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A Fortuitous Connection

Vice President Kamala Harris's Mother and Her NIH Collaborations

BY MICHAEL TABASKO, OD

Vice President Kamala Harris was raised in a family in which science was interwoven with everyday life. After all, her mother, Shyamala Gopalan (professionally known as Gopalan Shyamala) chose to make NIH a vital part of her remarkable career as a breast-cancer researcher. "NIH was such a huge part of my youth," said Harris. She and her husband, Second Gentleman Douglas Emhoff, were visiting NIH on January 26, 2021, to receive their second doses of the Moderna COVID-19 vaccine.

The NIH connection began in 1987 during a hilly bus ride in Colorado: Two scientists struck up a spirited conversation as the Rocky Mountains faded away through the bus's rear window. The pair had attended a scientific conference in Keystone, Colorado, and were headed to Stapleton International Airport in Denver. **Stephen Ullrich** would return to his lab at the National Cancer Institute (NCI) in Bethesda, Maryland, and Gopalan to Lady Davis Institute for Medical Research (Montreal, Canada). Their dialogue did not end there—the auspicious meeting catalyzed a collaboration that would give rise to

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Accelerating an End to Dementia

New NIH Center for Alzheimer's Disease and Related Dementias

BY MICHAEL TABASKO, OD

CREDIT: HENSEL PHELPS/ZGF DESIGN BUILD TEAM

A rendering of the new NIH Center for Alzheimer's Disease and Related Dementias, which plans to open its doors on the Bethesda, Maryland, campus in early 2022.

A formidable new player has arrived in the fight against neurodegenerative diseases: NIH's Center for Alzheimer's Disease and Related Dementias (CARD). Established in 2020 by the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS), the center will draw on the wealth of resources across NIH and around the world to develop treatments and preventions for Alzheimer disease and related dementias (AD/ADRD).

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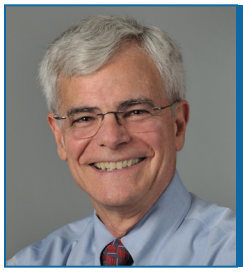


Being Mindful of Diversity and Inclusion in Selecting Scientific Speakers at NIH

BY MICHAEL GOTTESMAN, DDIR, AND ROLAND OWENS, DIRECTOR OF RESEARCH WORKFORCE DEVELOPMENT, OIR

The recent recognition of Juneteeth as a federal holiday acknowledges the essential contributions made to this nation by people of African descent and calls for us to "recommit ourselves to the work of equity, equality, and justice," as stated in President Biden's proclamation. "We celebrate the centuries of struggle, courage, and hope that have brought us to this time of progress and possibility," the President said.

Thus, Juneteenth is a reminder that diversity is strength and that the National Institutes of Health is the world's leading biomedical research institution by virtue of the diversity we attract. What better way to express this diversity than through the selection of speakers for our seminar series that reflect the amazing diversity of this nation.

NIH Director **Francis Collins** created quite a stir by calling for an end to "manels" (all-male speaking panels), coincidentally just days before Juneteeth in 2019. In spite of this initiative, we still keep seeing symposia at the NIH with a surprising lack of gender and ethnic diversity among the speakers, given the known diversity of the talent pool.

Those of us who organize seminar series and symposia have a great deal of control over the speed of dissemination of new scientific concepts. It is therefore important for us to be mindful and intentional about hearing from the full breadth of talented researchers. It is very easy to nominate the "usual suspects" when putting together a seminar series, but that is not the best way to promote scientific discourse.

To enhance diversity and inclusion in the Wednesday Afternoon Lecture Series (WALS), the Office of Intramural Research (OIR) has embraced several promising practices, which we will share here.

The best way to promote diversity and inclusion is to invite nominations from a large and diverse group of individuals. Each year, we invite WALS nominations from the entire NIH community. We especially encourage nominations from our diverse array of Scientific Interest Groups. In addition, we encourage nominations from groups such as the Women Scientists Advisors Committee and the Women of Color Subcommittee of the Working Group on Women in Biomedical Careers. We encourage other groups who feel that they are underrepresented to nominate speakers for the WALS and other seminar series. Feel free to recommend multiple candidates during the next call for speakers.

We also make sure that a diverse group of scientists are involved in the speaker selection process. We are fortunate that the OIR senior staff is such a group (https://oir.nih.gov/about/leadership-staff). Another practice that diversifies the WALS is favoring nominees who have not spoken at the NIH in the last five years.

Even organizers of more narrowly focused lab and branch seminar series and institutes and centers (IC)-sponsored symposia should be mindful of diversity and inclusion. The first point to consider is not to assume that you know every important researcher. NIH has several web-based tools for identifying top researchers in specific fields. To identify NIH scientists in the Intramural Research Program (IRP), search the NIH Intramural Database (https://intramural.nih.gov) and the IRP PI listing by research focus area (https://irp.nih.gov/our-research/scientific-focus-areas). To find NIH grantees in specific areas, you can search the NIH RePORTER (https://reporter.nih.gov). The NIH Office of Scientific Workforce Diversity (OSWD; https://diversity.nih.gov) has also developed a tool for identifying diverse groups of scientists in particular research areas.

If you require assistance with generating a list of diverse speakers on a particular topic, you can reach out to OIR, OSWD, or even your IC's extramural program officers.

We also recommend making note of outstanding scientists you see at meetings, on television, or as authors of journal articles, so that when the opportunity arises, you will have some people in mind. Before finalizing your speaker list, ask yourself whether your list reflects the diversity of the talent pool.

As stated on the OIR Diversity and Inclusion web page (https://oir.nih.gov/about/our-commitment-diversity-inclusion), a key part of our definition of inclusive excellence is "creating and fostering an environment in which all talented individuals are allowed to contribute." Research seminars and symposia greatly enrich the intellectual environment at NIH.

Let's all work together to make sure that all talented researchers are heard. ●

New Chief Officer for Scientific Workforce Diversity

Marie Bernard Is Helping to Make Change Happen

BY LAURA STEPHENSON CARTER

"We're at a tipping point," said **Marie Bernard**, NIH's new Chief Officer for Scientific Workforce Diversity (COSWD). She is leading NIH's efforts to diversify the national scientific workforce and expand recruitment and retention.

NIH has long recognized that teams made up of people from diverse backgrounds and experiences are better than homogenous teams at fostering innovative science and are more likely to engage in research that will benefit underserved populations. But change isn't happening fast enough. "Disparities seen in COVID deaths," among other disturbing events across the country, have inspired NIH to redouble its efforts. "Everyone is really focused," said Bernard, who has met with almost every institute and center (IC) director and is beginning meetings with scientific directors as well.

"Dr. Bernard is an accomplished physician-scientist and has championed diversity and inclusion efforts over her entire career," said NIH Director **Francis Collins** in a news release announcing her appointment as COSWD in May 2021.

Bernard, who was deputy director of the National Institute on Aging (2008–2021), has held key leadership roles—and has received many awards for her work—in a variety of NIH and national activities that are furthering diversity. She serves as a co-chair of NIH's UNITE initiative, an effort to identify and address structural racism within the NIH-supported and the greater scientific community. UNITE aims to establish an equitable and civil culture and reduce barriers to racial equity within the biomedical research workforce.

Since becoming acting COSWD in October 2020, she has been building on the strong foundation set by **Hannah A. Valantine**, NIH's first-ever COSWD who retired last year. Bernard heads the Office of Scientific Workforce Diversity (OSWD), which is striving to stimulate diversity inside as well as outside NIH. For the intramural research program, the OSWD is helping ICs recruit diverse candidates into senior-level scientist positions. Bernard also hopes to bring more senior tenured scientists to the Distinguished Scholars Program, which facilitates the hiring and career progression of tenure-track investigators who have demonstrated a commitment to promoting diversity and inclusion in the biomedical-research enterprise.

Marie Bernard

"There's no silver bullet" to make these changes happen, Bernard explained. "Sometimes change can be scary but we'll all be working together."

For example, she and her office can reach out to their broad networks of people and "make them aware that NIH is serious about having more diverse perspectives," she said. The OSWD has also developed a standardized approach for identifying candidates with diverse backgrounds and can help ICs in their recruiting efforts.

In addition, "we think there are opportunities to think about people from diverse backgrounds for standard lectures and [positions on Boards of Scientific Counselors] as regular or ad hoc members," she said. "Our office has a role to play in helping scientific directors and others better identify potential candidates with diverse backgrounds."

Prior to joining NIH in 2008, Bernard was the endowed professor and founding chair of the Department of Geriatric Medicine at the University of Oklahoma College of Medicine (Oklahoma City) and Associate Chief of Staff for Geriatrics and Extended Care at the Oklahoma City Veterans Affairs Medical Center.

She received her M.D. from the University of Pennsylvania (Philadelphia) and trained in internal medicine—and was chief resident—at Temple University Hospital (Philadelphia).

Bernard's research at the University of Oklahoma focused on nutrition and function in older populations, specifically underrepresented minorities. At NIH, she led a NIH-wide portfolio analysis—on inclusion of older adults in clinical trials—that contributed to NIH's updating its inclusion policies. In 2019, NIH updated its policy to "Inclusion Across the Lifespan," requiring inclusion of children and older adults. "We're pretty proud to have contributed to that," said Bernard. (*J Am Geriatr Soc* **67:**218–222, 2019; DOI:10.1111/jgs.15786)

"We have to do the work now to make [diversity in the scientific workforce] happen," said Bernard. "People seem to be committed to doing exactly that. We will to push ourselves, measure ourselves, and be transparent and accountable as well." ●

From the Visiting Fellows Committee

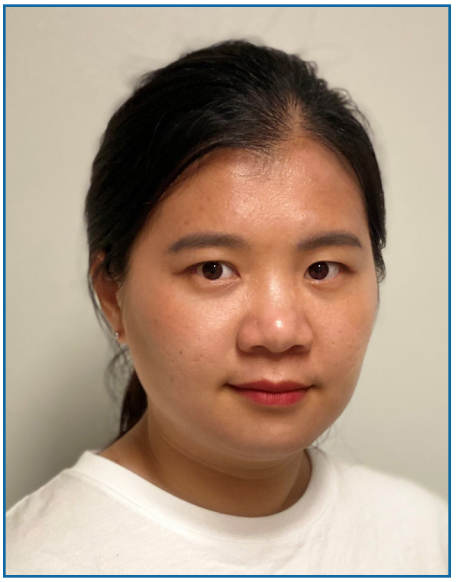
An Interview with VFC Co-chairs Vrushali Agashe and Zeni Wu

BY ERICA WYNNE-JONES, NIAID

The Visiting Fellow's Committee (VFC), a subcommittee of the Fellows Committee, serves the interests of visiting fellows (trainees from other countries) in their transition to life at NIH and in preparation for their future careers. The VFC holds events to help fellows adjust to American culture, promote multicultural friendships, and maintain and strengthen connections to their home countries. The *NIH Catalyst* interviewed VFC co-chairs **Vrushali Agashe** and **Zeni Wu**. Their responses have been lightly edited and condensed.

Vrushali Agashe, who is from India, has been at NIH since 2018. She is a postdoctoral fellow in the Clinical and Translational Immunology Unit in the National Eye Institute. She earned a B.S and M.S. in microbiology from the University of Mumbai (Mumbai, India); and an M.S. in biomedical sciences and a Ph.D. in comparative biomedical sciences from the University of Wisconsin at Madison (Madison, Wisconsin). When she's not working, she enjoys baking and exploring the Washington, D.C., metropolitan area with its abundance of hiking trails, museums, and excellent restaurants.

Zeni Wu, who is from China, has been at NIH since 2019. She is a postdoctoral fellow in the Metabolic Epidemiology Branch in the National Cancer Institute's Division of Cancer Epidemiology and Genetics. She earned an M.D. degree from Wuhan University (Wuhan, China) and M.P.H. and Ph.D. degrees in epidemiology from the National Cancer Center, Cancer Hospital, at the Chinese Academy of Medical Sciences and Peking Union Medical College (Beijing, China). Outside of work, she enjoys traveling, hiking, and playing basketball and musical instruments.



Zeni Wu (National Cancer Institute)

Vrushali Agashe (National Eye Institute)

Why did you choose to come to NIH?

VA: I met a couple of NIH postdocs during graduate school—one at a graduate student-organized networking event and the other at a university poster session. They convinced me to come to the NIH for my postdoc. Also, the incredible research and clinical facilities at the NIH are unparalleled.

ZW: During my Ph.D. training, I read great papers published by NIH scientists and enjoyed the lectures by them (when they visited, at international conferences, or in online courses). I think becoming a fellow at the NIH is a great opportunity.

Why did you decide to run for co-chair of the VFC?

VA: I had the pleasure of seeing some of the VFC events firsthand. On a personal level I also felt that this was a group that I shared a lot in common with. Additionally, I was aiming to develop soft skills (such as learning how to build a team) that scientists are generally not exposed to.

ZW: I think it's a great opportunity to meet fellows and work with them. In addition to doing my research, I have also learned how to organize events and coordinate with different people. This is an experience that is different from working with a mentor or collaborators.

What do you enjoy about being part of the VFC?

VA: It gives me something to do in addition to research. It also pushes me out of my comfort zone, something that I believe helps you grow and learn.

ZW: Making friends from all around the world and sharing experiences of different countries.

What are some challenges that visiting fellows faced during the COVID-19 pandemic?

VA: The biggest challenge was being unable to see family back home.

Also, many visiting fellows who live alone felt isolated. I know I did. Living in a 500-square foot studio apartment with no human interaction can be challenging, especially when your closest family might be several thousand miles away.

ZW: During the pandemic, several travel bans have been implemented, so uncertainty around going back home to visit family is a major concern for many visiting fellows. Also, since embassies of some countries are closed, or only have limited appointments, visiting fellows find it difficult to deal with visa-related concerns.

How has the VFC adapted to the COVID-19 pandemic and restrictions on gatherings?

VA: The transition from in-person to virtual events was certainly not easy. Credit goes to each and every member of the VFC who jumped in with their expertise and helped out with virtual events. Although limited in what we could do, the pandemic has opened doors. For example, everyone can attend virtual events and we now have representatives at several NIH campuses including in Baltimore; Research Triangle Park, North Carolina; and Fredrick, Maryland. In the future, we would like to continue to hold virtual events alongside in-person events.

ZW: We continue to organize activities under the physical-distancing guidelines. We have social-networking events and International Movie Nights via Zoom to have fun together. We also organize Science Voices from Home and Brown Bag Seminars. Both types of events provide useful information for fellows' career development. Most recently, we organized a virtual Division of International Services/VFC symposium to provide the most recent information on travel restrictions and J-1 and J-2 visa-related issues.

What do you miss from home?

VA: Apart from my family and friends, the food for sure.

ZW: Friends and food.

What is your favorite American thing you can't get at home?

VA: The individualistic nature of American society. Coming from a culture where the good of the society and family is put before one's individual desires, this is a welcome change.

ZW: I enjoy the diversity of the American culture and the way people respect different cultures and beliefs.

What aspect of American culture surprised you or was difficult to adjust to?

VA: When I came to the United States in 2010 for my Master of Science degree, I received a lower grade than expected in my first semester because I did not speak up in class. The concept that you needed to speak up, and that your grade depended on it, was very new to me.

ZW: One example is the health care system. In China, the hospital is usually available for walk-ins and to register to see any specialist on the same day. In the United States, you have to see a primary-care physician first and get a referral to a specialist. I didn't get used to this for my first six months here.

Do you have any advice for American fellows to help visiting fellows adjust to American culture?

VA: Invite them out for coffee or food or to your Thanksgiving or Christmas dinners. It is also helpful to acknowledge or ask about traditions that are happening in their home country, such as Chinese New Year or Diwali (in India). Remember, food is the biggest commonality—everybody eats.

ZW: American fellows are very nice and always willing to help. They are welcome to attend VFC events and can even become VFC members. It's a great way to interact with visiting fellows. ●

To learn more about the VFC go to https://www.training.nih.gov/felcom/visitingfellows2.

To join the Visiting Fellows LISTSERV newsletter (and keep up to date with social events, the Brown Bag Series, Science Voices from Home, and the English Conversation Club) go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=VISITINGFELLOWS&A=1.

To maintain and enhance connections to home countries, the VFC also hosts country support groups. To find contacts go to https://www.training.nih.gov/country_support_groups.

Erica Wynne-Jones is an Australian visiting postdoctoral fellow in the National Institute of Allergy and Infectious Diseases. She is currently doing a detail in the Office of Intramural Training and Education, where she works on educational programming. She is the Outreach Liaison on the Fellows Committee and is writing for and coordinating fellows' contributions to the NIH Catalyst *Training Page.*

Connection

CONTINUED FROM PAGE 1

new paths of discovery, many of which are still being explored today.

Ullrich was a senior staff fellow in **Ettore Appella's** group in the Laboratory of Cell Biology at NCI. His lab focused on tumor immunology and was working on identifying antigens that could inhibit tumor growth in mice. In the process they discovered that mammals had two isoforms of the heat shock protein (HSP)—HSP90-alpha and HSP90-beta. Initially observed in the cells of fruit flies (*Drosophila melanogaster*) responding to heat-induced stress, HSP90 had never been identified in mammals before. It was just becoming clear that HSPs played key roles in cellular machinery and were synthesized in response to a variety of stressors beyond heat including infection and malignancy. While serving a protective and quality-control function in normal cells, HSPs also appeared to play a role in facilitating pathology, such as in tumor growth. To test exactly how HSP activity changed when faced with disease, scientists first needed a biological model: Appella's lab had cloned the first mammalian HSP90 to be used for answering questions about the newly discovered protein. And they had developed the antibodies and DNA probes used to detect it.

Meanwhile, Gopalan was already a pioneer in the field of breast-cancer research. Born in Chennai (also known as Madras), India, she came to the United States and earned her Ph.D in nutrition and endocrinology from the University of California at Berkeley (Berkeley, California) at age 25. Her talent as a researcher took her to universities around the world, building relationships along the way. She became a leader in the study of progesterone receptors in both normal tissues and breast cancer, and was intrigued by the role that HSPs might play in tumor development.

After the Keystone conference, Ullrich sensed the possibilities of a joint effort and invited her to partner with NIH. "She was a generous collaborator and positive person, a kindred spirit and down to earth," he recalled. "She had a great sense of humor and liked to laugh at life's absurdities."

CREDIT: LAWRENCE BERKELEY NATIONAL LABORATORY

Shyamala Gopalan Harris (left) in her lab at Lawrence Berkeley National Laboratory. © 2010-2019 The Regents of the University of California, Lawrence Berkeley National Lab.

Gopalan's group in Montreal began collaborating with Ullrich and the Appella lab in 1987, and they produced two publications with lasting impact. Using NCI's antibodies and DNA probes, they were the first to show that both isoforms of HSP90 were regulated by estradiol in mouse uterine tissue (HSP90-alpha showed a significantly stronger response). This inaugural study established an important link between hormone modulation and a protein that could potentially be augmenting tumor growth (*Mol Cell Biol* **9:**3567–3570, 1989).

Gopalan "exhibited a level of energy and enthusiasm for scientific research that was contagious," said **Stephen Moore**, who was a senior staff fellow in Appella's lab and a co-author of the first study. "She was always asking the next question."

The second publication followed five years later and yielded similar results. This time the researchers used human mammary tissue and found a positive correlation between estrogen-receptor stimulation and the increased expression of HSP90. Their finding would have important implications for the treatment of breast cancer (*Breast Cancer Res Treat* **26:**95–100, 1993).

The formal partnership ended in 1992, but Gopalan maintained her relationship with NIH as a peer reviewer for the Biochemical Endocrinology Study Section and would visit the Bethesda campus each year to reconnect with colleagues. Gopalan eventually left Canada and returned to California to continue her work on the role of hormone receptors in breast-cancer development at Lawrence Berkeley National Laboratory (Berkeley, California). She was awarded several NIH grants supporting her research through 2001, and her lab published their findings in 2006 (*Cancer Res* **66:**10391–10398, 2006).

CREDIT: CHIA CHI "CHARLIE" CHANG, OD

Vice President Kamala Harris visited NIH on January 26 for the first time since taking office to receive her second dose of the Moderna COVID-19 vaccine—the first was administered in southeast Washington, D.C., on December 29, 2020. She remarked how "NIH was such a huge part of my youth" because her mother, who was a breast-cancer researcher, was funded by NIH and collaborated with NIH scientists. Judy Chan, a nurse practitioner in NIH's Occupational Medical Services, administered the vaccine.

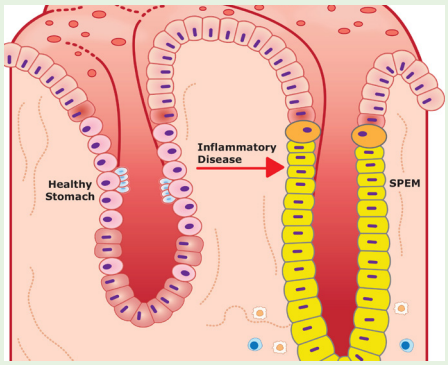
"What we started had real significance and promise," said Appella. The discovery that arose from his NCI lab over 30 years ago has branched out to influence our understanding of immunology in unexpected ways. Recent research has further defined the role of HSPs as molecular chaperones, coordinating the function of a wide range of proteins. HSPs can act as stabilizers not only for normal cells but for cancer, neurodegenerative diseases, and even viral and bacterial infections. Additional studies have shown that partial inhibition of HSP90 function may have profound antitumor effects and can even inhibit the replication of coronaviruses such as SARS-CoV-2, which causes COVID-19.

Successful women often wear more than one hat. Gopalan was simultaneously raising her two young daughters, Maya and Kamala, alongside a career rich in discovery and partnerships. "My first job was cleaning pipettes in my mother's lab," said Harris. "I grew up around science. [It was] taught to me by someone who was so profoundly passionate about a gift, which is what scientists give to us."

Gopalan died in 2009 after a battle with colon cancer, but her personal and professional legacy is clear. "I should not be surprised at the accomplishments of her daughter," said Ullrich. "It's comforting to know that some of [Shyamala Gopalan's] beautiful spirit lives on in her. The NIH community should be reassured knowing that Shyamala's daughter understands the important role of biomedical research for advancing our understanding of human disease." ●

Michael Tabasko is a science writer-editor for the NIH Catalyst.

Intramural Research Briefs



CREDIT: N IEHS

NIEHS: Glucocorticoids and androgens promote a healthy stomach pit (glands embedded in the stomach lining) by inhibiting inflammation, left, while their absence promotes inflammation and SPEM seen in a diseased pit, right. SPEM glands are also much larger than healthy stomach glands.

NIEHS: MALE HORMONES MODULATE GASTRIC INFLAMMATION IN MICE

NIEHS scientists reported that androgens, or male sex hormones, play a critical role in regulating gastric inflammation. Chronic gastric inflammation can lead to a precancerous condition in the stomach called spasmolytic polypeptide-expressing metaplasia (SPEM). Women suffer more frequently than men from inflammatory diseases, and this study sheds new light on the action of androgens as an inflammatory mediator.

Researchers first removed the adrenal glands (which secrete anti-inflammatory glucocorticoids) from both male and female mice. The removal resulted in spontaneous gastric inflammation and SPEM in females but not males. However, removal of both glucocorticoids and androgens abolished the male protective effects, triggering stomach inflammation equally in all mice. Treatment of female mice with androgens prevented gastric inflammation and SPEM and even reversed the pathology after the onset of the disease.

"The study showed that glucocorticoids and androgens act like brake pedals on the immune system and are essential for regulating stomach inflammation," said lead author **Jonathan Busada**. (NIH authors: J.T. Busada, K.N. Peterson, X. Xu, R.H. Oakley, D.N. Cook, and J.A. Cidlowski, *Gastroenterology* 2021)

[BY SATABDI NANDI, NIA]

NCATS: SMALL-MOLECULE COCKTAIL PROTECTS STEM CELLS FROM STRESS

NCATS researchers found that a combination of four drugs and compounds can protect induced pluripotent stem cells (iPSCs) from stresses commonly encountered when the cells are used in a laboratory setting. Stem cells are sensitive and can be easily damaged during the research process, posing a challenge to scientists.

A team of investigators led by **Ilyas Singeç** created a small-molecule cocktail, which they named CEPT, that greatly improves iPSC survival. The new cocktail proved useful for several common iPSC research tasks. For example, cells can be damaged when they are frozen for transport and later thawed for clinical use. Treatment with CEPT resulted in significantly better cell-survival outcomes than existing protocols during this cryopreservation process. The authors noted potential applications for this discovery across many biomedical fields including regenerative medicine and drug development. (NIH authors: Y. Chen, C.A. Tristan, L. Chen, V.M. Jovanovic, C. Malley, P. Chu, S. Ryu, T. Deng, P. Ormanoglu, D. Tao, Y. Fang, J. Slamecka, H. Hong, C.A. LeClair, S. Michael, C.P. Austin, A. Simeonov, and I. Singeç, *Nat Methods* **18**:528–541, 2021)

[BY HENRY DIECKHAUS, NINDS]

NIAAA: NEURAL CIRCUIT COMPETES TO INFLUENCE THE PERSISTENCE OF TRAUMATIC MEMORIES

NIH scientists and international colleagues have characterized key brain areas involved in the formation and loss of traumatic memories. When a person experiences trauma, their brain undergoes a process called persistence in which negative feelings become linked to cues and continue to provoke fearful behavior. Over time, exposure to trauma-associated cues without any adverse consequence leads to extinction (harmful association is forgotten).

The amygdala, the emotional processing region of the brain, is surrounded by distinct clusters of neurons called intercalated cells (ITCs). The researchers used in vivo calcium imaging to measure the activity of these clusters in mice during the simultaneous presentation of a mildly painful shock and a harmless auditory cue. The investigators then removed the painful stimuli and observed brain activity when the auditory cue was presented alone, such as occurs during extinction. The ITCs directly competed with each other for influence in a process called mutual synaptic inhibition, in which each distinct cluster could dial up—or down—the fear state. Furthermore, the study showed that this neural circuit linked the amygdala to other fear-regulating regions in the midbrain and prefrontal cortex.

According to lead researcher **Andrew Holmes**, studies targeting these brain areas could help identify patients at higher risk for conditions such as post-traumatic stress disorder and could provide insight into treatments for the persistence of traumatic memories. (NIH authors: O. Bukalo, A. Limoges, T. Rigg, T. Campbell, A. Mendez, C. Weinholtz, and A. Holmes, *Nature* **594**:403–407, 2021)

[BY ADAM LAZERE, NEI]

NIAID: SALMONELLA EXPLOITS INTESTINAL CELL DEFENSE TO AID GUT COLONIZATION

NIAID scientists have found that the immune response aimed at removing Salmonella bacteria from the gastrointestinal tract could instead be helping bacteria colonize the gut.

A common cause of gastroenteritis, Salmonella bacteria invade intestinal epithelial cells (IECs) and form a vacuole. The bacteria can either remain within the vacuole or escape into cytosol (cell fluid). Cytosolic bacteria trigger the IECs to expel the infected cell from the host in a protective response. However, previous studies have shown cytosolic Salmonella not only replicates rapidly, but also features adaptations that aides its invasion into new cells. This discovery led the scientists to question whether the bacteria were exploiting the host's defense strategy.

To test this hypothesis, the investigators genetically modified the bacteria to self-destruct when exposed to the IEC cytosol. Indeed, the mice infected with the self-destructing version showed reduced bacterial colonization and fecal shedding. (NIH authors: A. Chong, K.G. Cooper, L. Kari, O.R. Nilsson, C. Hillman, B.A. Fleming, Q. Wang, V. Nair, and O. Steele-Mortimer, *Cell Host Microbe* 2021)

[BY LEANNE LOW, NIAID]

NIDDK, NCI: KEY PROTEIN IMPROVES GLUCOSE HOMEOSTASIS IN TYPE 2 DIABETES

Type 2 diabetes (T2D) is caused by pancreatic beta cells that do not produce enough insulin; and peripheral tissues such as fat, liver, or skeletal muscle that do not properly respond to circulating insulin. Insulin resistance is known to occur in individuals with obesity and usually triggers an increase in beta-cell mass that can delay or prevent the development of T2D.

NIH scientists identified the beta-arrestin-1 protein (Barr1) as essential to proper functioning of pancreatic beta cells. The team inactivated the gene that codes for Barr1 in mice. These knockout mice were fed a high-fat diet to induce obesity. Compared with their control littermates, the knockouts exhibited a significant increase in blood-glucose concentration and reduction in insulin in both fed and fasting conditions.

Barr1 appears to promote the expression of a transcription factor that plays a key role in pancreatic development and the expansion of beta-cell mass—a finding the authors also confirmed in human beta-cell lines. "The results of this study support strategies to enhance Barr1 activity in beta cells as a therapeutic option for restoring glucose homeostasis and preventing T2D," said co-author **Jürgen Wess**. (NIH authors: L.F. Barella, M. Rossi, S.P. Pydi, J. Meister, S. Jain, Y. Cui, O. Gavrilova, G. Fulgenzi, L. Tessarollo, and J. Wess, *Nat Commun* **12**:Article number 3385, 2021)

[BY CHARLESICE GRABLE-HAWKINS]

NINDS, NICHD: GENETIC FORM OF CHILDHOOD ALS DISCOVERED

A team of researchers led by scientists at NIH and the Uniformed Services University (Bethesda, Maryland) have identified a gene responsible for a rare form of amyotrophic lateral sclerosis (ALS) in children.

The authors studied 11 children from around the globe with undiagnosed ALS-like symptoms, such as severely weakened or paralyzed muscles. Compared with sporadic adult ALS, the children's symptoms progressed more slowly but began as early as four years of age. The researchers analyzed the patients' DNA and found that they each had a mutation (either inherited or spontaneous) in *SPLTC1*, a gene associated with producing a class of fats called sphingolipids. Previously reported mutations in *SPLTC1* prompt the enzyme serine palmitoyltransferase (SPT) to overproduce toxic versions of these fats, causing hereditary sensory and autonomic neuropathy type1.

In the children, however, the mutation appeared to result in elevated plasma concentrations of normal sphingolipids caused by unchecked SPT activity. The investigators showed that the *SPLTC1* variant prevented the protein ORMDL from inhibiting SPT.

The scientists recognized a potential for treatment and created small interfering strands of RNA to target the *SPLTC1* mutation in vitro. Using the patient's skin cells, they tested the interfering RNAs and found they were effective in decreasing expression of the problematic gene and that sphingolipid synthesis returned to normal rates. The ultimate goal is to translate these ideas into effective treatments for patients who currently have no therapeutic options. (NIH authors: P. Mohassel, S. Donkervoort, M. Nalls, A.R. Foley, Y. Hu, C. Grunseich, A.R. Nickolls, N. Pourshafie, S.B. Neuhaus, D. Saade, Z. Piccus, C.E. LePichon, and C.G. Bönnemann, *Nat Med* 2021; DOI:10.1038/s41591-021-01346-1)

[BY EIMEAR HOLTON, NIAID]

CREDIT: NINDS

NINDS, NICHD: NIH researchers discovered a new form of ALS that begins in childhood and linked the disease to a gene called SPLTC1. As part of the study, NIH senior scientist Carsten Bönnemann (right) examined a young patient from the Apulia region of Italy.

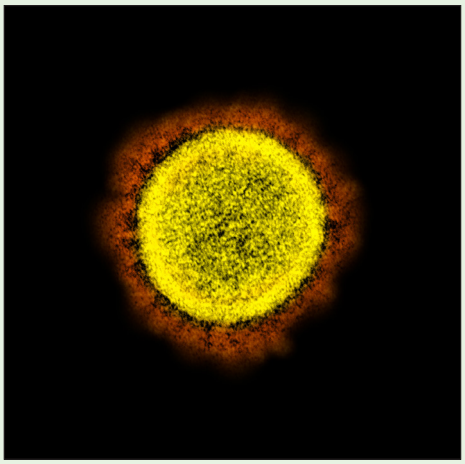
NIDDK, NHLBI: CLUES TO THE EFFICACY OF AN HBV TREATMENT

NIH scientists set out to learn why many people with chronic hepatitis B virus (HBV) do not respond to current treatment with pegylated interferon alpha (PEG-IFN-a). In a pilot study, the researchers studied blood samples and liver biopsies isolated from 13 people with chronic HBV infection before, during, and after treatment with PEG-IFN-a. They found that people responded better to the treatment when their body's natural killer cells (immune system cells that control viral infections) were activated. The researchers also found that people who developed more antibodies against PEG had less of a response, because these antibodies removed PEG-IFN-a from the blood. These findings may improve the efficacy of HBV treatment and may be applicable to similar drugs now being developed for other chronic diseases and cancer. (NIH authors: A. Nishio, F.J. Bolte, K. Takeda, N. Park, Z.-X. Yu, H. Park, K. Valdez, M.G. Ghany, and B. Rehermann, *Sci Transl Med* **13**:Issue 587, eaba6322, 2021)

[BY KATIE CLARK, NIDDK]

Read longer versions of these briefs at: https://irp.nih.gov/catalyst/v29i4/research-briefs.

COVID-19 Timeline at NIH (May–June 2021)



CREDIT: NIAID

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

May 3: A study led by NHLBI, NIDDK, NIAID, and NCI finds a proinflammatory immune pathway that affects the lungs of patients with severe COVID-19. Researchers used lab and computer models to test treatments that could help patients with severe lung infections recover faster. (*Sci Immunol* **6**:issue 58, eabg0833, 2021)

May 7: In an all-staff email, NIH Director **Francis Collins** reports that a pilot study has been launched at NIAID's Rocky Mountain Labs (Hamilton, Montana) that will detail the process for slowly increasing the density of scientific and technical staff in the labs.

May 10: The FDA expands its emergency-use authorization for the Pfizer COVID-19 vaccine to include adolescents 12–15 years of age.

May 10: The NIH Clinical Center updates its visitor policy, which had restricted during the COVID pandemic, to allow visitors for patients.

May 11: NIAID Director **Anthony Fauci** and CDC Director Rochelle Walensky testify before the Senate Health, Education, Labor, and Pensions Committee on efforts to combat COVID-19.

May 12: Outdoor dining returns to campus. Eurest Dining Services will prepare a rotating, themed barbecue for lunch every other Wednesday on the south lawn of Building 10.

May 13: The CDC updates its mask guidance: Except where locally required, fully vaccinated people can resume activities outdoors and indoors without wearing a mask or physically distancing. In an NIH-wide email later this week, **Francis Collins** asks for staff to be patient and continue to wear a mask at work as the new guidance does not yet apply to health care settings such as NIH premises.

May 13: The Trans-NIH Mental Health Response Team launches a new "How I Cope with Stress" campaign. Employees are encouraged to support one another by sharing how they cope with stress on social media using the hashtag: #NIHCopeWithStress.

May 14: In his email to all staff, **Francis Collins** recognizes the ongoing efforts of The Trans-NIH Mental Health Response Team for Mental Health Awareness Month and shares additional mental-health resources.

May 17: Eight U.S. Senators (many are members of the Appropriations Committee) and their staff tour the Vaccine Research Center to learn about the rapid development of safe and effective COVID-19 mRNA vaccines. Senators are also briefed on the RADx pipeline of new COVID-19 testing technologies and about emerging research on the impact of the COVID-19 pandemic on mental health.

May 19: In an all-staff email, **Francis Collins** updates mask guidance to allow unmasking in outdoor spaces where physical distancing is possible. Outdoor gatherings will continue to be limited to 50 people. Staff vaccination rate stands at 65% and masks will continue to be required inside all NIH buildings, except in rooms occupied by one person.

May 21: In his all-staff email, **Francis Collins** announces NIH is joining HHS sibling agencies and the White House in a digital day of action to distribute vaccine information and resources across all digital platforms, as part of the "We Can Do This" campaign.

May 25: **Francis Collins** testifies virtually before the U.S. House of Representatives Labor-Health and Human Services Subcommittee hearing on the Fiscal Year 2022 NIH Budget, and discusses a range of topics, including COVID-19, health disparities, and substance abuse.

May 26: Alongside several NIH institute directors, **Francis Collins** testifies in-person before the U.S. Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies at a hearing titled "National Institutes of Health's FY22 Budget and the State of Medical Research." A wide range of topics are discussed about the funding needed to advance biomedical research at NIH, including efforts to end the current COVID-19 pandemic.

May 28: **Francis Collins** sends his 85th pandemic-related email to staff. He announces the application process for Group C federal employees and trainees to return to the physical workspace will be reinitiated (it was paused October 2020).

June 1: A study led by NHLBI and NIAID finds that SARS-CoV-2, the virus that causes COVID-19, does not appear to pose a threat to the safety of the nation's blood supply. (*Transfusion* 2021; DOI:10.1111/trf.16511)

June 1: NIAID initiates a clinical trial in which adult volunteers who have been fully vaccinated against COVID-19 will receive booster doses of different COVID-19 vaccines to determine the safety and effectiveness of mixed booster regimens.

June 1: **Francis Collins** announces that two NIH-supported studies found that that COVID-19 mRNA vaccines are safe and effective for pregnant women with the potential to benefit both mother and baby. (*JAMA* **325**:2370–2380, 2021; *Obstet Gynecol* 2021)

June 2: The Employee Asymptomatic Testing Clinic on the 5th floor of the Clinical Center will no longer be open on Wednesdays.

June 3: An NICHD-led study finds that the experimental drug TEMPOL may be a promising oral antiviral treatment for COVID-19. TEMPOL can limit SARS-CoV-2 infection by impairing the activity of a viral enzyme called RNA replicase.(*Science* eabi5224, 2021)

June 3: An NIH Director's Blog post reports that NIH-funded researchers have discovered a way to detect where COVID-19 hotspots are emerging. (*Science*, eabh0635, 2021)

June 8: In his Director's Blog, **Francis Collins** announces that new NIH-supported studies found that some people can develop diabetes after an acute COVID-19 infection. (*Cell Metab* S1550-4131(21)00232-1, 2021; *Cell Metab* S1550-4131(21)00230-8, 2021)

June 11: In an all-staff email, **Francis Collins** announces that more than 80.4% of NIH staff have received at least one dose of the COVID-19 vaccine. He also explains that the vaccine clinic will be reducing its hours (see below). He gives special thanks to staff who screened people entering the Clinical Center and who ran the asymptomatic testing clinic.

June 14: NIH's Occupational Medical Health Service, which has been operating a daily COVID-19 vaccine clinic in the Clinical Center's B-1 cafeteria, will offer vaccines once a week, on Thursdays, through August.

June 14: A phase 3 clinical trial shows that the investigational vaccine NVX-CoV2373 by Novavax, Inc. (Gaithersburg, Maryland) demonstrated 90.4% efficacy in preventing symptomatic COVID-19 disease.

June 15: Pre-procedure testing guidelines for asymptomatic NIH patients without known high-risk COVID-19 exposure are updated: Certain procedures will no longer require SARS-CoV-2 pre-procedure testing.

June 15: **Francis Collins** highlights a new NIH-supported study that found a specifically engineered antibody delivered by a nasal spray dramatically reduced the amount of SARS-CoV-2 in the lungs of mice. (*Nature* 2021; DOI:10.1038/s41586-021-03673-2)

June 15: An NIH-led study finds evidence of SARS-CoV-2 infections in five states as early as December 2019, weeks prior to the first known cases. (*Clin Infects Dis* ciab519, 2021)

June 15: The day-long "NIH Summit on Anti-SARS-CoV-2 Antibodies for Treatment and Prevention of COVID-19: Lessons Learned and Remaining Questions" begins with opening remarks from NIH Director **Francis Collins**, Acting FDA Commissioner Janet Woodcock, and NIAID Director **Anthony Fauci**. The event features presentations on the current state of the science and sessions addressing the design, development, and real-world use of anti-SARS-CoV-2 antibodies.

June 17: The Biden Administration announces it will invest more than $3 billion to accelerate the discovery, development, and manufacturing of antiviral medicines as part of a strategy to develop the next generation of COVID-19 treatments.

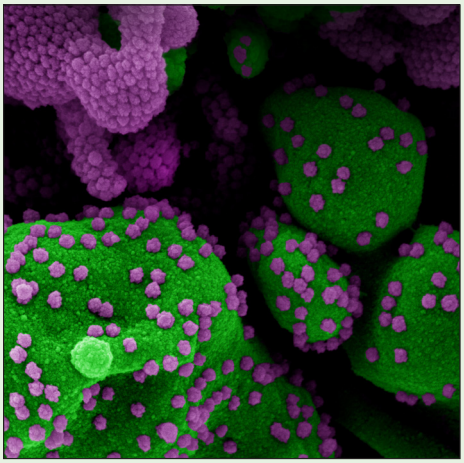
June 21: In an all-staff email, NIH Principal Deputy Director **Lawrence Tabak** announces that Group C federal employees, fellows, and trainees may now apply to voluntarily return to the physical workspace.

June 22: In his blog, **Francis Collins** explains how a new NIH-supported study attempted to answer the question of how immunity generated from COVID-19 vaccines differs from an infection. The data indicate that people who've had and recovered from COVID-19 still stand to benefit from getting vaccinated. (*Sci Transl Med* eabi9915, 2021)

June 22: An NIH team of researchers report that the prevalence of COVID-19 in the United States during the spring and summer of 2020 exceeded the known number of cases and that there were nearly 17 million undiagnosed cases by mid-July. (*Sci Transl Med* eabh3826, 2021)

June 23: NIAID begins a new observational study called MOMI-VAX designed to measure the development and durability of antibodies against SARS-CoV-2, the virus that causes COVID-19, in people vaccinated during pregnancy or the first two postpartum months. Researchers also will assess vaccine safety and evaluate the transfer of vaccine-induced antibodies to infants across the placenta and through breast milk.

June 24: A NIDA-funded study finds that adolescent marijuana use and binge drinking did not significantly change during the COVID-19 pandemic despite record decreases in the s perceived availability of marijuana and alcohol. The findings, based on a survey of 12th graders in the United States, challenge the idea that reducing adolescent use of drugs can be achieved solely by limiting their supply. (*Drug Alcohol Depend* 2021; DOI:10.1016/j.drugalcdep.2021.108822.)



CREDIT: NIAID

Colorized scanning electron micrograph of an apoptotic cell (green) heavily infected with SARS-COV-2 virus particles (purple), isolated from a patient sample. Image at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland.

June 24: In his blog, **Francis Collins** announces that NIH-funded researchers have developed a new metric to more accurately detect where COVID-19 hotspots are emerging. (*Science* eabh0635, 2021)

June 29: An adjuvant developed with NIH funding has contributed to the success of the COVAXIN COVID-19 vaccine, which was developed and is manufactured in India.

June 30: The NIH Director's Blog continues to cover COVID-19 and the work being done by NIH and NIH-funded researchers. ●

Read a more detailed version of this timeline, complete with links, at https://irp.nih.gov/catalyst/v29i4/covid-19-timeline-at-nih-may-june-2021.

CARD

CONTINUED FROM PAGE 1

CREDIT: CHIA-CHI "CHARLIE" CHANG, OD

Andrew B. Singleton is the new director of the NIH Center for Alzheimer's Disease and Related Dementias.

At the helm of the center is CARD Director **Andrew Singleton**, an NIH Distinguished Investigator who has published 655 studies during his 20-year career in NIA's Intramural Research Program (IRP). "Our program aims to serve as a hub for neurodegenerative research, centered [on] the area of understanding biology and anchored in genetics," Singleton said. "We are an extremely mission-focused group where people can come in and work on a very focused topic related to AD/ADRD for a set period of time."

The effort couldn't come sooner. AD, the most common form of dementia, currently affects over five million Americans. As the baby boomer generation ages, that number is expected to escalate to 13.8 million by the year 2050, representing an enormous cost to those diagnosed with the disease, as well as to caregivers and society as a whole. The looming public-health crisis hasn't gone unnoticed, however, and a transformative federal investment has poured into the AD/ADRD space over the past six years. NIA alone has seen its funding more than triple since 2015 to accelerate research focused on ending the devastation caused by these diseases. Singleton emphasized that, rather than compete with existing extramural endeavors, CARD seeks to fill in the gaps. "We're a large foundational initiative," he said. We are "focused on finding the places where there are resource needs, things that need to be done that are not getting done in the extramural world."

One of CARD's first such projects is already moving forward—the Induced Pluripotent Stem Cell (iPSC) Neurodegenerative Disease Initiative (iNDI). Led by NINDS's **Michael E. Ward** and NIA's **Mark Cookson**, the project aims to build a better understanding of how genetic mutations lead to the brain-cell damage underlying Alzheimer disease and other dementias. The iNDI is engineering a standardized library of stem-cell lines for 154 genetic variants known to contribute to AD/ADRD. The massive undertaking is the largest iPSC genome-engineering project to date and will offer scientists an invaluable resource to test promising treatments at the genetic level. Engineering and distribution of these lines is expected to take one year. A second phase will molecularly characterize the lines—a three-and-a-half-year process that will reveal the key networks and pathways involved in these diseases.

CARD's new home is under construction, just south of Building 10 on the NIH Bethesda campus, and will open its doors in early 2022. The temporary 24,000 square-foot, one-level modular facility will include laboratories, conference rooms, and office spaces. A collaboration of talent will be the driving force behind the state-of-the-art facility. A small number of permanent CARD staff will support groups that have expertise in AD/ADRD fields. Joining them will be a revolving series of independent research scholars.

"These are newer, extremely promising postdocs," said Singleton. "We give them resources to run a small group...and chase things." Singleton noted that over half of

CREDIT: NIH

CARD's new home is under construction, just south of Building 10 on the NIH Bethesda campus, and will open its doors in early 2022. The temporary 24,000 square-foot, one-level modular facility will include laboratories, conference rooms, and office spaces. A collaboration of talent will be the driving force behind the state-of-the-art facility.

the staff will be visiting investigators (both intramural and extramural) who want to commit 6–12 months to come and work in CARD space on an AD/ADRD related project. "And we're opening the possibility of investigators within the IRP who have an interesting idea in the AD/ADRD space to run a project in CARD."

Smoothing the path to innovation by streamlining data access is a priority, and CARD will make several powerful bioinformatic tools available to the AD/ADRD research community. These data platforms organize and decipher vast amounts of neurodegenerative data and will be accessed through one useable, open-source portal—enabling investigators to accelerate projects and collaborate more efficiently with colleagues. Other public-data resources are planned, too. The center will use long-read sequencing to analyze the genome of a large number of people diagnosed with AD/ADRD as well as healthy individuals. Singleton hopes that the resulting library will serve as a reference that scientists can use to predict genetic variations in people who haven't been directly sequenced. "We're trying to do this across diseases...and in ancestrally diverse individuals."

The road from basic clinical science to breakthrough treatment can be long and costly and is often fraught with failure. By leaning on the stable funding and exceptional expertise at the IRP, CARD is uniquely positioned to translate promising AD/ADRD targets and projects into something that private industry partners are comfortable taking on—a process known as "de-risking." For example, **Richard Youle** (NINDS) will lead AutoTac, a project that involves eliminating pathological tau protein aggregates that are associated with AD by targeting them for autophagic removal (a waste-disposal mechanism naturally present in cells).

A Timeline of Notable AD/ADRD Milestones at NIH

- **1984:** NIA funds Alzheimer's Disease Research Centers at major medical institutions across the United States.
- **1991:** NIA sets up the Alzheimer's Disease Cooperative Study, a nationwide medical network to collaborate on the development of Alzheimer treatments and diagnostic tools.
- **2005:** NIA's Alzheimer's Disease Preclinical Drug Development program is established.
- **2008:** IRP research explains the mechanism behind prion self-propagation, which has broad significance in understanding several common human diseases that feature amyloids, including Alzheimer disease.
- **2012:** The International Alzheimer's Disease Research Portfolio is launched in collaboration with the Alzheimer's Association. The database enables funders of Alzheimer research to share and review funding data.
- **2012:** The first National Plan to Address Alzheimer's Disease is created, following passage of the National Alzheimer's Project Act in 2011. NIH leads the research effort targeted to preventing and treating the disease.
- **2013:** NIH generates first batch of genomic data on Alzheimer disease.
- **2013:** IRP researchers identify several genetic variants associated with the development of Alzheimer disease.
- **2015:** IRP investigators identify blood biomarkers that predict who will develop Alzheimer disease years before symptoms develop.
- **2015:** Aimed at speeding discovery, congressional legislation requires that NIH prepare a professional judgment budget to estimate the additional funding needed each year to help reach the ultimate research goal of the National Plan—to effectively treat and prevent Alzheimer disease and related dementias by 2025.
- **2020:** FDA approves the first tau biomarker as a diagnostic tool for Alzheimer disease.
- **2020:** NIA and NINDS announce the establishment of CARD, construction plan launch, and the appointment of Andrew Singleton as acting director.
- **2021:** In an article published in *Neuron*, NIH researchers outlined their plans for the iPSC Neurodegenerative Disease Initiative, which will test more than 100 genetic mutations linked to Alzheimer disease and related dementias. (*Neuron* **109**:1080–1083, 2021)
- **2021:** NIH announces that, effective April 13, Andrew Singleton is the director of CARD.
- **2021:** The FDA approves aducanumab to treat people with Alzheimer disease. While the NIH provided no direct support for the development of the drug, NIA's years of funding have been integral to this and other promising therapeutic approaches to treating Alzheimer disease.

For links to information on this timeline, go to https://irp.nih.gov/catalyst/v29i4/accelerating-an-end-to-dementia.

Eventually, Singleton has his sights on a precision-medicine approach using genetic-based therapeutics. "That's a space we'd really like to move toward," he said. We'd "first [be] targeting monogenetic forms of disease and then hopefully building our toolkit against genetically complex diseases."

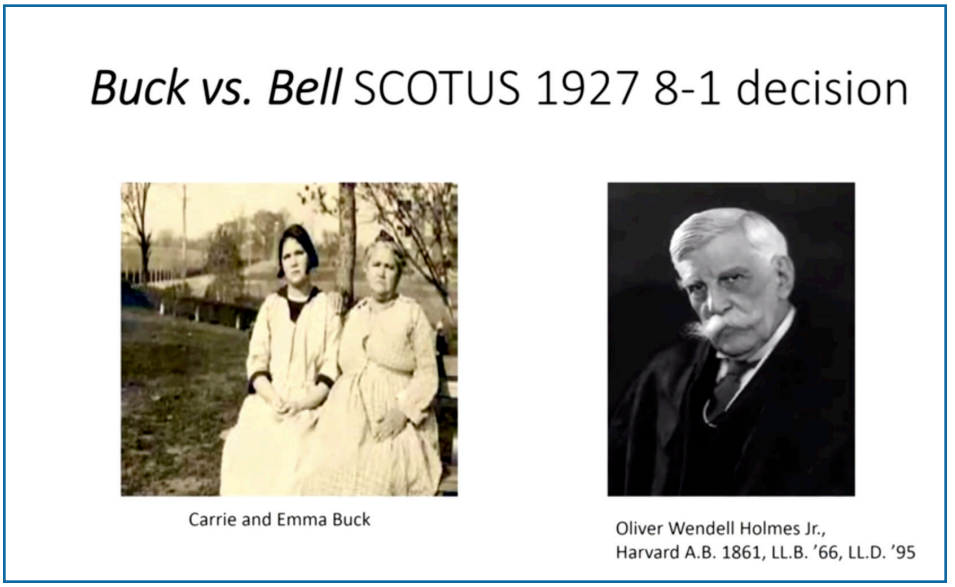
There is a palpable sense of hope on the horizon for an end to AD/ADRDs. "What makes me most excited is the unknown at the moment," said Singleton. "The new ideas that I don't know where they are going to come from or what they are going to focus on...and lastly and hopefully, trials—using the power of the Clinical Center and the resources we have here to do clinical trials in the AD/ADRD space." ●

To learn more about CARD, go to https://www.nia.nih.gov/research/card.

Unfit to Breed: America's Dark Tale of Eugenics

Former NIDDK Director Allen Spiegel Gives History of Medicine Lecture

BY MEGAN KALOMIRIS, NIAID



CREDIT: SCREENSHOT FROM ALLEN SPIEGEL'S PRESENTATION

Carrie Buck and her mother (left panel) were both labelled as "feebleminded," shorthand for unintelligent and undesirable. In the 1927 the Supreme Court case, Buck v. Bell, judges endorsed the surgical sterilization of Carrie Buck, who was pregnant due to rape at age 16. Officials at the institution where she was sent to keep the pregnancy secret wanted to sterilize her to prevent her from passing her perceived feeblemindedness to future generations. The landmark decision set a legal precedent for the roughly 60,000 other forced sterilizations that followed. (Right panel) Chief Justice Oliver Wendell Holmes Jr., who presided over the case.

In 1927, the Supreme Court determined Carrie Buck unfit to breed. Uneducated, poor, and pregnant due to rape at age 16, she was labelled "feebleminded," shorthand for unintelligent and undesirable. To hide her pregnancy, Buck was institutionalized at a colony for the feebleminded by her foster family. Officials at the colony wanted to sterilize her to prevent her from passing her perceived feeblemindedness to future generations. In the Supreme Court case, Buck v. Bell, judges endorsed her surgical sterilization as constitutional in an eight-to-one ruling. The landmark decision set a legal precedent for the roughly 60,000 other forced sterilizations that followed.

On April 22, 2021, **Allen Spiegel** gave a lecture at NIH on the unsettling history of the 20th century eugenics movement in America. Spiegel, who spent 33 years at NIH, is the former director of the National Institute of Diabetes and Digestive and Kidney Diseases (1999–2006) and was dean of the Albert Einstein College of Medicine in New York (2006–2018). He remains a faculty member at Albert Einstein, but stepping down as dean has afforded him more time to pursue personal interests, such as investigating the history of eugenics in America. The Office of NIH History invited Spiegel to share his knowledge on the subject as the first talk in the NIH "History of Medicine" lecture series.

Eugenics is broadly defined as the use of selective breeding to improve the human race. The main principle behind the early eugenics movement was the assumption that all human characteristics are borne of simple inheritance. Spiegel began his lecture with a comprehensive history of the movement. He explained that the idea of eugenics was largely developed and popularized in the late 1800s by Sir Francis Galton (a cousin of Charles Darwin), who applied the principles of natural selection to the human race. His ideas took root in America in the early 1900s and were championed by Harry Laughlin (a former teacher interested in animal breeding) and Charles Davenport (a prominent biologist). When Davenport was director of Cold Spring Harbor Laboratory (Cold Spring Harbor, New York), he founded the Eugenics Record Office (ERO), which became the epicenter of American eugenics; he recruited Laughlin to be ERO's superintendent and assistant director. Davenport examined family trees (pedigrees) in order to elucidate inheritance patterns for various observable traits. Some traits had a legitimate genetic source, such as Huntington disease and hemophilia. Others, Spiegel explained, did not. Davenport "collected pedigrees of families with pauperism...and my favorite, thalassophilia—love of the sea...as if [this was passed through simple inheritance]."

The assumption that all characteristics are genetically determined led to the widespread belief that desirable traits should be selected for. This was encouraged and celebrated through "fitter family" and "better baby" competitions, where judges rated families and children like people would rate livestock or pets at shows today. Additionally, the eugenics movement sought to eliminate undesirable traits in society—forcibly sterilizing people with unwanted characteristics to

prevent their contribution to the gene pool. Each state had their own criteria for which people should be sterilized including "the feebleminded," "moral degenerates," "mental defectives," and "habitual criminals." These criteria were vague and often biased against marginalized groups such as immigrants, people with disabilities, and the poor.

Acceptance of eugenics was prevalent in American society and academia in the early 1900s. For example, many Harvard faculty and graduates espoused these principles. Additionally, well-respected figures at the time such as the Rockefeller family, the Carnegie family, and U.S. President Woodrow Wilson showed vigorous support. In fact, these principles became so popular that Nazi Germany took notice, inspiring the Holocaust. A 1934 issue of *The New England Journal of Medicine* even addressed this fact, lauding Germany as "perhaps the most progressive nation in restricting fecundity among the unfit," and noting how "[the American people are probably] not ready for the adoption of the German plan."

The eugenics movement was rife with societal bias that defined which attributes made the best individual. And, in each country where eugenics was practiced, those biases colored a broad range of what was considered genetically ideal.

Spiegel illustrated the negative consequences of biases against groups deemed inferior, citing the example of Arno Motulsky, one of 900 Jewish people seeking to escape Nazi-occupied Europe aboard the ship the St. Louis. This ship was denied entry to the United States, according to Spiegel, because of restrictions on immigrant groups considered undesirable. Motulsky was later

CREDIT: ALBERT EINSTEIN COLLEGE OF MEDICINE

Former NIDDK Director Allen M. Spiegel, gave a lecture at NIH on the unsettling history of the 20th century eugenics movement in America..

able to emigrate to America and went on to an illustrious career as a pioneer in medical genetics. He is one of many remarkable individuals serving to demonstrate that no society practicing eugenics had accurately modeled the traits that characterize an ideal human, said Spiegel.

With the last forced sterilizations occurring in the 1960s, the eugenics movement is far from ancient history. At the end of his talk, Spiegel drew attention to advances in modern medicine that, if left unchecked, could conceivably cause a resurgence of these old ideas. Genetic testing already provides prospective parents with the opportunity to screen a fetus for genetic traits in utero, opening the potential to terminate offspring with traits unwanted by society.

On the horizon, genetic-editing technologies (such as the CRISPR/Cas9 method) might allow for modification of pre-implantation cells used for in vitro fertilization, or even the cells of an adult human. While these technologies hold extraordinary possibilities for treating illness and preventing suffering, they also have the potential to be used to enhance positive traits and delete those that are simply disliked by society.

Science continues to make giant leaps that improve how we treat disease. But history cautions us to temper our enthusiasm and consider the ramifications of using new knowledge. Spiegel concluded his lecture with some thoughts to keep in mind as modern medicine pushes forward: protecting society's marginalized groups; keeping a standard of bioethics and objectivity; and distinguishing between using technology to promote health versus using it to enhance desirable traits (and if we should even make those distinctions).

"I certainly don't have the answers to these questions," Spiegel said. "But I hope that [by] presenting this lecture to you...you will at least contemplate these [considerations] and...help us find a way forward." ●

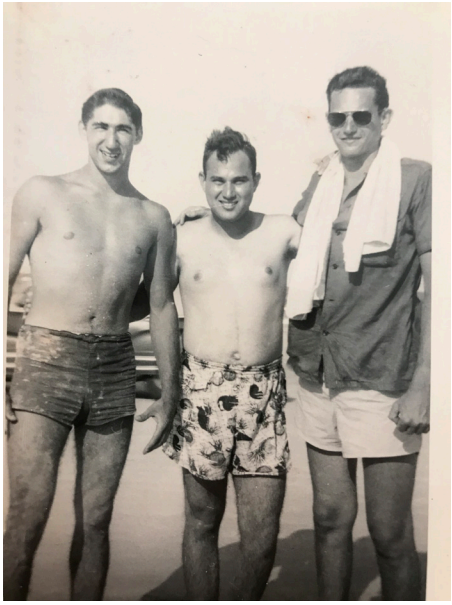
To view the videocast of the April 22, 2021, lecture, "A Brief History of Eugwenics in America: Implications for Medicine in the 21st Century," go to https://videocast.nih.gov/watch=41818.

Megan Kalomiris, a postbaccalaureate fellow in the Laboratory of Infectious Diseases in the National Institute of Allergy and Infectious Diseases, studies norovirus. After completing her NIH training in 2021, she will be attending the Science Communications Master's Program at the University of California at Santa Cruz (Santa Cruz, California).

Marshall Nirenberg's Old College Friend Visits NIH

Stories About Nirenberg Before He Became the Man the World Knew

BY JOSEPH PATRICK



CREDIT: DAVID ARONSON

In his college days, Marshall Nirenberg (right) enjoyed going to the beach with David Aronson (left) and other friends.

You would never believe how much meaning there can be behind catching a fly. For as long as I can remember I have had memories of my grandfather "Papa," David Aronson, catching flies with his bare hands, right out of the air, without ever harming the fly. My Papa worked with various animals throughout his 50+ years as a veterinarian in Pensacola, Florida, but he learned this trick from an unlikely source.

Papa went to the University of Florida (Gainesville, Florida) from 1948 to 1952, where he learned to catch flies with his roommate who was, at the time, studying caddisflies for his master's thesis in zoology. Who was this roommate? It was none other than **Marshall Nirenberg** (1927–2010), who later became an NIH scientist and a recipient of the 1968 Nobel Prize in Physiology or Medicine.

Marshall and my Papa met in 1948 and became roommates and fraternity brothers in Pi Lambda Phi in 1950 at the University of Florida. They were the only ones who stayed at the frat house during the summer so they "borrowed furniture" from the house to furnish an apartment and rented out rooms to pay for their tuition and fun money. They immediately formed a great bond—both had a keen interest in science, a love of the outdoors, and an affinity for having a good time.

For my entire life I have been fascinated by my Papa's stories about Marshall before he became the man the world knew. I never tired of hearing about Marshall and my Papa building a whiskey bar in the glove compartment of a sleek 1950 Dodge convertible, going to Daytona Beach to celebrate the 4th of July or, of course, catching hundreds of flies together. Marshall was also the person who introduced my grandfather to Sherlee Holmes on a blind date. She was a young, charismatic nursing student at a nursing school in Gainesville. Sherlee was good friends with Marshall, who was well known around the nursing school as a charmer. She went on to marry my grandfather and eventually became my grandmother.

Marshall and my Papa went their separate ways after college. My Papa was drafted into the Army and then went on to veterinary school at Auburn University (Auburn, Alabama). Marshall enrolled at the University of Michigan (Ann Arbor, Michigan) for his doctorate. They kept in occasional touch through the years and had the occasional meet-up including a 1980s visit to Washington, D.C., where Marshall, who had already gained a Nobel Prize and international fame, was still driving around in an old car with its bumper hanging off. He didn't drive it much though because he spent so much time in his NIH lab.

Despite having become world renown, Marshall was always keen on getting every last detail about my Papa's life whether it was stories about his family, news about his veterinary practice, or updates on the latest advancements in animal research and medicine. Marshall's curiosity about people was just as strong as his curiosity about science.

Although Marshall and Papa's friendship was relatively brief, my grandfather can still describe his memories of Marshall with such clarity and detail you would have guessed many of their escapades had happened last week. He always speaks of Marshall with fondness and admiration. Many of their stories played a big role in my own upbringing. I loved hearing them, reading articles by and about Marshall, and even writing school papers on him. It wasn't until college (at the University of Florida, where my three brothers and my parents also went), where my love of science started to blossom. I realized that all of my reading about Marshall had inadvertently given me quite the introduction to biology

CREDIT: DAVID ARONSON

Aronson (right) and a friend lean on Nirenberg's 1950 Dodge convertible. (Inside, the glove box has been converted into a whiskey bar.)

and genetics. Going into my junior year of college, I had the opportunity to intern at the NIH in a genetics lab within the National Institutes of Nursing Research.

In May 2019, **Tara Mowery** arranged for my mom (Judi Aronson Patrick), my grandfather, and me to visit NIH. Tara, who's chief of the National Library of Medicine's (NLM's) Visitor Operations, set up a VIP tour for us that included visiting the Nobel Laureate Wall in the NIH Visitor Center; going to NLM to view the profile video of Dr. Nirenberg, meet the NLM director, and look at Dr. Nirenberg's genetic-code chart in NLM's History of Medicine Department; having lunch with two NIH historians; visiting the Marshall Nirenberg exhibit in the Clinical Center (Building 10); and meeting a few of Marshall's colleagues. Everyone loved hearing my grandfather's stories, and he was thrilled to share them.

You never know how the people you meet will end up affecting your life and how the littlest of things and occurrences can have such everlasting meaning. ●

David Aronson, a retired veterinarian in Pensacola, turned 90 in January 2021. He practiced veterinary medicine for more than 50 years and received a Lifetime Achievement Award from the Florida Veterinary Medical Association in 2002. In addition to receiving many other awards, he served in leadership positions in several professional veterinary organizations.

Joseph Patrick is working as a data scientist for Booz Allen Hamilton's health-consulting office (Falls Church, Virginia) and pursuing his master's in biostatistics at George Mason University (Fairfax, Virginia). During college, he did an internship in a genetics lab within the National Institutes of Nursing Research.

CREDIT: JUDI PATRICK

CREDIT: TARA MOWERY

Aronson's VIP tour included a visit to the National Library of Medicine's (NLM's) History of Medicine Division and to the Marshall Nirenberg exhibit in Building 10. (Left) At NLM, Aronson is holding the leather case containing Nirenberg's Nobel Prize gold medal; a display case containing other Nirenberg memorabilia is behind him and so is a portrait Fielding Hudson Garrison (1870-1935) whose professional career was as a librarian, bibliographer, and medical historian at the Army Medical Library (later the National Library of Medicine). (Right) Reunited: Aronson pauses to admire the Nirenberg exhibit in Building 10.

CREDIT: LAURA S. CARTER

David Aronson and his family got to meet Alessandra Rovescalli, a scientist who trained in Nirenberg's lab and remained there for 12 more years. From left: Joseph Patrick, David Aronson, Alessandra Rovescalli, and Judi Patrick.

Lisa L. Cunningham Named NIDCD Scientific Director

Exploring Hearing Loss

BY NIDCD COMMUNICATIONS AND LAURA S. CARTER

Lisa Cunningham, Ph.D., is the new NIDCD Scientific Director.

The National Institute on Deafness and Other Communication Disorders (NIDCD), has named **Lisa L. Cunningham** scientific director and director of the Division of Intramural Research. She assumed her new position on April 11, 2021, and will oversee the NIDCD intramural research programs, which have roughly 165 employees working in 13 labs.

She is passionate about science," said NIDCD Director **Debara L. Tucci**. "Her extensive experience in basic, translational, and clinical research will be critical to advancing our shared vision of propelling new discoveries to the clinic and reducing the disease burden in our mission areas."

Cunningham has been in NIDCD's intramural program since 2011, becoming chief of the Section on Sensory Biology in 2014. The intramural program focuses on research on human communication disorders, with a primary interest in hearing and balance. The division's scientists have made great strides in deepening our understanding of inner-ear development and function, as well as how genetic variations and factors such as ototoxic drug exposure affect hearing and balance.

"The Division of Intramural Research has truly outstanding scientists, and the intellectually rich and collaborative culture of the division has positioned us to make important discoveries and to generate resources that will benefit the entire field," said Cunningham. "I am looking forward to building on the existing high quality of scientific research by recruiting a diverse faculty of researchers and facilitating the development of innovative therapies."

Cunningham originally trained as a clinical audiologist, having received her B.A. and M.A. in audiology from the University of Tennessee-Knoxville (Knoxville, Tennessee) and completed a clinical fellowship in audiology at Indiana University Medical Center (Indianapolis). Although she had initially planned for a career as a clinician, an auditory study she conducted as a Master's student, with her classmates serving as research subjects, abruptly changed her path. "We had created a tiny piece of new knowledge, and I was hooked," said Cunningham. "I knew then that research was what I wanted to do for the rest of my life."

She went on to receive a Ph.D. in neuroscience from the University of Virginia (Charlottesville, Virginia) and completed a postdoctoral fellowship at the University of Washington (Seattle). In 2004, she joined the faculty at the Medical University of South Carolina (Charleston, South Carolina) as an assistant professor. Her lab at MUSC conducted studies on heat shock protein (HSP)-mediated protection against ototoxic drug-induced hearing loss and the death of sensory hair cells (inner-ear cells that are fundamental to hearing and balance functions.)

Since coming to NIH in 2011, Cunningham has continued her work exploring the cellular and molecular mechanisms that underlie the survival or death of hair cells. An area of particular focus is hearing loss caused by medications, such as certain antibiotics or cancer drugs.

She and her team recently found evidence suggesting that the cholesterol-lowering drug atorvastatin can reduce hearing loss in patients undergoing cancer chemotherapy with cisplatin, which is toxic to hair cells and causes hearing loss in about 50% of treated patients. The data suggest that the concurrent use of atorvastatin during cisplatin-based chemotherapy does not affect the therapeutic efficacy of cisplatin. (*J Clin Invest* 131:e142616, 2021). Her team is pursuing this finding through a phase 3 trial, the first interventional trial for hearing loss to be conducted within the division.

Among Cunningham's numerous honors and awards are two NIDCD Director's Awards and an NIH Bench-to-Bedside Award. She has also been recognized for her commitment to mentoring, having received an NIH Graduate Partnerships Program Outstanding Mentor Award.

As academic dean of the NIH Oxford-Cambridge Scholars Program, Cunningham has helped to advance NIH on the world stage and to launch the biomedical research careers of a group of talented graduate students. She also serves as an elected member of the Council of the Association for Research in Otolaryngology, where she has worked on diversity programming and cultural awareness with the goal of ensuring that the field as a whole is inclusive, diverse, and welcoming. ●

Congressional Visit

Eight U.S. Senators Visit NIH in May

FROM THE *NIH RECORD*

A BIPARTISAN CONTINGENT OF United States senators and staff members visited NIH on May 17, 2021, for science briefings, a lab tour, and biotech demonstration. The group included U.S. Senators Tammy Baldwin (D-Wisconsin), Roy Blunt (R-Missouri), John Boozman (R-Arkansas), John Cornyn (R-Texas), Dick Durbin (D-Illinois), Roger Marshall (R-Kansas), Lisa Murkowski (R-Alaska), and Chris Van Hollen (D-Maryland). Many are members of the appropriations committee.

NIH director **Francis Collins** and National Institute of Allergy and Infectious Diseases Director **Anthony Fauci** welcomed the group at the Vaccine Research Center (VRC). A tour of a VRC lab, a demonstration of Rapid Acceleration of Diagnostics (RADx) technology, a briefing on mental health amid the pandemic, and a discussion of the potential "Advanced Research Projects Agency–Health" (ARPA-H) were packed into the afternoon. Senators and staff members were separated into two groups to facilitate occupancy in small spaces.

For the lab tour, VRC Director **John Mascola**, VRC Deputy Director **Richard Koup**, who is also chief of the Immunology Laboratory, and **Nancy Sullivan**, chief of the biodefense research section, joined in a discussion about vaccine development.

In a tent erected not far from the VRC, National Institute of Biomedical Imaging and Bioengineering Director **Bruce Tromberg** provided an overview of RADx and walked the delegation through several technologies including COVID-19 at-home tests, point-of-care tests, and lab tests. He highlighted efforts developed via RADx over the past year and showed a large sampling of new tests and products from 32 different companies. Each senator and staffer received a box of two at-home tests they could take with them.

CREDIT: CHIA CHI "CHARLIE" CHANG, OD

Vaccine Research Center (VRC) Director John Mascola (right) describes research on the Senators' tour of a VRC lab.

In a large conference room in the Porter Neuroscience Research Center (Building 35), National Institute of Mental Health Director **Josh Gordon** and Deputy Clinical Director **Joyce Chung** discussed mental health and COVID-19. Gordon provided an overview, with Chung presenting on intramural research efforts, collaborations, and preliminary findings on the impact of the pandemic on mental health.

Collins briefly discussed ARPA-H, a potential new health-research component devoted to scientific breakthroughs that would be housed within NIH. President Joe Biden proposed creating ARPA-H in a recent speech to Congress. Collins also talked about what the senators would see during their visit, which included several presentations on NIH's multifaceted response to the COVID-19 pandemic.

Afterward, on social media, Senator Blunt posted a message: "Thank you to National Institutes of Health (NIH) Director Dr. Francis Collins [and] researchers for giving us a terrific tour [and] presentation of their latest work to save lives. Because of medical researchers' ingenuity [and] drive, we are on the edge of finishing the fight against Covid [and] on a faster timeline than we thought possible a year ago." ●

This article was adapted from one that appeared in the June 11, 2021, issue of the *NIH Record*: https://nihrecord.nih.gov/2021/06/11/cadre-senators-visit-nih-take-home-tech.

Recently Tenured

ANIRBAN BANERJEE, NICHD

PHILIP CASTLE, NCI-DCEG

HOI SUNG CHUNG, NIDDK

REBECCA F. GOTTESMAN, NINDS

KATIE KINDT, NIDCD

ANIRBAN BANERJEE, PH.D., NICHD

Senior Investigator, Unit of Structural and Chemical Biology and Membrane Proteins, Eunice Kennedy Shriver National Institute of Child Health and Human Development

Education: Jadavpur University, Calcutta, India (B.Sc. in chemistry); Indian Institute of Technology, Kanpur, India (M.Sc. in chemistry); Harvard University, Cambridge, Massachusetts (Ph.D. in chemistry)

Training: Postdoctoral training in chemistry at Harvard University; postdoctoral training in ion-channel biophysics at Rockefeller University (New York)

Came to NIH: In 2012 as a Stadtman Investigator

Outside interests: Listening to bootleg recordings of Indian classical instrumental music; gardening; cooking; learning home-improvement skills

Website: https://irp.nih.gov/pi/anirban-banerjee

Research interests: I am motivated to learn the fundamental chemical principles underlying cellular processes. Currently, my lab and I are examining the structural and chemical biology of membrane proteins. We are obtaining detailed atomic descriptions of the proteins, connecting their structural chemistry with their cellular function in healthy human beings, and trying to understand how structural and functional aberrations are linked to human diseases.

We combine a variety of tools such as X-ray crystallography and cryogenic electron microscopy, protein and peptide chemistry, in vitro and in-cell functional assays using a range of biochemical and biophysical techniques, and most recently, high-resolution microscopy. We are currently pursuing studies in two different directions: 1) membrane-embedded enzymes and proteins that use lipids as substrates and 2) transporters that move transition metal ions across the membrane into the mitochondria.

In the first research area, we have solved the first high-resolution structures of members of the DHHC family of membrane enzymes that catalyze protein S-acylation, also known as protein palmitoylation, a form of posttranslational modification that is important in a range of physiological processes (*Science* **359:**eaao6326, 2018; *Structure* **25:**1337–1347.e6, 2017).

In the area of metal transport, we are investigating how iron—which is important in all kingdoms of life from microbes to humans—is transported across cellular membranes. Mitochondria are the cellular hot spot for the biology of iron in eukaryotes. Mitoferrin-1 and mitoferrin-2 are members of the mitochondrial carrier family and were thought to be the only major importers of iron into mitochondria, but no one knew for sure. We devised the first robust in vitro iron-transport assay and demonstrated that mitoferrin-1 does indeed transport iron (*J Biol Chem* **293:**3819–3828, 2018; DOI:10.1074/jbc.M117.817478).

We showed, using the same assay, that MavN," an unusually conserved protein in *Legionella pneumophila*, a bacterial pathogen that causes Legionnaire disease, is also an iron transporter that supports growth and invasion of Legionella in the host cell. (*Proc Natl Acad Sci U S A* **116:**17775–17785, 2019)

PHILIP CASTLE, PH.D., M.P.H., NCI-DCEG

Senior Investigator, Clinical Epidemiology Unit, Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute; Director, Division of Cancer Prevention, National Cancer Institute

Education: Carnegie Mellon University, Pittsburgh (B.S. in biological sciences); Johns Hopkins University, Baltimore (Ph.D. in biophysics); Johns Hopkins School of Hygiene and Public Health, Baltimore (M.P.H. in epidemiology)

Training: Cancer Prevention Fellow, NCI-DCEG

ROBIN STANLEY, NIEHS

Came to NIH: In 1999 for training; became a tenure-track investigator in 2003 and a senior (tenured) investigator in 2010; left NIH in 2011 and held leadership positions in different organizations (American Society for Clinical Pathology in Washington, D.C.; ImmuneXpress, Inc., in Seattle; Global Cancer Initiative, Inc., in Chestertown, Maryland; and National University Health System of Singapore in Singapore) before joining the Albert Einstein College of Medicine (New York) in 2014

Before returning to NIH: Tenured professor of epidemiology and population health, Albert Einstein College of Medicine

Outside interests: Traveling; enjoying food and wine; engaging in outdoor activities (hiking, biking, running, etc.)

Website: https://dceg.cancer.gov/news-events/news/2021/castle-tenure

Research interests: I am interested in the science and translation of cancer-prevention strategies, global health disparities research, and the epidemiology of human papillomaviruses (HPV) and cervical and anogenital cancers. My research program and group are focused on the discovery, development, evaluation, and validation of new technologies for the prevention of cancer, especially those that address global cancer health disparities. We are involved in the following studies: 1) impact of prophylactic HPV vaccination of Rwandan women living with HIV (WLWH); 2) optimal cervical cancer screening strategies in Rwandan WLWH; 3) the efficacy of different ablative treatments for the prevention of cervical cancer in Mozambican WLWH; 4) oral-cavity cancer screening in Assam, India; 5) morphologic and genetic markers of gynecologic cancer; 6) breast-cancer diagnostics in women living in low- and middle-income countries; 7) prophylactic HPV vaccination in pediatric females; and 8) FDA registration trial for self-collection and HPV testing for cervical-cancer screening in the United States.

I have led studies that have contributed critical insights to the design and conduct of randomized trials and cohort studies of the effectiveness of HPV vaccinations, screening regimens, and the natural history of cervical precancer and cancer. Another focus of my research has been the development and validation of new technologies for cervical cancer prevention including HPV tests, many of which have been approved for clinical use by the FDA. My work has enhanced clinical practice and informed the United States screening and management guidelines, notably the implementation of primary HPV testing for cervical cancer screening, and global cervical cancer prevention.

HOI SUNG CHUNG, PH.D., NIDDK

Senior Investigator and Acting Chief, Single-Molecule Biophysics Section, Laboratory of Chemical Physics, National Institute of Diabetes and Digestive and Kidney Diseases

Education: Seoul National University, Seoul, South Korea (B.S. and M.S. in chemistry); Massachusetts Institute of Technology, Cambridge, Massachusetts (Ph.D. in physical chemistry)

Training: Visiting fellow, Laboratory of Chemical Physics, NIDDK

Came to NIH: In 2007 for training; became a staff scientist in 2012 and a tenure-track investigator in 2015

Outside interests: Playing and hiking with his family

Website: https://irp.nih.gov/pi/hoi-sung-chung

Research interests: My lab studies the conformational dynamics of proteins using a technique called single-molecule Förster resonance energy transfer spectroscopy. In particular, we focus on intrinsically disordered proteins (IDPs) that are closely related to various human diseases. The primary goal of our research is to understand the mechanisms of binding and aggregation processes of IDPs.

In our investigations of the IDP binding mechanisms, we are exploring how molecular conformations evolve when two molecules approach each other, make contact, and form a bound complex. This information is contained in the moment of binding, which can be probed only by single-molecule spectroscopy. In a recent study, we experimentally probed how disordered proteins follow diverse transition paths as they fold and bind to a partner protein, one of the fundamental features of macromolecular dynamics predicted by theories (*Science* **368:**1253–1257, 2020).

We are also characterizing how proteins aggregate. Protein aggregates and oligomers are thought to be implicated in the development of neurodegenerative diseases such as Alzheimer and Parkinson diseases. However, oligomerization and aggregation have been extremely difficult to study due to the heterogeneity of the process. Single-molecule spectroscopy can characterize this complicated process by detecting individual

CONTINUED ON PAGE 22

Recently Tenured

CONTINUED FROM PAGE 21

molecular species without separation. Recently, we visualized the formation of fibrils of amyloid-beta peptide associated with Alzheimer disease. We found that the process is intrinsically heterogeneous, which explains highly diverse experimental results on the aggregation of this peptide (*bioRxiv* preprint 2020; DOI:10.1101/2020.09.10.290023).

REBECCA F. GOTTESMAN, M.D., PH.D., NINDS

Senior Investigator, Chief of the Stroke Branch, and Chief of the Stroke, Cognition, and Neuroepidemiology Section, National Institute of Neurological Disease and Stroke

Education: Columbia College, Columbia University, New York (B.A. in psychology); Columbia College of Physicians and Surgeons, Columbia University (M.D.); Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore (Ph.D. in clinical investigation)

Training: Residency in internal medicine (preliminary), Johns Hopkins Bayview Medical Center (Baltimore); residency in neurology and clinical and research fellowship in cerebrovascular neurology, Johns Hopkins Hospital (Baltimore)

Before coming to NIH: Professor, Neurology and Epidemiology, Johns Hopkins University

Came to NIH: In 2021

Outside interests: Spending time with family; running; baking

Website: https://research.ninds.nih.gov/researchers/faculty/rebecca-fran-gottesman-md-phd

Research interests: Before coming to NIH, I was an investigator at Johns Hopkins University, where my research focused on understanding the cognitive impacts of stroke and other vascular disease, as well as the short- and long-term associations among vascular risk factors, vascular disease, and dementias including Alzheimer disease (AD). I use epidemiology and brain-imaging methods to evaluate the vascular contribution to cognitive impairment and dementia, with an emphasis on the life course. In one of my studies called the Atherosclerosis Risk in Communities (ARIC) study, which had a large cohort, my lab and I found a significant association among midlife vascular risk factors—including obesity, hypertension, diabetes, smoking, and high cholesterol—and increased risk of elevated levels of amyloid plaques, a hallmark of AD. (*JAMA* **317:**1443–1450, 2017).

In another study in the ARIC cohort, we found that many of these midlife risk factors were associated with a higher risk of dementia (*JAMA Neurol* **74:**1246–1254, 2017).

In work led by **Keenan Walker** (now a PI in the National Institute on Aging), we found that adults with high blood pressure in midlife but low blood pressure in later life had an elevated risk of dementia (*JAMA* **322:**535–545, 2019).

At NIH, I will be continuing my work on modifiable risk factors for dementia, both in the ARIC cohort and also in the DISCOVERY study, a study of poststroke dementia that is enrolling stroke patients at 30 sites across the United States. I will also study cognitive outcomes in patients with stroke and traumatic brain injury, and disparities in these outcomes, and I will evaluate cerebral small-vessel disease and its relation to dementia.

KATIE KINDT, PH.D., NIDCD

Senior Investigator and Chief, Section on Sensory Cell Development and Function, National Institute on Deafness and Other Communication Disorders

Education: University of Wisconsin at Eau Claire, Eau Claire, Wisconsin (B.S. in biochemistry and molecular biology); University of California at San Diego, San Diego, California (Ph.D. in biomedical sciences)

Training: Postdoctoral fellowship at the Medical Research Council (Cambridge, England); postdoctoral fellowship at the Vollum Institute and Oregon Hearing Research Center at Oregon Health and Science University (Portland, Oregon)

Came to NIH: In 2013

Outside interests: Rock climbing; mountain biking; camping; backpacking

Website: https://irp.nih.gov/pi/katie-kindt

Research interests: My laboratory studies sensory hair cells, specialized mechanoreceptors that are required for hearing and balance. In mammals, auditory and vestibular organs are encased in the temporal bone, making it difficult to study how these sensory organs form or function in their native environment. We use zebrafish for our research because in contrast to mammals, embryonic and larval zebrafish are transparent and their hair-cell systems can be studied in vivo. Zebrafish use sensory hair cells to detect sound, maintain proper balance, and to detect local water movements. Many studies have shown that the same core genes are required for hearing and balance in zebrafish, mice, and humans. Therefore, we use this relevant, genetically tractable model by combining powerful functional and time-lapse imaging, electrophysiology, and behavioral analyses to comprehensively dissect the molecular and functional requirements underlying the assembly and function of hair-cell systems

in vivo. Our studies provide insight into how to replace and rewire hair cells after hearing loss. This fundamental knowledge is required to develop effective clinical treatments to restore hearing and balance in humans.

In a recent study, we showed that mitochondria regulate hair-cell synapses so they can develop and function correctly. Our results illustrate a mechanism in which presynaptic and mitochondrial Ca2+ (mito-Ca2+) couple to confer proper presynaptic function and formation. Our findings help explain why damage to mitochondria in the inner ear can lead to hearing loss (*eLife* **8:**e48914, 2019).

In the future we hope to expand this research to explore how evoked and spontaneous mito-Ca2+ influx are affected by pathological treatments such as age, noise, and ototoxins.

ROBIN STANLEY, PH.D., NIEHS

Senior Investigator and Head, Nucleolar Integrity Group, Signal Transduction Laboratory, National Institute of Environmental Health Sciences

Education: University of North Carolina at Charlotte, Charlotte, North Carolina (B.A. in mathematics and B.S. in chemistry); Yale University, New Haven, Connecticut (M.Phil. and Ph.D. in molecular biophysics and biochemistry)

Training: Postdoctoral fellowship in the National Institute of Diabetes and Digestive and Kidney Diseases

Came to NIH: In 2009 for training; became a Stadtman tenure-track investigator in NIEHS in 2014

Outside interests: Spending time with her family; running; reading; playing the piano

Website: https://irp.nih.gov/pi/robin-stanley

Research interests: My lab is using a multidisciplinary approach that combines structural, molecular, and cellular biology to explore the ribosome assembly pathway. All cells require ribosomes for the translation of messenger RNA into proteins. Ribosome biogenesis is one of the most energetically costly endeavors for a cell, and as a result, the process needs to be tightly regulated with cell-cycle progress and environmental stimuli. Eukaryotic ribosome biogenesis is a complex process that depends on hundreds of assembly factors. Dysfunction of the ribosome-assembly pathway gives rise to a group of human diseases known as ribosomopathies; deregulation of the pathway has been linked to many types of human cancers.

We seek to determine the molecular mechanisms that ensure the accurate and efficient synthesis of the ribosomal subunits. In one study (one of four of our studies selected as an NIEHS Paper of the Year between 2017 and 2020), we used cryoelectron microscopy (cryo-EM) to determine how an essential ribosome assembly drives ribosome production (*Nat Commun* **10:**513, 2019).

More recently we have begun to take a multi-disciplinary approach to study how SARS-CoV-2, the virus that causes COVID-19, processes viral RNA to evade detection by host-defense systems. Using cryo-EM-derived models of the SARS-CoV-2 nonstructural protein 15 endoribonuclease—in combination with biochemistry, mass spectrometry, and molecular dynamics—we revealed how this nuclease recognizes and cuts viral RNA. Our findings can be used to aid in the development of effective inhibitors against SARS-CoV-2 (*Nat Commun* **12:**article number 636, 2021).

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
DIPHR: Division of Intramural Population Health Research, NICHD
FAES: Foundation for Advanced Education in the Sciences
FARE: Fellows Award for Research Excellence
FelCom: Fellows Committee
FDA: Food and Drug Administration
FNIH: Foundation for the NIH
FNL: Frederick National Laboratory
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCBI: National Center for Biotechnology Information
NCCIH: National Center for Complementary and Integrative Health
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

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PHOTOGRAPHIC MOMENT

Cicada Time

CREDIT: GEOFF CARTER

In the Spring, millions of 17-year cicadas emerged full force on the NIH campus in Bethesda, Maryland. This one seems to be checking the time.

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