

March 19, 2021
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Intramural NIMH Looks at Pandemic's Mental Health Impact

BY ERIC BOCK

The Covid-19 pandemic's impact on daily life has negatively affected people's mental health, said Dr. Joyce Y. Chung during a recent virtual Clinical Center Grand Rounds.

"We know why things have changed," said Chung, NIMH deputy clinical director. "But do we really know how these changes have affected us? It's something that we really need to understand."

Public health actions, such as physical distancing and mask wearing, are critical to slowing the spread of Covid-19, but they have rapidly and dramatically changed our lives.

Schools transitioned to remote learning. Office employees teleworked while frontline workers, such as health care providers and grocery store employees, became essential. Large indoor social gatherings were discouraged. Families—especially those with older

SEE CHUNG, PAGE 10



Dr. Joyce Y. Chung

Mid-March marked 1 year since we entered the pandemic age—social distancing, mask wearing, nationwide lockdowns and maximum telework at NIH. Look for a special feature Apr. 2 on coping strategies and how people are acknowledging the historic anniversary.



Self-care images lead Wear Red Day 2021. See story, p. 12.

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LIVING TECHNOLOGY

Programmable Cells Poised to Benefit Biology, Disease Detection

BY RICH McMANUS

In the brave new world plausibly envisioned by MIT's Dr. James Collins in a recent Covid-19 scientific interest group lecture, wearable sensors may one day detect the arrival of whatever pandemic will almost certainly succeed Covid-19 as a global threat, and even the mask one dons on such an occasion might be capable of diagnosing what that bug tangled in the fibers happens to be.



Dr. James Collins

SEE COLLINS, PAGE 4

National Institutes of Health

A PATH PAVED BY MANY

Crowther Underscores the Value of Mentorship

BY DANA TALESNIK

Wherever in the world Dr. Mark Crowther may travel, there's usually a mentee he can visit. Crowther has trained and mentored countless successful academics who span the globe. Of all his achievements, the renowned clinician-scientist with hundreds of publications under his belt is proudest of the careers he has helped shape.

SEE MENTORSHIP, PAGE 6



Dr. Mark Crowther

'UNITE' LAUNCHED

NIH Targets Structural Racism in Biomedical Research

Earlier this month, NIH launched a wide-ranging, comprehensive initiative to end structural racism in biomedical research. A five-committee group—called “UNITE”—that consists of a cross-section of more than 75 NIH’ers from all 27 institutes and centers will guide the long-term initiative.

“The time for upholding our values and taking an active stance against racism, in all its insidious forms, is long overdue,” said NIH director Dr. Francis Collins, in a Mar. 1 statement. “As a science agency, we know that bringing diverse perspectives, backgrounds and skillsets to complex scientific problems enhances scientific productivity. NIH has long supported programs to improve the diversity of the scientific workforce with the goal of harnessing the complete intellectual capital of

SEE UNITE, PAGE 8

'Take Your Child to Work Day' Goes Virtual

NIH's "Take Your Child To Work Day" (TYCTWD) will be held virtually on Thursday, Apr. 22.

This year's online registration will be conducted in two phases. The first phase will begin on Tuesday, Mar. 23 at noon. The second phase will begin on Tuesday, Mar. 30 at noon.

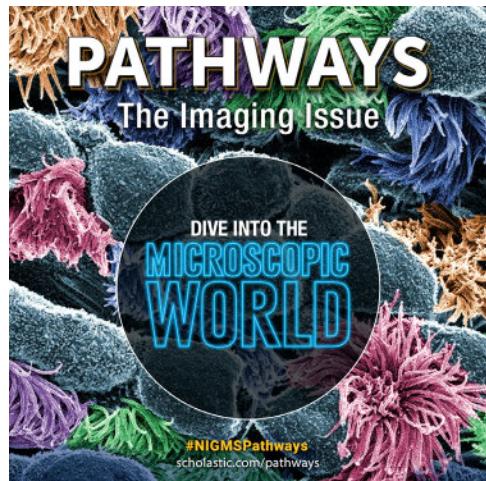
During the first phase, parents or guardians can register their child for only two "limited-space" activities each.

During the second phase, children may be registered for up to 2 additional limited-space activities for a maximum of 4 limited-space activities per child.

Open-space activities do not count toward the limited-space activities.

TYCTWD offers children in grades 1 through 12 an opportunity to explore career paths in science and public service at NIH.

Visit <https://takeyourchildtowork.nih.gov/Pages/default.aspx> for more information.



5th Pathways Issue Looks at Imaging

NIGMS has launched its fifth issue of Pathways, a collection of free Scholastic resources for grades 6 through 12. This issue is all about the microscopic world and the science of imaging. The goal of NIGMS' collaboration with Scholastic is to teach students about basic science, its importance to health and the many different career paths of researchers. Visit www.scholastic.com/pathways/index.html and download the free magazine and accompanying resources to help students learn about how scientific imaging technology allows researchers to unlock the mysteries of our cells and molecules. These discoveries can aid in learning about the body's normal and abnormal processes and lead to more effective, targeted treatments for illnesses.

NIH Will Enforce REAL ID Act In October

Starting Oct. 1, NIH will no longer accept driver's licenses or other forms of identification from

visitors seeking to enter campus unless those credentials are compliant with the REAL ID Act.

As a federal agency, NIH cannot admit visitors without an acceptable form of ID. These same standards apply to NIH staff who forget their ID badge and must access NIH facilities as a visitor. Patients, regardless of identification, will continue to be allowed on campus upon verification of their status on a protocol with the admissions office at the Clinical Center.



WHEN IDEAL IS NOT AN OPTION

Kern Finds Short Workout Better Than no Workout

The *Record* asked readers about their exercise regimens during cold weather. Stuart Kern, contract specialist, NIDA Office of Acquisition, NCATS section, replied below.

"I'm a year-round athlete, so the winter is always a time for working on my base conditioning in anticipation of cycling and running events later in the year.

Prior to the pandemic, my base miles were built into my commute. I biked the 8 miles from Silver Spring to my office at White Flint, and then extended my ride on the way home, or rode straight home and ran when I got there. With proper clothing and lights, I rode all through winter [2020] except those few days when we had ice or snow.

Once we were sent home, I shifted to single, longer rides or runs—either before or after my work day. That's great through the longer days of summer, but now in the winter I've shifted again. I enjoy running just before dawn, so on running days I get up and out early. On cycling days, I start my workday early and get out at lunchtime.

I also try to work through a core strength and flexibility routine a few times a week. We have some simple resistance items—elastic bands, simple

The REAL ID Act of 2005 established minimum security standards for state-issued driver's licenses and identification cards and prohibits federal agencies, such as NIH, from accepting for official purposes licenses and identification cards that do not meet these standards as of Oct. 1, 2021.

For additional information about the Real ID Act, visit: <https://www.dhs.gov/real-id>.



Year-round athlete Stuart Kern masked and in motion at left, and above, breaking for a bridge-crossing

weights, an exercise ball, two teenagers—which provide adequate resistance workouts for the muscle groups I don't use when cycling or running.

My biggest challenge is a mistaken notion that if I can't do a full ideal workout—like three sets of all exercises or a long run or a long ride—that it's not worth doing. I have to remind myself that one set of pushups, or a half-hour ride, or a run around the block is better than nothing at all. Likewise, it's all too easy to go directly to my chair and not take any stretching breaks through the day. I try, with mixed success, to get out of my chair regularly and do that one set of pushups, or stretch while I'm making a cup of coffee, or push the teenagers out for a walk.

For motivation, I've signed up for a few races later this year. They may be cancelled or when the time comes I may not feel it's safe to participate, but for now it gives me a target to shoot for. I follow friends on Strava, so we see each other's workouts—we trade encouragement, and there's the quiet satisfaction of knowing that I rode or ran on a colder or wetter day than they did. I also keep a simple written log of my workouts, so I can look back over the month and see whether I exercised on more days than I didn't. I keep an eye on the weather forecast for the week, plan on taking the worst day as an intentional rest day, and commit to getting decent workouts on the days before that."

Rural Health Seminar Examines Covid-19 Challenges

BY SALLY PAUSTIAN

NIH hosted a seminar examining the many ways the Covid-19 pandemic has affected health and health research in rural communities. The seminar highlighted commitments from all NIH institutes and centers to improve rural health across the country.

NIMHD director Dr. Eliseo Pérez-Stable introduced the seminar, explaining that race and socioeconomic status strongly affect health, and that rural communities already were experiencing significant disparities in health before the pandemic.

"We have a unique opportunity to expand and build on health care delivery through innovation and research by helping to mobilize and strengthen local efforts in rural areas to improve health outcomes," Pérez-Stable emphasized.

Dr. Marshall Bloom of NIAID's Rocky Mountain Laboratories elaborated on some of the differences in Covid-19 response between larger cities and small towns that have contributed to high rates of Covid-19 infection in many rural communities.

In a panel session moderated by NCATS deputy director Dr. Joni Rutter, speakers outlined real-world data on the effects of the pandemic in rural communities.

Dr. Brenda Eskenazi of the University of California, Berkeley, explained that many Latino farm workers in California have experienced life impacts during the pandemic, including increases in food insecurity, depression and anxiety. Dr. Randall Akee of UCLA pointed out that Covid-19 rates are higher in many racial and ethnic minority populations, such as Native Hawaiian and Pacific Islander populations that already have disproportionately higher rates of chronic disorders like diabetes and heart disease.

Tracking health in minority populations can be challenged by database structures, too. Akee noted that many public health databases do not disaggregate Native Hawaiians and Pacific Islanders from other Asian ethnicities and often list them as "Other."

Reducing exposure by staying at home also is complicated for many rural Americans.

In rural New Mexico, students from sexual and gender minority (SGM) populations who previously may have received social support and health resources in school, no longer have access to these benefits when school is virtual.

Dr. Cathleen Willging of Pacific Institute for Research and Evaluation said whether SGM students are able to receive confidential counseling or treatment from home may increase the disparities and isolation these students already faced before the pandemic. Also, many rural students have



Seminar presenters included (from l) Dr. Stacy Rasmus , Dr. Vincent Werito and Mysha Wynn.

unequal access to the internet to participate virtually. She advocated funding to promote broadband internet in rural communities as a common good to accelerate equitable access to much-needed resources during the pandemic.

In many rural communities, race and ethnicity are inextricably intertwined with other aspects that contribute to health, such as immigration status or socioeconomic status. A nuanced understanding of cultures is needed to identify and improve gaps in health outcomes.

Dr. Thomas Chavez of the University of New Mexico explained that many in undocumented communities view hospitals as a last resort to seeking urgent health care, and Covid-19 has increased the stress these communities experience because of lack of health insurance and fear of disclosing immigration status.

The University of New Mexico's Dr. Vincent Werito emphasized that, in the Diné community of Navajo Nation, Covid-19 has antagonized members' holistic sense of well-being and relationships.

Many researchers and community partners have responded to the Covid-19 crisis by strengthening the collaborations that help meet the unique needs of each rural community.

Dr. Giselle Corbie-Smith of the University of North Carolina School of Medicine and Mysha Wynn, executive director of Project Momentum, Inc., presented examples of partnerships in rural North Carolina that enable communities to solve their own problems.

Dr. Stacy Rasmus of University of Alaska, Fairbanks,



Healthy food provided on job sites addresses food insecurity during the pandemic.

PHOTO: ALICE AMMERMAN

and Billy Charles, tribal member of the Native Village of Emmonak in Alaska, explained that in rural Alaska, people cooperate as a community to survive and be resilient. Drs. Alice Ammerman of UNC and Carla Norwood, executive director of Working Landscapes, showed attendees some creative collaborations with local farms and restaurants to address the increase in food insecurity during the pandemic, such as a program that provides frozen, healthy meals made with local ingredients.

Drs. Lydia Bazzano and Angela Lambert discussed how relationships between communities and health care systems in Louisiana expanded during the pandemic to provide trusted information and "meet people where they are" to make healthy choices.

Closing the seminar, NIDDK director Dr. Griffin Rodgers emphasized that although Covid has deepened existing health disparities and illuminated the complex intersectionalities that drive rural health, NIH's commitment to improving health for everyone—including rural communities—offers researchers the chance to "transform these troubles into opportunities" for a healthier, more equitable future. He encouraged seminar attendees to "stay safe, stay healthy, and stay hopeful."

View an archived recording of the workshop at <https://videocast.nih.gov/watch=38788>. R



ON THE COVER: A healthy neuron

IMAGE: NIA

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Collins

CONTINUED FROM PAGE 1

That's thanks to the maturing field of synthetic biology, in which investigators are adapting the logic of the electronic circuit board to make gene circuits capable of rewiring living cells and endowing them with novel functions. So-called "wet circuits" are now being designed and built by scientists such as Collins, who is the Termeer professor of medical engineering & science at the Massachusetts Institute of Technology.

Starting with relatively simple genetic toggle switches, Collins and colleagues have created a range of chemical switches that "open up tremendous possibilities for biosensors...Synthetic gene circuits have opened up a whole range of logical functions to use in cells."

The technology enables programmable cells, or living technology, that can sense their environment, make a decision and act on it. Standing to benefit are not only medicine, but also energy, the environment, first responders, the military and agriculture, to name a few fields.

Yet multiple times throughout the hour of his lecture, Collins paused to remind listeners, "No matter how clever we think we are, biology still gets in the way of our best intentions and aspirations in synthetic biology."

Nonetheless, we are poised on the doorstep of an era of living diagnostics and living therapeutics, he said.

Proof of concept for the MIT team was their response years ago to a challenge from the Gates Foundation to create an inexpensive way to diagnose and treat cholera. Engineering, in mice, the bacteria *Lactococcus lactis*, the researchers invented a "theranostic," that responds only to the presence of cholera. By modifying the pH in cells, the therapy thwarts the dumping of cell fluids into the intracellular space, which is the hallmark of that nasty gut pathogen.

Virtues of the therapy are that it is "eminently manufacturable, inexpensive and can be lyophilized into pills or spiked into yogurt," Collins said. "These innovative developments in synthetic biology could make a difference for controlling pathogen outbreaks."

Thanks to the wizardry of a number of collaborators skilled in manipulating



MIT's Collins is one of very few people belonging to the National Academy of Sciences, the National Academy of Engineering, National Academy of Medicine and the American Academy of Arts & Sciences.

cell-free extracts, Collins described the possibility of encoding RNA switches within freeze-dried, paper-based systems—which don't require refrigeration—to create paper-based diagnostics that could be mailed around the globe to identify pathogens. It could tell first responders—within the "golden hour" when treatment is most effective—which antibiotic to reach for, and which to avoid.

Several years ago, Collins and collaborators pivoted from diagnostic work on bacteria and antimicrobial resistance to a focus on Ebola, to help with an outbreak in Africa. Within a day of taking on the challenge, his team had crafted a 24-sensor system at a cost of only 2 cents per sensor, capable of detecting multiple strains of Ebola.

Fifteen months later, in January 2016, they embarked on creation of a paper-based diagnostic for Zika virus. It took less than 2 months to create a freeze-dried amplification system embedded with RNA sensors that could tell Zika from dengue, chikungunya and yellow fever.

Almost inevitably, the scientists also began using CRISPR-cas9 gene editing technology to make a Zika diagnostic capable of teasing out its various strains; it debuted in 2016.

Collins described another paper-based diagnostic created to detect the gut microbiome and host response, to identify species present in stool samples.

"It was easy, inexpensive and provides a rapid readout of results," he said.

"But what we build doesn't always function," Collins cautioned. He and colleagues are now exploring "deep learning" platforms that can harness neural networks

to improve synthetic biology, particularly with respect to Covid-19.

Working with collaborators at Harvard and the Wyss Institute, Collins is now searching for design rules, new components and novel gene circuits that will enable the platforms to quickly diagnose diseases such as covid. They are using a kind of regulator known as a "toehold switch," which, according to Wyss "enables precise control over the expression of a gene of interest in response to a defined environmental stimulus in diverse synthetic biology applications."

A refinement of CRISPR known as SHERLOCK, pioneered by scientists at MIT and the Broad Institute, uses a variety of enzymes beside cas9 to detect substances at the sensitivity of a single molecule. It forms the basis of a diagnostic system enabling not only species identification, but also discrimination between strains and mutants within a strain, said Collins. Uses are not limited to bacteria, but viruses as well.

He envisioned a 4-pot multiplex system that could evaluate serum, urine, saliva and plasma simultaneously, with results as rapid as today's pregnancy tests.

Last May, the FDA issued the first CRISPR-dependent emergency use authorization for a Covid-19 diagnostic, reported Collins. "Ours compares well to the PCR-based test," he said. "You get output in less than an hour, which is much faster, and at only one-quarter of the cost."

Collins predicts a coming era of "wearable synthetic biology," wherein gene circuits could be inserted into clothing to see if a person is exposed to a pathogen or toxin, and perhaps even measure a bug's biological effect on the host. Already, a synthetic gene circuit has been developed that serves as a universal sensor for nerve toxins.

The "lab coat of the future" could be tailored with biosensors, and even johnnies—those embarrassing gowns worn by inpatients at hospitals everywhere—could include sensors enabling hospital epidemiologists to pinpoint sources of in-house infection.

Masks, too, could include inserts that respond to and analyze the water vapor in exhalations—such a system is now in demonstrations, said Collins.

"Any porous media, not just paper" can

host biosensors, he continued. Freeze-dried pellets could be encapsulated into portable field systems that can make vaccine antigens on the spot, Collins noted. A model has already been created, using diphtheria as an example. “We could have portable on-demand biomolecular factories.”

Observing that the Moderna vaccine against Covid-19 has its origins in synthetic biology, Collins said work has started on a BCG-based Covid vaccine. (BCG, or bacillus Calmette–Guérin, has long been used as a tuberculosis vaccine.)

“This is not Operation Warp Speed, but Operation Slow Speed,” he quipped. Tweaked using synthetic biology, the BCG-based vaccine would be “inexpensive, safe, easy to make, requires no refrigeration and involves only one shot,” said Collins. “We don’t know if it will be ready in time, but it could address the next pandemic, which is coming, but we don’t know when or where.”

Collins and colleagues are also taking a deep-learning approach to the discovery of novel antibiotics.

“Our antibiotic arsenal is declining while antibiotic resistance is increasing,” he said. “What features, if we look bond by chemical bond, contribute to bactericidal behavior?” Applying their technology to larger and larger libraries of compounds, they are identifying hundreds of new candidates.

“We would like to extend our work to the design of novel antibiotics,” Collins concluded, “and to antivirals, and to new treatments for cancer and other complex diseases.”

During a brief Q&A moderated by Collins’s first postdoc, Dr. Carson Chow, now at NIDDK, who described the talk as “Marvel-level science,” Collins was asked if biofabrics will be affordable for everyone.

“Our hope is that this new technology will be as cost-effective as possible,” he said. “Face masks can be made for small numbers of dollars. The more complicated clothing could be quite expensive. But wristbands are very low-cost. Athletes at the high school level could use them for monitoring their workouts.”

The complete talk—a great way to get excited about science all over again—is available at <https://videocast.nih.gov/watch=38876>. **R**

‘YOUNG BLOOD, OLD BRAINS’

Wyss-Coray To Deliver Mahoney Lecture, Mar. 31

Dr. Tony Wyss-Coray, a leading researcher in brain aging and neurodegeneration with a focus on age-related cognitive decline and Alzheimer’s disease, will present “Young Blood for Old Brains,” the Mahoney Lecture on Aging, on Wednesday, Mar. 31 at 3 p.m., via NIH videocast.

Wyss-Coray is the D.H. Chen professor in the department of neurology and neurological sciences, Stanford University School of Medicine; associate director, Center for Tissue Regeneration, Repair and Restoration Center of Excellence, Veterans Administration Rehabilitation R&D Service; and co-director, NIH Alzheimer’s Disease Research Center. He and the Wyss-Coray research team

are following up on earlier discoveries that showed that circulatory blood factors can modulate brain structure and function, and that factors from young organisms can rejuvenate old brains and, vice versa, factors from old mice are detrimental for young mice and impair cognition.

Evidence has indicated that the cerebrovasculature is an important target and that brain endothelial cells show prominent age-related transcriptional changes in response to plasma.

Scientists also have discovered that plasma proteins are taken up broadly into the brain and that this process varies between individual endothelial cells and with aging. Researchers are currently exploring the relevance of these findings for neurodegeneration. They also are seeking potential applications toward therapies on the molecular basis of this systemic communication with the brain by employing a combination of genetic, cell biology and proteomics approaches in model organisms and humans.

Wyss-Coray’s lab is part of the Glenn Center for Aging at Stanford University, the Stanford Neurosciences Institute’s Brain Rejuvenation Project and NIH Alzheimer’s Disease Research Center. He and his team are funded by the American Heart Association/Allen Initiative, NIA and the NOMIS Foundation.

He received his bachelor’s, master’s, Ph.D., and postdoctoral fellowship in the Institute of Clinical Immunology from the University of Bern, Switzerland. In 1993, Wyss-Coray moved to the United States to pursue a postdoctoral fellowship at The Scripps Research Institute.

Wyss-Coray joined Stanford in 2002. Prior to that, he was at the University of California, San Francisco; Gladstone Institute of Neurological Disease; and Veterans Affairs Palo Alto Health Care System.

He has received numerous awards, including the NIH Director’s Transformative Research Award, the NIH Director’s Pioneer Award and the NOMIS Foundation Distinguished Scientist Award. *TIME Magazine* named him among the “Health Care 50” most influential people transforming health care. Wyss-Coray is a member of the Society for Neuroscience, American Association for the Advancement of Science and International Society for Neuroimmunology.

Mahoney lectures are sponsored by NIA and named in honor of Florence Stephenson Mahoney (1899–2002), who devoted much of her life to successfully advocating for the creation of NIA and increased support for NIH.

Visit <https://videocast.nih.gov/watch=41454>, to watch the lecture.



Dr. Tony Wyss-Coray will present the Mahoney Lecture on Aging on Mar. 31.

Mentorship

CONTINUED FROM PAGE 1

"I think mentorship is the most important and valuable thing we can do in our scientific careers," said Crowther, who chairs the department of medicine at McMaster University in Ontario, Canada. Speaking at a recent virtual CC Grand Rounds Great Teachers Lecture, he offered numerous nuggets of sage advice for trainees and academics, young and old.

"Anybody has the ability to influence the course of development of many other people around them," he said.

Different mentors bring their own unique experiences, lessons and stories. They may be older or younger, more senior or junior, or come from different disciplines, but one



Dr. Meaghan Colling, a mentee who met Crowther when she was an NIH hematology fellow, introduces the lecture. "I could speak at length about the way he...demonstrated profound commitment to the development of his trainees, including me," from lessons on the ward to hours of brainstorming, despite his full academic load.

• • •

"Anybody has the ability to influence the course of development of many other people around them."

DR. MARK CROWTHER

• • •

thing is certain: cultivating relationships with many mentors throughout your career is critical to success, Crowther said.

The more-junior people will have to establish themselves as independent researchers and find their own niches. It's the mentor's job to enhance skills learned in clinical and research training and to guide, protect and provide occasional reality checks.

A self-described benign hematologist, Crowther said it's endlessly gratifying to help young people advance in their careers and to know he had even a little bit to do with their success. He's also eager to connect colleagues at all levels, especially when he can offer someone a time-saving resource.

"It always amazes me, what takes me literally 30 seconds can save [someone else] days or weeks of their time," he said.

Be generous with your contacts, Crowther said, offering advice that has come back to him in spades. If he texted the busiest professors at McMaster, they'd get back to him immediately. He is one of dozens

Crowther tells all budding academics of two career paths they can follow. For those with their hearts set on remaining at a specific institution or in a certain city, "you have to subvert your interest to the interest of the institution," he said. Figure out what that location will need and want at the time your training will finish, then go train to become adept at that specialty.

For those traversing the second path—to excel at their chosen specialty—Crowther says: "Find the best training you can and pursue it relentlessly." He recounted mentoring an exceptional resident from Kuwait who wanted to return to his country as the preeminent electrophysiologist. Crowther candidly advised him to stay at McMaster for cardiology but train in EP elsewhere to maximize his potential when he returns home.

Before the lecture, Crowther met virtually with NIH medical fellows, one of whom asked how to figure out what to pursue and where. Crowther responded with the story of a freshman undergrad named Alan, who really wanted to collaborate. Crowther kept ignoring his emails but finally succumbed, impressed with his enthusiasm.

"There's a fine line between persistence and stalking," Crowther quipped. Five years

of successful venous thromboembolism experts in his small city, all of whom choose to cooperate, rather than compete.

"As long as you are thoughtful about turf, and people get along, at least reasonably," he said, "the success is predicted by having a culture and a fertile ground into which new people can be deposited and grow with direct support."



Henry Ddungu

First job was making gravel for less than pennies a day in Uganda

Has risen through sheer hard work that we cannot even imagine in our cozy life

People like Henry are the best mentors as they lead by an example that we can aspire to but never actually



Crowther met his good friend and mentor Dr. Henry Ddungu (pictured here with his family) while running an outreach program in Uganda. "People like Henry are the best mentors as they lead by example," Crowther said.



Michael Gent

McMaster
University
Health Sciences



- A clear thinker of the highest order
- Tremendously generous with time and resources
- Probably the most influential of mentors on the actual career path I have followed

Some mentors serve up the harsh reality: The late Michael Gent, a McMaster professor and biostatistician, told Crowther to brush up on his English, handing him a copy of *Fowler's Guide to Modern English Usage*. Crowther remains grateful for the immense amount of time Gent spent editing his papers.

later, the two will have co-published more than 10 papers by the time Alan finishes first-year medical school.

"If you're looking for mentorship, ask questions, review the literature, attend meetings, get introduced to people and use the people who you know to introduce you to other people," he advised.

Too often, people rush to get their first faculty position, but "the more training you get at the beginning of your career," he said, "the better you're going to do through the course of your career." He looks back fondly on his 4 years as a clinical scholar. It didn't pay much at the time, but it paid dividends over the subsequent 20 years of his career.

Crowther also reflected on some of his most beloved mentors, many of whom he still turns to for guidance. Some he calls on sparingly, for an important, specific matter. Some he'd call on regularly, such as the late Dr. Bruce Barton, a hematologist from his hometown who introduced him to his first research job.

"Bruce inspired me as a medical student to pursue hematology," Crowther noted, "and insisted I go to the best place to get trained," even if it wasn't his institution.

Another cherished mentor is the renowned and very busy hematologist Dr. Jack Hirsh, who gave Crowther his first big

career break and was an invaluable mentor early in his career.

"Jack is a rock star in my world," Crowther said. "He's why I came to McMaster."

Other mentors frame priorities and keep you sane. For Crowther, that person is his longtime administrative assistant, Gail Campbell, who makes sure he doesn't overcommit.

"The pathway to success is paved by others," said Crowther. Mentorship circles will evolve over time. "Building a team to support a career path is critical, hard and slow."

As scientists become more senior, they begin to wonder what legacy they might leave.

"The legacy is not going to necessarily be their own productivity," Crowther concluded, "but the productivity and success, enjoyment and fulfillment of the many young people that we are honored to be able to contribute to over the course of our leadership lives." **R**



Dr. Kizzmekia Corbett briefs President Biden earlier this year.

NIAID's Corbett Named to Honor Lists by Two Magazines

TIME Magazine has named Dr. Kizzmekia Corbett to the TIME100 Next 2021 List. A viral immunologist and research fellow in NIAID's Vaccine Research Center, Corbett focuses on coronavirus biology. Her team's work has been central to the development of Moderna's Covid-19 vaccine and the Eli Lilly therapeutic monoclonal antibody.

NIAID director Dr. Anthony Fauci wrote Corbett's *TIME100 Next* profile. In it, he called Corbett a "rising star" in the immunology community whose "work will have a substantial impact on ending the worst respiratory disease pandemic in more than 100 years."

The *TIME* list "recognizes 100 emerging leaders who are shaping the future of entertainment, health, politics, business and more."

Corbett was also named one of *People Magazine's* Women Changing the World. She was featured as one of four of the many women behind Covid-19 vaccine development.



NIAID director Dr. Anthony Fauci (l) and NCI Surgery Branch chief Dr. Steven Rosenberg

Fauci, Rosenberg Win Dan David Prize

NIAID director Dr. Anthony Fauci and NCI Surgery Branch chief Dr. Steven Rosenberg have received the Dan David Prize for 2021, an international award endowed by the Dan David Foundation and headquartered at Tel Aviv University.

The awards are given in three categories—Past, Present and Future—"for achievements having an outstanding scientific, technological, cultural or social impact on our world."

Fauci received the Present award, which "recognizes achievements that shape and enrich society today," for his exceptional contributions to HIV research, being the architect of the U.S. President's Emergency Plan for AIDS Relief, heading NIAID, fighting for the recognition of novel approaches such as mRNA vaccines and "courageously defending science in the face of uninformed opposition during the challenging Covid-19 crisis."

Rosenberg won the Future award, which "focuses on breakthroughs that hold great promise for improvement of our world," for his landmark discoveries leading to the first cancer immunotherapies, ongoing efforts to develop immunotherapy for solid tumors, and "the combination of insight, care and fearlessness that enabled his translation of basic science to medical practice."

He shares the award with Prof. Zelig Eshhar, an Israeli immunologist at the Weizmann Institute of Science, and Dr. Carl June, an immunologist at the Perelman School of Medicine at the University of Pennsylvania.

"The Dan David Prize recognizes and encourages innovative and interdisciplinary research that cuts across traditional boundaries and paradigms," according to the prize's website. "It aims to foster universal values of excellence, creativity, justice, democracy and progress and to promote the scientific, technological and humanistic achievements that advance and improve our world."

UNITE

CONTINUED FROM PAGE 1

the nation. These efforts, however, have not been sufficient. To those individuals in the biomedical research enterprise who have endured disadvantages due to structural racism, I am truly sorry. NIH is committed to instituting new ways to support diversity, equity and inclusion, and identifying and dismantling any policies and practices that may harm our workforce and our science."

UNITE is an acronym for the five target areas and major strategies of the initiative:

U-understanding stakeholder experiences through listening and learning; N-new research on health disparities, minority health and health equities; I-improving the NIH culture and structure for equity, inclusion and excellence; T-transparency, communication and accountability with



"We cannot underestimate the challenges before us."

-NIH DIRECTOR DR. FRANCIS COLLINS



internal and external stakeholders; and E-extramural research ecosystem—changing policy, culture and structure to promote workforce diversity.

UNITE co-chairs are NIH principal deputy director Dr. Lawrence Tabak, NIH deputy director for management Dr. Alfred Johnson and NIA deputy director Dr. Marie Bernard, who also serves as acting NIH chief of scientific workforce diversity.

For the last 6 months or so, UNITE has been meeting to develop the foundation for the initiative. On Feb. 26, the group presented the concept to a special virtual meeting of the advisory committee to the NIH director (ACD). ACD members welcomed UNITE with enthusiasm and unanimous support.

"We're at an important juncture in our nation's experience and reckoning with race,"

said ACD member Dr. Roy Wilson, president of Wayne State University. "On the one hand, the spotlight really has been shone brightly in exposing the inequities that have disadvantaged Black people for centuries. This has had a positive effect in that many people and institutions are using this moment to assess their own contributions to systemic racism

scientific workforce and to promote cultural change in the scientific community."

As part of UNITE's launch, a new website <https://www.nih.gov/ending-structural-racism> went live with details of the initiative and resources for the public. In addition, a Request for Information (RFI)—<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-21-066.html>—seeks input from the public and stakeholder organizations. The RFI is open through Friday, Apr. 9; responses to the RFI will be made publicly available.

"We cannot underestimate the challenges before us," Collins noted in his statement. "Identifying and dismantling racist components of a system that has been hundreds of years in the making is no easy task. This is just the beginning of an effort that has a concrete goal of achieving racial equity but has no scheduled end point..."

"At the most fundamental level, the NIH mission is about the respect of human life and dignity, which should permeate all aspects of our lives and work. The National Institutes of Health is also known as the National Institutes of Hope. With optimism, I invite you to join NIH in our efforts to bring health and hope to all people—because together we're stronger." **R**

ENDING STRUCTURAL RACISM



As part of UNITE's launch, a new website went live with details of the initiative. Visit <https://www.nih.gov/ending-structural-racism>.

and make meaningful change. But I'm also bewildered at acts of overt racism that are being played out with increasing frequency and blatant openness. So, we have to leverage the positive momentum over the negative. NIH is in a unique position to move the needle in addressing systemic racism in the

NIH To Screen *Picture a Scientist* Documentary

In recognition of Women's History Month, the Office of Equity, Diversity and Inclusion and NHLBI will sponsor an on-demand virtual screening of the documentary film *Picture a Scientist* for the entire NIH community Mar. 22-26.

This 2020 official selection from the Tribeca Film Festival spotlights three researchers

who are reshaping the culture of science for women. In addition to recounting experiences of harassment and institutional discrimination, these empowering women offer new perspectives for making the sciences more diverse and equitable for all.

NIH is committed to cultivating an inclusive environment for people of all genders and backgrounds. All NIH staff, as well as family members and friends, can RSVP on the EDI

website to receive a reminder when the screening opens at <https://edi.nih.gov/pictureascientist>.

EDI and NHLBI also will co-host a panel discussion on Thursday, Apr. 8, about fostering a diverse, equitable and inclusive workplace for women at NIH. More information will be coming soon.

To learn more about *Picture a Scientist*, visit www.pictureascientist.com/.

Study Shows Promising Therapy for Drug-Resistant *Klebsiella pneumoniae*

A promising strategy to tame troublesome drug-resistant bacteria is bacteriophage, or phage therapy, which uses viruses instead of antibiotics. NIH scientists have used two different bacteriophage viruses individually and then together to successfully treat research mice infected with multi-drug-resistant *Klebsiella pneumoniae* sequence type 258 (ST258).

The bacterium *K. pneumoniae* ST258 is included on a CDC list of biggest antibiotic resistance threats in the U.S. High rates of morbidity and mortality are associated with untreated *K. pneumoniae* infections.

Phage therapy has been pursued for about a century, though clinical research has provided mixed results. In a new paper published in the journal *mBio*, NIH scientists noted the significance of this research given the lack of alternative treatment options for drug-resistant infections. Bacterial resistance has emerged against even the newest drug combinations, leaving some patients with few or no effective treatment options.

In research conducted at NIAID's Rocky Mountain Laboratories in collaboration with NCI, scientists treated mice with phage P1, P2 or a combination of the two, all injected at different times following ST258 infection. Each of the three experimental treatment regimens helped the mice recover from ST258 infection.



Scientists are studying whether phage therapy can treat multidrug-resistant *Klebsiella pneumoniae*.

PHOTO: MOTORTION/ISTOCK/GETTY

The scientists noted that recovery was more dependent on timing than dosage. Mice treated one hour after infection showed the strongest recovery, followed by those treated 8 or more hours after infection. Control mice treated with saline all quickly developed severe disease and died.

The scientists also checked the blood and tissue of phage-treated mice and found there were significantly fewer ST258 bacteria at all time points compared to control mice. Unfortunately, there also were signs that the ST258 bacteria had begun developing phage resistance, a finding the scientists are continuing to investigate.

This study represents a first step in evaluating phage therapy for treating severe *K. pneumoniae* ST258 infection in humans.

Law Enforcement Seizes More Illegal Drugs During Pandemic

An analysis of law enforcement seizures of illegal drugs in five key U.S. regions revealed a rise in methamphetamine and marijuana (cannabis) confiscations during the Covid-19 pandemic. Seizures of the two drugs were higher at their peak in August 2020 than at any time in the prior year. While investigators found that trends in heroin, cocaine and fentanyl seizures were not affected by the pandemic, provisional overdose death data show that the increased drug mortality seen in 2019 rose further through the first half of 2020.

In the NIDA study, published in *Drug and Alcohol Dependence*, investigators analyzed nearly 30,000 drug seizures from March 2019 through September 2020 in Washington, D.C./Baltimore, Chicago, Ohio, New Mexico and North Florida.

Measures to address the Covid-19 pandemic have limited social gatherings, closed international borders and reduced economic activity across many sectors. The findings suggest that the pandemic and its related restrictions may have affected the availability and demand of some, but not all, illegal drugs, and that availability may have increased in summer and fall of 2020 in the five regions under study.



Seizures of methamphetamine have risen during the pandemic in five regions studied.

PHOTO: BLUESHOT/ISTOCK/GETTY

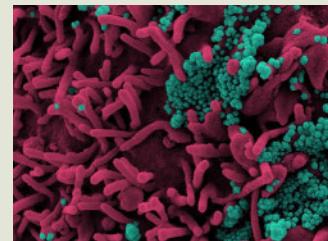
"Our understanding of how the Covid-19 pandemic affects drug use is evolving, but we do know that social isolation, even for short periods, can cause psychological distress that may drive some people to seek out psychoactive substances," said lead study investigator Dr. Joseph Palamar of New York University's Grossman School of Medicine and co-investigator on the National Drug Early Warning System. "It is critical for us to obtain a clearer picture of how the pandemic has influenced drug supply and demand, so that we may better mitigate potential harmful effects of changing drug use patterns."

Incidences of marijuana and methamphetamine seizures dipped at the beginning of the pandemic, with low points in April 2020, but confiscations subsequently rose, exceeding pre-Covid-19 seizure rates. Provisional CDC data show overdose deaths involving stimulant drugs, including methamphetamine, have increased 39 percent in the year ending in June 2020 compared to the year ending in June 2019.

NIH Halts Trial of Covid-19 Convalescent Plasma in Patients with Mild Symptoms

NIH halted a clinical trial evaluating the safety and efficacy of Covid-19 convalescent plasma in treating emergency department patients who developed mild to moderate Covid symptoms.

Launched in August 2020, the Clinical Trial of Covid Convalescent Plasma of Outpatients (C3PO) was being conducted at 47 hospital emergency departments across the U.S. and had enrolled 511 patients toward its 900-patient enrollment goal. It was studying the effectiveness of using convalescent plasma—blood plasma with antibodies derived from recovered patients—to treat adults.



Colorized scanning electron micrograph of a cell infected with SARS-CoV-2

IMAGE: NIAID

On Feb. 25, after analyzing interim trial data, an independent data and safety monitoring board (DSMB) determined that while the convalescent plasma intervention caused no harm, it was unlikely to benefit this group of patients. The DSMB then recommended that NHLBI stop enrolling new patients into the study.

Even if enrollment continued, this trial was highly unlikely to demonstrate that Covid-19 convalescent plasma prevents progression from mild to severe illness in at-risk emergency department non-hospitalized participants. More than 100,000 people in the U.S. and many more worldwide have already been treated with it since the pandemic began.

relatives in long-term care facilities—experienced isolation.

"It's quite odd to consider our lives one year ago today, what we were doing, what we took for granted and how we are living today," Chung said.

One survey conducted by the Centers for Disease Control and Prevention found that 40.9 percent of respondents experienced at least one adverse mental or behavioral health condition, including depression or anxiety, trauma or stress related to the pandemic, increased substance use to cope, or thoughts of suicide. She noted younger adults, racial and ethnic minorities and essential workers had disproportionately worse mental health outcomes.

Another study found the pandemic disproportionately affected older adults, frontline health care workers, people with pre-existing poor physical health and those unemployed with income insecurity.

NIMH's intramural research program quickly launched several projects in response to the pandemic. Specifically, the program wanted to study effects of Covid-19 stressors on mental health.

Chung led one project, a survey called the "Mental Health Impact of Covid-19 Pandemic on NIMH Research Participants and Volunteers," which enrolled more than 3,600 participants from all 50 states and 15 countries. Every 2 weeks for 6 months, participants completed a questionnaire about Covid-19, mental health symptoms and stress.

"One of the best things about the study, for me, was the connections we made across NIMH labs," she said. "Rather than working in silos, we formed a team that had people who had not necessarily worked this closely before."



Dr. Robert Lembo, director of education and training at the Clinical Center, introduces Dr. Joyce Chung at a recent CC Grand Rounds.

The study has three aims:

- to describe the relationship between stressors related to Covid-19
 - to determine whether mental health status moderates the relationship between stressors related to Covid-19
 - to identify risk and resilience factors among study participants

At the beginning of the study, Chung and her team asked participants about their medical and mental health history, functional impairment and alcohol and

drug use. Then, participants answered questions about their mental health, symptoms, distress and loneliness every 2 weeks for 24 weeks. They also had the opportunity to answer

open-ended prompts about their mental health. Once the study ended, participants completed an end-of-study assessment.

After the death of George Floyd and the racial injustice protests that followed across the United States, Chung and her team tried to increase the racial and ethnic diversity of the study population. They changed the design of recruitment materials and conducted a direct-mail campaign.

The participants included 194 patients who had enrolled in prior NIMH studies, so Chung knew their medical and mental health histories. She compared their responses to mental health symptom surveys before and after the pandemic started to "benchmark how our group of individuals were doing

compared to published reports of increased anxiety and depression."

Fifty-nine percent of respondents reported higher levels of anxiety, while 41 percent of respondents reported higher depression symptoms.

Chung noted that 174 of the participants who had enrolled in prior NIMH studies had undergone an in-person, comprehensive clinical evaluation. Of this subsample, 61 had a positive lifetime history of mental disorder and 113 healthy volunteers had a negative lifetime history of a mental disorder.

With the help of Dr. Francisco Pereira, an NIMH expert in machine learning, Chung is using data from the subsample to predict the mental health status of participants based on survey responses. This approach allows researchers to control for mental health status.

Going forward, having the ability to control for mental health status will help determine how the mental health effects of the pandemic are distributed. A preliminary analysis suggests the "consequences of Covid-19 are not evenly distributed across the study population." Researchers hope to release a more detailed analysis in the future.

The research team will be examining longitudinal patterns over the course of the pandemic using the repeated measures of mental health and distress to look for different clinical trajectories. They also want to identify risk and resilience factors that increase or decrease the mental health impact of pandemic stressors.

"There are broad and significant social and environmental stressors imposed by the Covid-19 pandemic on the general public," Chung concluded. "A focus on mental health is warranted and is an important area of clinical and research inquiry." **R**

NINDS's Moy Retires After 32 Years of Federal Service

BY SHANNON E. GARNETT

After 32 years of federal service—20 with NIH—Dr. Claudia Moy, an epidemiologist and program director in NINDS's Division of Clinical Research, has retired.

"There's never a good time to go and it was really hard to make the decision, but I'm excited about the next phase of my life," she said. She officially retired on Jan. 31.

Born in Connecticut and raised in a small town near Pittsburgh, Penn., Moy grew up surrounded by science. "Science has always been an interest for me," she said. "Both of my parents were scientists and as a student I worked summers in my father's organic chemistry lab in Pittsburgh."

She earned her bachelor of science degree in biology from Pennsylvania State University in 1974, and a year later, she began her federal career as a survey statistician in the Division of Health Interview Statistics at the National Center for Health Statistics, now part of the Centers for Disease Control and Prevention.

While at NCHS, Moy participated in the design and analysis of the National Health Interview Survey, which monitors the health of the U.S. population through collection and analysis of data on a broad range of topics; the National Health and Nutrition Examination Survey, a program of studies created to assess the health and nutritional status of adults and children in the U.S.; and the Hispanic Health and Nutrition Examination Survey, which gauges the health and nutritional status and needs of Hispanic and Latino populations.

Moy continued to pursue her education, earning a master of public health degree in epidemiology in 1986 from Johns Hopkins University School of Hygiene and Public Health, and her doctorate in epidemiology in 1989 from the University of Pittsburgh Graduate School of Public Health.

"As an undergrad, my focus was on life sciences, and then as a graduate student I was driven more toward public health, specifically epidemiology and clinical trials," she said.

Moy served as a graduate research assistant at the University of Pittsburgh from 1987 to 1989 and a postdoctoral fellow from 1989 to 1991. During this time her primary research focus was on the incidence and risk factors for type 1 diabetes, specifically looking at how genetic and environmental factors contribute to the wide geographic variation in diabetes incidence. She completed her dissertation research in Madrid, Spain, and afterwards



Dr. Claudia Moy

coordinated a large international registry collaboration for type 1 diabetes called Diabetes Mondiale or DIAMOND.

After leaving the University of Pittsburgh, Moy joined the faculty at the Wilmer Eye Institute at the JHU School of Medicine with joint appointments in the departments of ophthalmology and epidemiology and the Center for Clinical Trials. While there, she helped design, conduct and monitor multicenter clinical trials.

Before becoming an official member of the NIH family, Moy was part of its research community.

She conducted research in quality of life outcomes in people treated for ocular melanoma as an NEI-sponsored researcher, serving as co-investigator on the Collaborative Ocular Melanoma Study from 1991 to 2001 and as principal investigator on the Quality of Life: The Collaborative Ocular Melanoma Study from 1994 to 2001.

In 2001 she officially joined NIH as an epidemiologist and program director in the Clinical Trials Cluster of NINDS's Division of Extramural Research.

"Although I had no background in neuroscience, I saw the opportunity at NINDS as a chance to expand my skills while helping to build a new extramural program in clinical trial research," she said. "I will always be grateful to John Marler and so many others at NINDS for taking a chance on me."

At NINDS, Moy oversaw a portfolio of clinical trials and clinical research, primarily in stroke and other cerebrovascular diseases. Her main research interests were in clinical trials outcome measures—particularly measures of quality of life and of cognitive impairment associated with neurologic disease or therapy—clinical trials methodology, research integrity and protection of research subjects.

During her tenure, she served on countless NIH, trans-NIH and NINDS committees and working groups as well as some outside of NIH.

Among her most memorable initiatives were the development of the Neurological Quality of Life assessment tool—NeuroQOL—which spawned other similar projects across NIH, including PROMIS (Patient-Reported Outcomes Measurement Information System) and the NIH Toolbox.

NeuroQOL, PROMIS and the NIH Toolbox are used to measure health outcomes from the patient perspective.

Moy also helped develop the original Clinical Trials Methods Course—a "summer camp" for budding neurology trialists that was instrumental in boosting the careers of many successful NINDS grantees—and NINDS's clinical trial networks, NeuroNEXT and StrokeNet.

Moy's more recent projects focused on vascular contributions to cognitive impairment and dementia or VCID, which she described as "a new arena for me but also a rewarding experience."

Throughout her career, she received numerous awards and accolades, including many NIH Director's Awards, NINDS Director's Awards and NINDS Merit Awards. In 2011 she received the Common Fund Leadership Award and the NHLBI Outstanding Clinical Research Award in 2017.

Moy's plans for retirement are vast and include traveling, pursuing hobbies like baking, catching up on her recreational reading, learning French and cleaning her garage. She serves on the board of directors of Marlow Guitar International (MGI), a non-profit classical guitar society that hosts live performances with top-tier guitarists, runs an annual youth competition for local students and currently is collaborating with Walter Reed and the United Service Organization to bring guitar instruction to veterans with post-traumatic stress disorder. In retirement, Moy plans to be more active in MGI.

"These past 10 months of working from home have helped me realize how much I value, and miss, personal interactions with my friends and colleagues at work," she concluded. "It goes without saying that I hope to stay in touch with my happy hour buddies in the future. NINDS has been my home for 20 years—the longest time I have ever spent in one place! To any new staff, I would say you will never work with a finer, more dedicated and more collegial group of people." **R**

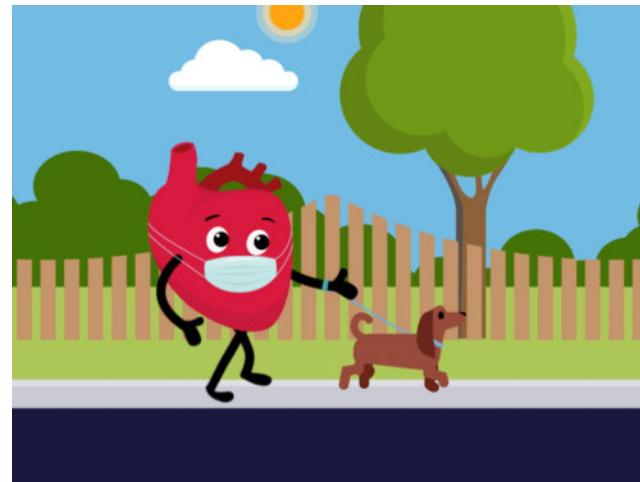
VOLUNTEERS

Food Allergy Study Recruiting

Food allergy? NIAID researchers are seeking volunteers ages 2 and older who have at least one food allergy to participate in a study to better understand how food allergies affect health. Participants receive a comprehensive nutritional evaluation and meet with a dietitian for individualized counseling. Compensation for participation is provided. For more information, contact the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY 1-800-877-8339) or email prpl@cc.nih.gov. <https://go.usa.gov/xGPsA>. Refer to study 15-I-0162

Dopamine Study Seeks Volunteers

NIDDK researchers seek healthy volunteers (18-45 years old) to participate in a study investigating how dopamine affects body weight and eating behavior. Participants must be able to visit the Clinical Center for 5 consecutive days to pick up food and then have a 5-day inpatient stay. For more information, call 1-866-444-2214 or prpl@cc.nih.gov (1-800-877-8339 TTY/ASCI). <https://go.usa.gov/xPTBn>. Refer to study 18-DK-0132.



Above and below, inspirational quote cards for social media remind people to take care of themselves for better heart health. At right, NHLBI also offered an animation about the value of daily self-care. To view the video, go to https://www.nhlbi.nih.gov/sites/default/files/inline-images/AHM_2021_Heart_Character_Selfcare.gif.

WEAR RED DAY 2021

Practicing Self-Care for a Healthy Heart During the Pandemic and Beyond

A global pandemic may have had much of the NIH staff working from home this year, but they still celebrated American Heart Month...just in a virtual kind of way. And for the annual kickoff—National Wear Red Day, Feb. 5—well, that was like none other.

This year's theme focused on the importance of self-care as a form of heart-health care. Studies show that devoting a little time every day to care for yourself can go a long way toward protecting the health of your heart.

Simple self-care, such as taking a moment to de-stress, giving yourself time to move more, preparing healthier meals and not cheating on sleep can all benefit your heart.

To spur this year's celebration, NHLBI's The Heart Truth program created inspirational quote

"To keep my heart healthy, I make exercise part of my routine. These dumbbell thrusters are a great cardio challenge!"

Francis S. Collins, M.D., Ph.D.
Director, National Institutes of Health



cards for social media that reminded people to take care of themselves. Cards featured NIH leaders engaging in various physical activities, including yoga, walking and weightlifting. A few showed heart-healthy meals, such as salads,

to emphasize the importance of good nutrition. Of course, people rocked plenty of red; some posted crimson-clad selfies online.

One of the biggest highlights was a virtual dance.

Hosted by NHLBI director Dr. Gary Gibbons and NHLBI communications director Dr. Lenora

Johnson, in partnership with the Office of Research Services and the R&W Fitness Center, the special event—beamed from Masur Auditorium in the Clinical Center—encouraged work-from-home dancers to get moving. They were treated to a 30-minute medley of popular songs and dances, all led and choreographed by fitness instructor Charissa Mobely. In all, 648 registrants from across the country took part.

If you missed the quote cards and the dance, don't worry. A compilation of heart-healthy resources is available online year-round, <https://www.nhlbi.nih.gov/heartmonth>.

And remember: Keep moving! It's never too late to join the growing effort to fight heart disease, the leading cause of death among women and men in the United States.

