NIAID clinical trial of the antiviral remdesivir.

In preparation for this eventuality, the CC recently took stock of its quarantine capacity. There are a total of 11 rooms in strict, airborne isolation: 7 in the special clinical studies unit and 4 inpatient rooms. These rooms meet optimum quarantine standards: negative pressure to outside air, HEPA filters and anterooms where staff can safely put on and remove personal protective equipment such as gowns and masks.

"Eleven is the number of patients, in terms of our facilities, that we could take care of the best," said Gilman, adding that there are additional, negative-pressure rooms that could house patients.

At the local level, the CC, which often collaborates with Walter Reed National Military Medical Center and Suburban Hospital, may expand that relationship to take in some of their coronavirus patients should the need arise during this viral pandemic. An agreement among the three hospitals, drafted after 9/11 and renewed ever since, fosters an even greater exchange in the event of a natural disaster or other national emergency, said Gilman.



Screening booths for patients and visitors were erected at the entrance to the Clinical Center on Mar. 12. It became mandatory, later in the month, for everyone to be screened.

PHOTO: RICH MCMANUS

"We have contingency resources for taking care of patients who may have to come to us from Suburban or Walter Reed," he said.

The hospital's leadership has been preparing for this pandemic at a precipitous pace. They engage in multiple meetings daily, making quick decisions and problem-solving as they go along. Gilman likened the pace to that of a critical military operation.

"I've been a physician over 40 years, and I've been through some pretty interesting times, including a lot of time in the Department of Defense taking care of young men and women [injured in battle], but I've never been through anything like this," he said. "I have a lot of experience with military operations and I would say that the pace here equals that of even the most well-organized military exercises and operations."

In addition to preparing for coronavirus patients and protocols, the CC is making significant changes every few days to help protect patients and staff while providing optimal patient care. One such change is updating its visitor policy.

"We've begun to tighten the visitor policy significantly, with the idea that we will tighten it even further should we have to," said Gilman.

As of mid-March, the CC was limiting each inpatient, even children, to one visitor at a time.

"It cuts down on the number of people we have to screen," said Gilman, "and helps protect not only our vulnerable patients but also our staff."

And, since Mar. 13, all patients and visitors entering the CC are screened for symptoms at the door [this policy became mandatory for all entrants to Bldg. 10 later in the month]. Staff who have a fever or other coronavirus symptoms first get screened by the Occupational Medical Service; some then get tested.

"Our department of laboratory medicine has done a great job of developing the ability to test patients and staff," said Gilman.

"We will do whatever the NIH, HHS or national leadership decides," he concluded.

Singh and her team search for mutations relevant to patients' cancer.

PHOTOS: CHIA-CHI CHARLIE CHANG

Singh

CONTINUED FROM PAGE 1

computer science at Princeton University's Lewis Sigler Institute for Integrative Genomics. "The mutations that you see across individuals can vary quite a bit."

Cancer is a disease where cells acquire genetic mutations that allow them to divide uncontrollably. These mutations can affect proteins, each of which play a critical role in the body.

Thanks to The Cancer Genome Atlas and other cancer genomics initiatives, researchers can access large datasets featuring data from thousands of tumor samples and several cancer types. Many researchers identify cancer genes by using programs that search for genes that mutate at a higher frequency than others do.

While these frequency-based methods are powerful, Singh believes they are insufficient because there are many cancer-relevant genes that are mutated at lower frequencies across tumors. "It makes sense to not just look at cancer data by itself as these frequency-based methods do, but instead, look at it within the context of other types of data that have been collected over the years about proteins and genomes," she argued.

Her group has built an algorithm to search through mutational patterns that involve how proteins interact with DNA, RNA and other molecules. The program incorporates cross-genomic and population information. The algorithm tries to identify whether mutations disrupt protein interactions.

In one test, her team used the algorithm to search through 11,000 tumor samples across 33 types of cancer. They uncovered several known cancer genes. Additionally, they identified several genes thought to be cancer genes as they have many mutations within sites where proteins interact with each other or with other biomolecules.

Singh and her group have developed another resource called the InteracDome, "which may have applicability in many other disease types because it allows you to see where mutations are hitting interaction sites."

Proteins work together within large networks. Some proteins, for instance, respond to DNA damage, while others play a role in cell growth. Mutations in any of the proteins associated with a particular function can alter the function. Further, proteins that are associated with the same function tend to be near each other in the network.

To find cancer-relevant mutations by leveraging these networks, Singh helped build a framework that considers somatic mutation data across individual tumors within the context of protein interaction networks. The idea is to find small subnetworks where many patients have mutations in at least one component protein—even if none of the proteins individually are frequently mutated across all the individuals' tumors. She also developed a network approach that additionally leverages known cancer genes.

To test her method, Singh's team searched a dataset featuring 278 individuals with a type of brain cancer called glioblastoma. Her approach showed "there's clear benefit to interpreting new potential disease genes in the context of previously known disease genes."

New research shouldn't be considered in isolation, she argued. "We should use this prior knowledge about proteins that are known to be cancer-relevant to somehow guide our network-based processes."

NIH Clinical Trial of Vaccine for COVID-19 Begins

A phase 1 clinical trial evaluating an investigational vaccine designed to protect against coronavirus disease 2019 (COVID-19) has begun at Kaiser Permanente Washington Health Research Institute (KPWHRI) in Seattle. NIAID is funding the trial. KPWHRI is part of NIAID's Infectious Diseases Clinical Research Consortium. The open-label trial will enroll 45 healthy adult volunteers ages 18-55 years over approximately 6 weeks. The first participant received the investigational vaccine on Mar. 16.

The study is evaluating different doses of the experimental vaccine for safety and its ability to induce an immune response in participants. This is the first of multiple steps in the clinical trial process for evaluating the potential benefit of the vaccine.

The vaccine is called mRNA-1273 and was developed by NIAID scientists and their collaborators at Moderna, Inc., a biotechnology company based in Cambridge, Mass. The Coalition for Epidemic Preparedness Innovations supported the manufacturing of the vaccine candidate for the phase 1 clinical trial.

"Finding a safe and effective vaccine to prevent infection with SARS-CoV-2 is an urgent public health priority," said NIAID director Dr. Anthony Fauci. "This phase 1 study, launched in record speed, is an important first step toward achieving that goal."

New Coronavirus Stable for Hours on Surfaces

The virus that causes coronavirus disease 2019 (COVID-19) is stable for several hours to days in aerosols and on surfaces, according to a new study from NIH, CDC, UCLA and Princeton University scientists published in the *New England Journal of Medicine.* The scientists found that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was detectable in aerosols for up to 3 hours, up to 4 hours on copper, up to 24 hours on cardboard and up to 2 to 3 days on plastic and stainless steel. The results provide key information about the stability of SARS-CoV-2, which causes COVID-19 disease, and suggests that people may acquire the virus through the air and after touching contaminated objects. The study information was widely shared during the past 2 weeks after the researchers placed the contents on a preprint server to quickly share their data with colleagues.

The NIH scientists, from NIAID's Rocky Mountain Laboratories in Montana, compared how the environment affects SARS-CoV-2 and SARS-CoV-1, which causes SARS.

SARS-CoV-1, like its successor now circulating across the globe, emerged from China and infected more than 8,000 people in 2002 and

2003. SARS-CoV-1 was eradicated by intensive contact tracing and case isolation measures and no cases have been detected since 2004. SARS-CoV-1 is the human coronavirus most closely related to SARS-CoV-2.

In the stability study the two viruses behaved similarly, which unfortunately fails to explain why COVID-19 has become a much larger outbreak.

The NIH study attempted to mimic virus being deposited from an infected person onto everyday surfaces in a household or hospital setting, such as through coughing or touching objects. The scientists then investigated how long the virus remained infectious on these surfaces.

Blood Test Method May Predict AD Protein in Brain

An advance in the development of a blood test could help detect pathological Alzheimer's disease in people who are showing signs of dementia.

IMAGE: LUCHSCHEN/ISTOCK GETTY

Researchers report an advance in the development of a blood test that could help detect pathological Alzheimer's disease (AD) in people who are showing signs of dementia. This approach could be less invasive and less costly than current brain imaging and spinal fluid tests. The blood test detects the abnormal accumulation of a form of tau protein known as phosphorylated-tau-181 (ptau181), which is a biomarker that suggests brain changes from AD. The study, funded by NIH, was published Mar. 2 in *Nature Medicine*.

Over the past 15 years, research advances in the development of biomarkers like tau protein have enabled investigators to more accurately diagnose AD, select research participants and measure response to investigational therapies. Tau and other biomarkers can be detected with PET scans of the brain and lab tests of spinal fluid. However, PET imaging is expensive and involves radioactive agents, and spinal fluid tests require spinal taps, which are invasive, complex and time-consuming. Simpler biomarker tests are still needed.

"The considerable time and resources required for screening research participants with PET scans and spinal taps slow the pace of enrollment for Alzheimer's disease treatment studies," said NIA director Dr. Richard Hodes. "The development of a blood test would enable us to rapidly screen a much larger and more diverse group of volunteers who wish to enroll in studies."

An international team of researchers used the new test to measure the concentration of ptau181 in plasma, which is the liquid part of blood that carries the blood cells. The samples were collected from more than 400 study participants.

Analysis demonstrated that the ptau181 in plasma could differentiate healthy participants from those with Alzheimer's pathology and differentiate those with Alzheimer's pathology from a group of rare neurodegenerative diseases known collectively as frontotemporal lobar degeneration.

NIH Researchers Stop Blood Vessel, Tumor Growth in Mice

Scientists at NIH and other institutions have devised a new strategy to stop tumors from developing the new blood vessels they need to grow.

Once thought to be extremely promising for the treatment of cancer, blocking molecules that stimulate new blood vessel growth (angiogenesis) has proven ineffective because tumor cells respond by producing more stimulatory molecules. The new strategy involves disabling key enzymes that replenish the molecule that cells need for the reactions that sustain new vessel growth.

The research team was led by Dr. Brant Weinstein, chief of the section on vertebrate organogenesis at NICHD. The study appears in *Nature Communications*.

Among the angiogenesis factors that stimulate new vessel growth is vascular endothelial growth factor (VEGF), which binds to a receptor on cell surfaces. This binding sets off a sequence of chemical reactions inside the cells lining the inside of blood vessels, culminating in new vessel growth. Previous attempts have sought to prevent this binding by targeting VEGF with antibodies or drugs, or by blocking the receptor so VEGF can't bind to it. However, tumors respond by producing more VEGF, overwhelming such efforts.

After binding occurs, an enzyme that converts the compound phosphatidylinositol-(4,5)-bisphosphate (PIP2) into inositol triphosphate, which is needed for the reactions that fuel new blood vessel growth, and diacylglycerol (DAG). Through a series of enzyme-assisted steps, DAG is converted back into PIP2, allowing it to be recycled, as needed.

The researchers showed that they could stop angiogenesis by blocking any of the enzymes in this PIP2 recycling series. They first halted angiogenesis in human cell cultures and zebrafish embryos by disabling the genes for one or more of the enzymes. They then targeted tumors in mice with drugs that block the recycling enzymes.

Compared to normal mice, the treated mice had less tumor and tumor blood vessel growth. Moreover, adding more VEGF depleted any remaining PIP2, further reducing blood vessel growth.

NHLBI also provided funding for the study.

Newer Anti-HIV Drugs Safest, Most Effective During Pregnancy

The antiretroviral drugs dolutegravir and emtricitabine/tenofovir alafenamide fumarate (DTG+FTC/TAF) may comprise the safest and most effective HIV treatment regimen currently available during pregnancy, researchers announced. Their findings come from a multinational study of more than 640 pregnant women with HIV across 4 continents. The study results affirm updated recommendations for HIV treatment in pregnant women set forth by the World Health Organization (WHO).

Previous research clearly has demonstrated that antiretroviral therapy (ART) to suppress HIV prevents perinatal HIV transmission and benefits the health of both mother and child. The current study compared three antiretroviral drug regimens and found that regimens containing dolutegravir (DTG) were more effective in suppressing HIV than a commonly used regimen containing efavirenz (EFV).

The phase 3 clinical trial is called IMPAACT 2010 or VESTED (Virologic Efficacy and Safety of Antiretroviral Therapy Combinations with TAF/TDF, EFV and DTG). It was sponsored by NIAID.

Dr. Lameck Chinula of UNC presented the findings Mar. 11 at the 2020 Conference on Retroviruses and Opportunistic Infections.

A variety of antiretroviral drugs used to treat HIV

IMAGE: NIAID

"When a woman living with HIV is expecting, she can be confident that the same antiretroviral therapy she takes every day to protect her own health also helps protects her future child from acquiring HIV," said NIAID director Dr. Anthony Fauci. "Findings from the VESTED study suggest that a drug regimen containing dolutegravir provides the safest, most effective HIV treatment available during this critical time for women and their infants."

Everybody dance! On the platform, fitness instructors Linda Bessacque (l) and Lakisha Wade (r) encourage crowd to get moving during Wear Red Day at the Clinical Center.

Above, Brittany Royall, a health communications specialist with NHLBI, distributes a heart-shaped sticker to a visitor in the C wing of Bldg. 31. Below, Chef Brendon McCalla presents baked tilapia with tomato sauce and basil, the special of the day, in the second floor cafeteria of Bldg. 10.

'EVERYBODY DANCE!'

'Wear Red Day' Stresses Social Support, Physical Activity

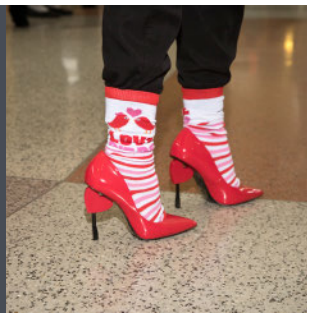
PHOTOS: STEVE CANNING

Each year on the first Friday in February, NHLBI, The Heart Truth and organizations around the country mark National Wear Red Day to bring greater attention to heart disease awareness as the leading cause of death for Americans.

As in previous years, NHLBI led NIH celebrations with a flash mob dance in the Clinical Research Center atrium, red food features and displays in campus cafeterias, Wear Red sticker and pin distribution in lobbies, pledge posters to be more active and a "hashtag our hearts" social media campaign featuring #HeartMonth, #MoveWithHeart, #WearRedDay and #OurHearts.

"Research shows that having social support makes being heart-healthy easier. Join the #OurHearts movement and show us how you, your friends, family, coworkers and others in your community are preventing heart disease. Learn more: https://go.usa.gov/xdZD5," read one NHLBI Twitter post.

The cafeteria crew in Bldg. 31 show their excitement for Wear Red Day by displaying heart-themed shirts, signs and red food.



Heart health on our minds—head to toe. Whoa, these red pumps are hard to beat!

ABOVE: Tawanna Berry (l) signs a pledge card for #OurHearts. At right, on Wear Red Day, NHLBI chief of staff Dr. Nakela Cook (r, red jacket) joins others in dance event in the Clinical Research Center atrium.

Jacobson Named Director of CSR Division

Dr. Ray Jacobson

Dr. Ray Jacobson has been named director of the Center for Scientific Review's Division of Basic and Integrative Biological Sciences.

He joined CSR in 2009 as a scientific review officer in the bioengineering sciences and technologies integrated review group (IRG). In 2015, he became chief of the biological chemistry and macromolecular biophysics IRG, overseeing a staff of 14 and 11 standing or recurring special emphasis panels.

At CSR, he has led the best practices committee, which highlights and clarifies current review policies for scientific review officers. Additionally, he has led pilot studies of changes to the review process, led the review of high-profile initiatives such as the Big Data to Knowledge program and the NIH Director's Transformative Research Awards and served as CSR liaison to other parts of NIH and other government agencies.

Before joining CSR, Jacobson was an assistant professor at the University of Texas MD Anderson Cancer Center, where his research focused on structural and biophysical aspects of eukaryotic RNA polymerase II general transcription machinery. He received his Ph.D. from the University of Oregon and did postdoctoral research in the molecular and cell biology department at the University of California, Berkeley.

Exec Sec's Crone Retires After 42 Years

BY DANA TALESNIK

Colleen Crone, a program analyst for OD's Executive Secretariat, will retire this spring following a 42-year NIH career.

A proud employee since the day she arrived, Crone started working at NIH as a GS-5 typist in the Clinical Center's diagnostic radiology department in January 1978, shortly after receiving her associate's degree.

"In a sense, I grew up here at NIH," she said. "I'd grown up in Frederick County and had always heard about people getting treated at NIH. It was always considered the Emerald City of medical research."

Crone went on to spend 4 rewarding years working for Dr. Michael Zasloff in NICHD's Human Genetics Branch. As a small-town girl, she especially looked forward to the lab holiday parties where she got a taste of different international foods and cultures.

In the first half of her NIH career, Crone also worked for NHLBI director Dr. Claude Lenfant and NEI scientific director Dr. Robert Nussenblatt.

"There's no question why they call this the crown jewel of the federal government," said Crone. "Wonderful, amazing things go on here."

Some of Crone's fondest NIH memories occurred during her 9 years working for Dr. Michael Gottesman, NIH deputy director for intramural research. She excitedly recounted meeting presidents, senators and celebrities and chatting on a first-name basis with Nobel laureates who frequented the office.

"I was often in awe of all the brain power in the meetings I attended," said Crone.

"Colleen had a 'can do' attitude about all of her work," said Gottesman." As my executive assistant, she was frequently called upon to deal with an unexpected or unfamiliar problem, and she always found her way to a desirable solution."

Colleen Crone ends her NIH career after 42 years.

PHOTO: DANA TALESNIK

For the past 12 years, Crone has worked for Exec Sec, the OD office that manages official correspondence and provides a range of other support to the NIH director and principal deputy director.

In her office, surrounded by files and family photos, next to an overstuffed day planner, sat a pink folder. One of her most fulfilling duties at Exec Sec, Crone said, is processing these "pink packages"—the awards and promotion packets for scientists and senior staff. Crone has always relished her support role, from typing articles and searching for information to managing her supervisor's calendar.

"I first met Colleen several years before I came to NIH at monthly meetings of the Council of Federal Executive Secretariats," said Crone's supervisor, Patrice Allen-Gifford. "Colleen wasn't just capable and helpful; her lively presence brightened those meetings. Five years later, when I became director of NIH Exec Sec, it was a joy to reconnect with Colleen. She is dedicated, thoughtful, caring—and fun!"

Crone recollected taking her sons, and later her grandsons, to Take Your Child to Work Day each year. She was planning to retire a little sooner but chose to stay through April so her grandsons could have one more TYCTWD experience [an event since canceled by the coronavirus pandemic] with her.

"I never expected to be retiring," said Crone. "I'm relatively healthy, I enjoy my work, I love my co-workers."

Her motivation? Crone is eager to spend more time with her two grandsons, Joel, 10 and JD, 7. She looks forward to taking the "Granny Cooper"—as her grandsons call her Mini Cooper—on frequent family road trips to Ocean City.

Crone also looks forward to having more time to go hiking and backpacking. She lives down the road from the Appalachian Trail and, has, in fact, hiked all 41 miles of it in Maryland.

"Coupled with her consummate professionalism, Colleen's spunk and stories about her 'munchkins' (grandkids) inspire easy laughter," said Allen-Gifford. "Most importantly, Colleen has deeply rooted admiration for the NIH family and mission, which drives her unwavering commitment. I will miss her. We all will miss her."

Virtual Town Hall Draws Tens of Thousands of Viewers

On the same day NIH announced that most of the Intramural Research Program would be reduced to a maintenance-only operation due to spread of the novel coronavirus, NIH director Dr. Francis Collins led an online virtual town hall meeting that drew more than 23,000 viewers and generated close to 2,000 emailed questions.

The Mar. 20 event in Wilson Hall included 30 minutes of presentations by NIH leadership and an online-interactive Q&A session for the rest of the hour that answered 19 questions.

"We at NIH are doing everything we can to continue to pursue our mission," said Collins, noting that one of his teleconferences from home had been interrupted by his cat's sneezing fit. "It's been a weird week, I grant you."

Takeaways from the session included:

• The decision to put the IRP into hibernation for all non-critical functions was made to lower physical proximity, Collins explained. "That's the most dangerous thing now...We do not want to be vectors ourselves."

• The IRP guidance extends to all laboratories, even those outside Bethesda.

• The requirement to telework for eligible NIH'ers is now extended from Apr. 3 to at least May 1. Supervisors have been asked to use maximum flexibility in managing telework.

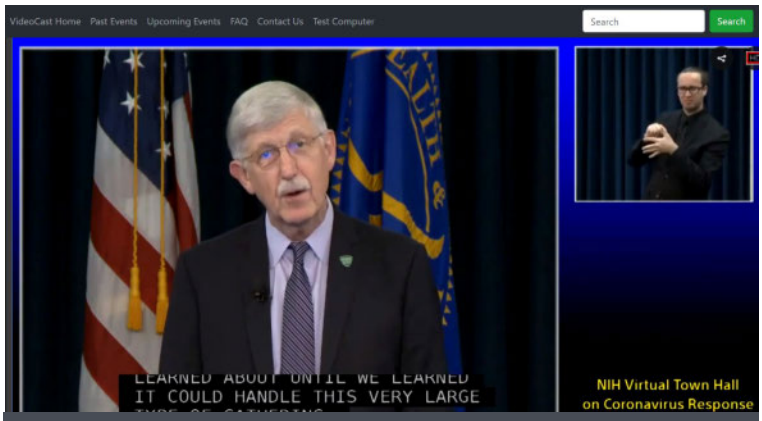
• It has been necessary to cancel the Summer Internship Program for young trainees at NIH for 2020.

• NIH'ers should be ready to share information about how to keep safe from coronavirus with their neighbors, Collins suggested.

• Six NIH'ers had tested positive for COVID-19 disease as of Mar. 20. [There were 28 by Mar. 27.] All have been asked to self-isolate and remain in contact with the Occupational Medical Service, which has added 22 staff to handle screening and calls.

• The Clinical Center, which began screening all patients and visitors on Mar. 13, has drastically reduced its census of both inpatients and outpatients and has cut its normal social traffic by more than 90 percent.

Asked how long social distancing—though Collins prefers the term physical distancing—will last, Collins said it hurt to send his own lab's staff home that day.



NIH director Dr. Francis Collins addresses the NIH workforce on Mar. 20 during an all-hands virtual town hall meeting. The full talk is archived at videocast.nih.gov.

The session had been scheduled to include NIAID director Dr. Anthony Fauci, who has become the nation's chief medical authority on COVID-19 and has been a ubiquitous presence on the national news. But he was at the White House's daily press conference, Collins explained. "Even Tony can't be in two places at once."

Also presenting at the meeting were (from l) NIH principal deputy director Dr. Lawrence Tabak, NIH deputy director for intramural research Dr. Michael Gottesman, Julie Berko, director of the Office of Human Resources, Dr. Tara Schwetz, NIH associate deputy director, and Colleen McGowan, director, Office of Research Services.

"I don't know how long it will last," he said. "We can't tell with any precision at this point." Much wider testing will be available soon, he noted, predicting, "We will probably have 4 to 5 times the number of cases we have now in a few weeks. It will be at least a month before we can tell whether social distancing is working. I have no crystal ball."

Collins concluded, "It's been a unique experience to do this virtually—I wish I could see all of you out there...There is no question that this is an unsettling time...But I am quite confident that we will get through this together. There will be stories told about this period in history for decades, maybe even centuries."

He reminded the audience that NIH also stands for the National Institutes of Hope: "That's what we are, after all, and I think we should claim that."

Quoting an editorial in that day's newspaper that included the observation that "the only thing more contagious than a virus is hope," he urged, "Be contagious with hope—to your neighbors, to your colleagues and in the mirror, to yourself."—**Rich McManus**

Also participating were (from l) Dan Wheeland, director, Office of Research Facilities, NIH deputy director for management Dr. Alfred Johnson, Dr. Sharon Milgram, director, Office of Intramural Training & Education, NIH deputy director for extramural research Dr. Michael Lauer, and CC CEO Dr. James Gilman.