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National Institutes of Health

DIRECTOR VISITS CARD, CUP

Collins Applauds Extraordinary Efforts at Construction Site, Utility Plant

BY CARLA GARNETT

"On time and on budget." Five words that are music to heads of organizations everywhere probably sounded especially sweet to NIH director (and resident musician-in-chief) Dr. Francis Collins recently as he made another stop on his "Gratitude Tour." He has visited several key staff and locations in 2021 to show his appreciation for employees and their continuous high-quality efforts in the midst of unprecedented, pandemic conditions.

On July 21, he took time to thank staff at two locations: the Center for Alzheimer's and Related Dementias (CARD), one of the largest construction projects on the Bethesda campus; and the Central Utility Plant (CUP), the main source of power and utilities for NIH operations in Bethesda.

"This is my chance to say thank you," Collins told the dozens of helmeted workers assembled outside the building going up on Service Rd. in the center of campus. "I know you have been working incredibly hard to support this project, to do something on a timetable that a lot of people said, 'Oh that's never going to work.' But you're meeting all these milestones and getting it done. What will go on in that building—as these remarkable scientists will tell you—will be major discoveries about Alzheimer's disease and related disorders, which we're all thinking

SEE **GRATITUDE**, PAGE 6

Inside the CARD, NIH director Dr. Francis Collins (third from l) gets a briefing on construction progress.

PHOTO: CHIA-CHI CHARLIE CHANG

'A HARD PIVOT'

Sadtler Pauses Tissue Engineering Project to Launch Antibody Protocol

BY DANA TALESNIK

Dr. Kaitlyn Sadtler

PHOTO: CHIA-CHI CHARLIE CHANG

Dr. Kaitlyn Sadtler arrived at NIH in September 2019, energized to study ways to regenerate injured tissues. She had her laboratory set up, ready to go in January 2020 but, 2 months later, when the pandemic struck, she soon found herself working on a completely different project.

SEE **SADTLER**, PAGE 4

2nd Article in a Series on Pandemic Pivots

Brooks Narrows Search for Therapeutics for Albinism-Related Vision Loss

BY AMBER SNYDER

Vision impairment is a common feature in most individuals with albinism, a condition in which the skin, hair and eyes (or some combination of the three) have reduced melanin pigmentation. Problems with eyesight can be so severe that people may be declared legally blind. Dr. Brian P. Brooks of NEI is investigating therapies to improve vision quality in patients with oculocutaneous albinism (OCA), which is the most

Dr. Brian P. Brooks

SEE **BROOKS**, PAGE 8

Health equity art winners announced. See p. 12.

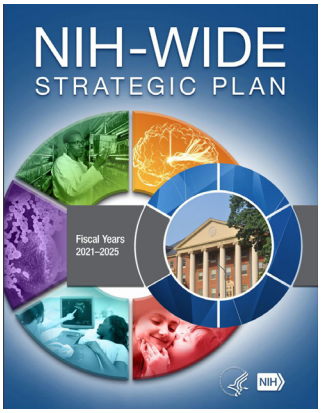
ALSO THIS ISSUE

NIH-Wide Strategic Plan Live

The NIH-wide strategic plan for fiscal years 2021-2025 is now live.

In order to advance its mission and fulfill requirements of the 21st Century Cures Act, NIH will update its strategic plan every 5 years. The most recent iteration, the *NIH-Wide Strategic Plan for Fiscal Years 2021–2025*, updates the previous plan for fiscal years 2016–2020.

The plan outlines NIH's vision for biomedical research direction, capacity and stewardship by articulating the highest priorities over the next 5 years. In addition, it provides illustrative examples of accomplishments under the last plan and new initiatives under this one.



The plan was developed through collaboration between leadership and staff across NIH and key stakeholders, including the research community, professional societies advocacy groups and the public.

Designed to complement and harmonize institute and center strategic plans that address individual missions, the NIH-wide plan can be viewed here: https://www.nih.gov/about-nih/nih-wide-strategic-plan#about.

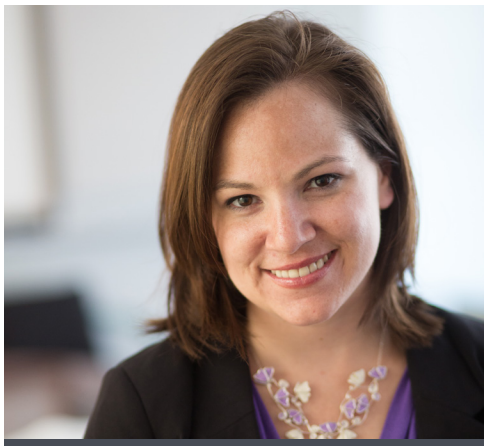
Musci To Present Next 'Mind the Gap,' Aug. 26

Join the Office of Disease Prevention for a Methods: Mind the Gap webinar with Dr. Rashelle Musci on use of integrated data analysis in prevention science. The webinar will take place on Thursday, Aug. 26 at noon ET.

The webinar will review the use of integrative data analysis (IDA) to harmonize extant school-based cluster randomized prevention trials with longitudinal follow-up.

Musci will extend the emerging techniques—related to measurement invariance and differential item functioning for factor analytic models—to develop an approach to IDA with outcome analyses. She will illustrate this approach using baseline data from six school-based prevention intervention trials with longitudinal follow-up.

The Dr. Ali and Rose Kawi professor in mental health, Musci is an expert in prevention science, child mental health and quantitative methods and measurement in public health. Her research focuses on advanced latent variable methodology for use in developmental science, exploring the intergenerational transmission of self-regulation and how



Dr. Rashelle Musci

that transmission may be impacted by universal prevention programming.

Musci holds a doctoral degree in human development, as well as a master of science degree in child development and bachelor of science degree in neurobiology, physiology and behavior from the University of California, Davis. Currently, she is an associate professor of mental health at Johns Hopkins Bloomberg School of Public Health.

Registration for the webinar is required at prevention.nih.gov/education-training/methods-mind-gap/integrated-data-analysis-prevention-science. The session will be recorded and available on the ODP website.

For more information, visit prevention.nih.gov/MindTheGap.

Winners Announced in ORWH Competition to Enhance Faculty Gender Diversity

NIH has awarded $50,000 each to 10 institutions for their efforts in enhancing faculty gender diversity. Last year, the Office of Research on Women's Health announced the competition aimed at increasing gender diversity among faculty members at colleges and universities and removing barriers for transformative change.

The NIH Prize for Enhancing Faculty Gender Diversity in Biomedical and Behavioral Science recognizes institutions that have acted to effect systemic change within their biomedical and behavioral science departments.

Winners of the competition are:

• WISELI: A Wise Approach to Gender Equity, Women in Science and Engineering Leadership Institute, University of Wisconsin–Madison

• A Framework to Promote Gender Diversity & Equity, Rochester Institute of Technology

• Promoting Women of Diverse Creative Expertise, Worcester Polytechnic Institute

• No One Size Fits All: FOCUS's Mosaic of Initiatives, Perelman School of Medicine, University of Pennsylvania

• Participatory Approaches for Gender Equity: CWIMS, Center for Women in Medicine and Science, University of Minnesota Medical School

• Enhancing Faculty Gender Diversity at MD Anderson; Office of Faculty Diversity, Equity and Inclusion; University of Texas MD Anderson Cancer Center

• FIU ADVANCE; Office to Advance Women, Equity & Diversity; Florida International University

• Leveraging Evidence to Enhance Faculty Diversity, University of Houston

• Gender Diversity in Medicine, Columbia University Vagelos College of Physicians and Surgeons

• Achieving Gender Equity at Boston University, Trustees of Boston University, Boston University Medical Campus

"Through the Prize for Enhancing Faculty Gender Diversity, NIH fosters supportive, inclusive and equitable environments in which women faculty members can further their careers in the biomedical and biobehavioral sciences," said ORWH director Dr. Janine Clayton. "Advancing women into leadership roles in the sciences is critical to producing good science. Diversity in the scientific workplace generates more innovative solutions; diverse teams are more productive and produce more impactful research."

ORWH also recognizes the following institutions as honorable mentions for their commitment to faculty gender diversity:

• Intersectional Directions: Faculty Success @ XULA, Xavier University of Louisiana

• Colorado Trails to Advance Gender Diversity, University of Colorado School of Medicine, Anschutz Medical Campus

• Women in Medicine and Science Program, Office of Faculty Affairs, Wake Forest School of Medicine

• University of Chicago: Using 3 R's to Elevate Women, Department of Medicine Women's Committee

• Promoting Women Scientists During Covid and Beyond, Mass General Brigham, Harvard Medical School

• Eye of the Tiger: Women with a Will to Thrive, Alliance for Women in Medicine and Science, Southern Illinois University School of Medicine

On Tuesday, Oct. 5, ORWH will host a forum, Effective Approaches to Fostering Faculty Gender Diversity, Equity, and Inclusion: Celebrating Progress, to recognize and promote the winners' effective, evidence-based practices, address challenges and improve the existing career paradigm for many women in biomedical and behavioral science.

Registration required to attend. Register at https://herox.zoom.us/webinar/register/7716260398030/WN_3Q_pJRNbQ9Cz7yLOLgSjTA.

Dr. Charmaine Royal of Duke University (l) and Dr. Genevieve Wojcik of Johns Hopkins University spoke at a recent NHGRI event.

GENOMICS 'BOLD PREDICTIONS'

Two Researchers Discuss Race and Ancestry

BY AMBER SNYDER

By 2030, "research in human genomics will have moved beyond population descriptors based on historical social constructs such as race," according to the fourth of 10 bold predictions released by NHGRI.

This prediction was discussed in a recent installment of the 10-episode "Bold Predictions for Human Genomics by 2030" seminar series. The virtual event featured two guest speakers: Dr. Genevieve Wojcik of Johns Hopkins University and Dr. Charmaine Royal of Duke University.

Wojcik conducts research to understand the role of ancestry and genetics in risk to address health inequities for diverse and admixed populations. An admixed population is one that is formed from the mixture of two previously isolated populations, whose new offspring have ancestors from multiple sources. Wojcik questioned the use of race/ethnicity to classify participants in genomic research, who are often admixed.

Graphing an individual's genetic ancestry against their racial self-identification revealed that there is no way to discretely group people based on genetics. "There is a continuous spectrum of diversity in human variation," she explained. "There are no real discrete cutoffs [to separate people], definitely not along national borders."

Wojcik cited the Hispanic/Latino group as a specific example, as people from that group can have ancestry from multiple continents (Europe, Africa and the Americas).

She also made a bolder prediction: that "research in human genetics will have rid itself of a Eurocentric bias (that is present in all areas of our research), moving beyond social constructs such as race with equity for all ancestries."

The term "diverse populations" is generally understood to mean non-white/non-European, and we currently have the most genomic data on people of European ancestry, even though they are not the most populous group in the world. The majority of researchers are of European descent, however, and the proportion of research in that group reflects that.

"It's important for us to see what systems are in place that created research and a knowledge base that looks like us, the people doing the research, and not the communities we are trying to help," Wojcik said.

Royal researches the ethical, social, scientific and clinical implications of human genetics and genomics, with particular interest in the intersection of genetics and race. She reminded viewers to look to the history of science and race as we think about how to move forward.

Royal and several colleagues conducted a survey several years ago on scientific opinion about the biological basis of race. The survey was targeted toward genetics professionals and anthropologists. The researchers found that geneticists largely disagree with statements such as "races don't exist" and "race has no biological basis," while anthropologists tended to agree with the statements. Both groups tended to be in agreement, though, about replacing race with a more appropriate and precise term, and that genetic ancestry plays a role in an individual's health.

How, then, do we integrate the useful information from race/genetic ancestry into an individual's health care without using terminologies that invoke racial bias? Many people in the scientific community agree that the concept of race is unlikely to vanish in the near future, and race as a social construct has a significant impact on health even if it does not exist as a real genetic distinction.

Royal also referenced an ongoing global study of different research cohorts that asked what descriptors they used for study participants. Given options such as race, ethnicity, ancestry, tribe and others, there was no clear consensus across the board. Options for self-identification vary widely across the world.

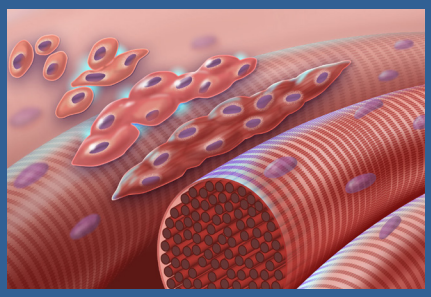
Royal's bolder prediction expressed her aspiration that "the field of human genetics and genomics will have become a visible and credible catalyst for dismantling racism on a global scale."

Genetics and biology have historically been used at times as a cover for inhumane acts such as the Holocaust and the eugenics movement. Royal also pointed to a recent *New York Times* article about sickle cell trait being cited as a cause of death for Black people in police custody, even though the condition is usually benign on its own (The individuals possess only one of the variants necessary for expression of the disease).

Wojcik and Royal both expressed hope that geneticists will come together in discussion about the utility of race versus ancestry in research, and to change the way that society thinks about the two.

"If we don't do it," Royal said, "who will?"

View the full presentation at https://www.youtube.com/watch?v=vVFwdMUIDGo&list=PL1ay9ko-4A8sm_n7QZ1Re0Y3fbUAvIC7VU&index=4. For details about the lecture series, visit https://www.genome.gov/event-calendar/Bold-Predictions-for-Human-Genomics-by-2030.



ON THE COVER: *Myoblast Fusion. Image depicts normal myoblast (early muscle cells with a single nucleus) fusing together to form myocytes (multinucleated musle cells) during myogenesis.*

IMAGE: DARRYL LEJA, NHGRI

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

Sadtler

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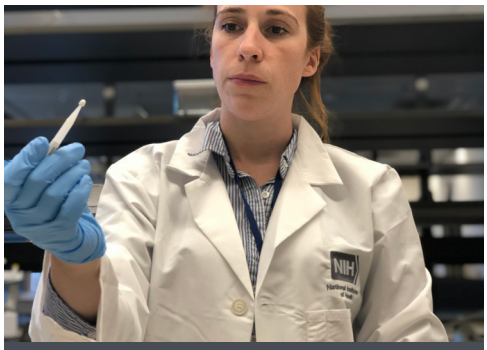
"It was very much a hard pivot," said Sadtler, an Earl Stadtman tenure-track investigator and chief of NIBIB's section for immunoengineering. "I didn't plan for infectious disease to be the main part of my lab. I had to change my mindset to start developing serologic assays for processing antibody tests."

The new project began with scientific curiosity and some chitchat. Wouldn't it be interesting to evaluate asymptomatic Covid infections, wondered Sadtler and NCATS colleague Dr. Matthew Hall over Twitter, of all places. Could they study people with potential undiagnosed infections? "Sure! We can do ELISAs!" she told Hall.

An ELISA (enzyme-linked immunoabsorbent assay) is a common lab technique to measure viral proteins and antibodies. A robotic setup can automate the steps to increase testing capacity.

"Little did I know that was a huge commitment on my end," Sadtler said. It required temporarily casting aside her original project. "But go big or go home, I guess!"

Sadtler and Hall connected with NIAID clinicians and soon launched the Covid protocol, enrolling 11,000 people nationally to test for Covid antibodies at multiple time points. In the collaboration among NIBIB, NCATS, NIAID and NCI's Frederick National Lab for Cancer Research, study participants received home-testing kits and mailed their dried blood samples to Sadtler's lab for analysis.



Sadtler holds up a microsampling device from the home blood collection kit used in the study.

PHOTO: NIBIB

It was almost fate that Sadtler came to work on a Covid project. Before the pandemic, she did her postdoctoral fellowship in immunology and bioengineering at MIT with Dr. Robert Langer, a cofounder of Moderna. There, she learned a bit about nanoparticle therapies and mRNA vaccines.

During her time in Boston, she connected with investigators at the Ragon Institute, one of whom was doing antibody testing research.

"So, while I was in the co-founder of Moderna's lab for my postdoc, I met somebody we'd [later] collaborate with to get an antigen construct to do our serology work down here at NIH," Sadtler said. "He wound up happily sending us the plasmid for the protein, and that's the one we used."

The biggest challenge early on was a technological one. "We were running so many assays, we broke the [ELISA] robot!" said Sadtler. A couple of replacement parts later, it was back up to speed.

"We're going to learn a lot from this study beyond just the proportion of people with antibodies," she said. Along with sending physical specimens, each participant answered demographic, health and vaccination questions.

From all of this, Sadtler and the team of NIH scientists hope to gain more insights about the geographic distribution of Covid and about antibody decay rates, since the study follows the same people over time. Did people with asymptomatic infections have vaccine reactions? Are antibodies from prior infection protective against Covid variants?

"We can correlate all of this within the subgroup analyses of different demographics, geographics, health and socioeconomic factors," she said.

As all the specimens and demographics rolled in and the assays were run, Sadtler found help managing and interpreting the large datasets from NIAID statisticians. "They do math that's far beyond me," she said.

Now, Sadtler is continuing this protocol while resuming her original project, studying how the immune system—which gets activated to prevent infection—can help build back damaged tissue following injury. Ultimately her group is working toward developing new materials and medical devices that can heal wounds faster.

She's also helping with 2 related projects: 1 looking at antibody responses in patients with rare diseases, and another working with 6 trauma centers to study infectious diseases, including the prevalence of SARS-CoV-2, among trauma patients.

Sadtler's unexpected pandemic project started with curiosity and took her on a research journey that kept getting bigger.

"I do think it shows the strength of having an interdisciplinary research community," she said, "so individuals coming in with, say, a bioengineering background [could apply their skills where needed during the pandemic]. Ultimately, it's that interdisciplinary nature of research that drives things forward."

The Results Are In

Results from the antibodies study reveal there were nearly 17 million undiagnosed Covid-19 cases in the U.S. by July 2020, far exceeding the known number of cases in a pandemic that has affected the country unevenly.

Analysis of participant blood samples—along with the collected health, demographic and socioeconomic data—offers insight into the undetected spread of Covid-19 and subgroup vulnerability to undiagnosed infection.

Sadtler's lab mates include (from l) Kenneth Adusei, Maria Karkanitsa and Tran Ngo.

PHOTO: NIBIB

"The estimate of Covid-19 cases in the United States in mid-July 2020, 3 million in a population of 330 million, should be revised upwards by almost 20 million when the percent of asymptomatic positive results is included," said NIBIB's Dr. Kaitlyn Sadtler, about the study published June 22 in *Science Translational Medicine*. "This wide gap between the known cases at the time and these asymptomatic infections has implications not only for retrospectively understanding this pandemic, but future pandemic preparedness."

NIH'ers Volunteered on Behalf of Social Justice

BY GORDON MARGOLIN

Would you volunteer to help solve some significant infractions of social justice?

Perhaps you would be followed or tracked by people in pickup trucks brandishing rifles—as happened to Drs. Norman Robbins and Stanley Rapoport. Or perhaps you could be threatened with instant death when trying to help peace marchers who had been brutally clubbed by state troopers—again as Robbins encountered. Or perhaps you would get arrested because you stayed in the homes of Black citizens and went around asking too many questions—as Rapoport experienced. You might even be involved in preparing hospitals and jails for race riots on the streets of Washington, D.C.—as did Dr. Jesse Roth.

These events really happened to NIH scientists during the 1960s Civil Rights movement. A somewhat little-known history, their experiences have been recently documented in oral histories conducted by the Office of NIH History and Stetten Museum.

In 1965 and 1966, four young scientists working at NIH, all members of the Public Health Service, volunteered to go to the southern United States on a government-sanctioned mission: to assess whether hospitals provided integrated health care and whether Black health-care workers were given equal access to education and jobs in hospitals. The NIH scientists were aware of Jim Crow laws and the disregard for the well-being of Black citizens who were segregated into hospital areas in which the quality of services and environment were notably substandard compared to areas reserved for Whites.

Segregation in Southern hospitals had continued despite two federal laws that called for equal treatment for all, namely, the Hill-Burton Hospital Construction Act of 1954, and the Title VI of the Civil Rights Act of 1964. Both laws demanded an end to discrimination, but neither had the administrative teeth to produce a result in medical care. Something more had to be done to mitigate the limited medical care available to people of color. In the Medicare Act of 1966, therefore, the federal government would only guarantee payment to hospitals that integrated as required by the law. If hospitals did not integrate, they would not receive Medicare funding.

State Library of Louisiana (http://www.state.lib.la.us)

Scene from Apr. 21, 1965. Crowds, police and photographers in the street during a race riot in Bogalusa, La. That summer Bogalusa became the battleground between Congress of Racial Equality activists and White supremacists in the Ku Klux Klan. Dr. Stanley Rapoport entered this volatile situation to inspect the local hospital for compliance to Medicare segregation rules.

PHOTO: STATE LIBRARY OF LOUISIANA

President Lyndon Johnson signed the 1965 Medicare bill in a ceremony held in Independence, Mo. Standing behind him were Lady Bird Johnson and Vice President Hubert Humphrey. Sitting next to him was President Truman and his wife Bess.

PHOTO: NATIONAL LIBRARY OF MEDICINE

The need for government investigators to assess the situation in each hospital in the South and to help hospital administrators implement the new laws were the reasons the federal government approached Public Health Service officers to volunteer in this endeavor. But there were hazards in undertaking these responsibilities. Many White Southerners wanted to maintain segregation and were often violently militant, as the volunteers soon discovered.

New oral histories from four of the NIH investigators who took up the challenge to help integrate health care provide stirring stories of their experiences. The example of Black protestors and the scientists' own participation in this volunteer project subsequently led these NIH'ers individually to additional acts of social justice on behalf of the underprivileged, socially disparaged and frequently mistreated people.

Find an introduction and links to the transcripts at https://history.nih.gov/display/history/Medicare+Hospital+Certification+Program+Oral+Histories.

Collins and the CARD construction crew signal progress on building the facility that will be devoted to research on Alzheimer's and related dementias.

PHOTOS: CHIA-CHI CHARLIE CHANG

Gratitude

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about in terms of ourselves and our families. This is the right moment for this campus, with its incredible critical mass of scientists. So, please remember the big picture...What you're doing is creating a new opportunity for one of the most pressing medical needs of our generation. Feel good about that. Even if you're having a tough day."

CARD project officer Mitch Taragin traveled to Florida to watch the building's modules under construction.

CARD project officer Mitch Taragin then led Collins and several other top leaders on a tour of the 1.3-acre site that broke ground just before Labor Day 2020. The CARD, or Bldg. T-44, consists of individual modular units that were built at a factory in Leesburg, Fla., just outside Orlando. Modules were then shipped via truck to Bethesda for assembly. A 600-ton capacity crane set each unit in place.

"We are still on schedule and still on budget" despite unusual workplace conditions due to the pandemic, Taragin announced at the tour's start. He has walked the job site every weekday since construction began.

A full-time federal employee since November 2019, Taragin has worked at NIH in some capacity since 2007. CARD marks his largest responsibility to date, managing some 70-plus onsite workers. In April, he traveled to Florida for several days to oversee the first units under construction.

"CARD will be NIH's most well-traveled building by far," quipped Matt Frazier, project manager for general contractor Hensel Phelps. Frazier explained that collectively the modules will have logged some 155,000 highway miles making their way from Florida to Maryland.

Once completed—target date February 2022—the 24,000-plus sq. ft. CARD structure will consist of 65 units, with about 12,000 sq. ft. of lab space and 9,000 sq. ft. for office areas. Approximately 130 scientists and support personnel will occupy CARD, beginning in spring 2022.

"I find it so rewarding to work on campus," Taragin said. "I look forward to coming to work every day and just knowing what our mission is, specifically for this project, which is helping to solve Alzheimer's and dementia."

[Take a virtual fly-through of the building: https://youtu.be/JK7YJHFiXDA.]

After seeing CARD progress, Collins and company took a brief hike across Service Rd. to visit NIH's CUP, one of the largest utility plants in the United States.

Dr. Farhad Memarzadeh, director of the Office of Research Facilities' Division of Technical Resources (DTR) and a leading researcher in bioenvironmental studies, led a tour of what is essentially the campus's nerve/circulatory system, the Central Utility Plant or CUP.

The CUP provides steam, chilled water and compressed air to the Bethesda campus,

In a CUP conference room, Collins congratulates staff on outstanding continuous operation.

Wall of screens: CUP staff monitor operations in real time from the control room shown above.

serving in excess of 12 million gross sq. ft. of clinical, research and administrative facilities, including the 240-bed hospital. The CUP is a critical facility for continuity of NIH operations.

Memarzadeh explained that the CUP collects more than 104 million live automated data points every day and conducts about a million advanced calculations during approximately 5,000 continuous analyses. Data is considered one of the most important commodities in CUP daily operation.

"Data is the currency and lifeline in a rapidly changing and technologically complex field," he pointed out. "In the last several years, DTR introduced and used three powerful drivers–exponential data collection, sophisticated distributed networks and highly advanced mathematical algorithms–to advance and improve the NIH CUP, making it one of the most technologically advanced utility plants in the country."

Since joining NIH in the early 1990s, Memarzadeh also has been a leading champion for energy conservation efforts and minimizing NIH's ecological footprint. With one of the largest cogeneration plants in the federal government, NIH produces about 40 percent of the campus's steam and electricity needs.

Of necessity, the CUP must operate 24/7 with no breaks, regardless of external conditions. Memarzadeh reported continuous service by both staff and equipment, despite the ebb and flow of the campus population due to the pandemic telework situation. In addition, the CUP maintained its energy efficiency and saved NIH hundreds of thousands of dollars in utility costs.

"I had no idea what all was going on inside these walls," Collins said, viewing images of the specially designed and uniquely modified combustion jet engine that powers NIH's cogeneration plant. "The outside is not nearly as impressive as the inside."

The touring group also got to see a simulated emergency, when operators launched an outage that monitors had to detect and address to prevent a serious utility shutdown.

Dr. Farhad Memarzadeh (l) and Collins, after a tour of the plant

Over the early days of the pandemic, before vaccine availability, the CUP was extra vigilant about preparing for potential emergencies or shortages in supplies as well as human resources.

"We just needed to make sure all the spare parts and the chemicals for the water treatment were available. because we didn't know how the supply chain was going to be affected," recalled Alamelu Ramesh, DTR deputy director. "But we had a plan. We always have a 3 months' supply on hand, so that we will never run out of things. Then the big issue was we really hoped and prayed that our operators didn't fall sick. We implemented all safety protocols, and we were very fortunate that everyone basically stayed healthy."

Above, CUP control room view of half of 60,000-ton chiller plant; below, Memarzadeh (r) points out CUP features.

Celebrating 15 years as an NIH'er, Ramesh remembers joining NIH in 2006 as an electrical engineer who designed buildings' electrical systems for private consulting firms. Memarzadeh recruited her as his deputy, where she oversees six branches as well as budget and staffing.

"It's absolutely fantastic," she said. "It's all because of Farhad that I'm here. People don't know this about him, but he makes this all work. We are like one big family."

Brooks

CONTINUED FROM PAGE 1

common form of albinism in the U.S.

Generally, "the less melanin is present, the worse vision tends to be," Brooks said in a recent Clinical Center Grand Rounds Lecture. Affected individuals have lower than normal visual acuity and are also more sensitive to light and glare because of their lack of pigmentation.

Albinism is an inherited condition, and there are multiple forms found throughout the world. Brooks focuses his research on OCA1, the most common form in North America. Individuals with this form of albinism have mutations in their tyrosinase gene. There are two subtypes of OCA1: OCA1A, in which patients have no tyrosinase activity, and OCA1B, in which patients have some tyrosinase activity.

Melanin is synthesized from the amino acid tyrosine, so a lack of tyrosine corresponds to a lack of melanin pigment. Tyrosinase, the enzyme that metabolizes tyrosine in the first step of melanin production, is either not produced at all or only made in small quantities.

Because tyrosinase is at the beginning of the melanin synthetic pathway, Brooks explained, a decrease in activity would be expected to affect both eumelanin (black/brown pigment) and pheomelanin (red/yellow pigment) in melanocytes, the cells that produce melanin.

Brooks's study found a trend where eumelanin was increased more than pheomelanin in the hair of participants after drug treatment. A higher eumelanin/pheomelanin ratio may help protect people with albinism from developing skin cancer.

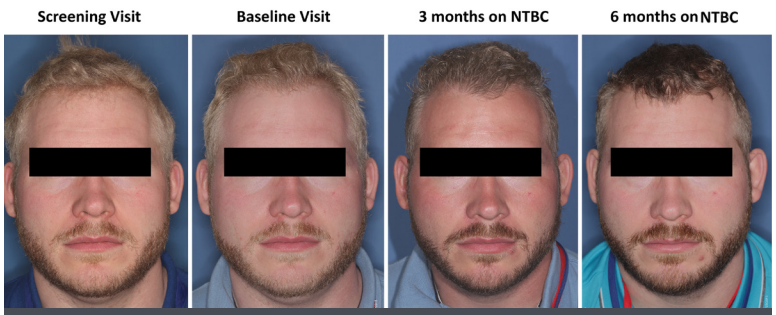
Most treatment for vision loss caused by albinism is only supportive. If there was a treatment to improve melanin pigmentation in patients with albinism, Brooks wondered, would that improve their vision function?

Brooks's patients include this young woman who has a complete form of albinism. She was not in the drug trial he discussed in the recent Grand Rounds lecture.

Melanin is found in the iris, retinal pigment epithelium (RPE) and choroid of the eye, and the lack of these pigments contributes to vision problems. Ideally, treatment would focus on identifying and treating affected individuals while still in utero, as the eyes develop, or in the first few years after birth as the eyes finish maturing.

Brooks identified the drug nitisinone (NTBC) as a potential treatment. It blocks tyrosine degradation, and he hypothesized that it would elevate tyrosine levels in patients with albinism, which would stabilize tyrosinase and allow it to increase melanin synthesis.

He first studied NTBC in mice, with promising results. Partly albino Himalayan mice represented OCA1B patients, and fully albino mice represented OCA1A patients. Young mice were fed NTBC for several months, and the OCA1B group developed darker skin pigmentation. The fully albino group showed no increase in skin pigment. The partly albino group also had a slight increase in iris pigmentation when viewed under a microscope.



In this illustration from Brooks's paper, a timeline of images of a man who had a response to the drug, from a screening visit to later points where he tanned and his hair became darker.

A closer look at the RPE, iris and choroid showed no change in the mature melanosomes (produced by melanocytes) that are responsible for producing melanin in the OCA1A mice, but a demonstrable increase in the OCA1B mice. Daily NTBC supplementation for pregnant OCA1B mice produced young that had darker fur and eyes than their parents.

After studying NTBC in mice, Brooks completed a 1-year pilot study of the drug in 5 patients with OCA1B (3 women and 2 men). He did not expect the drug to increase visual acuity in adults because of their mature visual system but expected to see some increase in melanin pigmentation. Study subjects were given a daily dose of NTBC; their hair, skin and eye pigmentation were monitored.

Responses varied on an individual basis, but there was a general increase in skin and hair melanin during the 1-year course of NTBC. Researchers did not observe a clinically significant increase in visual acuity, but believe that NTBC might produce better results in children because their visual systems are not fully developed.

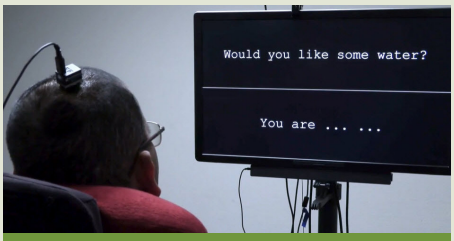
In terms of future research, Brooks and his team are working to identify new compounds that may be useful for increasing tyrosine in the body, and are also looking into therapies that target the RPE.

In collaboration with Dr. Kapil Bharti of NEI's ocular and stem cell translational research section, Brooks and his team have isolated blood cells from 2 patients with OCA1A and 2 with OCA1B and converted those cells to pluripotent stem cells. These new cells are then given cues to differentiate into RPE cells, which can be studied in the lab. They exhibit all the characteristics of cells with albinism, and will be important for identifying new therapies.

View the entire lecture at https://videocast.nih.gov/watch=42286.

Beyond Words: Device Helps Paralyzed Man Communicate

Researchers developed a device to decode brain activity into words in real time, allowing a person with paralysis to communicate in complete sentences. Part of an NIDCD-supported project, results from the study's first participant appeared in the *New England Journal of Medicine.*



Researchers developed a system that can successfully decode thoughts of words.

PHOTO: CHANG LAB, UCSF, *NEJM*

"This is an important technological milestone for a person who cannot communicate naturally, and it demonstrates the potential for this approach to give a voice to people with severe paralysis and speech loss," said co-lead author Dr. David Moses of the Weill Institute for Neuroscience at the University of California, San Francisco.

With previous brain-computer interfaces that help people who cannot articulate speech to communicate, the user must spell out messages one letter at a time. An interface that let the user generate whole words at a time would allow much more efficient and natural communication.

The first participant, a 36-year-old man identified as "Bravo-1," has been severely paralyzed for 16 years. The researchers implanted an array of electrodes onto a part of his brain that includes regions implicated in speech processing.

During a series of training sessions, Bravo-1 attempted to say each of 50 vocabulary words and sentences with these words many times. The electrodes recorded the brain activity associated with each attempt and transmitted it to a computer.

The researchers used machine learning to recognize patterns in the brain activity and associate these with the word the user was trying to say. A predictive text algorithm provided an "autocorrect" function like that used in texting.

To test the device, Bravo-1 attempted to say sentences using the 50-word vocabulary while the device decoded his brain activity in real time. The system decoded about 15 words per minute on average. Speech-decoding approaches become usable when the error rate is below 30 percent. For this system, the error rate was about 25 percent.

The team is working to increase the size of the vocabulary and the rate of speech. They also plan to conduct follow-up trials with more participants. *—Brian Doctrow, NIH Research Matters*

Youth-Onset Type 2 Diabetes Complications Arise by Young Adulthood

People with type 2 diabetes diagnosed during youth have a high risk of developing complications at early ages and have a greater chance of multiple complications within 15 years after diagnosis. The findings are the culmination of a first-of-its-kind trial funded largely by NIDDK.

Within 15 years of a type 2 diabetes diagnosis, 60 percent of participants had at least 1 diabetes-related complication, and nearly a third of participants had 2 or more complications, according to results of the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) follow-up study, called TODAY2. The findings were published in the *New England Journal of Medicine.*

Youth-onset type 2 diabetes is more aggressive than adult-onset diabetes.

IMAGE: FIZKES/ISTOCK/GETTY

"The original TODAY study showed that youth-onset type 2 diabetes is distinct from adult-onset diabetes; it is both more aggressive and more difficult to control," said Dr. Barbara Linder, NIDDK project scientist.

TODAY2 involved 500 original participants from the TODAY study, which began in 2004. The study, conducted at 15 centers across the country, compared 3 treatments for managing blood glucose: metformin—the only FDA-approved oral medication to treat type 2 diabetes in youth—alone or combined with another medication or intensive lifestyle intervention.

Overall, researchers saw a steady decline in blood glucose control over 15 years. In addition, 67 percent of participants had high blood pressure. Nearly 52 percent had dyslipidemia, or high fat levels in the blood. Nearly 55 percent had kidney disease; 32 percent had nerve disease and 51 percent had diabetic eye disease.

"Compared to what we see in adults with type 2 diabetes, the participants in TODAY2 developed complications much earlier in their disease course and at a much faster pace over time," said TODAY2 study chair Dr. Philip Zeitler of the University of Colorado School of Medicine. The findings underscore the importance of early, intensive treatment.

Discovery Paves Way for New Sight-Saving Therapy

NEI-funded research offers a new path for preventing glaucoma vision loss. A form of gene therapy protects optic nerve cells and preserves vision in mouse models of glaucoma. The findings were published in *Cell.*

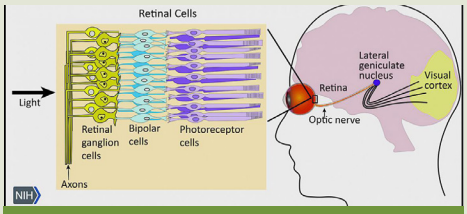


IMAGE: NEI

Glaucoma, a leading cause of visual impairment and blindness, results from irreversible neurodegeneration of the optic nerve, the bundle of axons from retinal ganglion cells that transmits signals from the eye to the brain to produce vision. Available therapies slow vision loss by lowering elevated eye pressure, but some glaucoma progresses to blindness despite normal eye pressure.

"Our study is the first to show that activating the CaMKII pathway helps protect retinal ganglion cells from a variety of injuries and in multiple glaucoma models," said the study's lead investigator, Dr. Bo Chen of the Icahn School of Medicine at Mount Sinai.

The CaMKII (calcium/calmodulin-dependent protein kinase II) pathway regulates key cellular processes and functions throughout the body, including retinal ganglion cells in the eye.

Using an antibody marker of CaMKII activity, Chen's team discovered that CaMKII pathway signaling was compromised whenever retinal ganglion cells were exposed to toxins or trauma from a crush injury to the optic nerve. Administering the gene therapy to mice just prior to the toxic insult and just after optic nerve crush increased CaMKII activity and robustly protected retinal ganglion cells.

Among gene therapy-treated mice, 77 percent of retinal ganglion cells survived 12 months after the toxic insult compared with 8 percent in control mice. Six months following optic nerve crush, 77 percent of retinal ganglion cells had survived.

Similarly, boosting CaMKII activity via gene therapy proved protective in glaucoma models based on elevated eye pressure or genetic deficiencies.

"If we make retinal ganglion cells more resistant and tolerant to the insults that cause cell death in glaucoma, they might be able to survive longer and maintain their function," Chen concluded.

NIDCD Division Director Jordan Retires

BY PATRICIA BLESSING

Dr. Craig A. Jordan, director of the NIDCD Division of Extramural Activities, retired in August after 37 years at NIH. Since 2003, he led DEA and served as executive secretary for NIDCD's advisory council.

At his last council meeting this past May, it was fitting that he received a virtual standing ovation from council members and NIDCD staff. While Jordan was flattered by the sentiment, his entire career has centered around going the extra mile with grantees, researchers, peer reviewers, council members and NIDCD and NIH colleagues to resolve issues, develop management strategies and encourage scientists in the early stages of their research careers.

"Craig will truly be missed at NIH and we are grateful for his outstanding contributions to the mission of our institute," said NIDCD director Dr. Debara Tucci. "While he is highly regarded in his role as executive secretary to the council, I also admire his unwavering commitment to his staff and the extramural community."

Tucci presented Jordan with the highest award given at NIDCD, the Exceptional Service Award, for his sustained outstanding service in support of the institute's mission.

His dedication has been recognized by numerous NIH awards for his work on the Early-Stage Investigator Program, the American Recovery and Reinvestment Act, the Pioneer Award Program, NIDCD advisory council operations and enhancing peer review and the funding opportunities process. He is particularly proud of his early-career role in helping to build DEA into the widely respected force it is today. Treasuring this respect from the research community, he never felt compelled to look elsewhere for career satisfaction.

Before joining NIH, Jordan was a predoctoral fellow and research assistant in the microbiology department at the University of Texas Medical Branch in Galveston. He received his bachelor's degree in biology at Ohio State University and his Ph.D. in medical microbiology at the University of Texas Medical Branch.

In 1984, Jordan joined the National Institute of Neurological Disorders and Stroke as a staff fellow. He became an NINDS senior staff fellow before joining NIDCD as a scientific review administrator in 1990. He was promoted to chief of DEA's Scientific Review Branch in 1996. He served as acting DEA director from 1996 to 1999 and again from 2002 to 2003. In 2003, Jordan was officially selected as DEA director.

Dr. Craig A. Jordan

Jordan rounded out his professional career by representing NIDCD in the community and encouraging staff to join him in NIH health and exercise events, the Combined Federal Campaign and Take Your Child to Work Day activities. He now looks forward to more days of bike riding, traveling and spending time with family, friends and his grandchildren.

AFTER 33 YEARS OF FEDERAL SERVICE

NINDS's Warren Pursues New Direction

BY SHANNON E. GARNETT

When Margo Warren, director of media relations in NINDS's Office of Neuroscience Communications and Engagement, first came to NIH in 1988, her coworkers treated her to lunch at a Chinese restaurant in Bethesda. "My fortune cookie said, 'You are headed in the right direction.' I kept that fortune for years and stayed at NIH ever since," she said.

Now, after 33 years of federal service—all with NIH—Warren's fortune has led her in a new "right" direction, straight to retirement. She officially retired on July 31.

"In journalism school we used to joke about public relations—PR—being the dark side," Warren said. "But PR at NIH is anything but. I have always been proud to work at NIH because we aren't selling anything, we aren't pushing any agenda, we are only providing news about biomedical research. Our job in communications at NIH is to make the very technical very understandable for the media and our enormous body of stakeholders, the taxpaying public. There is a saying about how science isn't completed until it's communicated, and that is what we do."

Warren earned her bachelor of arts degree in journalism and Latin from the University of Arizona (UA) in 1976, where she was an award-winning investigative reporter and feature editor of the *Arizona Daily Wildcat*—UA's student newspaper. However, after graduation, she found that journalist positions were scarce.

"I had always been a writer and studied journalism in high school and college," she said. "I wanted to stay in journalism but the year I graduated I couldn't find a job. Interest in journalism was at its peak and Woodward and Bernstein had just broken Watergate [1976] in the *Washington Post*.

She eventually landed a job in the Community Relations Office and Tucson Film Commission in Tucson's City Hall. There her PR career was born. She was assistant director of the office—providing counsel on PR-related matters to the mayor, city council and numerous department heads.

Margo Warren (l) and NINDS Communications Director Alissa Gallagher take "cellfies" with a giant plush neuron at a meeting in San Diego.

"I had lots of great experiences there including hosting a public affairs radio and television show, and managing the Tucson Film Commission, which marketed the city as a movie location," Warren recalled. "I got to drive Sydney Poitier around for location scouting, sit in on an interview with Richard Pryor and have drinks with Billy Wilder. We

also handled the protocol for a state visit by Imelda Marcos."

In 1983, Warren left Tucson and City Hall to come to Washington, D.C., as communications director at the National Water Alliance—an environmental coalition on Capitol Hill chaired by then Sen. Dennis DeConcini (D-AZ). There she arranged editorial boards and media tours, edited the quarterly newsletter and coordinated efforts for a national public service media campaign.

In 1988 Warren joined NIH in the NIA communications office as a public affairs specialist. She organized a promotional campaign for large-scale national clinical trials, developed press releases and articles for the media, trained scientists for interviews with print and broadcast media and managed the institute's audiovisual collection and exhibit program.

A couple of years later, in 1990, she moved from NIA to NIAID. "I had been at NIA for 2 years and wanted to be busier," Warren remembered. "I got my wish after getting hired in the NIAID press office during the AIDS crisis. I remember writing a press release on AZT [azidothymidine] as a treatment for pregnant women, while a group of ACT-UP protesters were shouting outside of Bldg. 31—seven stories below my office. I worked with a reporter from *People* magazine who was interviewing Dr. [Anthony] Fauci for the 25 Most Intriguing People of the Year edition...in 1990!"

Warren made her final institute stop in 1991 when she became part of the NINDS family, where she has served in many roles—including writer, editor, media trainer, chief of the Health Education and Public Liaison Branch, project officer for the communications contract with Ogilvy Public Relations Worldwide, and director of media relations—and has worn numerous hats (Those who know her know the hats were always stylish and that she had the perfect designer shoes, handbags and jewelry to match).

She played an active role in stroke education after the announcement of the institute's groundbreaking study on the first treatment for acute stroke, tPA (tissue plasminogen activator).

"In my time at NIH I have been witness to and part of the astounding story of stroke going from an untreatable, disabling and sometimes fatal disease to a treatable disease," she said. "Before 1995, people viewed stroke as a hopeless condition. It took many years of effort to radically change the mindset of doctors and patients who simply didn't know stroke was an emergency. Now there are thousands of stroke treatment centers, a new generation of stroke specialists and nonstop advances in imaging technology and improved treatments."

Warren was a driving force behind NINDS's national campaigns—Know Stroke, Know the Signs, Act in Time and Mind Your Risks. Her stroke education efforts even took her to California where she hobnobbed with Hollywood executives in a successful attempt to promote the importance of stroke and tPA on the hit medical TV drama *ER*.

In addition, she coordinated NINDS's press activities for a broad range of neurological disorders—working closely with media to gain coverage for important scientific findings. She was a founding member of the NINDS nonprofit forum—a meeting that connects patient advocate groups with NIH and NINDS staff—and a member of the executive committee of the Brain Attack Coalition, a group of leaders in the stroke field.

Through the years, Warren has served on various NIH, NINDS and trans-NIH committees and working groups, and she has received top awards for her previous feature writing and investigative reporting, scores of NIH and NINDS group and individual merit awards, a Plain Language award for the NIH Stroke website (www.stroke.nih.gov), and an NINDS Director's Award for the Mind Your Risks campaign. In 2011, she was inducted into the UA Journalism Alumni Hall of Fame.

But, perhaps, more meaningful were the heartfelt accolades she has received from her colleagues since she announced her retirement.

On her digital kudos board, many noted her quick wit, infectious laugh, congenial personality, unmatched work ethic, tenacious drive to promote science and unwavering ability to put everyone—from young interns to junior staff to those in top leadership—at ease, regardless of the circumstances.

Even in her parting words, Warren continued to put science first.

"I have been so proud to see Dr. Fauci again being recognized as a national hero in medicine, in 1990 with AIDS and now with Covid," she said. "If there has been any good to come out of the pandemic, it may be that the public now recognizes the value of NIH, who we are and what we do."

In retirement Warren plans to return to her love of writing by writing a book and working on her travel blog, "Margo on the Go." An avid tennis player, she aspires to spend every day on the courts, travel and spend time with her husband, Darr, and two grown sons, Peter and Franky. R

Warren and husband H. Darr Beiser in their beloved Tucson, earlier this year. They plan more frequent visits now that she's retired.

VOLUNTEERS

Participants Wanted for Kids' Study

Help NIAID fight the flu. Scientists are investigating what happens in kids' immune systems after receiving a flu vaccine. Researchers are enrolling children who have received a flu vaccine in the past and plan to get the current seasonal flu vaccine by injection. Participation will take place at home. Participants will not receive any vaccinations as part of this study. Contact the Office of Patient Recruitment by phone (800-411-1222) or email (prpl@cc.nih.gov). For details, visit: https://www.clinicaltrials.gov/ct2/show/NCT04963166. Refer to study #000488-I.

Above, **1st place teen**. "A Playground is Just a Small City" by Larisa Kachko of Maryland depicts a playground where children and adults from all backgrounds and abilities can play.

At left, **1st place adult**. "In This Together" by Zarrin Tashnim of New York uses imagery inspired by the Bronx to highlight the importance of clean environments, access to healthy food and breaking generational cycles of illness through quality preventive care.

Above, **2nd place adult**. "The American Dream" by Kirandeep Kaur, California. Justice is depicted holding the Staff of Hermes (symbol of medicine) with the background of the pride flag. Her scale is balanced with children of different ethnicities sitting on it.

Below, **3rd place adult**. "Healthcare Access Pass" by Adam Vossen of California visualizes an access pass that allows everyone regardless of their race, class, or gender to receive health care, replacing the inaccessible monetary requirements of modern health care.

NIMHD Announces Winners of First Health Equity Art Challenge

BY GINA ROUSSOS AND SHELLY POLLARD

In 2020, NIMHD marked 10 years as an institute, 20 years as a center, and 30 years since establishment of the NIH Office of Minority Programs, making for a 10-20-30 celebration! Looking for new ways to bring national awareness to minority health and health disparities, NIMHD hosted its first Envisioning Health Equity Art Challenge as an anniversary activity. Teens and adults were invited to submit original artwork expressing NIMHD's vision for the future: an America in which all populations will have an equal opportunity to live long, healthy and productive lives.

NIMHD received 70 entries from 25 states and Puerto Rico, each expressing the artist's unique vision of health equity. A team of NIMHD extramural, intramural and administrative staff selected the winners for each category. Winners received a cash prize: $3,500 for 1st place, $2,500 for 2nd place and $1,500 for 3rd place.

"At NIMHD our vision is to promote health equity and we have been a leader in raising national awareness about the prevalence and impact of health disparities," said NIMHD director Dr. Eliseo Pérez-Stable. "Our anniversary celebration provided an opportunity to hear from others by sponsoring the Envisioning Health Equity Art Challenge."

"I was amazed by the passion and creativity displayed in each of the entries," said Dr. Gina Roussos, project lead for the challenge. "I am excited for NIMHD to share these six talented artists with the world."

To view the winning art and artists online, visit NIMHD's YouTube page https://www.youtube.com/watch?app=desktop&v=QckirBvHcWo&feature=youtu.be.

Below (from l): **2nd place teen**. "Working Together to Bring Health for All" by Katie Bonilla of Georgia shows working together to create a healthy nation with equitable health for all, no matter race, ethnicity or background; **3rd place teen**. "Medical Equality" by Arielle Clark, Maryland. Equal medical services are in reach of hands of all races and ages.