NIH RECORD

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National Institutes of Health

'WE FOLLOW THE SCIENCE'

President Biden Pays NIH a Call

BY CARLA GARNETT

Curbing the coronavirus pandemic is President Joe Biden's top priority. To stress the urgency, he stopped by NIH, source of a powerful weapon against Covid-19—biomedical research.

On Feb. 11—after just more than 3 weeks in office—Biden toured the lab where the Moderna vaccine was co-developed by scientists at the Vaccine Research Center. While there, the President also was briefed on investigations into Covid therapeutics and diagnostics and other topics by NIH director Dr. Francis Collins, NIAID director Dr. Anthony Fauci, who also is Biden's chief

SEE **PRESIDENT**, PAGE 6

At NIH on Feb. 11 are (from l) VRC deputy director Dr. Barney Graham, President Joe Biden, NIAID director Dr. Anthony Fauci, White House Covid Response Coordinator Jeff Zients, NIAID research fellow Dr. Kizzmekia Corbett and NIH director Dr. Francis Collins.

PHOTO: CHIA-CHI CHARLIE CHANG

RETHINKING THE HIERARCHY

Law Professor Proposes New Health Care Architecture

BY DANA TALESNIK

Dr. Barak Richman

It's tough to innovate on a large scale. There comes a time, though, when advances within a sector compel us to reevaluate the bigger picture.

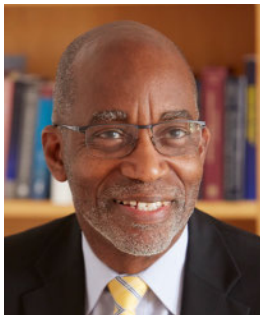
Dr. Barak Richman, a professor of law and business at Duke University, proposes a new framework for the U.S. health sector, one he believes would be more affordable and sustainable. He shared his ideas at a recent virtual NIMH Director's innovation lecture.

Within our current health care system,

SEE **RICHMAN**, PAGE 8

Housing Segregation a Central Cause of Racial Health Inequities

BY ERIC BOCK



Dr. David Williams

Structural racism in the housing system is a fundamental cause of racial health inequity in the United States, said Dr. David Williams during a recent NIMHD/NINR Joint Directors' Seminar on the Science of Structural Racism.

"We will not make the progress we would like to make in reducing health inequities if we don't address it," said Williams, professor of African and African-American studies at Harvard University and the Florence and

SEE **WILLIAMS**, PAGE 4

NIAID division directors brief White House science chief at VRC. See story, p. 2.

ALSO THIS ISSUE

NIMHD Seminar To Host Mokdad, Mar. 11

Dr. Ali Mokdad will deliver the next lecture in the virtual NIMHD Director's Seminar Series on Thursday, Mar. 11 at 2:30 p.m. He will present "Disparities in Life Expectancy."

Mokdad is a professor of health metrics sciences at the Institute for Health Metrics and Evaluation and chief strategy officer for Population Health at the University of Washington. As a public health researcher, Mokdad has published groundbreaking work on local-level disease trends and some of the leading risk factors for poor health. His work on obesity is among the most highly cited in the field.

Dr. Ali Mokdad is NIMHD's next virtual Director's Seminar Series speaker.

For reasonable accommodation, call (301) 402-1366 or the Federal Relay, 1-800-877-8339. The talk will be videocast at https://videocast.nih.gov.

To learn about the NIMHD Director's Seminar Series, visit https://nimhd.nih.gov/news-events/conferences-events/directors-seminar-series/.

NHGRI's Dr. Daniel Kastner recently was awarded Sweden's Crafoord Prize.

Kastner Earns Sweden's Crafoord Prize

The Royal Swedish Academy of Sciences recently awarded this year's Crafoord Prize in Polyarthritis to Dr. Daniel Kastner, NHGRI scientific director. The prize, worth 6 million Swedish kronor (approximately $700,000) this year, is one of the major international science honors, with subject areas that complement the Nobel Prizes and rotate from year to year.

The prize's website cited Kastner "for establishing the concept of autoinflammatory diseases. He has identified the mechanisms responsible for familial Mediterranean fever, TRAPS and other diagnoses within this group. They are genetic diseases that are unusual in most of the world, but may have a higher incidence in some areas. One or two of every thousand people in the eastern Mediterranean have familial Mediterranean fever, while TRAPS was initially discovered among families in Ireland and Scotland."

The Crafoord Prize is awarded by the Royal Swedish Academy of Sciences and the Crafoord Foundation in Lund, with the academy being responsible for selecting the laureates. Its subject areas rotate every year, between mathematics and astronomy, the geosciences, biosciences and polyarthritis (such as rheumatoid arthritis). The polyarthritis prize—instituted because the donor, Holger Crafoord, suffered from severe rheumatoid arthritis toward the end of his life—is only awarded when there has been scientific progress that motivates a prize.

At a coronavirus research response briefing in the VRC on Feb. 10 are (clockwise) Dr. Eric Lander (front, c), Kei Koizumi, Dr. John Mascola, Dr. Cliff Lane. Dr. Emily Erbelding, Dr. Alan Embry and Dr. Anthony Fauci. Several other NIH'ers participated via video conference.

PHOTOS: CHIA-CHI CHARLIE CHANG

White House Science Chief Lander Visits NIH

Dr. Eric Lander, President Biden's nominee to lead the White House Office of Science and Technology Policy (OSTP), visited NIH on Feb. 10. Accompanied by OSTP Chief of Staff Kei Koizumi, Lander met at the Vaccine Research Center with NIAID director Dr. Anthony Fauci, who also serves as Biden's chief medical advisor.

OSTP Chief of Staff Koizumi (l) and Lander (c) chat with Fauci.

Fauci gave an overview of NIAID with a focus on vaccine development; VRC director Dr. John Mascola provided a VRC overview with an emphasis on Covid-19 vaccine research.

"Both emphasized the importance of prior basic research in speeding the development of a vaccine," noted Dr. Cliff Lane, NIAID deputy director for clinical research and special projects, who also attended the meeting at the VRC, along with Dr. Emily Erbelding, director of the Division of Microbiology and Infectious Diseases (DMID), and Dr. Alan Embry, chief of DMID's Respiratory Diseases Branch.

Joining the gathering by video were VRC deputy director Dr. Barney Graham; Dr. Daniel Rotrosen, director of the Division of Allergy, Immunology and Transplantation; NIAID principal deputy director Dr. Hugh Auchincloss; and Dr. Carl Dieffenbach, director of the Division of AIDS.

Lane and other division directors briefly discussed what their divisions are doing as part of the NIH Covid-19 response.

VRC director Mascola (l) provides a VRC overview with an emphasis on Covid-19 vaccine development, as Lane (c), Erbelding and other division directors discuss their work.

Humidity from Masks May Lessen Severity of Covid-19

NIDDK's Dr. Joseph Courtney breathes into a sealed box while wearing a mask.

PHOTO: NIDDK

Research has shown masks help protect the wearers and those around them from Covid-19. Now, NIH investigators have uncovered another potential benefit: the humidity created inside the mask may offer another layer of protection.

The study, led by NIDDK and published in the *Biophysical Journal*, found that face masks substantially increase the humidity in the air that the mask-wearer breathes in. This higher level of humidity in inhaled air may explain why wearing masks has been linked to lower disease severity in people infected with SARS-CoV-2.

"We found that face masks strongly increase the humidity in inhaled air and propose that the resulting hydration of the respiratory tract could be responsible for the documented finding that links lower Covid-19 disease severity to wearing a mask," said the study's lead author, NIH distinguished investigator Dr. Adriaan Bax. "High levels of humidity have been shown to mitigate severity of the flu, and it may be applicable to severity of Covid-19 through a similar mechanism."

High levels of humidity can limit the spread of a virus to the lungs by promoting mucociliary clearance (MCC), a defense mechanism that removes mucus—and potentially harmful particles within the mucus—from the lungs. High levels of humidity can also bolster the immune system by producing special proteins, called interferons, that fight against viruses. Low levels of humidity have been shown to impair both MCC and the interferon response, which may be one reason why people are likelier to get respiratory infections in cold weather.

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"This research supports the importance of mask-wearing as a simple, yet effective way to protect the people around us and to protect ourselves from respiratory infection."

–NIDDK DIRECTOR DR. GRIFFIN RODGERS

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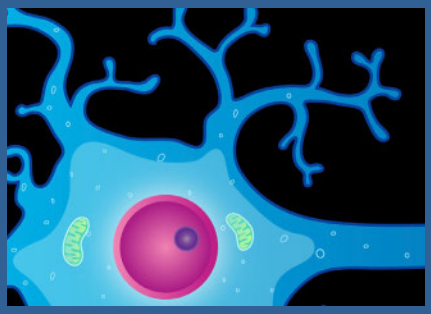
"This research supports the importance of mask-wearing as a simple, yet effective way to protect the people around us and to protect ourselves from respiratory infection, especially during these winter months when susceptibility to these viruses increases," said NIDDK director Dr. Griffin Rodgers.

NIH distinguished investigator Dr. Adriaan Bax

The study tested 4 common types of masks: an N95, a 3-ply disposable surgical mask, a 2-ply cotton-polyester mask and a heavy cotton mask. To measure the level of humidity, researchers had a volunteer breathe into a sealed steel box. When the person wore no mask, the water vapor of the exhaled breath filled the box, leading to a rapid increase in humidity inside the box.

When the person wore a mask, the buildup of humidity inside the box greatly decreased, due to most of the water vapor in the mask becoming condensed and being re-inhaled. To ensure no leakage, the masks were tightly fitted against the volunteer's face. Measurements were taken at three different air temperatures, ranging from 46 to 98 degrees Fahrenheit.

All four mask types increased the level of humidity of inhaled air, but the humidifying effects were greatest at lower air temperatures. The thick cotton mask led to the most increased level of humidity at all temperatures. R



ON THE COVER: *Illustration of neuron with dendrites and nucleus*

IMAGE: NIMH

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

Williams

CONTINUED FROM PAGE 1

Laura Norman professor of public health and chair of the department of social and behavioral sciences at Harvard's T.H. Chan School of Public Health.

Structural racism—also known as institutional or systemic racism—is a societal system that "categorizes and ranks populations and groups, devalues and disempowers some groups," he explained. It "leads to the development of negative attitudes and beliefs, prejudice and stereotypes, differential treatment and discrimination by both individuals and societal institutions."

Residential segregation, or "the physical separation of the races by forcing residents into different areas," is one of the most prominent examples of structural racism. The system was developed in the South and expanded to the North. He said it has been "locked in place" since 1940.

Historically, the segregation of African Americans has been unique. While other groups are segregated depending on income levels, segregation is higher for African Americans at all income levels. But not by choice.

"Studies show African Americans show the highest preference for residing in integrated areas [compared to] any other group," he said.

Williams compared segregation to toxic emissions produced by an industrial plant in a neighborhood. Both are often imperceptible and cause illness and death. When they appear, valuable resources such as quality schools, safe playgrounds and housing, good jobs, clean air and water, transportation and health care, all disappear.

In the 100 largest metropolitan areas in the U.S., studies show two-thirds of all African-American children, 58 percent of Latino children and 53 percent of indigenous American children live in low-opportunity neighborhoods. Almost two-thirds of non-Hispanic whites and Asian kids live in high- or very high-opportunity neighborhoods.

Residential segregation is one of the most prominent examples of structural racism, said Williams.

"There are striking differences in access to opportunity at the neighborhood level," Williams said.

Residential segregation is just one aspect of systemic racism. Other examples include immigration and border policy, political participation, the criminal justice system, workplace policies and home mortgage discrimination.

Acts of interpersonal racism also adversely affect health, he noted. Everyday discrimination, such as being treated with less courtesy and respect or receiving poorer service, predicts adverse health outcomes that have enormous health consequences, such as higher levels of type 2 diabetes, heart disease, breast cancer, poorer sleep and obesity.

People who experience these little indignities are biologically older than their chronological age, Williams said. Some research studies found African Americans are biologically 7.5-10 years older than non-Hispanic whites who are the same chronological age based on their physiology.

"One of the consequences of this is the earlier onset of diseases and greater severity of diseases," he said.

Going forward, Williams said public health researchers must better understand how poor neighborhoods and substandard housing lead to stress. They also need to identify exposure to non-traditional stressors, such as the viewing of traumatic videos of persons being beaten, arrested or detained or being shot by police, that adversely affect health.

"Addressing segregation will not be easy," Williams said. "There are deep fears of segregation and its impact on the United States."

Williams indicated that although there are not many success stories, there is the Purpose Built Communities model that shows it is possible to create mixed-income housing that addresses all of the challenges faced by poor communities simultaneously, and markedly improve public safety, education, employment and child care.

NINR director Dr. Shannon Zenk and NIMHD director Dr. Eliseo Pérez-Stable share a lighthearted moment with Williams during the Q&A.

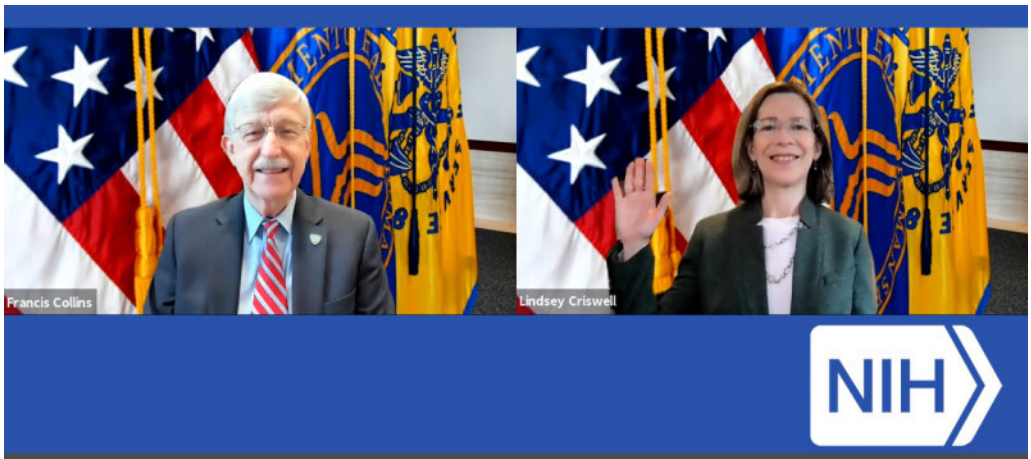
NIAMS Director Sworn In

Dr. Lindsey Criswell has officially joined the NIH community as director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Her virtual swearing-in ceremony was held on Feb. 16. NIH director Dr. Francis Collins administered the oath of office.

As NIAMS director, Criswell will oversee the institute's annual budget of nearly $625 million, which supports research into the causes, treatment and prevention of arthritis and musculoskeletal and skin diseases.

Acting director Dr. Robert Carter has returned to his position as deputy director of NIAMS.



NIH director Dr. Francis Collins administers the oath of office virtually on Feb. 16 to NIAMS director Dr. Lindsey Criswell.

VIRTUAL 'COFFEE' EVENT, MAR. 9

MI Program Opens Recruitment Season

The NIH Management Intern (MI) Program recruitment season is underway, coordinated by the Training Center in the Office of Human Resources. The program offers highly motivated NIH employees an opportunity to transition from their current field into an administrative management career.

"When I graduated from nursing school, my dream job was to help seriously ill children and their families navigate the difficult road to recovery," recalled former MI Kathleen Tepas, legislative coordinator in NIAAA's Office of Science Policy and Communications. "I immediately gravitated to the one hospital devoted to enhancing life and reducing the burden of disease and disability. Twenty years ago, I stepped nervously into the Clinical Center atrium on my very first day with a head full of ambition and a heart ready to support patients embarking bravely on biomedical research studies.

"It was thrilling to be an active part of an incredible team devoted to conquering disease and bringing quality of life back to those who suffered in what can best be described as the heartbeat of the 'National Institutes of Hope.' Over the years I found myself more and more curious about how NIH operated as a federal agency...I was fortunate to discover NIH supports a program designed to expose scientific or medical personnel such as myself to [administrative] processes and was thrilled to be selected for the class of 2013."

Management interns gain valuable experience and insight through rotations in a variety of administrative management areas for 2 years.

Rotations are available in these career tracks:

- Administrative Management
- Financial Management
- Grants Management
- Human Resources Management
- Communications
- Contracts Management
- Information Technology Management
- Management or Program Analysis

Program features include access to a senior-level mentor, an individual training budget, an opportunity to participate in challenging projects and committees, and face-to-face interactions with NIH leaders.

"I was able to meet the executive officers of each of the institutes and centers, sit in on advisory council meetings and shadow our Health and Human Services colleagues downtown," Tepas noted. "Through my various rotations I learned about the different grants available to researchers and the important steps needed to continue their efforts, from the first time a grant is reviewed to its renewal application seeking to expand on preliminary results. I was able to hear how NIH leaders and scientists share their findings at congressional briefings, highlighting the importance of continued research to develop new therapies and evidence-based prevention methods...Twenty years after that first step into the Clinical Center, I still work for an incredible team devoted to conquering disease and providing quality of life for those who suffer, but in a slightly different way...Had I not been part of the MI program and had the experiences I had, I might not be in the position I love now. Today I still enjoy the vast network of mentors and leaders I cultivated during my time as an intern. I continue to push my career to new horizons..I am grateful for the MI program jump-starting this exciting new career path and can't wait to see where the next 20 years will take me at NIH."

Former MI Kathleen Tepas, in front of the U.S. Capitol early in her career

For program details, eligibility requirements and information on the application process, visit https://hr.nih.gov/training-center/programs/intern/mi/management-intern-program-mi.

A "Coffee with an MI," run solely by current management interns, will be held on Mar. 9 from 1 to 2:30 p.m., via WebEx. Registrants can drop in to ask questions and hear more about MI experiences. To register, send an email to mi_info@od.nih.gov. For reasonable accommodation to participate, email at least 4 days before the session.

The MI job vacancy announcement opens Mar. 22 and closes Mar. 26 in USAJobs.gov (https://www.usajobs.gov/). Current GS-7 through GS-12 NIH employees are invited to apply.

Flanked by Collins (l) and Fauci (r) on stage in Kirschstein Auditorium, the nation's Commander-in-Chief addresses the NIH workforce.

PHOTOS: CHIA-CHI CHARLIE CHANG

President

CONTINUED FROM PAGE 1

medical advisor, and VRC director Dr. John Mascola.

VRC deputy director Dr. Barney Graham, chief architect of the prototype pathogen preparedness strategy combined with the mRNA vaccinology approach of biotech partner Moderna, and research fellow Dr. Kizzmekia Corbett, coronavirus team lead in NIAID's Viral Pathogenesis Laboratory, also talked with Biden.

"It's incredible," POTUS declared. "It's a place where our top minds spend years researching vaccines and treatments for all kinds of viruses and, partnering with academia and industry, prepare for the next one—because there will be others. HIV, SARS, West Nile, Zika, Ebola and, today, Covid-19. To all of you, your work made possible the remarkably rapid development of the Covid-19 vaccines we have today... People were initially talking years, if not decades before we'd have a vaccine. On behalf of a grateful nation—and I don't say that lightly—I want to thank you and your families for your work and your sacrifice. For there's no doubt your families sacrificed a great deal for the endless hours you put in to save the rest of us."

'We Give Back'

Taking the stage at the Natcher Bldg., Biden praised Collins and Fauci for agreeing to stay in their positions as the new administration assumed office.

"Our nation is fortunate to have both of you in these critical roles and that goes for all the world-class doctors, scientists and researchers working at NIH," said the 46th Commander-in-Chief, who acknowledged Covid's toll. "I know it hasn't been easy. The devastation of this pandemic, the loss of life and livelihoods, hasn't spared the scientific community. Labs closed. Research delayed. Careers disrupted—especially for those in

'HE LISTENED...HE CARED'

In Lab Tour, Biden Connects with Scientists

When President Biden visited the Dale and Betty Bumpers Vaccine Research Center at NIH on Feb. 11, VRC deputy director Dr. Barney Graham and research fellow Dr. Kizzmekia Corbett described various aspects of vaccine development science.

"I showed a 3C model of the whole virus to show how the spike molecule was on the virus surface," Graham recounted. "I then showed a 10 million X-enlarged 3D model of the spike protein. I had other models of the prefusion and postfusion forms of RSV F and some of our new nanoparticle designs for influenza, but didn't have time for those."

At left, Dr. Barney Graham and President Biden bump elbows. Above, Dr. Kizzmekia Corbett talks vaccine science with POTUS.

Corbett talked about how her group decided on the protein sequence for making the spike protein in different forms for assay development, cryoelectron microscopy, probes for antibody discovery and vaccine.

"[We] designed the vaccine insert sequence [over a weekend]," Corbett recalled.

In response to the science blitz and research briefing, Biden inquired about how the investigators themselves were coping.

"He was interested in our personal experience and our families' experience of going through this pandemic response over the last year," Graham noted. "He listened and he cared. At the end of the lab tour I mentioned that my wife (Dr. Cynthia Turner-Graham) and grandson (D.J.) both asked me to say hello from them. [The President] pulled out his cell phone and asked for my wife's number, then called her and proceeded to have a 5- to 10-minute call with her while everyone else waited."

This is the second meeting with a U.S. President in less than a year for Graham and Corbett. They met with President Trump on Mar. 3, 2020. Graham's work has placed him in this position several times over the last couple of decades.

"I had the opportunity to meet with President Obama in December 2014, when he came to thank us for our work on Ebola during the West African outbreak," Graham recalled. He also met with President Bush who visited in 2003 to learn about VRC work post-9/11.

What stood out for Corbett was "POTUS ad hoc calling Dr. Graham's wife for casual conversation and gifting us with the POTUS challenge coin."

"I never imagined meeting an active president as a research fellow," she said.

training. Yet for every moment of despair in this past year, you and all the heroes and heroines on the frontlines and at the frontiers of this pandemic remind us who we are. We are Americans. We never give up. We never give in. We give back. We follow the science and find the answers."

Biden thanks NIH'ers for their example during the pandemic.

In addition to thanking the scientific enterprise, the President also came to NIH to cite progress in his national strategy to fight Covid-19 and to discuss the American Rescue Plan, which bolsters economic recovery.

Besides getting 100 million people vaccinated in his first 100 days in office—a goal also announced at NIH 2 weeks previously by Vice President Kamala Harris—Biden's strategy addresses nationwide shortages of vaccine and vaccinators.

Already the administration has "increased the weekly supply of vaccine shipped to the states by almost 30 percent," Biden reported. Just that afternoon, his team had negotiated with two major pharmaceutical manufacturers, Moderna and Pfizer, to supply 100 million more doses each of their vaccines. They were also able to accelerate the delivery timeline by a month. By July, he intends to have enough vaccine to immunize 300 million Americans.

"Within 3 weeks [through] round-the-clock work with so many people, we've now purchased enough vaccine supply to vaccinate all Americans," said the President. "Now we're working to get those vaccines into the arms of millions of people."

'Administering a Dose of Hope'

One thousand more federal staff have been deployed to vaccination sites around the country, he noted.

On Super Bowl Sunday, the National Football League invited the Biden administration to use all 30 stadiums as mass vaccination stations. Biden accepted the offer, and the federally run centers will target areas that have been hardest hit by the illness.

Recalling the words of a nurse involved in giving the vaccine shot, POTUS said the vaccinator described the experience as "'administering a dose of hope'...We're going to get those doses of hope out at new and large-scale vaccination centers set up by the federal government."

Retired doctors and nurses, including some from FEMA, the Department of Defense and the U.S. Commissioned Corps, are being recruited back to work as vaccinators.

"Our end goal is beating Covid-19," Biden declared. "That brings us to the challenge that remains: We remain in the teeth of this pandemic. January 2021 was the deadliest month we've had—we lost over 100,000 of our fellow citizens."

Mask Up, It's Patriotic

Ending his visit, Biden said all citizens can help get the nation through this crisis.

"Masking remains the easiest thing to do to save lives," he said. "Everyone needs to mask up. I know it's a pain in the neck. It's a patriotic responsibility...Mask up, America. Mask up."

Biden noted that NIH and the broader "scientific community repurposed labs to work on Covid-19, developed therapeutics, new diagnostic technologies and vaccines in record time. You're highlighting lessons learned on the importance of pandemic preparedness, public-private partnerships, real-time data-sharing and most of all, speed and efficiency without compromising science and good conscience."

Science has modeled the example for everyone else, Biden concluded.

"You're a good group of people—I've been out here many times, trying to help my son who passed away with cancer...We have to do what you all do here at NIH and across the scientific community. We have to keep the faith—with purpose, with vision and with every dose of hope we have...You're the best America has to offer, NIH. Thank you from the bottom of my heart."

First Lady Biden Virtually Visits NCI

First Lady Dr. Jill Biden recently virtually visited the National Cancer Institute to learn about advances in cancer research.

"There is one challenge that unites us all, one thread of pain that runs through every community, North and South, rich and poor, in the best of times, the depth of this pandemic and that's cancer," said Biden on Feb. 3, the day before World Cancer Day.

NCI director Dr. Ned Sharpless welcomed the First Lady to NCI.

NIH director Dr. Francis Collins and NCI director Dr. Ned Sharpless welcomed the First Lady. During her visit, three scientists from NCI told Biden about recent advances in cancer research. She thanked NCI staff for their contributions to cancer research.

"Cancer touches us all and because of that your work touches us all," she said.

The theme for this year's World Cancer Day is "I Am and I Will" with a subtheme of "Together, all of our actions matter."

View the recording at https://www.youtube.com/watch?v=VUSUi2wBtUE&feature=youtu.be.

Dr. Jill Biden spoke with several experts in cancer research including (from l) Sharpless, Dr. Worta McCaskill-Stevens of NCI Community Oncology Research Program; Dr. Stephanie Goff of the Center for Cancer Research's Surgery Branch and Dr. Ligia Pinto of NCI's Vaccine, Immunity and Cancer Program.

Richman

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there's been great modular innovation over the years, from new medicines to surgical techniques, among other groundbreaking interventions, he noted.

"But if the last 40 years of innovation have taught us anything," said Richman, "it's that we also need to pursue organizational innovation. We need to develop a new architecture that can really harness new capabilities, reduce costs and improve quality and productivity."

Such a transformation involves rethinking our approach to health care delivery, he said, so we're no longer constrained by the existing architecture. Rather than centering care around available resources—hospitals, physicians, payors—the new structure would be built around patients, who could then better access the kinds of medical services they need.

"We really want to resist thinking only about how we deploy our resources," Richman said. "Instead, we might want to think about how we can deploy or create or provide high-value services."

The current hierarchical architecture puts hospitals at the center of health care delivery. But in this top-down system, doctors have increasingly become tethered to hospitals and insurers, which continues to inflate health care costs, he said. Meanwhile,

despite the digital advances of the past 25 years—from the internet to smartphones—health care productivity remains ossified.

"The way we have delivered health care has not really responded to dramatically significant technologies that have really transformed and reorganized most other sectors in the economy," argued Richman.

Digital technologies have unleashed myriad opportunities for health care, linking patients to health information sources and telemedicine consultations, digitizing health records and enabling data analytics to automate diagnostics and guidance. These technologies, he asserted, enable and necessitate a reorganization of U.S. health care delivery.

Richman suggested a business model that reworks power centers and priorities. Interrelationships are critical in providing high-quality care, along with the location and organization of care, which affect cost, quality, patient behaviors, convenience and optimized use of new technology.

Empowering the Patient

The new model would sever the local hospital from the main architecture of health care delivery. Instead, doctors and insurers would collaborate with patients, who could shop around for hospitals and other primary and chronic care needs.

Richman's work on antitrust issues led him to consider a new health care model. Removing hospitals from the epicenter of the current architecture offers new possibilities to contract with other hospitals, which in turn resolves antitrust problems by stimulating competition. Providers would still be the main organizers and visionaries of health care, but they wouldn't have to play a role in day-to-day delivery.

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"The way we have delivered health care has not really responded to dramatically significant technologies that have transformed and reorganized most other sectors in the economy."

-DR. BARAK RICHMAN

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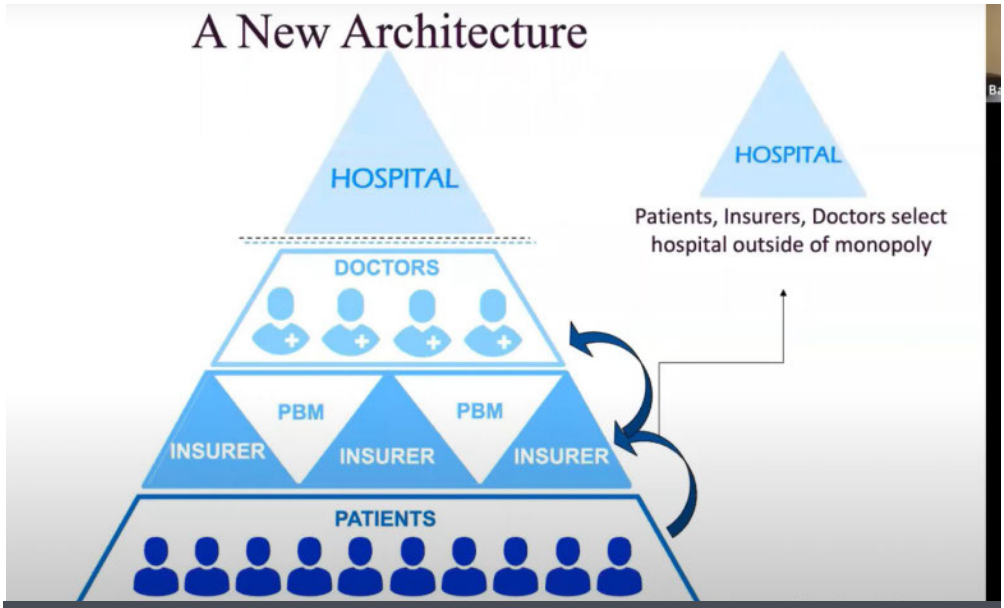
"With digital medicine and different kinds of arrangements and relationships, we can think more of a bottom-up approach," he said, which delivers care to patients in a cost-effective way.

Need for a New Framework

One case that exemplifies how an innovative idea was hampered by our existing health care architecture is the effort to develop an electronic health records system. After 8 years and a massive federal subsidy, an integrated, interoperable system remains elusive. Why? "Hospitals built the electronic health records to duplicate and reinforce the kind of architecture we currently have," Richman explained.

Another model, one undertaken by France, instead organizes health care



Richman advocates for a decentralized model of health care delivery that removes the local hospital from the epicenter, instead empowering the patient.

IMAGES: FLATICON.COM/FREEPIKCOMPANY

In France, individual health records are stored electronically on insurance cards.

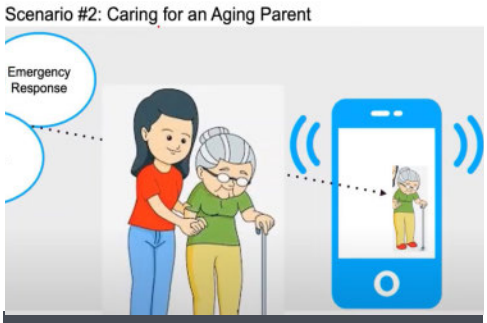
IMAGE: GIE SESAM-VITALE

delivery around the patient. There, individual health records are stored electronically on insurance cards, allowing patients to bring their personalized information to any provider.

In the U.S., some tech companies are investing in new patient-centered health services. But can this be done, asked Richman, without constructing a new architecture?

Lessons of a Pandemic

Our relationships with each other, our health providers and digital technology have evolved over the past year due to the Covid-19 pandemic. In March, telemedicine surged 50 percent; by August, these video-calls with doctors rose by 3,500 percent. But the pandemic also illuminated a problematic side of technology—the proliferation of misinformation and conflicting sources of health information.



Caring for an aging parent could be done digitally, suggests Richman.

IMAGES: FLATICON.COM/FREEPIKCOMPANY

"We need to shift the source of information...to trusted providers," said Richman. "The entire information ecosystem really needs to change, and there's no reason that our providers—who know us and our communities and who we have relationships with—cannot be much more active in disseminating information to us."

Looking to the Future

Richman envisioned several scenarios within a restructured health sector. With telehealth, a parent with a sick baby could receive care without having to leave the comfort of home. Caring for an aging parent also could be done digitally, suggested Richman. The technology already exists to monitor potential emergency triggers in the caregiver's absence. A new architecture, he said, could offer safer, more cost-effective independent living.

Another prospective improvement is surgery, such as hip replacement. Local hospitals often charge high prices yet may not even specialize in that area, said Richman. Imagine implementing destination medicine—the potential to shop elsewhere for care—reducing costs by expanding both competition and patient choice.

A new architecture could integrate specialists into primary care, while telemedicine further expands patient choice and the radius of care, since doctors wouldn't necessarily have to be local. Rather than a hierarchical relationship with doctors, patients could have a more direct relationship, perhaps through a new information ecosystem.

Even though patients might not regularly see doctors physically, Richman said, "We'd have them much more integrated into our daily lives—whether through telemedicine, some kind of digital interface or other information system—having them much more actively engaged in providing us with information and direction."

During the Q&A, Richman was asked how a new framework might affect vulnerable and marginalized populations. Caring for low-income and other vulnerable populations, who likely suffer from comorbidities, requires an integrated strategy, he said, which individual providers can't accomplish.

"That only accentuates the need to have a comprehensive approach to delivering care in a different kind of architecture that's patient-centered," Richman said. "All of the intersections between the social determinants of health and health care delivery are going to have to be a part of developing this new architecture." R

Han Named NCI Senior Scientist

Dr. Paul Han has been named senior scientist in the Behavioral Research Program (BRP), Division of Cancer Control and Population Sciences at the National Cancer Institute.

Dr. Paul Han

BRP initiates, supports and evaluates a comprehensive program ranging from basic behavioral research to the development, testing and dissemination of interventions in areas such as tobacco use, screening, dietary behavior and sun protection.

In addition to his senior scientist role, Han will serve as an adjunct investigator in NCI's Clinical Genetics Branch in the Division of Cancer Epidemiology and Genetics.

Han's background bridges the disciplines of behavioral and health services research. His research interests include risk communication, shared decision-making, predictive modeling and examining clinical problems in cancer care, genomic medicine and palliative and end-of-life care.

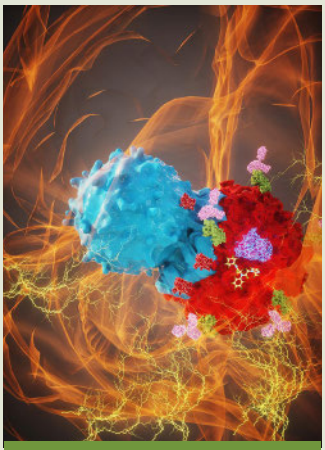
"With Paul's expertise in shared decision-making, health communication and most recently lung screening, I believe he offers an exceptionally useful clinical perspective to our work at NCI," said Dr. William Klein, BRP associate director.

Prior to joining NCI, Han served as the director of the Center for Outcomes Research and Evaluation at the Maine Medical Center Research Institute, and associate professor of medicine at Tufts University School of Medicine. He led statewide initiatives to promote lung cancer prevention and screening and to study the implementation of cancer genomic testing in clinical practice. Han has authored more than 150 papers and book chapters in peer-reviewed medical literature and has been active in initiatives to promote shared decision-making and teach risk communication skills to medical students and physicians.

Han earned his medical degree from New York University School of Medicine. He received a master of arts in bioethics and a master of public health from the University of Pittsburgh. He completed internal medicine residency training at the University of California, Los Angeles, and an NCI Cancer Prevention Fellowship.

Combination Treatment for Glioma Shows Promise

Gliomas are common brain tumors that comprise about one-third of all cancers of the nervous system. In an NIH-funded study, researchers tested a novel combination treatment on mice with tumors with characteristics similar to human astrocytomas—a type of slow-growing glioma—and found tumor regression in 60 percent of the mice treated. These encouraging results, published in the *Journal of Clinical Investigation,* could be the first step toward developing a treatment for this type of brain cancer.



Artist's rendering of a glioma cell under attack from the immune system

PHOTO: ELLA MARUSHCHENKO

A team of researchers at the University of Michigan Rogel Cancer Center specifically tested inhibitors of the compound D-2-Hydroxyglutarate (D-2-HG), which is produced by cancer cells, on a mouse version of astrocytoma carrying mutations in two genes, along with an inactivated form of a tumor-suppressor protein gene.

When the implanted mice were treated with a drug to block the production of D-2-HG along with standard of care radiation and temozolomide (chemotherapy) treatments, their survival significantly improved. Looking more closely at tumor cells grown in dishes, the researchers saw that blocking D-2-HG caused the cells to become more susceptible to radiation treatment. However, the treatment also increased the amount of an "immune checkpoint" protein, which tumors use to turn off T-cells and evade the immune system.

Inhibiting this immune checkpoint protein with an additional drug resulted in an even greater improvement in survival, because the mouse's own immune system was able to attack the tumor. Importantly, this combination therapy also led to immunological memory against the glioma, meaning the mouse now had T-cells tailored to the specific tumor. Because gliomas almost always grow back after treatment, these T-cells make the animal better prepared to fend off regrowth.

These preclinical results produced by this combination therapy could represent a key advance in developing an improved treatment regimen, which combines D-2-HG and immune checkpoint inhibition, radiation and temozolomide for patients with astrocytomas.

Four Potential Therapeutics for Covid Enter Phase 2/3 Testing

Enrollment has begun to test additional investigational drugs in the Accelerating Covid-19 Therapeutic Interventions and Vaccines (ACTIV) program.

ACTIV, sponsored by NIAID, is a public-private partnership that creates a coordinated research strategy to prioritize and speed development of promising Covid-19 treatments and vaccines. The new agents entering the randomized, placebo-controlled study are part of ACTIV-2, an adaptive trial designed to test investigational agents in non-hospitalized adult volunteers experiencing mild to moderate Covid-19 symptoms.

The added sub-studies will test four interventions for safety and efficacy: SNG001, an inhalable beta interferon delivered by nebulizer, (Synairgen); AZD7442, a long-acting monoclonal antibody combination that will be studied as both an infusion and an intramuscular injection (AstraZeneca); and Camostat mesilate, an orally administered serine protease inhibitor that may block SARS-CoV-2, the virus that causes Covid-19, from entering cells (Sagent Pharmaceuticals).

The first volunteer enrolled in the SNG001 substudy on Feb. 10. The other agents under study are expected to begin enrolling participants soon.

If an investigational agent shows promise by demonstrating safety and reducing Covid-19 symptoms through 28 days following administration, the ACTIV-2 trial then moves to a phase 3 study to gather additional critical data from a larger pool of volunteers. ACTIV-2 trials compare outcomes of multiple interventions with a shared group of placebo recipients.

To qualify for ACTIV-2, participants must have tested positive for SARS-CoV-2 in the outpatient setting within 10 days and started experiencing symptoms within 8 days of enrolling. To be eligible for the AZD7442 infusion study, participants must be at higher risk—due to age, smoking and/or certain co-morbidities—of progressing to severe Covid-19.

Genetic Study of Lewy Body Dementia Supports Ties to Alzheimer's, Parkinson's

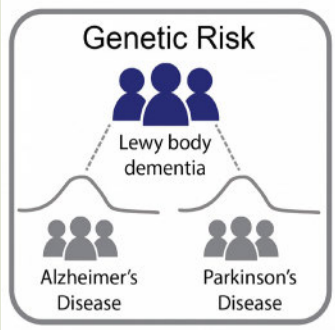
In an NIH-led study, scientists found that five genes may play a critical role in determining whether a person will develop Lewy body dementia (LBD), a devastating disorder that riddles the brain with clumps of abnormal protein deposits called Lewy bodies. These deposits are also a hallmark of Parkinson's disease. The results, published in *Nature Genetics,* not only supported the disease's ties to Parkinson's but also suggested that people with LBD may share similar genetic profiles to those who have Alzheimer's disease.

Lewy body dementia usually affects people over 65 years old. Early signs include hallucinations, mood swings and problems with thinking, movements and sleep. As the disease worsens, patients become severely disabled and may die within 8 years of diagnosis. There currently are no effective treatments.

"Patients [with LBD] often appear to suffer the worst of both Alzheimer's and Parkinson's diseases," said NINDS investigator Dr. Sonja Scholz, senior author of the study. "Our results support the idea that this may be because Lewy body dementia is caused by a spectrum of problems that can be seen in both disorders."

In the study, led by Scholz and NIA senior investigator Dr. Bryan Traynor, investigators compared the chromosomal DNA sequences of 2,981 LBD patients with those of 4,931 healthy, age-matched control participants. Samples were collected from participants of European ancestry at 44 sites across Europe and North America.

Initially, they found the sequences of five genes from LBD patients differed from those of the controls. It was the first time two of the genes, called BIN1 and TMEM175, had been implicated in the disease. These genes may also have ties to Alzheimer's and Parkinson's diseases. The other three genes, SNCA, APOE and GBA, had been implicated in previous studies, and thus, strengthened the importance of the genes in LBD.



An NIH-led genetic study found that Lewy body patients had higher chances of developing Alzheimer's or Parkinson's disease than age-matched controls.

SCHOLZ LAB/NINDS

Researchers replicated their initial results, finding differences in the same five genes in another study. They also found the genetic profiles of the patients in this study had higher chances of suffering from either Alzheimer's or Parkinson's disease than the control subjects.

"We hope these results will act as a blueprint," said Scholz, "for understanding the disease and developing new treatments."

NICHD's Basser Honored for Developing Imaging Techniques

Dr. Peter Basser of NICHD is a co-recipient of the 2021 Technology Award from the Eduard Rhein Foundation.

Dr. Peter Basser of NICHD

According to the award citation, Basser, who leads NICHD's section on quantitative imaging and tissue science and Division of Translational Imaging and Genomic Integrity, was honored for developing diffusion tensor magnetic resonance imaging (DT-MRI), which has implications for planning surgery and radiotherapy, characterizing brain disorders and visualizing nerve fiber pathways (tractography). The technique allows researchers and clinicians to make detailed three-dimensional maps of brain pathways that could not be detected with earlier imaging techniques.

With DT-MRI, radiologists can now diagnose and assess many diseases and disorders and help neurosurgeons better plan operations to target diseased tissue while sparing healthy tissue.

Tractography provides a wiring diagram of the brain, allowing neuroscientists to study anatomical connections between different brain areas.

The Germany-based foundation was established in 1976 by Rhein, an inventor, publisher and author. Its goals are to promote scientific research, learning, arts and culture by granting awards for achievements in radio, television and information technology.

Basser shares the award with Dr. Denis LeBihan, who co-developed DT-MRI. The two will receive the award in November at a ceremony in the Hall of Fame Deutsches Museum in Munich.

Retired NEI Senior Investigator Datiles Mourned

BY PAUL COPPOLA

Retired NEI senior investigator, eye physician-scientist and medical officer Dr. Manuel "Manny" Datiles III passed away on Feb. 12. In his nearly 40-year career at NEI, he worked to find the causes and possible cures for blinding cataracts. He was recognized around the world for his expertise in cataract documentation, pathogenesis and medical treatment and prevention.

Dr. Manny Datiles receives an HHS Innovation Award in 2011.

PHOTO: CHRISTOPHER SMITH

Datiles trained as a basic eye researcher at NEI and as an eye clinician and surgeon at Johns Hopkins Hospital, sub-specializing in cataract and corneal diseases. He became NEI's primary cornea and cataract clinical investigator, serving as chief of the cataract and cornea section of the Ophthalmic Genetics and Clinical Services Branch in 1992. He helped open the NIH operating room for eye surgery and performed hundreds of complex anterior segment eye procedures on research patients from around the world.

In the lab, he worked with the late Dr. Jin Kinoshita to demonstrate that aldose reductase inhibitor (ARI) drugs could prevent cataracts in animal models. ARIs are now used to prevent cataracts in diabetic dogs. He also co-discovered a novel lens protein in guinea pigs, the zeta-crystallin, with NEI protein chemist Dr. Sam Zigler.

In collaboration with NASA physicist Rafat Ansari, Datiles co-developed a special clinical device based on a dynamic light-scattering technique and used it to show that oxidation-caused loss of a lens protein—alpha-crystallin, a molecular chaperone—leads to the formation of human age-related cataracts. This finding will help hasten the development of non-surgical anti-cataract drug treatment for use in many parts of the world where cataract surgery is not available. This was Datiles' most important professional goal.

Datiles also helped care for hundreds of NCI and NHLBI patients who received stem cell transplants. He led a clinical trial of blood serum eye drops for patients who developed severe dry eye as a consequence of therapy.

He published more than 100 peer-reviewed papers, reviews and book chapters. He helped train many young eye physician-scientists from around the world who are now senior faculty and leading clinicians and scientists.

He received awards from the Department of Health and Human Services, the American Academy of Ophthalmology, NEI, NIH, Johns Hopkins University, University of Santo Tomas and the University of the Philippines as well as many civic and charitable societies for his contributions.

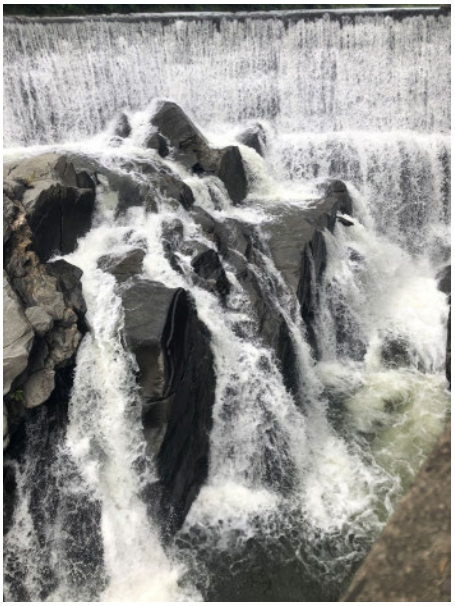
After retirement he served as a special volunteer at NEI, a member of the NIH institutional review board, and as an adjunct associate professor of ophthalmology at Johns Hopkins University School of Medicine.

He is survived by his wife, Jacqueline, 6 children and 4 grandchildren. R

VOLUNTEERS

Volunteers Needed for Asthma Study

People of African ancestry have a higher incidence of asthma and allergic diseases compared to other population groups. Researchers at NHGRI are investigating whether there is a genetic cause for this. Understanding the role that genes play may someday lead to better treatments for these conditions. Consider volunteering, if you are at least 18 years of age and self-identify as Black, African, African American or African Caribbean—both healthy volunteers and adults diagnosed with asthma are needed. For more information, contact the Office of Patient Recruitment at (866) 444-2214, (800) 877-8339 TTY/ASII or prpl@cc.nih.gov. Refer to study #19-HG-0092. Online https://go.usa.gov/x7RXQ.



A program officer at NICHD shared photos (clockwise from above) of the Ottauquechee River in Hartford County, Vermont, taken last August at various levels of the river, in and around the village of Quechee.

PHOTOS: DEBORAH HENKEN

Nature Springs Forth

A while back, the *Record* asked readers for images found in nature, as the pandemic made the Great Outdoors even more attractive. As we move into March, thoughts of spring make these photos a timely sight. To share your images, send hi-resolution photos with short captions to nihrecord@nih.gov.

Winter Color at Great Falls. Above, **Dr. Michael Bender**, program director, NIGMS Division of Genetics and Molecular, Cellular and Developmental Biology, captured a painted bunting near the Great Falls Visitor Center on the C&O Canal in late January.

Busy Bees Offer Respite in Pandemic. At right, **Mary Dunne** of the OD Office of Management, found solace in photographing her garden in the early days of the pandemic.