THE NIH CATALYST

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Introducing the Newest Laskers

BY LAURA STEPHENSON CARTER, OD, AND JOANNA CROSS, NIMH

WHETHER THEY ARE STUDYING EYE diseases, host-pathogen interactions, neurodegenerative diseases, preventing graft-versus-host disease in stem-cell transplants, blood cancers, pediatric sarcomas, or brain tumors known as gliomas, the eight newest Lasker Clinical Research Scholars are already hard at work in labs and clinics throughout NIH.

The Lasker Clinical Research Scholars Program is an "intramural–extramural" NIH program in partnership with the Albert and Mary Lasker Foundation. The program funds a small number of exceptional clinical researchers in the early stages of their careers to help them achieve independence. The scholars can work as principal investigators at NIH for five to seven years and then can either remain on the intramural tenure track or move—with three years of funding—to a university or other research institution.

Read on to learn about the newest Laskers, what their research is, the discoveries they've made, how they got interested in science, and what excites them about their work. You can read longer versions of the interviews online at https://irp.nih.gov/catalyst/v27i2/introducing-the-newest-laskers.

To learn more about the program, go to https://www.nih.gov/research-training/lasker-clinical-research-scholars.

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Center for Cellular Engineering

New Name and New Location for Cell-Processing Center

BY LAURA STEPHENSON CARTER

DANIEL SOÑÉ

Taking part in the groundbreaking for the newest cell-processing facility are (from left) NHLBI Director Gary Gibbons; NIAID Director Anthony Fauci; NIH Deputy Director for Intramural Research Michael Gottesman; Office of Research Facilities (ORF) construction project officer Hamideh Alehossein; ORF Director Dan Wheeland; NIH Director Francis Collins; HHS Assistant Secretary for Health Admiral Brett Giroir; Clinical Center (CC) CEO James Gilman; CC Department of Transfusion Medicine Chief Harvey Klein; and CC Cell Processing Section Chief David Stroncek.

SOON YOU WILL BE SEEING GIANT CONSTRUCTION CRANES HOISTING MODULES FOR a new cellular-processing facility onto the East Terrace of the NIH Clinical Center (CC), a.k.a. Building 10. The facility represents the most recent expansion of the CC's Department of Transfusion Medicine's (DTM's) growing capacity to support intramural cellular-therapy protocols. On January 22, 2019, the official groundbreaking ceremony took place, with NIH director **Francis Collins**, hospital CEO **James Gilman**, Assistant Secretary for Health Admiral **Brett Giroir** (U.S. Department of Health and Human Services), and others on hand to celebrate. The day also marked the formal recognition of the transition of DTM's Cell Processing Section to its new identity as the Center for Cellular Engineering (CCE).

The CCE will "enable intramural researchers to be on the leading edge" of cellular

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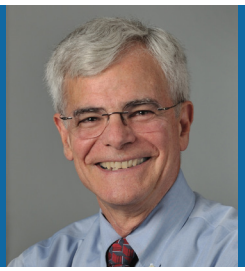
Breaking Through the Data Bottleneck

BY ANDY BAXEVANIS, OD AND NHGRI, AND MICHAEL GOTTESMAN, DDIR



One of the hallmarks of our intramural research environment is the rapid development and implementation of cutting-edge technologies that drive discovery and innovation, greatly facilitating our ability to respond to urgent public-health needs as they arise. The use of these new high-throughput, data-intensive technologies has found its way into almost all areas of scientific inquiry within the intramural research program (IRP), including genomics, computational chemistry, molecular modeling and simulations, structural biology, biomedical imaging, proteomics, metabolomics, and systems biology. The pace with which IRP scientists within these fields are generating biological and biomedical data continues to increase at breakneck speed—but that, in turn, poses its own problem: a data bottleneck. Breaking through that bottleneck requires new ways to easily and effectively use novel computational approaches that allow us to analyze this flood of data.

Back in 2013, with the ever-growing amount of data being generated across the IRP, it became obvious that we were quickly reaching the point at which we would no longer be able to meet the computational needs of our scientists without significantly expanding Biowulf, our large-scale central biomedical-computing resource. We were at a critical junction where not having enough horsepower to pursue computationally intensive projects could have a potentially devastating effect on our research goals as well as a serious impact on our ability to attract (and retain) the best and brightest scientists within the IRP. A collective "call to action" was issued to develop a plan to ensure that we had the kind of world-class computational support that would make us a leader in biomedical computing. The concerted effort to achieve this rather lofty goal involved more than 100 individuals from all corners of the NIH and an investment of $70 million in funding from NIH's Capital Improvement Fund. Our computational landscape now looks vastly different. In November 2017, Biowulf became the first supercomputer completely dedicated to advancing biomedical research that was listed among the top 100 most-powerful computers in the world.

The architecture of "Biowulf 2.0" is notable in that it is designed for general-purpose scientific computing, meaning that its architecture provides both the power and flexibility to meet the wide variety of computational needs of IRP investigators. With 100,000 computer cores, 35 petabytes of storage, a 100-gigabit connection to the modernized NIH network, and over 600 available scientific software applications, Biowulf is being put to good use. Half of all IRP investigators' research programs are now actively using Biowulf to process and analyze their research data, an overall doubling from just three years ago. This increased usage is reflected in number of manuscripts published by our scientists, with 5 percent of all peer-reviewed papers from the IRP based on data that were generated or analyzed using Biowulf. Many of these papers are featured on the CIT High-Performance Computing (HPC) Team's Twitter feed (@nih_hpc), where you can learn more about the studies described in these papers by searching on the very appropriate hashtag #PoweredByBiowulf.

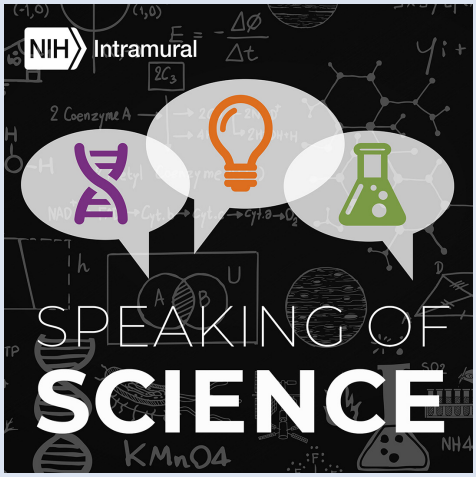
Beyond the impressive capabilities of Biowulf 2.0, the IRP also benefits immensely from the HPC team's expertise, greatly facilitating our ability to make best use of this remarkable resource. The team members spend a significant amount of time providing training and support to IRP scientists, both in formal classroom settings and through their monthly "Coffee Shop Consults" across campus. Also, in response to the increasing demand for training, the HPC team has also released an online, self-paced "Introduction to Biowulf" course that covers a wide variety of basics accompanied by hands-on exercises. Whether a beginner or a seasoned coder, any researcher can benefit from the expertise and diligent assistance of the Biowulf staff. You can learn more about their services by visiting the HPC website at https://hpc.nih.gov.

Of course, when it comes to a fast-paced arena such as supercomputing, there is no rest for the weary. As we come to the end of the IRP's current five-year plan for HPC, we have already started developing a new five-year plan to continue to sustain and capitalize on our investments. The new plan will focus not only on continuing to meet increasing demand but, more importantly, will look to take our HPC program in

new directions based on the ever-changing computational needs of our researchers. This effort would necessarily include investigating new architectures and technologies that would allow us to move more strongly into areas such as deep learning and artificial intelligence. These kinds of approaches have already shown great promise in several clinically relevant areas such as diagnostic pathology and in the study of molecular dynamics. Any new vision for HPC should also take advantage of the significant advances that have been made in cloud computing, particularly in the context of advancing multicenter collaborative studies. The NIH has already taken a significant first step in this direction with the launch of the Science and Technology Research Infrastructure for Discovery, Experimentation, and Sustainability (STRIDES) Initiative in July 2018. The initiative is already helping to advance NIH's goals for increased data sharing and enhancing collaborations through the use of cloud-based tools and services.

As biomedical research becomes even more computationally intensive, the creativity of NIH computational scientists and thoughtful investments by NIH leadership will be essential to ensure that the IRP remains a cutting-edge research institution. As we look forward, we welcome your input as we identify new challenges and set priorities for the future of biomedical computing in the IRP. More importantly, we encourage all of you to take advantage of these shared computational resources, incorporating them into your research as an "enabling technology" that can jump-start major initiatives and truly push the boundaries of biomedical science. ●

Andy Baxevanis is the director of Computational Biology in the Office of Intramural Research. He is also a senior scientist in the Computational and Statistical Genomics Branch of the National Human Genome Research Institute. For more on Biowulf, go to https://hpc.nih.gov.



New Podcast

BY BEN CHAMBERS, OD

Looking for your new podcast obsession? Tune in to "Speaking of Science," a new audio show featuring NIH intramural research program (IRP) scientists who are working at the cutting edge of biomedicine. In the first three episodes, hear from **Nehal Mehta** (a Lasker Clinical Research Scholar in the National Heart, Lung, and Blood Institute) on how treating the inflammatory skin condition psoriasis can help heal heart disease; **Christine Alewine** (a Lasker Clinical Research Scholar in the National Cancer Institute) on testing new immunotoxin strategies to treat pancreatic cancer; and **Bill Gahl** (director of the Undiagnosed Diseases Program) on inborn errors of metabolism and the Undiagnosed Diseases Network.

Listen and subscribe at https://irp.nih.gov/podcast. Tell your friends about the podcast and, if you have a moment, please leave a review on your favorite podcast platforms. ●

Explore more on the IRP Website at: https://irp.nih.gov.

Other Gems

Did you know that the IRP website also has news releases describing recent advances by intramural researchers; hot papers; "I Am Intramural Blog"; and events. To see what's happening, go to the "News and Events" page at https://irp.nih.gov/news-and-events.

You can also find snapshots of the IRP's accomplishments featuring the most outstanding research that helped to advance biomedical knowledge.

For instance, IRP investigators at the National Institute of Dental Research (now the National Institute of Dental and Craniofacial Research) spearheaded studies in the 1940s and 1950s that showed the rate of tooth decay in children who drank fluoridated water fell more than 60 percent.

A sampling of other important NIH accomplishments:

- **1974:** First rotavirus vaccine developed
- **1976:** Interleukin-2 was discovered
- **1981:** Discovery of the disease agent that causes Lyme disease
- **1985**: First detection and screening of HIV
- **1994:** First successful treatment of childhood schizophrenia
- **2001:** Work leading to the production of the first commercially available vaccine against human papillomavirus
- **2013:** Vaccine developed for all four dengue viruses

Find out more at https://irp.nih.gov/accomplishments. ●

From the Fellows Committee

NIH Career Symposium Broadens Its Scope

BY ALLISON DENNIS, NICHD, AND CRAIG MYRUM, NIA

NIH MEDICAL ARTS

The NIH Career Symposiums, which have been held every year since 2008, offer NIH trainees lots of ideas for moving ahead in their careers.

The intensity of day-to-day research can sometimes make career planning a neglected priority. Luckily, the 12th annual NIH Career Symposium, scheduled for May 10 this year, offers trainees an efficient yet extensive way to explore a wide range of career opportunities. In addition to more than a dozen panels consisting of professionals representing a diversity of career options, the symposium also offers "skill blitzes" to help attendees gather the tools and resources that are critical for job searches. And organizers are broadening the scope of the symposium this year in an effort to offer something for everyone.

"The planning committee is expanding the idea of career-themed panels this year," said **Lori Conlan**, director of Postdoctoral Services and Career Services at the Office of Intramural Training and Education. "We plan to start the day with a series of broad introductory sessions aimed at capturing the current state of the field for industry, academia, and everything else." Everything else, or "E-squared" as Conlan lovingly calls it, includes careers in policy, communications, tech transfer, and other areas outside of academia and industry. According to a national survey, only 57.7 percent of U.S. postdocs plan to seek a research-focused academic career and 17.8 percent plan for a career in industry.

The 2019 Career Symposium will therefore highlight a wider range of career options. The morning introductory sessions are intended to inspire fellows to select the most-appropriate career panels to attend later in the day.

The afternoon panel sessions will cover a wide spectrum of careers including those in academia, industry, and government as well as jobs in policy, patents and tech transfer, and communications. The planning committee is carefully selecting panelists who can answer the most-pressing questions that trainees have. For example, industry panelists will draw from their first-hand experiences to describe the differences in work culture and hierarchical structure between small and large biotech companies.

For the academia sessions, panelists will provide advice on transitioning from a postdoc to a faculty position as well as offer a behind-the-scenes glimpse into how applicants are evaluated. In addition, due to popular demand—and the need for bioinformaticians and data crunchers—the "Data Science" panel will return.

Other afternoon sessions will help fellows explore career opportunities away from the bench. One panel will feature former NIH trainees who use their science skills to find success in investment and consulting. Another will highlight the careers of those engaged in education outreach to foster ties between the general public and science. And still another will have people in policy and administrative roles who are interested in shaping the future of science and society.

People who've attended these career symposiums in the past have high praise for their experience. "I learned a great deal about industry-related jobs at the [2017] symposium," said **Xin Huang**, a postdoctoral fellow at the National Human Genome Research Institute and a member of the Career Symposium Committee. "As a result, I decided that R&D [research and development] in industry was the career path for me—and still is."

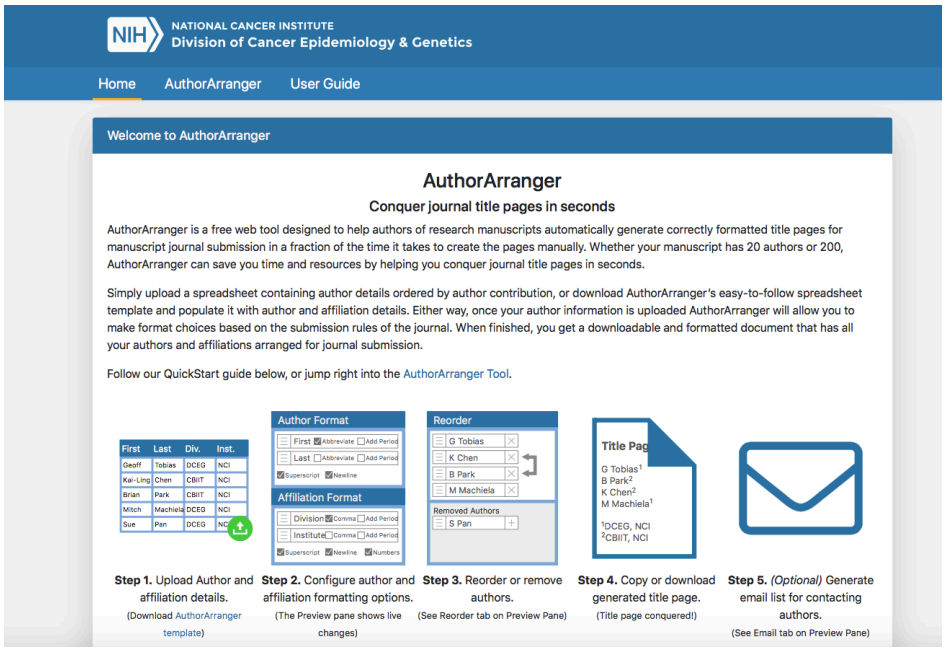
Delany Torres Salazar (a research fellow in the National Institute of Mental Health), who recently joined the planning committee, has found that experience to be as valuable and rewarding as the symposium itself. "It was at the symposium that I first learned about part-time positions in the government that you can pursue while you are still a trainee," he said. Thanks to what he learned at the symposium, he sought and started a detail as a scientific review officer (SRO) at the National Institute of General Medical Sciences. A year later, he parlayed that experience into offers from two institutes to become a full-time SRO. ●

For more up-to-date information, visit the NIH Career Symposium website at https://www.training.nih.gov/nih_career_symposium. You will also find detailed synopses of all past career symposiums.

AuthorArranger

New Tool Helps Quickly Format Manuscript Title Pages

BY GEOFFREY TOBIAS AND MITCHELL MACHIELA, NCI-DCEG



Either way, once your author information is uploaded, AuthorArranger will allow you to make format choices based on the journal's submission rules. When finished, you get a downloadable and formatted document that has all your authors and affiliations arranged for journal submission.

AuthorArranger paves the way for new and simplified approaches for generating and submitting manuscripts and supporting materials to scientific journals for rapid dissemination of research findings. As technology and web interfaces continue to evolve, our hope is that additional tools like AuthorArranger speed up the process of submitting manuscripts for publication. ●

In the population sciences, as in other disciplines, it is common for large studies to have hundreds of contributors with affiliations that span the globe. For example, a physics publication set the record for number of contributors with 5,154 authors and 344 affiliations that spanned 24 pages (*Phys Rev Lett* **114:**191803, 2015; DOI:10.1103/PhysRevLett.114.191803). Likewise, a genetics paper had 1,014 authors, indicating this trend in authorship spans scientific disciplines and is only increasing as improved methods of communication and technology propel a structural shift in scholarly publication practices [*G3 (Bethesda)* **5:**719-40, 2015; DOI:10.1534/g3.114.015966].

When submitting manuscripts to journals, researchers are expected to arrange—in order of contribution—the author names, titles, and affiliations on the title page and format them according to a particular journal's style. It's an arduous process that can take several hours to complete. Although referencing tools and custom scripts can aid in alleviating some of the pain in generating manuscript title pages, these tools are not widely available and often require some amount of manual input.

To help speed up the submission process, our team created AuthorArranger (https://authorarranger.nci.nih.gov/#/), a freely available, easy-to-use, web tool that enables users to conquer journal title pages in a small fraction of the time it takes to create the pages manually. Simply upload a spreadsheet containing author details ordered by author contribution, or download AuthorArranger's easy-to-follow spreadsheet template and populate it with author and affiliation details.

AuthorArranger was created by **Mitchell Machiela** and **Geoffrey Tobias** (both in NCI's Division of Cancer Epidemiology and Research) in collaboration with programmers in NCI's Center for Biomedical Informatics and Information Technology. Support for AuthorArranger came from the 2018 DCEG Informatics Tool Challenge. To start using the AuthorArranger tool, go to https://authorarranger.nci.nih.gov/#/.

PLEASE SHARE YOUR NEW METHOD

The *NIH Catalyst* occasionally publishes articles about new methods developed by NIH intramural researchers. If you developed a new method and would like to share the news with other readers of this publication, please contact us at catalyst@nih.gov or call 301-402-1449.

Matthew Hoffman Is New NIDCR Scientific Director

Commitment to Mentorship, Diversity, and Equity

BY EMILY PETRUS, NINDS

The National Institute of Dental and Craniofacial Research (NIDCR) made **Matthew Hoffman**'s appointment as scientific director (SD) official in July 2018 after he served two years as Deputy SD.

Mentorship and increasing the diversity of NIDCR's workforce are two of his main priorities. Hoffman credits NIDCR's nonhierarchical structure, established by the previous SD **Robert Angerer**, as being an exceptional tool for recruiting a diverse group of investigators. In NIDCR, five small branches have been replaced with all 26 PIs operating as one branch, and administrative committees now take care of the nuts and bolts of running a smooth operation. This setup provides leadership opportunities for more investigators at all levels to serve on committees.

In addition, new investigators each establish a mentoring committee made up of at least one senior NIDCR scientist, and up to four others chosen by the new investigator. This arrangement reduces the dependence on a branch chief and increases opportunities for collaboration for the new investigators.

Another invaluable recruitment tool is that the Clinical Center provides access to patients with rare diseases. Some new recruits have the opportunity to obtain cells from patients with rare diseases to make induced pluripotent stem cells to study the disease. This access allows investigators to study patient genetic and cellular abnormalities and develop treatment strategies accordingly. This "strong human gene-therapy program...will be a major advantage to translate discoveries in the future," he said.

Hoffman also mentioned NIDCR's commitment to using new imaging and genomic technologies and working with the corresponding big data; these endeavors are supported by NIDCR's new imaging core and the the Genomics and Computational Biology Core, which NIDCR shares with the National Institute on Deafness and Other Communications Disorders. For new investigators, these cores provide access to technologies that might otherwise require a large financial outlay.

Matthew Hoffman, new SD for NIDCR.

One of Hoffman's first decisions as SD was to choose a deputy SD whom he could trust to support his endeavors to recruit a diverse and productive group of investigators at NIDCR: senior investigator **Marian Young**, whom he called "a strong scientist [with] great enthusiasm for mentoring."

His belief that an institute should not depend on one person to run it and his immediate desire to develop leadership skills throughout the institute speaks to his commitment to mentorship, diversity, and equity in his institute.

In addition to being an SD, Hoffman is a senior investigator in the Matrix and Morphogenesis Section and is continuing to conduct his own research. He and his lab focus on how salivary glands develop from progenitor cells to functional glands and how they are damaged in people who are treated with radiation for head and neck cancer or who have diseases such as the autoimmune disorder Sjögren syndrome. He and his team are using what they learn to figure out ways to repair and regenerate salivary glands. Lack of salivary-gland function results in severe dry mouth, which reduces a person's quality of life and can lead to serious oral-health problems.

Hoffman earned a B.D.S. from the University of Otago School of Dentistry (Dunedin, New Zealand) and was a dental house surgeon at the Wellington Hospital Board (Wellington, New Zealand). After winning a Fulbright scholarship, he pursued M.S. and Ph.D. degrees at the University of Rochester School of Medicine and Dentistry (Rochester, New York). He came to NIDCR in 1994 as a visiting fellow in the laboratory of **Hynda Kleinman** in the Cell Biology Section of the Laboratory of Developmental Biology. He became a staff scientist in 2000; a tenure-track investigator in 2004; and a tenured senior investigator in 2011.

In his spare time, he enjoys tramping (that's New Zealand for hiking), camping, and swimming. He swims on the Masters Team for the District of Columbia Aquatics Club, where he met his partner Brady. Together they've backpacked and swum in countless countries. Hoffman's favorite adventure location is Fiordland National Park in New Zealand, but the Sierra Nevada mountains in California are "an acceptable alternative" in the United States, he said with a grin. ●

Former NIDCR SD, Robert Angerer

Strengthened NIDCR's Intramural Research Program

BY EMILY PETRUS, NINDS

Robert Angerer, who was NIDCR's SD until 2016.

Matthew Hoffman has a tough act to follow: former NIDCR SD **Robert Angerer** who implemented changes to strengthen the institute's intramural research program. Angerer introduced a more rigorous Board of Scientific Counselors (BSC) review system; enhanced training opportunities and staff diversity; and flattened the hierarchical system of governance that inhibited the advancement of younger investigators. He also expanded clinical collaborations and funneled resources to newly tenured and clinically oriented investigators.

NIDCR's scientific productivity benefitted from more rigorous BSC reviews by focusing on science quality, mission relevance, mentoring, and collaboration. This new review system provided clear goals for investigators to pursue; encouraged increased collaborations between and among intramural and extramural scientists; and resulted in the proper allocation of funds to increase support for newly tenured PIs.

Angerer also strove to support trainees at all career levels. His commitment to training was evident in his dedication to enhancing diversity—NIDCR recruited five female tenure-track scientists and a female clinical director during his tenure as SD.

He also expanded NIDCR's clinical research program by hiring core staff and clinical researchers to create an academic hospital environment. Angerer promoted a NIDCR research rounds seminar open to all of NIH and merged NIDCR's Institutional Review Board (IRB) with the Combined Neurosciences IRB to enhance the development of clinical-research protocols.

Angerer is a well-known expert in the field of developmental biology. Throughout his career he collaborated with his wife, **Lynne Angerer**, until her death in 2013. Together they obtained Ph.D.s from Johns Hopkins University (Baltimore) in 1973; did their postdoctoral training at the California Institute of Technology (Pasadena, California); established labs at the University of Rochester (Rochester, New York); and arrived at NIH in 2004.

Robert became NIDCR's scientific director and Lynne became chief of NIDCR's Developmental Mechanisms Section. They pioneered in situ hybridization to detect the expression of messenger RNA in embryonic tissue; used the sea urchin genome to develop microarray techniques to detect transcription factors and signal transduction pathways for the development of the ectoderm (neural and non-neural tissue); detected new neural precursors which arose from endoderm (gut) tissue (this finding was a challenge to the prevailing dogma that nerves develop only from other embryonic tissue); and described the signaling underlying embryo patterning. These discoveries and others were significant contributions to the understanding of early embryonic development. ●

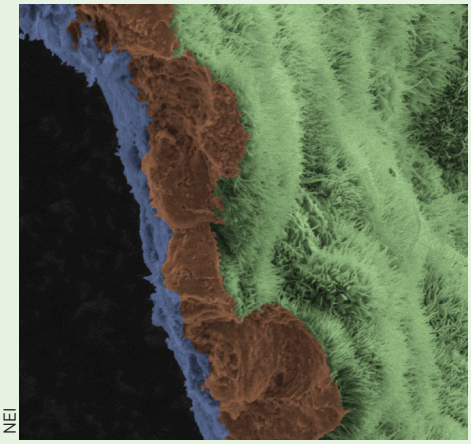
NIEHS Was Affected by Government Shutdown

Most of NIH was not affected by the partial government shutdown (December 22, 2018, to January 25, 2019) because it is funded through the passage of the Labor Health and Human Services (HHS) Funding Bill. But a few people at the National Institute of Environmental Health Sciences (NIEHS) in Durham, North Carolina, weren't so lucky. The NIEHS Superfund Research Program (SRP), which is funded by the Interior Appropriations Bill, experienced a lapse in appropriations, and 12 NIEHS employees were furloughed as a result. There was no delay in awarding Superfund Research grants, but normal oversight of grant-funded research did not happen.

Superfund Research Program

Since its inception in 1987, the SRP has applied a multidisciplinary approach to research focused on providing a solid foundation that environmental managers and risk assessors can draw upon to make sound decisions related to Superfund and other hazardous waste sites. The program supports peer-reviewed research in university-based centers, encompassing collaborations at over 100 institutions; provides funding for Small Business Innovation Research/Small Business Technology Transfer Research grants designed to foster the commercialization of relevant technologies, products, and devices; and funding for individual research grants to address specific issues that complement the multiproject center grants. The SRP also has a strong training component, which supports graduate students and postdoctoral researchers and funds a variety of outreach efforts to facilitate the translation of research findings to the communities and organizations most concerned with hazardous substances, with the ultimate goal of improving public health. ●

Intramural Research Briefs



NEI

NEI: A scanning-electron-microscope image shows a polarized retinal pigment epithelial (RPE) cell monolayer on a biodegradable scaffold. The image is colored to highlight the scaffold in blue, and three RPE cells in brown. The apical process of cells in RPE monolayer are light green.

NEI: STEM-CELL THERAPY PREVENTS BLINDNESS IN ANIMAL MODELS OF RETINAL DEGENERATION

Researchers at NEI used a novel stem-cell-based therapy to prevent blindness in rat and pig models of the advanced "dry" form of age-related macular degeneration (AMD). Specifically, induced pluripotent stem cells (iPSCs) that were programmed to become retinal pigment epithelial (RPE) cells were derived from the blood cells of three human AMD patients. During the progression of AMD, RPE cells often die, which leads to the death of the photoreceptors and thus to blindness. In the study, the iPSC-derived RPE cells were transplanted into normal and laser-induced degenerating retinas of animals and integrated into the retina. The study provides preclinical evidence of the safety and efficacy of iPSC-derived RPE cells as a treatment for AMD and a framework for the translating iPSC therapies into clinical trials. (NIH authors: R. Sharma, V. Khristov, A. Rising, B.S. Jha, R. Dejene, N. Hotaling, Y. Li, Q. Wan, C. Zhang, M.M. Campos, K.J. Miyagishima, D. McGaughey, R. Villasmil, M. Mattapallil, H. Qian, W. Wong, S. Miller, A. Marminishkis, J. Amaral, and K. Bharti, *Sci Transl Med* 11:eaat5580, 2019; DOI:10.1126/scitranslmed.aat5580)

[BY CLAIRE MCCARTHY, NCI]

NCI, NLM: ARTIFICIAL INTELLIGENCE OUTPERFORMED HUMANS IN IDENTIFYING CERVICAL PRECANCER

Investigators at NCI, NLM, and Global Good (Bellevue, Washington) developed an artificial-intelligence approach, called automated visual evaluation, that can analyze digital images of a woman's cervix and accurately identify cervical precancers. More than 60,000 digitized cervical images were used to train a deep-learning algorithm to recognize patterns of precancerous changes. When this approach was compared with human experts in the evaluation of Pap tests, the algorithm was better at identifying precancer. Moreover, this new method could potentially improve cervical-cancer screening in low-resource settings where cervical-cancer is a leading cause of death. (NIH authors: S. Antani, Z. Xue, K. Yu, L.R. Long, M. Demarco, J.C. Gage, A.C. Rodriguez [consultant to NCI], N. Wentzensen, and M. Schiffman, *J Natl Cancer Inst* 2019; DOI:10.1093/jnci/djy225)

[BY CLAIRE MCCARTHY, NCI]

NIAID (VRC): INVESTIGATIONAL TREATMENT FOR EBOLA IS SAFE

NIAID investigators at the institute's Vaccine Research Center and their collaborators found that intravenous mAb114 is safe, well-tolerated, and easy to administer to treat Ebola. The treatment is also being offered to Ebola patients in the Democratic Republic of Congo under compassionate use and as a phase 2/3 clinical trial of multiple investigational treatments. (NIH authors: M.R. Gaudinski, E.E. Coates, L. Novik, A. Widge, K.V. Houser, E. Burch, L.A. Holman, I.J. Gordon, G.L. Chen, C. Carter, M. Nason, S. Sitar, G. Yamshchikov, N. Berkowitz, C. Andrews, S. Vazquez, C. Laurencot, J. Misasi, F. Arnold, K. Carlton, H. Lawlor, J. Gall, R.T. Bailer, A. McDermott, R.A. Koup, J.R. Mascola, B.S. Graham, N.J. Sullivan, and J.E. Ledgerwood, *Lancet* 2019; DOI:10.1016/S0140-6736(19)30036-4)

[BY MOHOR SENGUPTA, NEI]

NIAID (ROCKY MOUNTAIN LABS): TICK SALIVARY GLANDS MAY HOLD SECRET FOR HOW VIRUSES ARE TRANSMITTED

The salivary glands of *Ixodes scapularis* (more commonly known as black-legged ticks or deer ticks) may hold the secret to preventing tick-borne infections. Tick-borne flaviviruses (TBFVs) have been on the rise in North America for the last two decades and cause roughly 15,000 infections each year. Flaviviruses include dengue, Zika, West Nile, yellow fever, and, in North America, the Powassan virus (POWV), which can cause encephalitis.

NIAID

NIAID: This confocal microscope image shows a cross-section of a tick salivary gland infected with Langat virus (green). Two rounded structures on the right, called acini, are shown attached to a duct (yellow). The lower acinus is infected, as denoted by the green fluorescent signal.

Tick bites are especially dangerous because the TBFVs, found in ticks' salivary glands (SGs) are rapidly transmitted. In just 15 minutes, an infected tick can transmit POWV to a human host or other mammal. Concentrations of TBFVs were higher in the SGs of engorged, or fed, ticks and only certain kinds of SGs are infected. The scientists also identified a tick gene that is involved in infection. These findings might point to transmission pathways that could be blocked and open doors to new methods of preventing infections. (NIH authors: J.M. Grabowski, O.R. Nilsson, E.R. Fischer, D. Long, D.K. Offerdahl, D.P. Scott, and M.E. Bloom, *mBio* 2019; DOI:10.1128/mBio.02628-18)

[BY AUTUMN HULLINGS, NCI]

NINDS: NEURODEGENERATIVE DISORDERS MAY BE TRIGGERED BY HYPERACTIVE IMMUNE RESPONSE

Researchers at NINDS found, in experiments using fruit flies (*Drosophila melanogaster*), that the body's immune system may play a critical role in the damage caused by aging brain disorders. The study involved altering the activity of the Cdk5 protein kinase, a group of proteins that are important in early brain development and may be involved in neurodegenerative diseases (such as Parkinson and Alzheimer diseases), degeneration of neurons, impaired autophagy, and accelerated aging. The researchers showed that increased activity of Cdk5 slowed autophagy and starts a chain reaction that triggers an increase in the innate immune response, which in turn causes the immune system to attack and kill the body's own neurons. The researchers suspect that this destructive chain reaction may occur during several neurodegenerative disorders. These conclusions provide a new way of looking at the progression of neurodegenerative diseases and could offer alternative solutions for stopping or slowing them. (NIH authors: A.K. Shukla, J. Spurrier, I. Kuzina, and E. Giniger, *Cell Rep* **26**:131–144.e4, 2019; DOI:10.1016/j.celrep.2018.12.025)

[BY AUTUMN HULLINGS, NCI]

NIAID: WITH HIV, UNDETECTABLE EQUALS UNTRANSMITTABLE

The HIV undetectable = untransmittable (U=U) concept has been validated by NIAID scientists who reviewed and summarized results from large clinical trials and cohort studies. The U=U concept suggests that people infected with HIV who achieve and maintain an undetectable viral load by taking antiretroviral therapy (ART) cannot sexually transmit the virus to others. The studies showed that no HIV transmission occurred in heterosexual and male-male couples, in which one partner is uninfected and the other has HIV and a durably suppressed viral load. For U=U to work as an HIV-prevention strategy, the undetectable viral load must be sustained by taking ART daily as prescribed. The authors point out, however, that ART adherence may be difficult when those infected with HIV don't have access to quality health care and that it's important to implement programs that help patients remain in care and to address the challenges in their lives that result in their stopping therapy. (NIH authors: R.W. Eisinger, C.W. Dieffenbach, and A.S. Fauci, *JAMA* **321**:451-452, 2019; DOI:10.1001/jama.2018.21167)

[BY NATASHA MCMASTERS, NCI]

NEI: FAULTY MOLECULAR MASTER SWITCH MAY CONTRIBUTE TO RETINAL DEGENERATION

In a recent study, NEI researchers explored the role of transforming growth factor–beta (TGF-beta) signaling in the retina. They found that a signaling pathway controlled by TGF-beta could be involved in the progression of age-related macular degeneration (AMD). Using mouse models, the researchers ablated the TGF-beta receptor (TGFBR2) in the retinal microglia, which led to the loss of the microglia's ability to sense TGF-beta signaling. The study also showed evidence of an activated, inflammatory gene-expression signature and of failure in the microglia's ability to sense endogenous environmental signals. This homeostatic misbalance has cascading effects on the retina—the neighboring Müller cells, a type of retinal glial cell, began to show signs of distress, and retinal neurons began to fail and die. The pathological changes are similar to what happens in the progression to late AMD. TGF-beta, therefore, may represent an important therapeutic target for treating AMD. (NIH authors: W. Ma, S.M. Silverman, L. Zhao, R. Villasmil, M.M. Campos, J. Amaral, and W.T. Wong, *eLife* 2019; DOI:10.7554/eLife.42049)

[BY AMRITA MANDAL, NICHD]

NIDCD, NCCIH: GENETIC VULNERABILITY TO MENTHOL IN CIGARETTES

NIH researchers found that a genetic variant is linked to the preference for menthol-flavored cigarettes among African-Americans. Mentholated cigarettes have been gaining a larger share of the cigarette market in the United States even as overall smoking has declined over the past 50 years. Nearly 83 percent of African-American smokers prefer mentholated cigarettes versus only 24 percent of white smokers and 32 percent of Hispanic smokers.

Researchers from NIDCD, NCCIH, and other institutions analyzed protein-coding genes and took surveys of smoking habits in 1,300 adults (in groups that included multiethnic and African-American smokers) and found that a variant of the *MRGPRX4* was in five to eight percent of African-Americans and absent from other demographics. Smokers with this variation were five to eight times as likely to reach for mentholated cigarettes as for nonmentholated ones.

The protein of *MRGPRX4* was identified as a G-protein-coupled cell-surface receptor associated with detecting irritation rather than taste. Menthol suppresses the activity of this receptor, an effect that is enhanced in those with the variant. The study predicts that menthol provides an anesthetic-like effect through this signaling pathway, making mentholated cigarettes less irritating. A potential genetic vulnerability to mentholated cigarettes among African-Americans could be used to help inform public-health policy decisions about the use of menthol in cigarettes. (NIH authors: D. Risso, E. Sainz, A. Barik, C. Frigerio-Domingues, and D. Drayna, *PLoS Genet* **15**:e1007916, 2019; DOI:10.1371/journal.pgen.1007916)

[BY MEGAN ROEGNER, NIDDK]

Read more briefs and longer versions of these online: https://irp.nih.gov/catalyst/v27i2/research-briefs

Lasker Clinical Research Scholars

CONTINUED FROM PAGE 1

CATHERINE ANN CUKRAS, M.D., PH.D., NEI

Lasker Clinical Research Scholar, Division of Epidemiology and Clinical Applications, Clinical Trials Branch, National Eye Institute

Education: Princeton University, Princeton, New Jersey (Bachelor of Science and Engineering); Washington University, St. Louis, Missouri (M.D.–Ph.D.)

Training: Intern, Presbyterian Hospital (Philadelphia); residency in ophthalmology, Scheie Eye Institute, University of Pennsylvania (Philadelphia); Medical Retina Clinical Fellow, NEI

Came to NIH: In 2007 for training; became a staff retina clinician in 2009; named Lasker Clinical Research Scholar in 2018

Website: https://nei.nih.gov/eyeclinic/about/cukras

Research focus: Clinical research in retinal degenerative diseases. I use multidisciplinary approaches to understand the patterns of photoreceptor dysfunction and degeneration in disease and to design and implement interventional clinical trials.

What discoveries have you made?

Our study investigating the findings of dark-adaptation abnormalities in age-related macular degeneration (AMD) has led to significant contributions in understanding disease pathophysiology. Our study of patients with hydroxychloroquine-induced retinal toxicity (the drug is used to treat malaria, rheumatoid arthritis, lupus, and other autoimmune diseases), has led to important findings in understanding the sequence of events in induced retinal degeneration.

What is exciting about your work?

That it furthers progress on treating and preventing blindness.

What do you like to do outside of work?

Spend time with my husband, three kids, and puppy. The NIH is like family and I am lucky to be able to be part of an environment that fulfills me and enriches me as a person.

JOHN P. DEKKER, M.D., PH.D., NIAID AND CC

Lasker Clinical Research Scholar, Chief, Bacterial Pathogenesis and Antimicrobial Resistance Unit, Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Diseases; Director, Genomics Section, Microbiology Service, Department of Laboratory Medicine, NIH Clinical Center

Education: Wesleyan University, Middletown, Connecticut (B.A., M.A.); Harvard University, Boston (Ph.D.); and Harvard Medical School, Boston (M.D.)

Training: Resident in Pathology and Edgar Taft Fellow in Medical Microbiology, Massachusetts General Hospital, Boston

Came to NIH: In 2013 as staff physician and co-director of the Bacteriology, Parasitology, and Molecular Epidemiology Sections of the Microbiology Service in the Department of Laboratory Medicine, NIH Clinical Center

Website: https://www.niaid.nih.gov/research/john-p-dekker-md-phd-fcap

Research focus: The evolution of bacterial pathogens, host-pathogen interactions, and mechanisms of antibiotic resistance in these organisms.

Tell us more about your recent research.

We have begun to study the utility of nanopore sequencing for the diagnostic identification of antibiotic-resistance genes in bacteria. Using this method, which offers an extremely rapid approach to genomic sequencing, it is possible to identify all of the antibiotic-resistance genes in bacteria isolated from a patient in a matter of hours. Other work focuses on in vitro models of adaptive evolution to understand how bacterial antibiotic resistance emerges and evolves during the course of treatment in patients. We have recently begun to study how some bacteria can increase their mutation rates by turning off DNA-repair mechanisms, thus possibly facilitating more rapid adaptive evolutionary escape from attacks by the host immune system and antibiotic treatment.

How did you get interested in your field?

I grew up in a house that always had the latest issue of the *New England Journal of Medicine*, which both of my parents read, open on the kitchen table. As an undergraduate, I was introduced to the field of biophysics; in medical school, I became interested in infectious diseases and the biology and evolution of microorganisms, and I came to appreciate the profound importance of the problems caused by the evolution of antibiotic resistance in bacteria. The field of medical microbiology allows me to connect basic biological questions relating to bacterial evolution with fundamentally important clinical aspects of antibiotic resistance and infectious disease.

CHRISTOPHER G. KANAKRY, M.D., NCI-CCR

Lasker Clinical Research Scholar, Center for Cancer Research, National Cancer Institute

INTERVIEWED BY JOANNA CROSS, NIMH

Education: Harvard College, Cambridge, Massachusetts (A.B. in history and science); Duke University School of Medicine, Durham, North Carolina (M.D.)

Training: Residency in internal medicine, fellowship in medical oncology, fellowship in hematology, all at Johns Hopkins University School of Medicine (Baltimore)

Came to NIH: In 2014 as an assistant clinical investigator in NCI-CCR's Experimental Transplantation and Immunology Branch; in 2018 became a Lasker Clinical Research Scholar

Website: https://irp.nih.gov/pi/christopher-kanakry

Research focus: Translational laboratory and clinical research on allogeneic hematopoietic-cell transplantation; gaining a better understanding the use of post-transplantation cyclophosphamide to prevent graft-versus-host disease (GVHD).

What discoveries have you made?

It has to do with understanding how post-transplantation cyclophosphamide prevents GVHD. It was believed that cyclophosphamide prevents GVHD by selectively *eliminating* alloreactive T cells. However, my research in mice shows that post-transplantation cyclophosphamide only *impairs* those T cells. These findings should facilitate the development of new strategies to improve transplantation outcomes that are based on biology and not on a flawed understanding.

What do you enjoy about your work?

Developing new understandings in the lab that can be taken directly to the clinic; and also taking clinical observations to the lab, where I can learn about the biology. My goal is to use this improved scientific understanding to improve patient outcomes. I also find great enjoyment in teaching and mentoring trainees at all levels both in the lab and in the clinic.

What do you like to do outside of work?

Spend time with my two young children; sing with the City Choir of Washington; swim; and teach Sunday School to fourth graders at my church.

MOST PHOTOS BY CHIA-CHI CHARLIE CHANG. OTHER PHOTOGRAPHERS FOR KANAKRY, LYONS, AND SCHOLZ.

JONATHAN J. LYONS, M.D., NIAID

Lasker Clinical Research Scholar and Chief, Translational Allergic Immunopathology Unit, Laboratory of Allergic Diseases, National Institute of Allergy and Infectious Diseases

Education: Pomona College, Claremont, California (B.A. in chemistry); Jesus College, Cambridge University, Cambridge, England (two terms as a humanities student); Keck School of Medicine, University of Southern California, Los Angeles (M.D.)

Training: Residency in internal medicine (later served as chief resident) at the University of California at San Diego (San Diego); clinical fellow in allergy and immunology, NIAID

Came to NIH: In 2011, for NIAID clinical fellowship in allergy/immunology; in 2014, became an assistant clinical investigator in NIAID's Genetics and Pathogenesis of Allergy Section; in 2017, named a Lasker Clinical Research Scholar and chief of the Translational Allergic Immunopathology Unit

Website: https://irp.nih.gov/pi/jonathan-lyons

Research focus: Using human immunogenetics to identify how alterations in signaling, protein expression, and metabolism can affect anaphylaxis and myeloproliferative disease.

What discoveries have you made?

I have been involved in the discovery of many single-gene disorders that lead to severe allergic diseases or reactions, and there are several more in the pipeline. One of these discoveries was the identification of a genetic trait we have called hereditary alpha-tryptasemia, which is associated with severe allergic reactions as well as several other difficult-to-treat symptoms.

How did you get interested in your field?

I have always wanted to understand how things worked and find a deeper meaning underlying it all. I remember being a grade schooler and learning for the first time that if you looked closely enough, solid things are really not "solid" at all, and I was hooked. My desire to find that deeper meaning directed me toward a career as a physician. Ultimately, my fascination with the complexity of immunologic responses

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Laskers

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and the diseases and reactions they cause, and a desire to better understand these processes to inform therapies, is why I chose the field of allergy and immunology.

What about you might surprise people?

That I played football in college and I am a huge underground hip-hop fan.

SONJA W. SCHOLZ, M.D., PH.D., NINDS

Lasker Clinical Research Scholar and Chief, Neurodegenerative Diseases Research Unit, National Institute of Neurological Disorders and Stroke

Education: Medical University of Innsbruck, Innsbruck, Austria (M.D.); University College London, Queen Square Institute of Neurology, London, United Kingdom (Ph.D. in neurogenetics)
Training: Postdoctoral fellowship in neurogenetics, National Institute of Aging; postdoctoral fellowship in neuroscience, Georgetown University (Washington, D.C.); internship and adult neurology residency, Johns Hopkins University Medical Center (Baltimore)
Came to NIH: In 2005 for training (2005–2009); returned in 2015 as assistant clinical investigator in NINDS; became Lasker Clinical Research Scholar in 2018
Website: https://irp.nih.gov/pi/sonja-scholz

Research focus: Unraveling the genetic causes of complex neurodegenerative diseases, including Lewy body dementia, multiple-system atrophy, and related Parkinsonism syndromes. We aim to advance our understanding of these conditions and improve diagnostic accuracy and targeted treatments.

What discoveries have you made?

My genomic research has had a significant impact on our understanding of genetic risk involved in neurodegenerative diseases, including the discovery of genes underlying Parkinson disease, Lewy body dementia, ataxia, and rare Parkinsonism disorders. In addition, I was part of an international team that developed the NeuroChip genotyping platform, a high-throughput genotyping array that allows us to rapidly screen individuals for known disease-associated genetic variants.

What do you find exciting about your work?

The knowledge that understanding the molecular mechanisms of a disease paves the way for treatments in the near future. As a neurologist who sees patients afflicted with these diseases, this knowledge is the most important dimension of what I do and what gets me up in the morning.

What about you might surprise people?

I have a glider pilot's license.

H. NIDA SEN, M.D., M.H.S., NEI

Lasker Clinical Research Scholar, Head, Unit on Clinical Translational Immunology, Laboratory of Immunology, National Eye Institute

Education: Hacettepe University Medical School, Ankara, Turkey (M.D.); Duke University, Durham, North Carolina (M.H.S.)
Training: Residency in ophthalmology, Ankara Training and Research Hospital (Ankara, Turkey); clinical fellowship in uveitis and ocular immunology, NEI; residency in ophthalmology, George Washington University (Washington, D.C.)
Came to NIH: In 2001 for training; returned in 2008 as a staff clinician; became Lasker Clinical Research Scholar in 2018
Website: https://nei.nih.gov/eyeclinic/about/sen

Research focus: Developing outcomes measures, biomarkers, and targeted therapies for the treatment of uveitis, an immune-mediated eye disease, and improving our understanding of the pathways driving it.

What discoveries have you made?

I developed a standardized grading system for scleritis (inflammation of the white part of the eye) using NEI's electronic ocular-image database. The system is used in clinical studies and has been adopted by an open-source electronic medical-record system in the United Kingdom. I was also one of the first to investigate the possible association between the gut microbiota and uveitis.

What is exciting about your work?

The opportunity to combine clinical research with translational research. I feel fortunate to be able to perform clinical studies and trials with a mechanistic component and collaborate with the best in the field. It is the perfect example of bench to bedside, though in my case its more of a "bed to bench to bedside."

Read longer profiles online at https://irp.nih.gov/catalyst/v27i2/introducing-the-newest-laskers.

JOHN (JACK) F. SHERN, M.D., NCI-CCR

Lasker Clinical Research Scholar, Pediatric Oncology Branch, Center for Cancer Research, National Cancer Institute

Education: University of Notre Dame, South Bend, Indiana (B.A. in preprofessional studies); The Medical College of Georgia, Augusta, Georgia (M.D.)
Training: Residency in pediatrics, University of Chicago Comer Children's Hospital (Chicago); combined fellowship in the pediatric hematology and oncology training program, Johns Hopkins University (Baltimore) and National Cancer Institute
Came to NIH: In 2010 for training; became assistant clinical investigator in 2015; became Lasker Clinical Research Scholar in 2018
Website: https://irp.nih.gov/pi/jack-shern

Research focus: Defining the biology, genetics, and epigenetics of pediatric sarcomas with the goal of developing novel therapies.

What discoveries have you made?

I led a project that collected patient tumor samples from rhabdomyosarcoma and applied sequencing technology. We gave the research community a list of targets to develop therapies toward.

How did you get interested in your field?

I have always been interested in understanding how things work. I come from a family of architects and engineers, and in many ways what we do in science and medicine is similar in that we first study the problem and then try to build solutions.

What is exciting about your work?

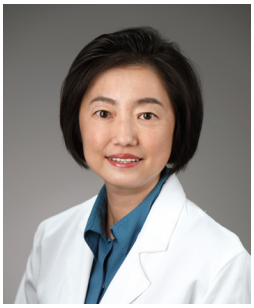
I love the discovery and inventiveness that goes with working in the laboratory; putting together diverse teams of brilliant people and challenging them with an unsolved problem; and having the opportunity to take discoveries from the laboratory and use them to help patients in the clinic.

Would you like to tell us anything else?

To the trainees, I would say be persistent and take chances. The NIH is a great place to train and to get involved with big projects that will change fundamental understandings and the way we do medicine.

JING WU, M.D., PH.D., NCI-CCR

Lasker Clinical Research Scholar, Neuro-Oncology Branch, Center for Cancer Research, National Cancer Institute



Education: Capital Medical University, Beijing, China (M.D.); University of Texas Medical Branch, Galveston, (Ph.D. in neuroscience)
Training: Postdoctoral fellow in anatomy and neuroscience, University of Texas Medical Branch (Galveston, Texas); residency in neurology (including chief resident), University of Texas Health Science Center (Houston); and a clinical neuro-oncology fellowship, University of Texas MD Anderson Cancer Center (Houston)
Before coming to NIH: Co-director, Brain Tumor Program, Lineberger Comprehensive Cancer Center, and tenure-track assistant professor, Department of Neurosurgery and Neurology, University of North Carolina Medical School (Chapel Hill, North Carolina)
Came to NIH: In 2015 as a staff physician.
Website: https://irp.nih.gov/pi/jing-wu

Research focus: Identifying clinically relevant challenges in patients with primary brain tumors, namely gliomas with mutations in the *IDH* gene; developing hypothesis-driven laboratory projects in preclinical models; and translating results into clinical trials to determine predictors and mechanisms of treatment responses or resistance.

What discoveries have you made?

At UNC, I observed that patients with IDH-mutant gliomas respond to chemotherapies better than those with wild-type gliomas. I later discovered that IDH mutations make gliomas even more sensitive to chemotherapy; in collaboration with colleagues, we discovered two proteins that repair the DNA damage induced by chemotherapies. Based on my preclinical findings, I designed and opened the first clinical trial with TG02 (an agent that penetrates the blood-brain barrier) in recurrent glioblastoma.

What is exciting about your work?

Having the privilege of taking care of my patients in both a clinical setting and using clinical challenges to further translational research in the laboratory.

Would you like to tell us anything else?

I am forever thankful for those who helped me when I needed it the most. I have always felt privileged to have the opportunity to take care of my patients during the difficult times of their lives. It is most rewarding to know that my research may bring hope to patients and help relieve their suffering. It is the trust and encouragement from these patients that motivate me to keep going in the field of neuro-oncology.

If I had more time I would … sign up for a ballroom dancing class or take some piano lessons. ●

Center for Cellular Engineering

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PERKINS AND WILL, DPR CONSTRUCTION

Architectural rendering of CCE's new modular facility to be built on the East Terrace of Building 10.

engineering, said Collins at the ceremony.

The CCE is expected to meet the increasing demand for customized cellular-therapy products and services that are needed for personalized treatments. Products include CAR-T cells for cancer immunotherapies; pluripotent stem cells to treat macular degeneration; and gene therapies for epithelial cancer. The CCE will also provide leadership, best-practices research, support, and training in cellular engineering. There are already 34 clinical-trial protocols underway that rely on the CCE; by 2020, 12 more protocols are expected to be added.

The CCE's existing cell-processing facilities include laboratories to develop and characterize novel cellular products and 11 rooms for cellular engineering. The demand for cells is increasing rapidly so, in addition to soon-to-be-built CCE modules on the East Terrace (which are expected to be completed within a year), additional space is being renovated on the 12th floor of the CC's E-wing. The CCE is operating under the guidance of DTM Chief **Harvey Klein**, Deputy Chief **Bill Ward**, and Section Chief **David Stroncek**. ●

Meet the Patients

Seven-year-old Cole is being treated at the NIH Clinical Center for a rare genetic disease called DADA2 (deficiency of the enzyme adenosine deaminase 2), caused by mutations in the *ADA2* gene. The disease can cause recurrent strokes, severe systemic inflammation, immune deficiency, and damage to body tissues and organs. Cole is enrolled in a clinical trial being run by **Jennifer Kanakry,** (National Cancer Institute) who relies on the CCE to provide engineered cells.

"The trial is aimed at studying new ways to hopefully improve the safety and efficacy of a transplant, even for problems with the immune system where the risk of the transplant not taking [is] high," said Kanakry. "The Center for Cellular Engineering is critical to allow us to provide a potentially life-saving, curative therapy to our patients as quickly as possible."

NCI senior investigator **Dennis Hickstein** is also counting on the CCE for his research on a rare bone-marrow-failure syndrome called GATA2 deficiency. "The [CCE] is critical for enabling freshly harvested bone-marrow cells from the donor to be infused into the recipient in a timely manner," he said. "Bone-marrow transplantation in diseases such [as] GATA2 deficiency relies upon the ability of the normal donor cells to replace the defective bone-marrow cells. The sooner that the cells are infused, the sooner the patient will acquire a new blood and immune system."

One of his patients is Jahleel, who has GATA2 deficiency. She received a bone-marrow transplant of 200 million bone-marrow cells per kilogram from her father. ●

To read more about Jahleel, go to http://bit.ly/2Ee9cLl.

THE CHILDREN'S INN AT NIH

During his stay at the NIH Clinical Center, seven-year-old Cole was visited by D.C. United soccer player Jalen Robinson. Under the care of Jennifer Kanakry and her team, Cole received a stem-cell transplant for a rare genetic disease.

LIANNE PRIEDE, NCI

Jahleel, an NIH Clinical Center patient with a rare bone-marrow-failure syndrome called GATA2 deficiency, received a bone-marrow transplant of 200 million bone marrow cells per kilogram from her father (left) under the care of NCI senior investigator Dennis Hickstein and his team.

New Institute Directors in NCCIH and NIBIB

NCCIH: Helene Langevin

Helene Langevin, an expert in integrative health, was sworn in as director of the National Center for Complementary and Integrative Health (NCCIH) on November 26, 2018. Her research interests have centered on the role of connective tissue in chronic musculoskeletal pain and on the mechanisms of acupuncture and manual and movement-based therapies. Her recent work has focused on the effects of stretching on inflammation-resolution mechanisms within connective tissue.

Before coming to NIH, Langevin was the director of the Osher Center for Integrative Medicine, which is jointly based at Brigham and Women's Hospital and Harvard Medical School (both in Boston). She was also a professor-in-residence of medicine at Harvard Medical School and a visiting professor of neurological sciences at the University of Vermont Larner College of Medicine (Burlington, Vermont).

As NCCIH director, Langevin oversees the continued development of an evidence base for the diverse medical and health-care systems, practices, and products that are not generally considered part of conventional medicine. NCCIH has an annual budget of approximately $142 million with which it funds and conducts research to help answer important scientific and public-health questions about natural products, mind and body practices, and pain management. The center also coordinates and collaborates with other research institutes and federal programs on research into complementary and integrative health.

Langevin received an M.D. degree from McGill University (Montreal). She completed a postdoctoral research fellowship in neurochemistry at the Medical Research Council Neurochemical Pharmacology Unit (Cambridge, England) and a residency in internal medicine and a fellowship in endocrinology and metabolism at The Johns Hopkins Hospital (Baltimore). She was the principal investigator of several NIH-funded studies and has authored more than 70 original scientific papers.

Langevin expects to continue her research in an intramural lab that has been established in the National Institute of Dental and Craniofacial Research. She is interested in exploring how to keep connective tissue flexible and free from pain, slow aging, and increase the health of the whole body.

NIBIB: Bruce J. Tromberg

The new year brought a new director for the National Institute of Biomedical Imaging and Bioengineering (NIBIB): **Bruce J. Tromberg**, a pioneering leader in the field of biophotonics. Biophotonics is a combination of biology and photonics (the physical science of the generation, detection, and manipulation of light or photons). Before coming to NIH, Tromberg was a professor of biomedical engineering and surgery at the University of California at Irvine and the director of the Beckman Laser Institute and Medical Clinic (Irvine, California).

Tromberg's research involves the use of light to image and conduct therapy at the molecular, cellular, and tissue levels. He specializes in new technology development as well as the bench-to-bedside clinical translation, validation, and commercialization of promising methods designed to improve human health.

In addition to serving as NIBIB director, Tromberg will be continuing his research at NIH. He plans to establish the Section on Biomedical Optics (SBO) in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. "The SBO will develop new bedside and wearable sensor technologies for quantitative measurements of tissue composition and metabolism," he said. "These devices can be translated to the clinic for guiding clinical decisions and understanding dynamic biological processes."

As NIBIB director, Tromberg will oversee NIBIB's annual budget, which in FY2019 is $389 million. Although a portion of the research budget is allocated to intramural laboratories at NIH, the majority supports a portfolio of more than 800 active grants awarded to universities around the nation and internationally.

Tromberg has conducted extensive NIH-supported research and has been the principal investigator for multiple NIH grants going back as far as 1994. As a high-school student, he volunteered in a National Cancer Institute laboratory on the NIH Bethesda campus. He earned a B.A. in chemistry and psychology from Vanderbilt University (Nashville, Tennessee) and a Ph.D. in chemistry from the University of Tennessee (Knoxville, Tennessee). He did his postdoctoral work at the Beckman Laser Institute and joined the faculty of UC Irvine in 1990. He has co-authored more than 450 publications and holds 18 patents for biophotonics technologies and their applications in areas such as cancer, neuroscience, and vascular disease. ●

Recently Tenured

JONAS S. ALMEIDA, NCI-DCEG

TODD S. MACFARLAN, NICHD

ALISON ANNE MOTSINGER-REIF, NIEHS

PHILIP SHAW, NHGRI

JONAS S. ALMEIDA, PH.D., NCI-DCEG

Senior Investigator and Chief Data Scientist, Division of Cancer Epidemiology and Genetics, National Cancer Institute

Education: Faculty of Sciences, University of Lisbon, in Lisbon, Portugal (B.S. in plant biology); Faculty of Sciences and Technology, New University of Lisbon, Lisbon, Portugal (Ph.D. in biological engineering)

Training: Postdoctoral training in microbial ecology and in computational statistics and machine learning at University of Tennessee (Knoxville, Tennessee) and Oak Ridge National Laboratory (Oak Ridge, Tennessee)

Before coming to NIH: Professor (tenured) and Chief Technology Officer, Department of Biomedical Informatics, Stony Brook University (Stony Brook, New York)

Came to NIH: In 2019

Selected professional activities: Participation in the International Society for Computational Biology and the American Society for Clinical Pathology with a focus on hands-on conferences, hackathons, and integrative data science

Outside interests: Dragging the family outdoors; sailing and kayaking are his favorite sports

Website: https://dceg.cancer.gov/about/staff-directory/biographies/A-J/almeida-jonas

Research interests: To accelerate the investigation of the epidemiologic and genetic causes of cancer, I am developing innovative methods to advance the computational infrastructure that will allow researchers to conduct precision-prevention studies of cancer. I lead a multidisciplinary research program that combines systems biology, computational statistics, and software engineering for biomedical applications.

The intersection of computational biology and data sciences has become a new frontier for engineering-software ecosystems for precision medicine. I seek to identify consumer-facing solutions for cancer prevention that use cloud computing, web applications, and machine learning. I am exploring this interrelated computational ecosystem by developing portable software solutions that can migrate between data sources (from consumer genomics to wearable sensing devices) and different contexts of application (for patients, caregivers, and others). This system is a new realm for participative computation, one that changes individual behavior and scales collective cognition in a manner sometimes described as "The Planet of the Apps."

As NCI-DCEG's chief data scientist, I have the dual responsibilities of 1) leading efforts for the integrated creation, management, and analysis of data-intensive knowledge bases, establishing cost-effective scalable researcher-facing analytic infrastructure, and defining new infrastructure to extract, manage, and analyze data in a scalable way to support epidemiological research; and 2) conducting independent research to advance real-time analytics of cancer "Big Data." My work provides support for the data and technology infrastructure used by a new prospective multicenter cohort study that will serve as an important DCEG-wide resource.

TODD S. MACFARLAN, PH.D., NICHD

Senior Investigator, Section on Mammalian Development and Evolution, National Institute of Child Health and Human Development

Education: Pennsylvania State University at State College, Pennsylvania (B.S. in biochemistry and molecular biology); University of Pennsylvania School of Medicine, Philadelphia (Ph.D. in cell and molecular biology)

Training: Postdoctoral training, The Salk Institute (La Jolla, California)

Before coming to NIH: Senior research associate, The Salk Institute

Came to NIH: In 2012 as an Earl Stadtman Investigator

Selected professional activities: Editor for *Mobile DNA*; class dean for the NIH Oxford-Cambridge Scholars Program for graduate students

Outside interests: Spending time with his wife and two children; playing soccer and basketball; coaching youth sports; running; hiking; listening to music

Website: https://irp.nih.gov/pi/todd-macfarlan

Research interests: At NICHD, our central mission is to ensure that every human is born healthy. Despite much progress in understanding the many ways a mother interacts with her fetus during development, we still know little about the molecular changes that promoted the emergence of placental mammals over 100 million years ago from our egg-laying relatives, or about the mechanisms that continue to drive phenotypic differences among mammals. One attractive hypothesis is that retroviruses and their endogenization into the genomes of our ancestors played an important role in eutherian evolution by providing protein-coding genes such as syncytins (derived from retroviral *ENV* genes that cause cell fusions in placental trophoblasts) and novel gene-regulatory nodes that altered expression networks to allow implantation and the emergence and continued evolution of the placenta.

The primary interest of my lab is to explore the impact of these endogenous retroviruses (ERVs), which account for about 10 percent of our genomic DNA, on embryonic development and on the evolution of new traits in mammals. This interest has led us to examine the rapidly evolving Kruppel-associated box zinc-finger protein (KZFP) family, the single largest family of transcription factors (TFs) in most, if not all, mammalian genomes. Our hypothesis is that *KZFP* gene expansion and diversification has been driven primarily by the constant onslaught of ERVs and other transposable elements (TEs) on the genomes of our ancestors as a means to transcriptionally repress them.

This hypothesis is supported by recent evidence demonstrating that most KZFPs bind TEs and that TEs and nearby genes are activated in *KZFP*-knockout mice. In the next several years we will continue to explore the impacts of the TE-KZFP arms race on the evolution of mammals. We will also begin a new phase exploring whether KZFPs play broader roles in genome regulation than just gene silencing and how these functions affect mammalian development.

ALISON ANNE MOTSINGER-REIF, PH.D., NIEHS

Senior Investigator and Chief, Biostatistics and Computational Biology Branch, National Institute of Environmental Health Sciences

Education: Vanderbilt University, Nashville, Tennessee (B.S. in biological sciences; M.S. in applied statistics; and Ph.D. in human genetics)

Before coming to NIH: Professor, Department of Statistics, and Core Director, Bioinformatics Consulting and Service Core, North Carolina State University (Raleigh, North Carolina)

Came to NIH: In 2018

Selected professional activities: Statistical Board of Reviewing Editors, *Science*

Outside interests: Parenting two young boys at home

Website: https://www.niehs.nih.gov//research/atniehs/labs/bb/index.cfm

Research interests: I am interested in developing new analytic methods that can be applied to real data—such as large-scale genetics and genomics data—to find genetic

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

factors that may predict complex disease as well as people's responses to drugs and environmental chemicals. For example, in my research on the response to cancer chemotherapies, I use cell-line models of drug response to look for genetic factors that can predict who will respond. Being able to predict mechanisms of action helps us better understand the biology of drug response, points to biomarkers, and helps us move toward personalized medicine.

The Biostatistics and Computational Biology Branch, which I lead, carries out basic and applied research dealing with statistical issues of relevance to environmental health. We are developing new methodologies and applying existing techniques in novel ways to address environmental health problems. We also advise NIEHS intramural scientists on computational study design and on database and statistical issues through both long-term and short-term collaborations in research projects throughout the institute.

In particular, we focus on developing and applying 1) animal toxicology and carcinogenicity experiments and improved statistical methods to analyze our findings; 2) methodologies for epidemiological and clinical human studies; 3) new bioinformatics techniques for harvesting information from high-dimensional genomic, gene-expression, and proteomic data; 4) new design and analysis approaches in statistical genetics; and 5) broadly applicable statistical approaches.

PHILIP SHAW, B.M., B.CH. (SURGERY), PH.D., NHGRI

Senior Investigator and Head, Neurobehavioral Clinical Research Section, Social and Behavioral Research Branch, National Human Genome Research Institute

Education: Oxford University, Oxford, England (B.A. in experimental psychology. B.M. and B.Ch. in medicine and surgery); Kings College, London (Ph.D. in psychological medicine)

Training: Residency in internal medicine at three hospitals in London: National Hospital for Neurology and Neurosurgery (neurology), Hammersmith Hospital (clinical pharmacology, cardiology), and Royal Free Hospital (infectious diseases, HIV medicine); residency in psychiatry, Maudsley and King's College Hospitals (London); fellowship in child psychiatry, New Children's Hospital (Sydney, Australia)

Before coming to NIH: Lecturer in neuropsychiatry, Institute of Psychiatry (London)

Came to NIH: In 2004 as a clinical research fellow and staff clinician, Child Psychiatry Branch, National Institute of Mental Health; became an Earl Stadtman Investigator in 2011

Selected professional activities: Member of the American College of Neuropsychopharmacology

Outside interests: Doing CrossFit (half-heartedly)

Website: https://irp.nih.gov/pi/philip-shaw

Research interests: My main interest is in the genetic, social, and environmental factors that influence the development of brain and behavior, especially in attention-deficit-hyperactivity disorder (ADHD). The ultimate goal is to provide tools to aid diagnosis and prognosis, and to develop individualized treatments that reflect the diversity of the genetic, behavioral, and neurocognitive problems found in ADHD.

ADHD is a highly heritable disorder, but only a small fraction of the genes that are likely to contribute to this complex disorder have been identified. My group aims to further genomic discovery by focusing not only on the clinical features of ADHD but also on the underlying brain features. We focus on the brain's structural and functional connections, particularly on how they develop over time. We have already identified the connections that are both heritable and associated with symptom severity and now use these features as targets for gene discovery and understanding.

Not all children with ADHD simply "grow out of the disorder" by adulthood; about a quarter of them have the full syndrome into adulthood, and many more have impairing symptoms. We have looked at the neural factors underpinning these variable adult outcomes. We found that among individuals who remitted from childhood ADHD by adulthood, the structure of cortical regions supporting attention and cognitive control veered toward typical dimensions, or "normalized," over the course of development. By contrast, those who had persistent symptoms into adulthood showed fixed, nonprogressive deficits. We use multimodal imaging to map how adult outcomes of childhood ADHD are underpinned by changes in the brain's structural and functional connections. We hope to translate these findings into clinically useful tools that can help predict the adolescent and adult outcome of a child's ADHD. This work could help target clinical treatments toward those most at risk of poor outcomes.

Furthermore, in collaboration with the National Institute of Mental Health, we aim for novel interventions grounded in our understanding of the neural and genomic contributors to ADHD. For example, we are developing a study in which a child with ADHD can use real-time feedback on his or her brain underactivation during an attention-demanding task to "normalize" this activation, thus improving attentional skills and symptoms. Through this intervention we aim to greatly accelerate the normalization of brain activity that underpins remission. ●

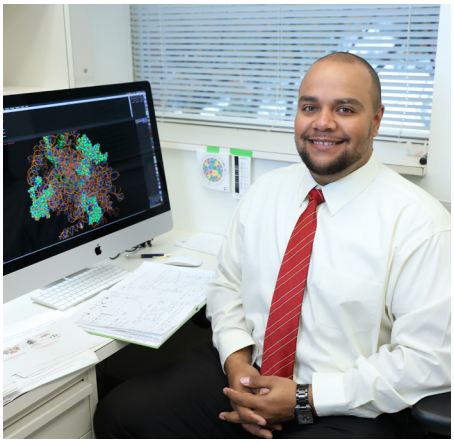
Bringing a Diversity of Perspectives to NIDCR Science

Using Biochemistry to Understand Developmental Disorders

BY CATHERINE EVANS, NIDCR

For biochemist Jason Collins, a postdoc in the National Institute of Dental and Craniofacial Research (NIDCR), it's the promise of the scientific "aha" moments that keep him coming back to the bench every day. "There's an excitement and adrenaline rush when all the pieces finally come together," he said. "Being able to share that with others, especially when it could benefit human health, is really exciting."

With this drive to discover, Collins became the first recipient of the NIDCR director's Postdoctoral Fellowship to Enhance Diversity in Dental, Oral, and Craniofacial Research. The award will enable Collins to work for up to five years in the Stem Cell Biochemistry lab of **Achim Werner**, who is exploring molecular signaling pathways that underlie craniofacial disorders.



CHIA CHI CHARLIE CHANG

Jason Collins is the first recipient of the NIDCR director's Postdoctoral Fellowship to Enhance Diversity in Dental, Oral, and Craniofacial Research.

Collins will draw on his expertise in ribosomes to understand cell processes that go awry during development to cause craniofacial malformations. His first insights into ribosomes emerged from his earlier postdoctoral work at the Scripps Research Institute campus in Jupiter, Florida. He studied how defects in the production of ribosomes could lead to conditions such as anemia, cancer, and craniofacial malformations. "When you bypass quality-control steps during ribosome maturation, the ribosomes have the potential to produce aberrant proteins that can cause dysfunction," Collins said. "We think this leads to disease."

Collins grew up in a military family in Germany and discovered his aptitude for biochemistry in high school. Later, at Old Dominion University in Norfolk, Virginia, one professor's influence sparked Collins's interest in the field as a career. He stayed at Old Dominion after graduation and completed his Ph.D. in biomedical sciences, and his insights into protein folding and misfolding in Alzheimer disease garnered several journal articles and a book chapter.

Collins is excited to continue his training at NIH, where he's found the collaborative environment suits him well. When he applied for the NIDCR fellowship, "what struck me was the sense of community and the many resources that are available to facilitate an interdisciplinary environment," he said. "Science [is] collaboration and discussing ideas with others in order to discover new and better ways to answer important questions."

This notion strikes at the heart of the NIDCR director's diversity fellowship, which is designed to enable scientists from diverse backgrounds and life experiences to bring different perspectives, creativity, and individual enterprise to address complex scientific problems. "Taking steps to support the inclusion of early-career scientists from underrepresented groups is an investment in development of a stronger, more dynamic research environment," said NIDCR Director **Martha Somerman**.

"We encourage applicants with a commitment to enhancing the diversity of the biomedical field and pursuing independent, highly competitive careers in dental, oral, and craniofacial research," said **Deborah Philp**, director of NIDCR's Office of Education, whose own doctoral work was supported by an NIH diversity program—the Division of Minority Opportunities at the National Institute of General Medical Sciences.

At NIDCR, Collins is trying to understand a molecular-signaling pathway, first discovered by his mentor Werner, that affects ribosome production during neural-crest stem-cell formation. These stem cells are produced during early embryo development and give rise to the facial bones, cartilage, and teeth. Werner and Collins suspect that changes to ribosomes in neural-crest stem cells during development could underlie Treacher-Collins syndrome, a disorder causing abnormal growth of the teeth and bones of the head and face. Collins's work might identify potential treatment targets for the syndrome and similar disorders—precisely the kind of lightbulb moment that motivates him to keep discovering.

"I'm driven to understand the world around us and how we can make it better for others," Collins added. "With science, you can do that." ●

This article first appeared on the NIDCR News and Events webpage: http://bit.ly/2GMIUU6.

ONLINE ONLY at https://irp.nih.gov/catalyst/v27i2: Nobelist Michael Young Delivers WALS Lecture; Behavioral and Social Sciences Research Festival 2018

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Also, we welcome "letters to the editor" for publication and your reactions to anything on the *Catalyst* pages.

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PHOTOGRAPHIC MOMENT

Memorial Trees

BY ADRIAN CARCAMO, NCI

Of the over 8,000 trees on the Bethesda campus, 24 are memorial trees and 50 are commemorative. Memorial trees honor people; commemorative trees honor an institute, department achievement, or milestone.

The most recent memorial tree is a kousa dogwood, planted last year in memory of **Sang-A Park**, a native of South Korea, who came to NIH in 2016 as a visiting postdoctoral fellow in the National Institute of Dental and Craniofacial Research's Mucosal Immunology Section. She died after being hit by a car on campus in January 2018. Her tree is native to China, Japan, and Korea. In late spring, it will produce white flowers in the courtyard west of Building 30, where she once worked. ●

Read the whole article at https://irp.nih.gov/catalyst/v27i2/memorial-trees.

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