

A NIMBLE IRP RESPONDS Su Examines Genetic Susceptibility to Severe Covid-19 Infection

BY RICH MCMANUS

When the global pandemic caused by a novel coronavirus made its debut in late 2019, NIAID's Dr. Helen Su was studying inborn errors of immunity in patients with viral infections, mostly rhinoviruses, which cause colds, and influenza. Why, she wondered, was there such variability of outcomes in people infected with the same virus?

In a remarkable example of the NIH Intramural Research Program's nimbleness, she and her colleagues quickly pivoted to studies of SARS-CoV-2 when it became

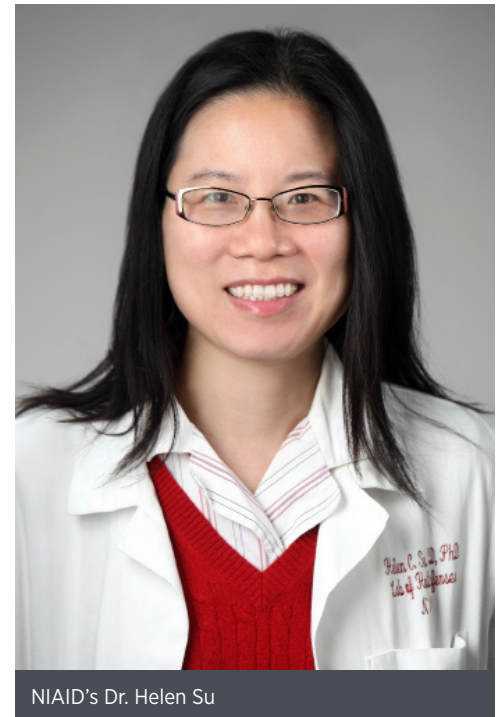
apparent that Covid-19, the disease caused by the virus, was spreading fast and becoming, in at least a small portion of patients, life-threatening.

By now, most people know the risk factors for Covid infection: advanced age, obesity, pre-existing cardiovascular and pulmonary issues, "and, I'm sorry to say," continued Su, "being male."

To that list can be added two informative outliers, she said: Those with a monogenic predisposition to get very sick, and their opposite—those whose genetic makeup seems to confer protection.

Su, who is chief of the human immunological diseases section in the Laboratory of Clinical Immunology and Microbiology, has joined forces with 15 principal investigators from 4 NIH institutes and centers to better understand Covid-19 pathogenesis, especially in those patients suffering acute respiratory syndrome.

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NIAID's Dr. Helen Su



How are readers keeping fit in winter? See p. 12.

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ASK THE RIGHT QUESTIONS Google Engineer Discusses Machine Learning in Medicine

BY DANA TALESNIK

Not long ago, it was the stuff of science fiction. Today, it's all around us: Our cell phones recognize images and speech, detect faces and auto-complete our sentences. Computers can learn to track customer habits to predict purchases and target advertising. They can also learn to detect fraud and deflect spam. Machine learning can interpret data for increasingly accurate predictions, and it has vast potential



Philip Nelson

SEE MACHINE LEARNING, PAGE 6

HARM IN SLEEP DISPARITIES Webinar Looks at Relationship Between Sleep, Housing, Cardiovascular Health

BY ERIC BOCK

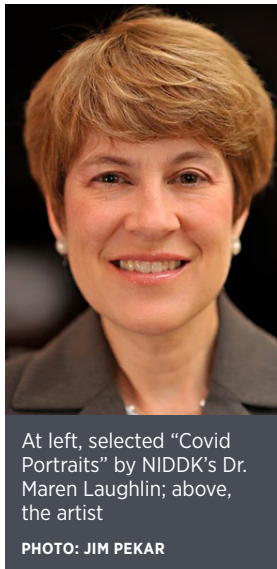


Dr. Dina Paltoo

Poor housing conditions and poor sleep can damage cardiovascular health and interfere with sleep, said Dr. Dina Paltoo, NHLBI's assistant director for scientific strategy and innovation.

"Where we live and how we're separated is very important," she said, opening a recent Housing, Sleep and Cardiovascular Risk webinar organized by NHLBI's National Center on Sleep Disorders Research. "Our

SEE SLEEP, PAGE 8



At left, selected “Covid Portraits” by NIDDK’s Dr. Maren Laughlin; above, the artist

PHOTO: JIM PEKAR

PAINTING THE PANDEMIC
NIDDK Employee Shares Artistic Talents

In the early days of the pandemic, NIDDK’s Dr. Maren Laughlin picked up her paintbrush to find comfort and connection. The program director for integrative metabolism research in the Division of Diabetes, Endocrinology and Metabolic Diseases had an idea—to portray people wearing their masks. A few months later, 25 colorful mixed media “Covid Portraits” in acrylic and fabric on canvas are the result, now on display in the Clinical Center near the Covid-19 testing check-in station.

“When we first learned about the pandemic’s



“Covid Portraits” by Laughlin are shown on display at the Clinical Center.

PHOTO: MAREN LAUGHLIN

shutdowns and public health measures that were necessary to try to contain the virus, there was so much anxiety across the community, and a strong sense of isolation,” said Laughlin. “These portraits celebrate people who choose to wear masks out of respect for each other’s health during this confusing and scary time and illustrate how unique and beautiful they are despite the mask. I hoped to provide a little connection during a time of physical distancing.”

When Laughlin got the idea for the portraits, she put out a call to family and friends for masked selfies and promised to paint a portrait of everyone who sent her a photo. Overall, the project took 4 months to complete and includes people from across the U.S. and two from France. Along with the display at the Clinical Center, some of the paintings have been displayed at a local venue during mask-sale fundraisers.

“Everyone who sent their selfies will have a unique souvenir of 2020,” said Laughlin. “Hopefully the portrait will remind them how we came together in new ways, even while staying apart physically.”—Alyssa Voss

NINR Holds Workshop on Reducing Inequities in Maternal Health

Last fall, NINR convened a workshop on innovative models of care for reducing inequities in maternal health. The workshop, co-sponsored by NICHD, NIMHD, ORWH and the Tribal Health Research Office, explored how nurses, midwives and birth companions can improve maternal and infant health for women in U.S. communities affected by racial discrimination, socioeconomic inequities and other system-level factors that contribute to maternal health inequities. More than 500 viewers tuned in. An archived recording of the workshop is available at <https://videocast.nih.gov/watch=38172>.

Among the key points:

- Research is needed that focuses on understanding the structural inequalities and system-level

factors affecting childbearing women in health disparity communities, including policies that result in decreased access to health care, lower quality care and disparate outcomes.

- Successful, innovative programs that are using person-centered, team-based approaches must be made sustainable and scalable.
- Respectful incorporation of community-generated knowledge and community members into models of care and maternal health research teams is important.
- The needs of pregnant women are met by respecting, listening to and supporting them, as well as communities and the health care workforce.
- A team-based approach that involves midwives, doulas or community health workers provides valuable person-centered care that results in positive maternal and infant outcomes, especially during the Covid-19 pandemic.

In the discussion sessions, participants shared lessons learned and identified research opportunities to improve maternal health care in underserved communities.

“DEMOCRATIZING HEALTH DATA”

NIMHD Director’s Seminar To Host Boulware, Feb. 4

NIMHD will host Dr. L. Ebony Boulware as the next virtual Director’s Seminar Series speaker on Thursday, Feb. 4 at 2 p.m. She will present “Where the Cloud Meets the Ground: Democratizing Health Data to Improve Community Health Equity.” This seminar was originally scheduled for last March.



Dr. L. Ebony Boulware

Boulware is the Eleanor Easley professor of medicine and director of the Clinical and Translational Science Institute at Duke University. A general internist and clinical epidemiologist, Boulware conducts research that empowers families and doctors with knowledge and tools to make healthy decisions and better manage chronic diseases.

The talk will be videocast at <https://videocast.nih.gov>. For reasonable accommodation, call (301) 402-1366 or the Federal Relay at 1-800-877-8339. Learn about the NIMHD Director’s Seminar Series at <https://nimhd.nih.gov/news-events/conferences-events/directors-seminar-series/>.

SHARING MY SCREEN

An Editor's Farewell

It is the hallmark of any great institution that it includes more people who worry about what kind of people they are than people who don't worry about what kind of

people they are. It might not be the most glamorous situation, but it does provide something precious: Hope.

No one pulls their PIV card out in the morning and comes within NIH's gates—or logs on from home—without the faith that their work somehow contributes to the alle-

viation of suffering in the world. We spend our healthy years trying to assure health for ourselves and for others. Nothing to apologize for there.

To do this kind of work in your own hometown, among people you admire, who make you laugh, who provide banking services, recreation, friendship, spiritual guidance, free flu shots, the opportunity to give blood, immense and relentless education, and

employment as wide as you can imagine—all within a 25-minute bike ride from home—sounds like love to me.

It was my pleasure, and my fortune, as *NIH Record* editor to help provide this great

• • •

“We used to call [the NIH Record] ‘The Second Best Thing About Payday.’ But it always meant more to me than a paycheck.

—RICH MCMANUS

• • •

institution's biweekly love letters to itself for almost 34 years.

We used to call it “The Second Best Thing About Payday.” But it always meant more to me than a paycheck. I hope that was evident.—**Rich McManus** **R**



Rich McManus (l) retired Jan. 1 after 38 years in NIH's information community. He was editor of the *NIH Record* from 1987 to 2020. In this 2018 photo, he interviews staff at NIH's power plant.

PHOTO: CHIA-CHI CHARLIE CHANG

New Covid-19 Website Features Research Response

NIH recently launched a new website, covid19.nih.gov, that provides the research community and the public with trusted, up-to-date, accurate information about research on Covid-19 at NIH and across the NIH-supported research community.

The website offers NIH Covid-19–related information in one location, including funding opportunities and research news on vaccines, treatments and testing. Users can search funding information for Covid-19 research by state, institution, congressional district and more.

To support ongoing efforts to direct the public to evidence-based information on Covid-19, the website also provides information and resources on joining clinical trials and donating plasma, and directs users to the Centers for Disease Control and Prevention, the State Department and other federal agency websites.

Visit covid19.nih.gov to learn more.



ON THE COVER: An aquatic research specialist in NICHD's section on vertebrate organogenesis took first place in the 46th annual Nikon Small World Photomicrography Competition for this image of a juvenile zebrafish.

IMAGE: DANIEL CASTRANOVA, NICHD

The NIH Record

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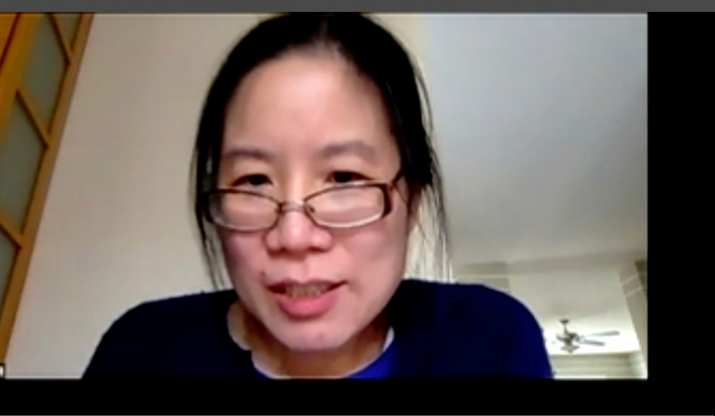
Associate Editor: Carla Garnett
Carla.Garnett@nih.gov

Staff Writers:
Eric Bock • Eric.Bock@nih.gov
Dana Talesnik • Dana.Talesnik@nih.gov

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Su and her collaborators underscored the importance of type I IFNs in host immunity against SARS-CoV-2 infection. This pathway could be a potential target for therapeutic intervention, they suggest.

Su

CONTINUED FROM PAGE 1

As part of the Covid Human Genetic Effort, co-led by Dr. Jean-Laurent Casanova at the Rockefeller University, HHMI and INSERM, and NIAID's Covid-19 Consortium, they are also working closely with investigators at the Uniformed Services University of the Health Sciences, New York, Paris and clinical teams in Italy to generate mountains of data on innate responses to infection.

"We had the freedom to sequence whoever we wanted to, regardless of age," said Su. "We sequenced all comers."

Mostly clinical immunologists, the team is looking for genetic variants responsible for acute disease. They have identified several loci of interest, in pathways involving type 1 and type 3 interferon, which are involved in susceptibility to respiratory viruses.

"It has been a thrill and an honor to watch our PIs apply their diverse talents to this pandemic," noted NIAID scientific director Dr. Steve Holland, who introduced Su's recent lecture—the 20th episode in a series begun last spring by the NIH Covid-19 scientific interest group. "It's been incredible to watch the fury and the enthusiasm with which this has been attacked."

Death is not a frequent or common outcome of covid infection, but neither is it extremely rare, said Su.

Sifting the human immune system for vulnerabilities to Covid-19 is no easy task.

"The immune system is extremely complex and dynamic," said Su. "When it

is unleashed, it is a powerful force."

At least 1,800 genes are involved in immune function, she said. And there are more than 420 distinct diseases where scientists know the underlying genetic lesion.

Inborn errors of immunity—Su's specialty—are estimated to affect about 1 in 4,000 live births. They can be grouped into categories, depending on which arms of the immune system are affected.

"It's not just white blood cells," Su explained, but

also "intrinsic immunity, involving many kinds of cells not typically thought of as immune-related."

The investigators found that impaired type 1 interferon production is associated with worse Covid-19 disease. Patients with this defect were more likely to require ventilator support.

The team focused on 13 genes that are important to type 1 interferon response, gathering both whole genome and whole exome data. They found that more than 3 percent of seriously ill patients had deleterious mutations in a number of these genes, resulting in loss of function.

Narrowing their focus to just 3 genes—IRF7, IFNAR 1 and IFN-alpha2—the investigators examined more than 1,000 patients critically ill with Covid-19, using as a comparison group more than 600 patients who were either asymptomatic or had mild cases, in addition to 1,200 healthy controls.

In about 10 percent of those seriously ill, autoantibodies to type 1 interferons were found—their own immune systems were neutralizing their ability to respond to SARS-CoV-2.

"These are really potent neutralizing autoantibodies to certain cytokines," said Su. "They exert a lot of biological function. And they are over-represented among men and older patients."

She admitted, "There is a lot we still don't know about autoantibodies, but they do predispose people to infection." She estimates that about 10 percent of critically ill Covid-19 patients have neutralizing autoantibodies.

"Knowing the defects allows us to better

treat these patients," she explained.

It is not yet clear whether administering interferons directly would be helpful, or if neutralizing autoantibodies can be removed by plasmapheresis, she said.

"Loss of interferon function early in infection is not good," Su concluded. "But there is still a lot to be understood...Too much and too little interferon are both bad things."

In a brief Q&A session, Su was asked if there are genetic or antibody tests that could signal a person at higher risk of severe Covid disease.

"Technically, it would not be very hard to do," she said, "but the interpretation is a little more difficult. What do you actually tell a person about risk? We need more research for concrete answers. Even if a person has a genetic defect, there is variable penetrance. It's not clear what kind of information would be actionable."

The full lecture is available at <https://videocast.nih.gov/watch=38875>. **R**

ORWH Releases New E-Learning Courses

ORWH recently expanded its e-learning course offerings with "Sex as a Biological Variable: A Primer" and the final two modules of the "Bench to Bedside: Integrating Sex and Gender to Improve Human Health" course.

The NIH Policy on Sex as a Biological Variable (SABV) articulates NIH's expectation that sex, as a biological variable, will be factored into research designs, analyses and reporting in vertebrate animal and human studies. The SABV primer consists of four independent, interactive modules designed to help the research community—including trainees and researchers at all career stages, NIH grant applicants and those engaged in peer review—account for and appropriately integrate SABV across all phases of biomedical and biobehavioral research. ORWH developed the primer in partnership with the National Institute of General Medical Sciences.

ORWH also released the final two modules of Bench to Bedside, developed in partnership with the Food and Drug Administration's Office of Women's Health.

The SABV primer, all six of the Bench to Bedside modules and the previously released "Introduction: Sex- and Gender-Related Differences in Health" course are available free. Visit <https://orwh.od.nih.gov/career-development-education/e-learning> for more information.



Workshop co-chairs Dr. Rada Dagher and Dr. Nancy Jones led the meeting.

NIMHD Workshop Explores Effects of Work on Health Disparities

BY BETHANY HOFFMAN

The National Institute on Minority Health and Health Disparities recently hosted a 2-day online workshop—the Role of Work in Health Disparities in the United States—to understand and address the role of work as a social determinant that contributes to health disparities.

The multidisciplinary workshop convened experts from the fields of health disparities, population sciences, labor economics, occupational health, epidemiology and organizational sociology and psychology to consider work as a social determinant and to identify priority research areas, potential mechanisms and interventions to address the role of work in health disparities.

Workshop co-chairs Dr. Rada Dagher, scientific program director in clinical and health services research at NIMHD, and Dr. Nancy Jones, scientific program director in community health and population sciences at NIMHD, took turns leading the meeting.

The first day provided an overview of current knowledge and conceptual grounding of research on work and health disparities, addressing theoretical foundations; concepts, measures, indicators and analytical approaches; and the challenges of operationalizing the concept of work. Day two addressed key mechanisms such as occupational segregation, worksite segregation, life course and intergenerational transmission; and systemic-level influences and pathways.

For U.S. adults, the experience of work is strongly influenced by their social identities, such as race/ethnicity, immigrant status, socioeconomic status, gender, sexual minority status and rural/urban residence. All these factors are associated with health disparities. However, most occupational disparities research to date has focused on hazardous exposures in the workplace. Meanwhile, health disparities research has seldom studied

the role of work in explaining health disparities.

Dagher said that studying the contribution of work to health disparities can help tackle a number of disparities underlying current health crises in the United States, such as Covid-19, maternal mortality and opioid use disorders.


NIMHD director Dr. Eliseo Pérez-Stable began the workshop by saying, “We acknowledge that work and occupation are primary social determinants of health. One of the questions I want to see discussed in this workshop is, how does this differ from what we already get from socioeconomic status, race, ethnicity and place?”

Dr. Sarah Burgard of the University of Michigan gave the keynote address, “The State of the Science for Research on Work and Health Disparities.” She explained that work had not been studied as a social determinant of health as much

as, for instance, education because it is challenging to measure the effects of work on health across the lifespan; most influences appear over time and can be connected to the complex paths of many different aspects of work.

Prominent epidemiological sociologist Dr. Bruce Link of the University of California, Riverside, presented “The Importance of Work in Fundamental Cause Theory,” in which he discussed how work structures major health-relevant aspects of our lives as a source of flexible resources such as money, knowledge, prestige, power and beneficial social connections, as well as a source of exposures and an important place where racism/discrimination occurs.

Organizers, speakers, and discussants agreed that the workshop was a success, sparking groundbreaking discussion of new approaches and interdisciplinary synergies to the underexplored effects of work on health disparities.

A complete videocast of the workshop is available at <https://nimhd.nih.gov/news-events/conferences-events/hd-workshop.html>. 

New NEI Director Speaks with FAPAC

Last July, NIH director Dr. Francis Collins named Dr. Michael F. Chiang as new director of the National Eye Institute. The Federal Asian Pacific American Council (FAPAC) NIH chapter recently had the opportunity to speak with Chiang about his career development, work-life balance and the unique challenges for the Asian American, Native Hawaiian and Pacific Islander (AANHPI) community.

Chiang’s career as a clinician-scientist began at Harvard Medical School, where he was originally interested in computational neuroscience and wanted to become a neurosurgeon. After 3 years of research focused on visual science in the lab of Dr. Richard Masland, he decided to focus on the intersection between technology, vision science and ophthalmology.

After training, he began to work at Columbia University, where he applied information technology to vision research and vision care. With the support from three mentors with expertise in ophthalmology, biomedical informatics and telemedicine research, Chiang initiated his innovative work to design and build a telemedicine system for diagnosis for ROP (retinopathy of prematurity). This led to the implementation of telemedicine as part of standard ROP care in pediatric ophthalmology.

In spite of the intense research, he was passionately engaged in teaching and mentoring, which involved a lot of one-on-one sessions with students and residents. In 2010, Chiang was recruited to Oregon Health Science University’s Casey Eye Institute. In building the ROP program, Chiang led the team and mentored a large group of research



Dr. Michael Chiang and his family

fellows, graduate students and clinical trainees.

More recently, he has started working on ROP with artificial intelligence, along with bioinformatics analysis, as well as data science. He predicts that knowledge discovery in the medical world will be significantly advanced by big data and analyses.

From his personal development, Chiang recognized that traditional Asian culture poses limitations in speaking up, which may be a unique challenge for AANHPI. He has learned through his career about the importance of effective communication of ideas, particularly in science, as more collaboration is required.

Throughout his career, Chiang has treasured the support of his family, particularly his wife Lydia, who is a pediatrician. He has a very active family, as his two daughters have always been involved in sports and the whole family enjoys skiing in winter. During the ongoing pandemic, due to quarantine at home, Chiang and his family have been enjoying movies together.

For the full interview, visit <https://www.fapac.org/resources/Documents/NIH%20Chapter/FAPAC%20Headlines%202020%20Winter%20Edition.pdf>.—Catherine Yu, Xinzhi Zhang

Machine Learning

CONTINUED FROM PAGE 1

for biomedical applications.

A subset of artificial intelligence, machine-learning programs train computers to learn by example, explained Philip Nelson, director of engineering at Google Research, who spoke at a recent NIA artificial intelligence working group webinar. Such a program, Nelson said, showing a photo collage, could quickly discern the chihuahuas from the blueberry muffins. The magic is in the data, he said, which machine-learning programs use to look for patterns and correlations to make their own predictions.

“One of our hopes in applying machine learning in scientific contexts,” said Nelson, “is that it will discover these correlations and previously undiscovered patterns for humans to follow-up and understand what the root mechanisms might be, and to essentially propose new theories.”

One type of machine-learning model uses neural networks for complex, deep learning tasks. After a sluggish start, said Nelson, neural nets—circuitry that can learn distinguishing features from raw data and root out unwanted correlations—are getting sharper and faster with bigger models.

“If you give [the networks] a lot of data, they really start learning, quite impressively,” he explained, excited about breakthroughs during the past decade. “Neural nets needed the power of today’s computation hardware.”

Ever since the Deep Blue supercomputer beat chess grandmaster Garry Kasparov in the late 1990s, the best chess players have been programs written by many engineers over many years, noted Nelson. But now, a neural net-based system called AlphaZero, starting from just the rules of the game and learning by playing itself, is a far better



Retinal fundus photos are taken to screen for diabetic retinopathy.

PHOTO: GOOGLE



Google’s Philip Nelson illuminates some of the ways machine learning is transforming science and medicine.

player than the work of all those engineers. “These networks are starting to best programmers at their own jobs, too,” he said.

Nelson doesn’t see this technology replacing doctors, but rather assisting them in a wide range of medical applications. One exciting area is diagnostics. Google recently teamed up with physicians to apply its Inception image-recognition model to detect diabetic retinopathy (DR). The condition, which can cause vision loss, even blindness, in people with diabetes, is not symptomatic until later stages, making early detection critical.

“When we were able to get enough data and apply modern machine learning,” said Nelson, “the results were spectacular.”

The Google team designed and trained a neural network using 130,000 retinal images that were graded by 54 ophthalmologists over an 8-month period. In the ensuing clinical trial involving thousands of patients, the results of which were published in a Dec. 13, 2016, *JAMA* article, their algorithms had high sensitivity and specificity for detecting DR from these images.

“We were basically as good as a board-certified ophthalmologist in diagnosing the

image,” said Nelson. Two years later, after further improvements in the training data, he reported, “We are now as good as a panel of retinal specialists.”

It turns out, their machine can also predict age, sex, blood pressure and refractive error from

the images. “We can predict your risk of a significant cardiovascular event on par with the Framingham score just from retinal fundus photos, without seeing the rest of your labs,” he said. They’re even able to see anemia in the fundus. “These machines now are able to see things that humans have never seen before.”

Nelson also cautioned about the risks of both false-positives and false-negatives. For example, a third of diabetics will develop DR, so diabetics should have their eyes checked every year. But that

can be expensive and inconvenient, and many people don’t even know they have diabetes. That’s why automated screenings, at pharmacies or even train stations, could be effective. But too many false-positives might overwhelm a health care system with otherwise healthy patients, he warned.

On the other hand, when neural networks assist a doctor reading a scan, studies have shown that false-negatives are more problematic. Doctors are good at dispensing with false-positives, but if the machine misses an issue, the doctor is likely to miss it too. People tend to trust computers too much, Nelson said. “We want our models to be as accurate as possible, and it’s also important to optimize the operating point and the user interface for the human workflow around any machine-learning-based system.”

Another emerging area for machine learning is pathology. Can machines emulate a cytotechnician, highlighting areas of concern for the doctor to check? Can machines analyze slides and recapitulate what pathologists would say? “One of the most exciting areas to me,” said Nelson, “is can we directly predict the outcomes or the therapies from the slide?”

Accuracy, though, depends on slide quality—whether the image is in focus. How likely is it, for example, that there is cancer in those pixels?

“If you were that patient, if this makes the difference between being treated properly or not, if you’re the 1 in 1,000, all this matters,” Nelson said. “We needed to build an image-quality model to run alongside our diagnostic models to help us understand the confidence in our predictions.”

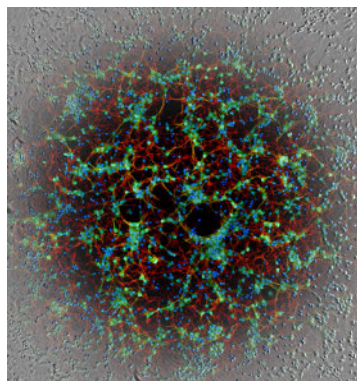
Machine learning can also distinguish one

image from another using a deep-learning technique called image regression. The machine is trained on pairs of correlated images, for example an unlabeled phase contrast microscopy image, and that same sample labeled with immunohistochemistry (IHC).

“The machine doesn’t understand biology,” Nelson said, “but if it can learn morphological patterns from the unlabeled image consistent with biological features shown by IHC, it can learn to predict those features in-silico without having to actually label the sample.”

This can be especially useful in a pathology context, he added, where many simultaneous immune stains can be predicted while leaving the tissue otherwise unmodified, so it can be used for sequencing or other biochemical assays.

Another promising area for machine learning is phenotypic drug discovery, said



In-silico labeling can distinguish neurons from other cells.

Nelson. A neural network can be trained to predict an embedding, a small vector, that represents an image such that similar images produce vectors that are closer together. These embeddings can then be used to extract the visual variation seen in controls, to identify when a drug or treatment changes the cells and, most importantly, indicate which of these changes are alike.

In one experiment, researchers tested three drugs with the same mechanism of action. The embeddings for cells treated with these drugs clustered near each other but had three distinct sub-clusters because each drug had different secondary effects. What’s more, scientists could see the effects early.

“The images of the cells would move in embedding space very early, at very low doses,” Nelson said. Differences were then visible in that space when the dose

increased. Many companies have begun using this technology.

The ability to morphologically cluster cells can give us new insights into the mechanisms of action of drugs, the effects of drugs in combination, and even treatments that might bring damaged cells back to a healthy state, explained Nelson. The hope for these technologies is to identify new patterns—new “Aha!” moments—that might lead scientists to new insights.

Machine-learning technology is already affecting health care, biology discovery and many other fields, he concluded.

“The potential is almost boundless, from imaging and diagnostics, to genomics, to wearable devices and other new biomarkers, to insights from medical records. These correlation engines might help us rethink longstanding biomedical challenges in the search for better outcomes. With machine learning, its eventual impact will be transformative. You have to start by asking the right questions.” **R**

FROM CLIQUE TO CLICK

Broaden the Sharing of Data, Researcher Argues

BY KELLY LENOX

Practices for sharing research data need to be fundamentally redirected toward broad availability, with appropriate privacy controls, according to Dr. James Byrd. The University of Michigan physician-scientist spoke recently at NIEHS.

“Nothing illustrates the need for data-sharing more than the pandemic we are in,” he said in the virtual presentation. For example, the SARS-CoV-2 vaccines being approved by the Food and Drug Administration were created using the publicly available genome sequence of the novel coronavirus. Byrd mentioned numerous advantages to robust data-sharing practices, including:

- More reproducible results
- New analyses, especially those that differ from the purpose data were originally gathered
- Better data-archiving, increasing the value of society’s original investment in the research
- Reducing burden on authors for finding and providing old data to future researchers
- Improving citation and linking of research data, which will enhance the visibility and recognition of authors, data producers and curators.

The current state of access differs markedly from that scenario. “Research data are often difficult or even impossible to access,” Byrd said. He cited a 2014 study showing that the older a paper is, the less available are the data its findings are based on.

Citing numerous examples of authors who built high walls around their data, Byrd illustrated pitfalls, including inability of other researchers to confirm findings. Scientists who will only share data with researchers whose viewpoints they agree with are taking a clique approach to research, he said.

So Byrd took a practical step and established the Research Symbiont Awards for researchers who make their data easy for others to access and use.

“Clique considerations need to be abandoned,” he said. “A reputation for sharing must improve researchers’ lot in life if we want [sharing] to be frequent and stable.”

The Research Symbiont Awards are one form of recognition. More important is for funding organizations to consider a researcher’s track record for data-sharing, so researchers’ lives could be improved by receiving more grants.

Dr. Kristi Pettibone of the NIEHS Program Analysis Branch invited Byrd and hosted the virtual talk. “As funders, we want to promote data-sharing to maximize resources and promote better science,” she said.



Dr. James Byrd suggested that part of establishing a rubric for evaluating past data-sharing should be challenging researchers to uncover problems that might arise, so they may be avoided.

PHOTO: SCOTT SODERBERG

To illustrate the impact of robust sharing, Byrd turned to 2018 Symbiont winner Dr. Morgan Ernest from the University of Florida. She assembled a dataset during graduate school and postdoctoral studies in ecology. Her research has been cited more than 10 times, mostly for reuse of the data.

“This type of sharing should influence her chance of [future] funding, since it amplifies the impact of the research funding Dr. Ernest received,” Byrd argued. “Reviewers might not know an individual’s reputation, so we need a rubric or metric [to convey that information].”

Such a measure must address privacy protection for any study participants whose data are being shared. One such metric is used

by grant reviewers for Alex’s Lemonade Stand, a foundation that supports research on childhood cancer. Byrd hopes more organizations will step up, including NIH.

Sleep

CONTINUED FROM PAGE 1

socioeconomic status is linked to where we live and sleep. This can give rise to our access to care and food.” Socioeconomic status also affects sleep quality and quantity, she added.

Dr. Mario Sims underscored the influence of housing on cardiovascular health. He is the Jackson Heart Study’s chief science officer and a professor in the department of medicine at the University of Mississippi Medical Center.

Recently, he led an effort to draft and publish a scientific statement from the American Heart Association. The statement reviewed and summarized research on the links between housing and cardiovascular health and overall well-being. Health is affected by four aspects of housing: stability, quality and safety, affordability and accessibility, and neighborhood environment.

“Housing is a prominent social determinant of health,” Sims said. “It should be considered when evaluating prevention efforts to reduce and eliminate racial, ethnic and socioeconomic disparities.”

The Jackson Heart Study is evaluating the causes of cardiovascular disease in



Dr. Dayna Johnson and Dr. Mario Sims spoke recently at a Housing, Sleep and Cardiovascular Risk webinar organized by NHLBI’s National Center on Sleep Disorders Research.

“There’s clearly a need to understand the multiplicity of socioeconomic, physical and psychosocial factors that impact racial inequities,” said Sims.

Sleep plays an important role in health, said Dr. Dayna Johnson, assistant professor

sleep disorders spend more money annually on medical bills for sleep-related health problems.

“Racial and ethnic minorities, lower socioeconomic individuals and sexual minorities all are disproportionately affected by insufficient sleep and some sleep disorders,” Johnson said.

These sleep disparities can be attributed to social determinants such as discrimination,

inconsistent work schedules and stress, as well as environmental factors at the housing and neighborhood level. Examples include inopportune light exposure, toxins, adverse temperature, noise and violence. Each of these factors consistently affects sleep duration and quality.

She noted that a few studies indicate racial sleep disparities are reduced by at least 50 percent when accounting for neighborhood environment. Another study she led found that those who live in mobile homes or trailers had higher odds of worse sleep compared to those living in an apartment or house.

To improve the sleep of people who will live in the homes they design, Johnson suggested that developers incorporate features that promote sleep health, such as insulation, ventilation and sound-proofing. Individuals can hang curtains to prevent artificial light from entering a bedroom and avoid screen-time before bed. Public officials could design and implement policies that eliminate homelessness and housing insecurity.

“Context matters,” Johnson concluded. “It’s important to think about how individuals are nested in social relationships, living conditions, neighborhoods and communities, our built environment, institutions and social and economic policies.” **B**



“Context matters. It’s important to think about how individuals are nested in social relationships, living conditions, neighborhoods and communities, our built environment, institutions and social and economic policies.”

—DR. DAYNA JOHNSON



African Americans. More than 5,300 men and women who live in Jackson, Miss., are enrolled. African Americans are more likely to be concentrated in areas with higher poverty. Data from the Jackson study show that areas with higher poverty rates have higher rates of heart disease.

Residents of neighborhoods with greater violence smoked cigarettes at a higher rate, had worse sleep outcomes and had an increased risk of cardiovascular disease and type 2 diabetes, particularly African-American women.

in the department of epidemiology at Emory University’s Rollins School of Public Health.

The American Academy of Sleep Medicine recommends adults 18 and over get at least 7 hours of sleep per night on a regular basis. Not getting enough sleep affects a person’s heart, memory, immune system, metabolism and emotional well-being.

The most common sleep disorders are insomnia and sleep apnea. In many cases, these conditions are undiagnosed, particularly in low socioeconomic and racial/ethnic minority populations. People with

Study Links Metabolic Syndrome to Higher Cardiovascular Risk in Patients with Psoriasis

Psoriasis, a chronic inflammatory skin disease, has long been known to increase the risk of



Psoriasis patients are more prone to having metabolic syndrome, increasing their risk of cardiovascular disease.

PHOTO: LIPOWSKI/ISTOCK/GETTY

cardiovascular disease, which includes heart attack and stroke. Now, researchers have identified a key culprit: the presence of metabolic syndrome (MetSyn), a condition that includes obesity, diabetes, high cholesterol and hypertension, and is highly prevalent among psoriasis patients.

The findings, which could lead to new ways to help prevent cardiovascular

disease among people with psoriasis, appeared online in the *Journal of the American Association of Dermatology*. The study was funded by NHLBI.

“Metabolic syndrome, so common among our psoriasis patients, drives up coronary artery disease in this population by increasing the plaque buildup that clogs the heart’s arteries,” said Dr. Nehal Mehta, preventive cardiologist and head of NHLBI’s Laboratory of Inflammation and Cardiometabolic Diseases. “Our study shows that, of the MetSyn components, hypertension and obesity contribute the most to coronary plaque buildup, and hence can be good targets for intervention.”

Partly because it worsens vascular and systemic inflammation, psoriasis, a common skin disease affecting 2-3 percent of adults, not only increases but speeds up atherosclerosis, the plaque buildup that clogs arteries and can lead to heart attack and stroke. Metabolic syndrome affects about 25 percent of adults and is on the rise, and its prevalence is even greater among patients with psoriasis.

To reach their conclusions, Mehta and his team conducted an observational study of the NIH Psoriasis, Atherosclerosis, and Cardiometabolic Initiative cohort, which included 260 patients with psoriasis, 80 of whom met the criteria for metabolic syndrome. All participants underwent CT scanning to take pictures of their coronary arteries using a technique called cardiac computed tomography angiography (CTA).

The study found that systemic inflammation, insulin resistance and blood cholesterol were

significantly higher in the participants who had both psoriasis and metabolic syndrome. And those with MetSyn had higher coronary artery plaque buildup, a high-risk factor for heart attacks that was assessed by CTA.

Obesity is the most salient aspect of MetSyn. The researchers suggest that identifying metabolic syndrome, especially waist circumference, can help assess cardiovascular disease risk in clinical settings for patients with psoriasis.

Pregnant Women in Third Trimester Unlikely to Pass Covid-19 to Newborns

Pregnant women who are infected with SARS-CoV-2, the virus that causes Covid-19, during the third trimester are unlikely to pass the infection to their newborns, suggests an NIH-funded study. The study—supported by NICHD, NHLBI and NIAID, and published in the *JAMA Network Open*—followed 127 pregnant women who were admitted to Boston hospitals during spring 2020.

Among the 64 pregnant women who tested positive for SARS-CoV-2, no newborns tested positive for the virus. Data is still pending on women infected earlier in their pregnancies.



Pregnant women in their third trimester are unlikely to pass Covid-19 to their newborns.

PHOTO: YACOBCHUK/ISTOCK/GETTY

“This study provides some reassurance that SARS-CoV-2 infections during the third trimester are unlikely to pass through the placenta to the fetus, but more research needs to be done to confirm this finding,” said NICHD director Dr. Diana Bianchi.

The team found that pregnant women with Covid-19 had detectable levels of virus in respiratory fluids like saliva, nasal and throat secretions, but no virus in the bloodstream or the placenta. They also evaluated the development of maternal antibodies, and how well those antibodies passed through the placenta to the fetus (an indicator of potential immune protection from the mother).

The researchers observed lower-than-expected levels of protective antibodies in umbilical cord blood. In contrast, they found high levels of influenza-specific antibodies, presumably from maternal flu vaccination, in the cord blood samples of both SARS-CoV-2 positive and

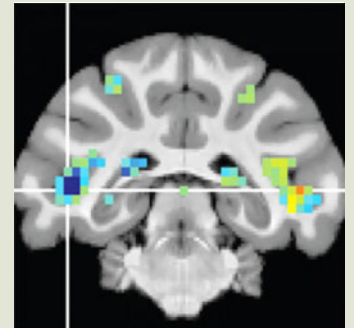
negative women. The researchers suggest these findings may indicate that SARS-CoV-2 antibodies do not pass through the placenta as easily as other maternal antibodies.

These findings could help improve care of Covid-positive mothers and guide strategies for vaccinating them.

NIH Researchers Discover Brain Area Crucial for Recognizing Visual Events

NIH researchers report that a brain region in the superior temporal sulcus (fSTS) is crucial for processing and making decisions about visual information. The findings, which could provide clues to treating visual conditions from stroke, appeared recently in the journal *Neuron*. The study was funded by NEI and NIMH.

“The human visual system recognizes, prioritizes and categorizes visual objects and events,” said Dr. Richard Krauzlis, chief of NEI’s section on eye movements and selective attention and senior author of the study.



fMRI scans reveal activity changes in the fSTS.

PHOTO: RICHARD KRAUZLIS

“We were surprised to learn that the fSTS is a crucial link in this story-building process, passing information from an evolutionarily ancient region in the midbrain to highly specialized regions of the visual cortex.”

While aspects of visual processing begin in the eye, crucial steps in visual attention start in the superior colliculus, a part of the midbrain that handles a variety of sensory input. Neuronal activity in the superior colliculus tells the brain to notice an event in the visual field and decide if it is significant.

Using fMRI, researchers found that some fSTS neurons fired in response to specific images, a property found only in areas of the brain that manage high-level processing. Without the contribution of the superior colliculus, many of these object-specific neurons in the fSTS failed to fire in response to their favored object.

These findings are particularly relevant to a condition known as visual neglect, which can occur in people after a stroke or other brain injury that affects brain areas involved in visual attention. People with visual neglect can see all the objects and events in their visual field, but often aren’t aware of the events on the affected side, especially when the visual field is cluttered.

NINDS Deputy Director for Management Gormley Retires After 34 Years at NIH

BY SHANNON E. GARNETT

After 34 years of federal service—all with NIH—Dr. Maureen Gormley, deputy director for management, NINDS, is ready for her next adventure. She officially retired on Dec. 31.

“With my younger daughter starting college this fall, it seemed like a good time for me to focus on my next career chapter,” she said.

Gormley earned her bachelor of science degree in nursing in 1985 from Boston College and a master of public health degree in 1987 from Yale University. In 2010 she earned a master of arts degree and in 2014 a doctor of philosophy degree—both in human and organizational systems from Fielding Graduate University in Santa Barbara, Calif. Her dissertation examined workplace stigma toward employees with intellectual disabilities.

She first came to NIH in 1986 as a summer student in the PHS Commissioned Officer Student Training and Extern Program (COSTEP). PHS COSTEP allows health-related undergraduate, master’s and doctoral students to train alongside active-duty officers during school breaks and become inactive PHS officers upon completion of the program.

“When I graduated, I had two job offers—one with a consulting company and the other with NIH,” Gormley shared. “The dean of my graduate program told me that the decision was a no-brainer, adding that ‘there are hundreds of consulting companies, but only one NIH.’”

She joined NIH in 1987 as an administrative fellow in the Clinical Center and rose through the ranks, undertaking increasingly challenging administrative duties and responsibilities in a variety of roles—assistant hospital administrator, director of quality improvement, special assistant to the

director and chief of administrative management and planning.

From 1987 to 1989, she also worked as a clinical nurse for the Meridian Healthcare Corp. at the Layhill Skilled Nursing and Rehabilitation Center in Silver Spring.

In 1999, Gormley became chief operating officer of the Clinical Center. She consulted on leadership development, strategic

planning and organizational effectiveness, and used her background in nursing and health services administration to make significant and lasting contributions to the hospital—both in terms of efficiency of operations and continuous improvement of patient services.

Gormley left the Clinical Center in 2016 to become NINDS executive officer.

She encouraged and nurtured a positive workforce culture with

strong employee engagement and accountability, and developed leadership strategy for continual improvement.

“When I left the Clinical Center, I really missed my daily interactions with patients—many of whom I got to know personally over the years,” she said. “In that environment, it was easy for me to feel that my work was

Among her most rewarding accomplishments are her efforts to support CC patients and help launch the careers of individuals with intellectual disabilities.

“I was at the Clinical Center for a long time and am most proud of the work I did to support the patients,” she said. Her standout examples included leading the implementation of a hospital-wide continuous quality improvement program, developing the first CC strategic plan, identifying the need for and establishing patient hospitality services, overseeing activation of the Mark O. Hatfield Clinical Research Center and the Edmond J. Safra Family Lodge, and serving as the first executive secretary of the NIH Advisory Board for Clinical Research.

She also introduced a school-to-work transition program known as Project SEARCH that has successfully trained and hired youth with intellectual disabilities into the mainstream NIH workforce.

“I am especially proud of the NIH Project SEARCH program,” she said. “In 2010, I responded to a ‘cold-call’ email from a teacher at the Ivymount School in Rockville asking if I would be willing to consider hosting a school-to-work transition program for youth with intellectual disabilities at NIH. Ten years later, the program is still going strong. With almost every institute involved, we have trained dozens of Project SEARCH interns, many of whom have been hired at NIH into mainstream federal and contract positions.”

Although Gormley has retired from

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“...Over the years, I have come to realize that the best leaders combine hard work and deep knowledge with a sense of humility and humanity.”

-DR. MAUREEN GORMLEY

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important because I could do something almost every day that made a difference. NINDS has a special culture because everyone is so driven by the mission, but at the same time, down to earth and friendly. My transition was very easy.”

Throughout her career, Gormley has received numerous awards and accolades and has served on countless NIH, trans-NIH and NINDS committees and working groups as well as some outside of NIH.

federal service, she will continue to provide counsel to NINDS’s Office of the Director. She said she will miss the people.

“Having great working relationships with people is not only the way to get things done at NIH, but it is also the way to have fun,” she noted. “I love helping people and find much gratification in establishing healthy teams in support of our mission.”

She revealed, however, that she will not miss “the litany of activities focused on



Dr. Maureen Gormley

compliance and regulations, such as continual data calls, rather than direct support of the science.”

In retirement, Gormley plans to continue her coaching and strategic consulting work, take long walks with her husband, run with her two daughters, and travel with family and friends—preferably to places with palm trees.

“I have witnessed much change at NIH—from sleeping overnight at the hospital as Y2K threatened to take down our information systems to watching a perimeter fence change the culture of the campus following 9/11,” she concluded. “What has always remained the same is the tireless commitment of all members of the staff for the mission of NIH. And, over the years, I have come to realize that the best leaders combine hard work and deep knowledge with a sense of humility and humanity.”

NCI’s Hildesheim Retires

Dr. Allan Hildesheim, senior investigator and former chief of the Infections and Immunoepidemiology Branch (IIB), retired from NCI’s Division of Cancer Epidemiology and Genetics after 33 years of service at the end of 2020.

As the inaugural chief of IIB, Hildesheim built a multidisciplinary research program focused on the interplay of infection, immunity and inflammation on cancer risk and helped translate those findings into important advances in cancer prevention, risk stratification and screening. As an investigator, he devoted his career to the study of host and viral factors involved in the pathogenesis of DNA virus-related tumors.

Hildesheim began his career at NCI in 1987 as a predoctoral fellow in the precursor to DCEG, the Division of Cancer Etiology. He earned his Ph.D. in epidemiology from Johns Hopkins School of Hygiene and Public Health in 1991 and completed his doctoral dissertation studying the interactions of herpes simplex virus 2 (HSV2) and human papillomavirus (HPV) in cervical cancer with Dr. Louise Brinton in the Invasive Cervical



Dr. Allan Hildesheim

Cancer Study in Latin America. Through this work, Hildesheim established numerous collaborations that would lay the groundwork for his subsequent studies in nasopharyngeal cancer (NPC) and cervical cancer.

Over the course of his career, he built a comprehensive research program dedicated to understanding the causes of NPC, a cancer associated with Epstein-Barr virus (EBV), and its early detection.

He conducted large studies of both sporadic and familial NPC in Taiwan

examining the role of viral, environmental and genetic factors, resulting in the identification of novel gene candidates, many of which had biological functions that could modulate responses to EBV infection. These studies created an extensive biospecimen collection, providing a rich resource for interdisciplinary molecular epidemiology evaluations. He extended this work to a large 30,000-person NPC screening program in Southern China to evaluate the impact of EBV-based markers and

clinical management procedures for the early detection of NPC.

Hildesheim was pivotal in establishing large-scale international cohort efforts that required extensive cross-discipline and cross-cultural collaborations. His contributions to natural history studies of HPV and cervical cancer in Guanacaste, Costa Rica, revealed insights into the performance of then-novel HPV and cytologic screening techniques. He and collaborators designed and launched the HPV Vaccine Trial in Costa

Rica, which was the only publicly funded HPV vaccine trial initiated prior to vaccine licensure.

More recently, his collaborations have extended to the Chile Biliary Longitudinal Study, which explores the etiology and natural history of gallbladder dysplasia and biliary cancer and seeks to identify risk stratification and prevention strategies. His seminal contributions have produced nearly 400 peer-reviewed publications.

“As founding chief of IIB, Allan guided the branch with his scientific vision and passion,” said Dr. Eric Engels, chief of IIB. “His expertise in designing molecular epidemiology studies has advanced the understanding of virus-related cancers and his commitment to international research collaborations, in regions of the world where the burden of these cancers is high, has made a lasting impact on public health.”

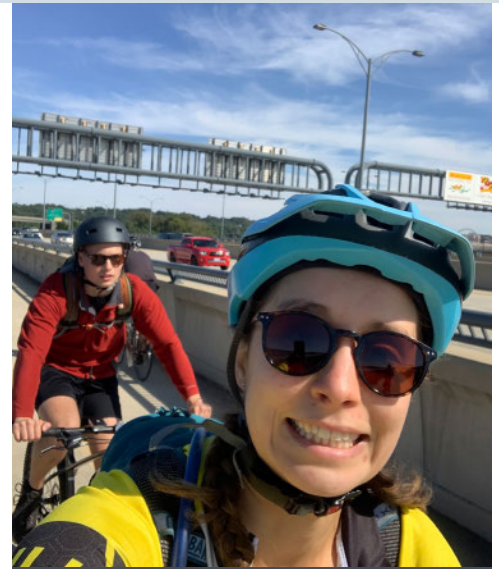
Over the last three decades, Hildesheim has mentored numerous fellows, staff scientists and junior investigators who have gone on to successful careers at NCI and other institutions. His dedication to mentorship was recognized with an NCI Outstanding Mentor Award. “Those who had the opportunity to be mentored by Allan became better scientists through his guidance and generosity,” said Dr. Aimée Kreimer, senior investigator in IIB.

In addition to his ambitious research program, Hildesheim served on many intramural and extramural committees and advisory boards. He is the recipient of numerous awards, including the HHS Secretary’s Award for Distinguished Service for groundbreaking research in human papillomavirus leading to the development of a vaccine for the prevention of cervical cancer. **R**

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“[Hildesheim’s] expertise in designing molecular epidemiology studies has advanced the understanding of virus-related cancers and his commitment to international research collaborations, in regions of the world where the burden of these cancers is high, has made a lasting impact on public health.”

—DR. ERIC ENGELS

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At left, Dr. Nancy Breen and husband, at Cumberland on the C&O canal; above, Charlotte Langner and Joe Krzeski, a postbac fellow in NICHD, explore the DMV via bike. Not shown but also on the ride was NCI postbac Joey McKenna.

TAKE A HIKE, OR RIDE A BIKE Readers Stay Active, Healthy

The *Record* recently asked how readers were moving toward their fitness goals these days—especially as seasons change and temperatures drop. Below are a few first responses. Send yours with a photo to nihrecord@nih.gov.

C&O Canal Caper

“I’m an NIH volunteer since my retirement from NIMHD (previously I worked at NCI) in December 2019. With travel plans canceled, my husband and I decided to explore all 184 miles of the C&O canal, stretching from Georgetown to Cumberland, Md. We walked or biked the entire length.”—**Dr. Nancy Breen**

Telework Forces Route Adjustments

As the pandemic moved us to this telework situation, I continue to cycle but had to adjust a bit since I lost the mileage I would gain from my

bike commute. That was 26 miles daily, so while teleworking I couldn’t always get out long enough to rack up those miles. While it had been warm out, I would do some night riding. My favorite routes were through Rock Creek Park or downtown at night. During the winter, I’ve resorted to more indoor riding on our Peloton bike. But with the right clothing and bike [See bike photo on p. 1], I can easily manage the winter weather. I’ll break out the gravel or mountain bike and get the insulated clothing on for some winter riding and work through any snow we may get. I’ve also started doing some hiking and recently hiked a loop at Old Rag.—**Steve Friedman, SEER Program Manager, NCI**

Exploring D.C. via Bike Trail

My friends Joey, Joe and I have been exploring

the D.C. area by bike and even did a 63-mile D.C. perimeter bike ride! Starting at NIH, we took Rock Creek Park to Silver Spring, continued down the Sligo Creek Parkway, got lost a bit, then followed the Northwest Branch of the Anacostia River to Alexandria. Then we hopped onto the Mt. Vernon trail, took a quick tour of the National Mall, then headed back to NIH via the Capital Crescent trail.—**Charlotte Langner, postbac IRTA fellow, NIAID Branchley Laboratory**



Steve Friedman atop Old Rag, and at right, at the Wright Brothers Memorial at Kitty Hawk, wearing the new NIH Bike Club kit

