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NIH Dental Clinic

Brace Yourself for Collaborations

BY GERIANN PIAZZA, NIDCR

Many intramural clinical investigators and research nurses may be unaware of the NIH Dental Clinic tucked away on the first floor of the NIH Clinical Center, despite the fact that the dental group began caring for patients since 1953. The clinic is well known, though, for its wisdom-tooth studies: recent studies on tooth and tissue samples collected during the removal of wisdom teeth as well as past studies to test the efficacy of pain medications. And, the Dental Clinic's consult services can guide the overall treatment plan for Clinical Center patients and lead to multidisciplinary-research collaborations between the National Institute of Dental and Craniofacial Research (NIDCR) and other institutes.

Over the past five years, NIDCR has renovated the Dental Clinic and recruited many board-certified staff and investigators—including NIDCR Clinical Director **Janice Lee** and three additional oral and maxillofacial (jaw and face) surgeons—**Kalpakam Shastri**, **Bonnie Gitman**, and **Andrea Burke**. In addition, Clinical Center patients now have access to oral-medicine specialist **Pamela Gardner**, hospital dentist **Bob Range**, and dental hygienist **Laurie Brenchley**. Patients with complex medical conditions such as Sjögren syndrome (an autoimmune disease that typically includes dry mouth and dry eyes and is often associated with rheumatologic disorders)

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New Partnership with Spanish Neuroscientists

Second Set of Cajal Drawings on Loan from Spain

BY CHRISTOPHER THOMAS, NINDS

COURTESY OF CSIC INSTITUTO CAJAL, MADRID, SPAIN

A Ramón y Cajal original: A drawing of Calyx of Held synapses, which are unique neuron communication points used in hearing. It's one of seven original Ramón y Cajal's drawings on display in the Porter Neuroscience Research Center.

On October 28, 2015, neuroscientists from Spain and the NIH gathered in the Porter Neuroscience Research Center (PNRC) for a daylong symposium that honored Santiago Ramón y Cajal, the Spanish scientist who in 1906 shared the Nobel Prize in Physiology or Medicine in recognition of his work on the structure of the nervous system.

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A Red Alert for the NIH

BY MICHAEL GOTTESMAN, DDIR

The intramural research program (IRP) depends heavily on input from outside experts to evaluate our laboratory and clinical research activities, including reviews by our Board of Scientific Counselors (BSC) and occasionally more global outside advice such as the recent Long-Term Planning Report from a subcommittee of the Advisory Committee to the Director (ACD) (http://acd.od.nih.gov/reports/ACD-IRP-WG-report.pdf). Most recently, in response to serious deficiencies discovered in May 2015 in the Clinical Center's Pharmaceutical Development Section (PDS), NIH Director **Francis Collins** commissioned a report from an ACD subcommittee called the "Red Team," chaired by Norman Augustine, formerly chief executive officer of Lockheed Martin, to determine the underlying causes of the PDS problems and to recommend a way forward designed to prevent similar problems from happening in the future.

The Red Team report was released on April 21, 2016. It concluded that deficiencies in practices in the PDS facilities—failure to comply with current good manufacturing practice (cGMP), a tendency to put research priorities ahead of safety concerns, and lack of reporting deficiencies up the chain of command so that corrective actions could be undertaken—were to some extent systemic and not limited to the PDS (http://www.acd.od.nih.gov/presentations/Red_Team_presentation.pdf).

These issues, if not attended to quickly, have the potential to put patients and, in some cases, staff at risk. In fact, some of the other facilities at the NIH that prepare sterile materials for use in clinical research were found to suffer from similar deficiencies incompatible with FDA requirements and have either been closed or are undergoing remediation. It is important to note that none of these problems have resulted in any direct harm to patients. But to maintain the deserved reputation of the Clinical Center as one of the best places in the world to participate in clinical research, we must take the findings of the Red Team very seriously and embrace its 11 wise, thoughtful recommendations. The report and its recommendations were relayed to institute and center directors, scientific directors, clinical directors, and the entire NIH clinical research community in a series of meetings on April 21 and 22, 2016.

> If the proposed recommendations are implemented, the IRP can provide the essential degree of patient safety while continuing its record of extraordinary scientific accomplishments.

The Red Team noted that in some cases it appeared that an emphasis on research was placed ahead of patient safety, and this emphasis must change. Such a change may require some investigators to reset their priorities and all of us to fortify our attention to patient care. The NIH clinical staff is highly dedicated to patient care, but that does not mean that we cannot improve our clinical-care practices and oversight even further. And the requirement "if you see something, say something" puts us all on notice that any concerns about practices that might threaten patient safety need to be reported to supervisors and beyond until appropriate action is taken. An improved system to accomplish this anonymously, if necessary, will be put into place.

There will be organizational changes to oversee and enforce new safety and compliance standards including a new Research Support and Compliance Unit (RSCU) in the Office of Intramural Research; a new Clinical Practice Committee to set standards for all clinical practice at the NIH; and an external hospital board, similar to those that oversee most U.S. hospitals, to ensure compliance with the highest standards of care.

On April 21, Dr. Collins announced that Laura Forese, executive vice president and chief operating officer of the New York–Presbyterian hospital system, will be the first chair of this new board. She is an orthopedic surgeon and has extensive experience in managing a vast hospital system.

Our very own **Kathryn Zoon**, formerly the scientific director of the National Institute of Allergy and Infectious Diseases, and before that, the director of the FDA's Center for Biologics Evaluation

and Research, will be the interim director of RSCU. She will work with me to help establish the office and oversee the development of a governance system that ensures compliance with regulatory and safety requirements at the NIH. These experienced leaders will make sure that we make all of the needed practice and policy changes that are outlined in the Red Team report.

The last sentence of the report captures the essence of the evaluation: "If the recommendations proposed herein…are implemented, the IRP can provide the essential degree of patient safety while continuing its record of extraordinary scientific accomplishments." As with the many valuable recommendations that we have received over the years, our prompt and complete attention to this advice will make the NIH an even more effective research institution in which we clearly incorporate compliance with applicable regulations and policies into our scientific culture. (Please see the new "Guidelines and Policies for the Conduct of Research at the NIH" at https://oir.nih.gov/sourcebook/ethical-conduct.) ●

To see a videocast of the April 22, 2016, NIH Clinical Center Town Hall meeting at which Red Team report was presented, go to http://videocast.nih.gov/launch.asp?19639 (NIH only).

ACD Long-Term Intramural Research Program (LT-IRP) Planning Working Group

- **Presentation**: http://acd.od.nih.gov/presentations/2014-12-11_ACD_LT-IRP_Cato.pdf.
- **Report**: http://acd.od.nih.gov/reports/ACD-IRP-WG-report.pdf).

Michael Gottesman's essay on the IRP long-term planning report in the July-August 2015 issue of the *NIH Catalyst*: http://irp.nih.gov/catalyst/v23i4/from-the-deputy-director-for-intramural-research.

Attention Intramural Investigators

Do You Know About NIH's Bench-to-Bedside Program?

BY PAT PIRINGER, JULIE ORLANDO, AND HANA SMITH, CC

Scientific collaboration is the name of the game these days, but did you know that NIH's Bench-to-Bedside (BtB) program was the first formal intramural effort that encouraged NIH investigators to seek funding for collaborative projects that involved other institutes and centers (ICs)? Established in 1998 by NIH Clinical Center Director **John Gallin**, the program has fostered longstanding, successful partnerships between basic and clinical researchers and has supported cross-institute projects that have accelerated the translation of promising laboratory discoveries into new medical treatments. BtB awards have financed research on AIDS, behavioral and social sciences, minority health and health disparities, women's health, pharmacogenomics, rare diseases and rare-diseases drug development, and other areas.

At first, the BtB program monies came from the Clinical Center's carryover funds, but by 2000 other NIH ICs were stepping in to help. Since 2003, most BtB awards have been provided by the Office of AIDS Research, the Office of Rare Diseases Research, the Office of Behavioral and Social Sciences, the Office of Dietary Supplements, the Office of Research on Women's Health, and the National Institute on Minority Health and Health Disparities. In addition, the Office of Intramural Research funds worthy BtB projects—intramural only—that might not fit into the other partners' research categories. And sometimes, other ICs may fund highly ranked projects when BtB program funds are not available.

In 2006, the program's scope expanded to encourage partnerships between intramural and extramural investigators. Since then, more than 90 percent of BtB projects have included an extramural collaborator (including investigators from international institutions).

Each BtB award—which provides investigators with small seed grants of up to $135,000 a year for two years—helps spur new collaborative translational research projects. About 20 percent of the BtB projects have gone on to receive funding from other sources including from the Opportunities for Collaborative Research at the NIH Clinical Center (U01) program.

Become Part of BtB's Success Story!

Look for the 2016 BtB Call for Proposals to be launched early this summer. Remember, the program provides an excellent opportunity to seed new research as well as to establish collaborations with intramural investigators outside your own institute or with extramural investigators. BtB offers intramural PIs the experience of applying for and receiving award funds in a manner that aligns with the NIH grants process.

To learn more about the program, join a pre-application information session on Tuesday, May 24, 9:30–11:00 a.m. in the Clinical Research Center's Medical Board Room (Building 10, Room 4-2551). Program administrators will be available to answer questions, and previous awardees will share their BtB experiences. You can also visit http://www.cc.nih.gov/ccc/btb/ or e-mail your questions to BenchtoBedside@mail.nih.gov. ●

FROM THE FELLOWS COMMITTEE

National Postdoctoral Association Helps Enrich Postdoc Training

BY CRAIG MYRUM, NIA

As researchers, we have seen how scientific investigations have evolved from the simple to elaborate, advanced, multimethod studies that often rely on collaborations among scientists from different disciplines. As postdocs, we know that we need training to keep pace with this ever-changing research world.

The NIH Fellows Committee (FelCom) has a long history of helping to identify ways of enriching the training experience at NIH. Not only does FelCom work closely with the Office of Intramural Training and Education to improve training, but it also has teamed up with the National Postdoctoral Association (NPA). NPA facilitates positive change for postdocs everywhere and in so doing advances the research enterprise in the United States.

Ten NIH representatives gathered with more than 380 others (including postdocs, faculty, administrators, and others) from across the country at NPA's 14th Annual Meeting held in Grand Rapids, Michigan, this March. There they laid out strategies to expand career-development programs for postdocs and discussed the challenges and opportunities faced by postdocs worldwide.

Attendees also discussed ways to enhance core competencies that are essential to a professional career, whether it's in academia, industry, government, a nonprofit, or an entrepreneurial business: discipline-specific conceptual knowledge; research skill development; communication skills; professionalism; leadership and management skills; and responsible conduct of research. As part of the discussion, FelCom NPA liaison **Didier Chalhoub** (National Institute of Aging) presented a poster on the Fellows Award for Research Excellence (FARE), which recognizes the outstanding scientific research performed by NIH's intramural postdoctoral fellows. "The fact that FARE is organized by the postdocs for the postdocs captivated the attention of many," said Chalhoub. "Some even asked to use it as a model [at] their universities."

Given that there are 3,000 postdocs in NIH's intramural program at any given time, FelCom can serve as an example to other postdoctoral communities for how to improve training experiences.

"The NPA presents great leadership opportunities for postdocs," too, said Chalhoub. "Members can join committees and work on projects they are passionate about." NPA's five core committees are Advocacy, Outreach (to disseminate NPA activities and goals), Meetings, Resource Development, and POSTDOCket (NPA's quarterly newsletter). In addition, "NPA [is] a great networking platform."

The NPA organizes the annual National Postdoc Appreciation Week every September as a way to recognize the significant contributions that postdoctoral scholars make to research and discovery. NIH campuses and institutions across the country and even around the world participate by holding special events. Stay tuned! ●

To learn more about FelCom, attend or call in to its meetings, which are held on the first Thursday of every month at 4:00 p.m. in Wilson Hall (Building 1). Find out how by subscribing to the Fellow-L LISTSERV (go to https://list.nih.gov and search the "Public Lists" for Fellow-L).

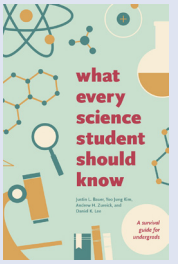
Websites for more information

- **FelCom: https://www.training.nih.gov/felcom**
- **NPA: http://www.nationalpostdoc.org**
- **OITE: https://www.training.nih.gov**

NIH ALUMNI NEWS

What Every Science Student Should Know

Two former NIHers are among the co-authors of *What Every Science Student Should Know* (University of Chicago Press, 2016). **Andrew H. Zureick** was a trainee in a summer internship program (SIP) in the National Eye Institute in 2010, and **Yoo Jung Kim** was a summer intern at the National Cancer Institute (2012) and an Intramural Research Training Award fellow at the National Human Genome Research Institute (2014–2015).



The book, written by four medical students who are graduates of Dartmouth College (Hanover, New Hampshire) and former editors-in-chief of the *Dartmouth Undergraduate Journal of Science*, aims to help aspiring scientists navigate the college experience, choose a major, master study skills, do scientific research at the undergraduate level, find a job, and continue to love science.

"I know this is something I personally wish I had read before my SIP experience," said Zureick, who graduated from Dartmouth in 2013 and is now a medical student at the University of Michigan Medical School (Ann Arbor, Michigan). "I imagine motivated SIP interns would likewise derive great benefit from it."

"The book was originally inspired by my experiences at the NIH," said Kim, a 2014 Dartmouth graduate and now a medical student at Stanford University School of Medicine (Stanford, California). "Some of the students interviewed for the book are also former NIH interns."

NIH is mentioned several times in the book including "a plug for the NIH Summer Internship Program," said Zureick. ●

Senator Mikulski's Farewell Visit to NIH

Continuing to Advocate for NIH

BY EMILY PETRUS, NINDS

Soon-to-retire U.S. Senator Barbara Mikulski (D-Md.) promised to continue to be an advocate for NIH in a town hall meeting held in Masur Auditorium on April 11, 2016. She had spent the day visiting with NIH Director **Francis Collins** and other institute directors, reassuring them and the assembled crowd that although this will be her last year as Maryland's senator, she will continue to fight for increased NIH funding. Senator Mikulski, who served for 10 years in the U.S. House of Representatives (1976–1986) and 30 years in the U.S. Senate (1986–2016), has often described herself as "working her earrings off" for NIH. So Collins presented her with a backup pair—ones emblazoned with the NIH logo.

Collins and Mikulski both spoke of the remarkable progress biomedical research has made over the past decades, from discovering and mapping the human genome to reducing cancer and heart disease mortality rates. The senator also highlighted her role as an advocate for the inclusion of women in clinical trials and health research, which led to the formation of the present-day NIH Office of Research on Women's Health.

Senator Mikulski outlined her priorities for her final year on the Senate Appropriations Committee. She has served on that committee since 1987, and in 2012 became the first woman and the first Marylander to chair it. She is now vice chair. Three principles would guide her actions, she said: Do no harm, meaning no sequesters or shutdowns; make sure that current successful programs do not lose funding; and find new money for programs such as the BRAIN initiative, precision medicine, and the "moonshot" initiative to end cancer.

She addressed a future challenge facing scientific research—the declining quality of K-12 education in science, technology, engineering, and mathematics fields. "We need to stand up for the future," said Mikulski. "We need to make sure we have education [that] isn't determined by your ZIP code." She also addressed the affordability and accessibility of college and graduate school and proposed a 20-year term limit on student loans.

"To serve is in my DNA," said Mikulski. "If you take the sample… you'll find the serve gene." Until her last hours in office, Senator Mikulski has vowed to continue her fight for the future of biomedical research.

"No matter where I go, I will continue to be your advocate," said Mikulski. "I will never forget you."

As a thank you, Collins presented the senator with a plaque sporting a gold-plated petri dish and read the engraved message aloud: "For her extraordinary vision, boundless enthusiasm, and tireless efforts on behalf of biomedical research during her 40 years in Congress, her work has been vital to ensuring the National Institutes of Health remains the National Institutes of Hope for all of human kind." ●

To watch the videocast online, go to http://videocast.nih.gov/launch.asp?19608.

ERNIE BRANSON

ANNOUNCEMENTS

Kudos to NIH Scientists

NIAID Director **Anthony Fauci** is the recipient of the Canada Gairdner Global Health Award for 2016 "for his many pioneering contributions to our understanding of HIV infections and his extraordinary leadership in bringing successful treatment to the developing world."

Clare Zhu, who participated in the summer internship program at NIDA in **Lei Shi's** lab in 2015, was a finalist in the Intel Science Talent Search. Zhu, age 17, of Irvine, California, studied the topography of G-protein-coupled receptors (GPCRs), which are prime targets for designer therapeutic drugs treating a wide range of conditions.

Katie Kindt, acting chief of NIDCD's Section on Sensory Cell Development and Function, and **Andre Larochelle**, an investigator in the NHLBI Regenerative Therapies for Inherited Blood Disorders lab were among the 105 researchers named as recipients of the Presidential Early Career Awards for Scientists and Engineers (PECASE), the highest honor bestowed by the United States government on science and engineering professionals in the early stages of their independent research careers.

The journal *Nature* named cryoelectron microscopy (cryo-EM) the "Method of the Year" for 2015. This technique is being pioneered by **Sriram Subramaniam** and his NCI colleagues. They were able to visualize the beta-galactosidase protein with single-particle cryo-EM at a level of near-atomic detail. Cryo-EM maps showing the contacts between small molecules and proteins can help to explore questions such as why one drug is better than another or why certain drugs fail. ●

Proteins and Processors

A Chat with NIH's Chief Data Scientist, Philip Bourne

BY BRANDON LEVY, NIMH

At first blush, Philip Bourne sounds a lot like the name of a secret agent. The Australian-born chemist has spent much of his career working with supercomputers, occasionally taking a break to fly small airplanes or take transcontinental journeys on his motorcycle. But unlike Jason Bourne of the Bourne film franchise, *Philip* Bourne uses his special skills to help researchers ply massive piles of data to produce new scientific breakthroughs.

Hired as the NIH's associate director for data science in 2014, Bourne administers an approximately $100 million funding enterprise called the Big Data to Knowledge program, or "BD2K" for short. The ultimate goals of the initiative, Bourne said, are to establish the NIH as a leader in data science, train scientists to take advantage of so-called "Big Data" in their research, and create policies and processes that will guide the use of Big Data. NIH launched the BD2K venture in 2012 and now funds 13 research centers across the United States. BD2K also provides many benefits to NIH intramural scientists including programs that teach individuals to train others in the use of basic data-science tools; hackathons in which researchers can examine unrelated data sets to generate novel findings; and a virtual commons where both intramural and extramural investigators are starting to access each other's data and store their own.

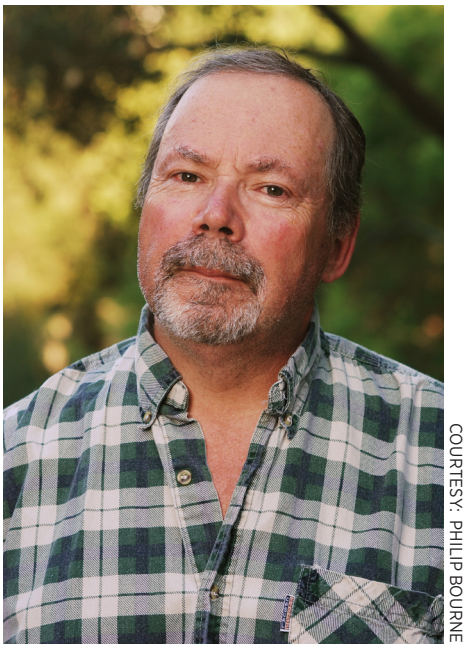
While some define Big Data as simply the accumulation of large quantities of information, Bourne takes a different view. "For me, the important thing is aggregation of data that [come] from different sources," Bourne said. "But when you put them together, it opens up new possibilities and [enables] new discoveries." As an example, Bourne pointed to a recent project that combined data from a smart-phone application with information from the crowd-sourced review website Yelp to identify correlations between the concentration and type of restaurants in a city and the physical-activity levels and weights of the city's residents.

Bourne has taken a somewhat nontraditional path to becoming NIH's resident guru of data science. His first love was actually chemistry, which he decided to pursue because his high-school chemistry teacher told him he would never succeed in the field.

"I think it was his way of inspiring me," Bourne chuckled. "I think he knew all along that I would rise to the challenge."

But the momentous advancements in computer technology that occurred during his undergraduate years at Flinders University (Bedford Park, South Australia) also sparked an interest in that area. These developments enabled physical chemists such as Bourne to create computer models of how the atoms that make up important biological compounds are positioned in space. "It's that three-dimensional arrangement that confers the function of a molecule and how it interacts with other molecules," he explained.

As a postdoctoral fellow at the University of Sheffield (Sheffield, England), Bourne used these models to determine the structure of the iron-storage protein ferritin found in human red blood cells, a discovery that shed light on how the human body processes iron (*Nature* **288:**298–300, 1980). Bourne has also used his expertise to model the structure and behavior of drug molecules, information that pharmaceutical companies can use to make therapies more effective and reduce side effects. "One of the things I've always pushed for is the idea of translation," Bourne said. "I'm not particularly interested in publishing a paper on a new interaction or a new tool. I'm much more interested in seeing this [research] translated into something that has an impact on health care."



COURTESY: PHILIP BOURNE

Hired as the NIH's associate director for data science in 2014, Philip Bourne administers an approximately $100 million funding enterprise called the Big Data to Knowledge program.

The importance of Bourne's computer skills to his research interests made the transition to data science a natural one. When he began working in the Department of Biochemistry and Molecular Biophysics at Columbia University (New York) in 1981, he wanted to use computer simulations to examine how neurotoxins bind to certain receptors in the nervous system. Columbia's computers were so bad, however, that Bourne complained to the dean about them. The dean offered to raise money for a new computer center

if Bourne would help build it and run it. Bourne agreed.

But after managing the facility for four years, the advent of the Human Genome Project pulled Bourne back into research. Sequencing a genome requires the use of computer algorithms to identify and link together overlapping regions of DNA fragments to form a continuous sequence. Bourne assisted in the assembly of human chromosome 13. "Doing that, I realized that this was the future of biomedicine," he said. "I wanted to get back to research rather than run a computer center for other people."

In 1995, Bourne moved to the University of California at San Diego (La Jolla, California), where he taught classes in the Department of Pharmacology and conducted research in the San Diego Supercomputer Center. He eventually became the director of the center's Integrated Biosciences Program and associate director of the university's Protein Data Bank, an online platform through which scientists around the world can upload and use information about the structures of biological molecules.

At the same time, he began studying evolution through the lens of protein structure. By examining the spatial organizations of proteins found in different organisms, Bourne and his collaborators were able to produce what Bourne calls "the tree of life"–a chart depicting the evolutionary closeness of 174 species (*Proc Natl Acad Sci U S A* **102**:373–378, 2004). According to Bourne, this work would have been impossible without resources, such as the Protein Data Bank, that provide access to large collections of other researchers' data.

"And that's why I'm so intrigued with what's going on now—more and more of biomedicine is involving [the] re-use of other people's data," he explained. "It's becoming an increasingly important part of what we do every day."

So when NIH Director **Francis Collins** asked Bourne to run the NIH's brand-new data-science initiative, Bourne jumped at the opportunity.

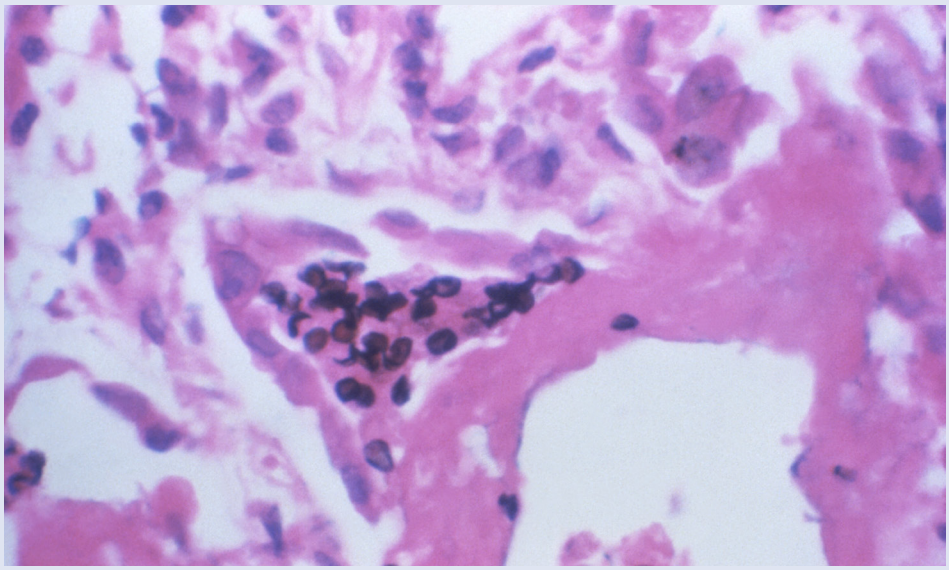
When Bourne is not using computers to scrutinize the shapes of proteins or launch new research programs, he enjoys using them to communicate about his other great love: motorcycles. An avid enthusiast since the age of 16, Bourne maintains a travel blog that describes his many long-distance trips, including a nearly 5,000-km excursion around western Australia in 2009, a 5,000-km jaunt through Eastern Europe in 2010, and the trip he undertook from San Diego to Virginia after he accepted his position at NIH. In the near future, he hopes to ride his bike out to Yellowstone National Park. NIH's colossal datasets will be awaiting his return. ●

COURTESY: PHILIP BOURNE

An avid motorcycle enthusiast since the age of 16, Bourne maintains a travel blog that describes his many long-distance trips, including a nearly 5,000-km excursion around western Australia and a 5,000-km jaunt through Eastern Europe.

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CDC: Centers for Disease Control and Prevention
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
FAES: Foundation for Advanced Education in the Sciences
FARE: Fellows Award for Research Excellence
FelCom: Fellows Committee
FDA: Food and Drug Administration
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



FRANCIS W. CHANDLER, CDC

Clinical Center researchers help sequence nearly the entire genomes of three species of Pneumocystis, a fungal pathogen that causes pneumonia and has caused thousands of deaths in immunosuppressed people such as those who've had transplants or are infected with HIV/AIDS. Shown here, a lung tissue sample extracted from a patient ill with pulmonary pneumocystosis. The dark spots in the alveolar spaces are the fungal organisms.

CC: RESEARCHERS SEQUENCE GENOME OF A FUNGUS THAT CAUSES LIFE-THREATENING PNEUMONIA

Clinical Center researchers, in collaboration with scientists at Leidos Biomedical Research (Frederick, Maryland) and the Broad Institute (Cambridge, Massachusetts), have sequenced nearly the entire genomes of three species of Pneumocystis, a fungal pathogen that causes pneumonia in humans, mice, and rats. Over the past 30 years, the pathogen has caused thousands of deaths in immunosuppressed people such as those who've had transplants or are infected with AIDS or the human immunodeficiency virus. Efforts to combat Pneumocystis infection have been stymied by a lack of knowledge about its genome that makes it impossible to culture the organism in the lab or manipulate its DNA.

The investigators discovered that Pneumocystis is extremely well adapted to its mammalian hosts. "Our findings suggest that Pneumocystis has developed unique mechanisms of adaptation to life exclusively in mammalian hosts, including dependence on the lungs for gas and nutrients and highly efficient strategies to escape both host innate and acquired immune defenses," the investigators wrote in their paper.

The newly acquired genomic information may lead to methods for growing Pneumocystis in the lab and allow researchers to test medications designed to kill the fungus. The information could also permit the investigators to alter the organism's genes and determine how various genetic changes affect its ability to infect and harm its host. (NIH authors: L. Ma, G. Kutty, H. Wang, L. Bishop, E. Davey, R. Deng, X. Deng, G. Fantoni, E. Gogineni, G. Handley, C. Huber, Y. Liu, M. Sassi, X. Song, L. Walsh, Y. Xia, and J.A. Kovacs, *Nat Commun* 7:10740, 2016; DOI:10.1038/ncomms10740)

NIAAA: MARIJUANA-USE DISORDER IS COMMON AND OFTEN UNTREATED

In 2013, the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) established new diagnostic criteria that combine marijuana dependence and abuse into a single disorder—marijuana-use disorder. NIAAA researchers conducted a study using the DSM-5 criteria and reported that marijuana-use disorder is common in the United States; is often associated with other substance-use disorders, behavioral problems, and disability; and often goes untreated.

The researchers applied the DSM-5 criteria to their analysis of data collected in 2012 and 2013 from a nationally representative sample of more than 36,000 American adults via the third National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III). The analysis found that 2.5 percent of adults in the United States had experienced marijuana-use disorder in the past year and 6.3 percent suffered from marijuana dependence at some point in their lives. In addition, marijuana-use disorder was strongly associated with other substance-abuse and mental-health disorders, including alcohol-use disorder, major depressive disorder, and post-traumatic stress disorder. Marijuana dependence was also found to produce considerable mental disability. Finally, the study showed that only seven percent of people with past-year marijuana-use disorder and 14 percent of those who had experienced marijuana-use disorder at some point in their lives received treatment for the condition. The study authors noted the urgency of identifying and implementing effective prevention and treatment for marijuana-use disorder and the importance of educating the public about the dangers associated with marijuana use. (NIH authors: T.D. Saha, B. Huang, R. Pickering, S.M. Smith, J. Jung, H. Zhang, B.F. Grant; *Am J Psychiatry* DOI: 10.1176/appi.ajp.2015.15070907; NIDA contributed funding)

NICHD: PRETERM BIRTH AND AIR POLLUTION

Roughly nine percent of American women of reproductive age have asthma, according to the Centers for Disease Control and Prevention. Maternal asthma is associated with a higher risk of pregnancy complications and preterm birth (before the 37th week of pregnancy)

COMPILED BY BRANDON LEVY (NIMH); NIDCR BRIEF SUBMITTED BY DAVE VANNIER (NIDCR)

as well as health problems for infants. In a recent study, researchers at NICHD and other institutions determined that pregnant women with asthma may be more likely to give birth prematurely when exposed to high concentrations of certain traffic-related air pollutants. Although previous studies showed that concentrations of certain air pollutants increase the risk of preterm birth, the NICHD study is the first to examine the effect of air-pollutant exposure before conception and very early in pregnancy. The researchers analyzed data from more than 223,000 single births occurring between 2002 and 2008 across the United States. They also examined daily measurements of six air pollutants in the regions surrounding the hospitals to assess the potential effects of air pollution.

The study found that higher concentrations of the traffic-related pollutants nitrogen oxides and carbon monoxide during the three months before conception and the first seven weeks of pregnancy increased the incidence of preterm births more in mothers with asthma than those without. Increased exposure to small particulate matter late in pregnancy had the same effect. The researchers hope their findings will prompt additional studies aimed at reducing the risk of preterm births in women with asthma. (NIH authors: P. Mendola, M. Wallace, B.S. Hwang, D. Liu, R. Sundaram, and K.L. Grantz, *J Allergy Clin Immunol* DOI:10.1016/j.jaci.2015.12.1309)

NINDS: NMDA RECEPTORS MAY HELP THE BRAIN DETECT MOTION

A series of experiments performed by NINDS scientists suggest that a protein called the N-methyl-D-aspartate (NMDA) receptor helps neurons in the eye and brain filter out background noise to detect movement. NMDA receptors have long been associated with learning and memory but have never before been linked to motion perception.

The researchers passed bars of light across retinas isolated from mice and recorded the electrical responses from neurons called directionally selective retinal ganglion cells (DSGCs), which are activated by stimuli moving in specific directions. By exposing the DSGCs to moving bars of light set against backgrounds of varying brightness, the NINDS team discovered that NMDA receptors helped the neurons send consistent signals about the direction of each bar's motion despite variations in the level of background light. The NMDA receptors did this by amplifying the cells' responses to the bars via a process called multiplicative scaling.

The results shed light on how neurons distinguish useful information in the visual environment from irrelevant inputs. The researchers now hope to examine whether NMDA receptors play a role in other visual processes as well. (NIH authors: A. Poleg-Polsky and J.S. Diamond, *Neuron* **89**:1277–1290, 2016)

NIAID: FACTORS THAT MAY INFLUENCE INFLUENZA VACCINE EFFECTIVENESS

The system for predicting the effectiveness of the seasonal flu vaccine may need to be changed, according to a study conducted by NIAID researchers. Currently, seasonal flu vaccines are designed to induce high concentrations of protective antibodies against hemagglutinin (HA), a protein found on the surface of the influenza virus that enables the virus to enter a human cell and initiate infection. However, there are wide variations in the effectiveness of recent vaccines.

The researchers conducted a clinical trial —called a human challenge study—in which 65 healthy volunteers (aged 18 to 50 years) were exposed to naturally occurring 2009 H1N1 influenza type A virus and monitored for eight weeks. The flu challenge study was conducted at the NIH Clinical Center in the specially designed Clinical Studies Unit, which has distinct isolation and infection-control features. The researchers found that higher concentrations of antibody against a different flu surface protein—neuraminidase (NA)—were a better predictor of protection against flu infection and its unpleasant side effects. NA, which is not currently the main target antigen in traditional flu vaccines, enables newly formed flu viruses to exit the host cell and cause further viral replication in the body.

Participants who had high concentrations of HA antibodies were considerably less likely to develop mild-to-moderate influenza during the eight-week period and also fought off the illness more quickly than those with lower concentrations of HA antibodies. However, both groups experienced roughly the same number and severity of flu symptoms. On the other hand, those with high concentrations of NA antibodies were not only less likely to get sick but also experienced symptoms that were less numerous, less severe, and briefer than those with low NA antibody concentrations or high HA antibody concentrations.

Participants with high concentrations of both types of antibodies were the most protected against the virus. The findings suggest that NA antibodies may be a better predictor of influenza immunity than HA antibodies and should be taken into account when estimating the efficacy of future vaccines. (NIH authors: M.J. Memoli, A. Han, L. Czajkowski, S. Reed, R. Athota, T. Bristol, S. Fargis, K. Risos, J.H. Powers, R.T. Davey, Jr., and J.K. Taubenberger, mBio 7:e00417-16, 2016; DOI:10.1128/*mBio*.00417-16)

NIDCR: THE HEALTHY ORAL IMMUNE SYSTEM AND PERIODONTAL DISEASE

NIDCR and University of Manchester (Manchester, England) researchers have identified the immune cells that reside in the gingival tissues surrounding the teeth. This study is the first detailed immunophenotyping of human oral tissues and provides a foundation for characterizing the healthy oral immune system and will help scientists track changes that occur under disease conditions. (NIDCR authors: N. Dutzan, T. Greenwell-Wild, and N. Moutsopoulos, *Mucosal Immunol* DOI:10.1038/mi.2015.136) ●

Read more online at http://irp.nih.gov/catalyst/v24i3/research-briefs.

Dental Clinic

CONTINUED FROM PAGE 1

ERNIE BRANSON

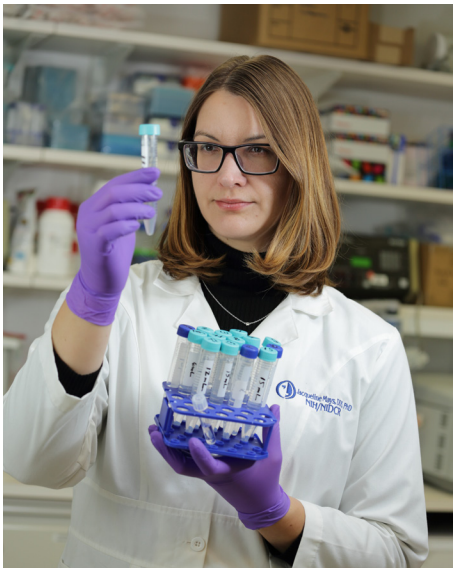
Over the past five years, NIDCR has renovated the Dental Clinic and recruited many board-certified staff and investigators including NIDCR Clinical Director Janice Lee shown here with a patient.

can see two physicians who specialize in rheumatology: **Alan Baer** (his primary appointment is at Johns Hopkins) and **Brian Walitt** (his primary appointment is in the National Institute of Nursing Research). Other important members of the clinical team include specialists in pediatric dentistry and periodontics (for gum-tissue disorders), dental assistants, and research nurses.

"We're here to help NIH clinical investigators understand how the disease they are studying impacts oral health," said NIDCR Deputy Scientific Director and former Clinical Director **James Melvin**. "The oral cavity is a big part of overall systemic health. We can explain what oral health means for their research."

"Five years ago, things were very quiet," said Assistant Clinical Investigator **Jacqueline Mays**, whose clinical care and laboratory research focus on oral mucosal immunity. "There wasn't the bustling research enterprise that there is now. There certainly wasn't the critical mass of dentists and scientists together to push the translational research enterprise. That has really grown."

Mays, who treats people who have had organ and stem-cell transplants at the Clinical Center, is an example of how NIDCR's five clinical investigators work with the dental clinical team and also collaborate with investigators at other institutes. In the lab, Mays uses salivary proteomics and immunology techniques to determine what triggers graft-versus-host disease (GVHD), a process in which transplanted cells sometimes attack the transplant patient's tissues. People with GVHD who are referred to Mays may be part of transplant-research protocols at the National Cancer Institute, the National Heart, Lung, and Blood Institute, or the National Institute of Allergy and Infectious Diseases. About 85 percent of Dental Clinic patients are referred by intramural investigators at other institutes.



ERNIE BRANSON

Assistant Clinical Investigator Jacqueline Mays, whose clinical care and laboratory research focus on oral mucosal immunity, treats people who have had organ and stem-cell transplants at the Clinical Center. In the lab, Mays uses salivary proteomics and immunology techniques to determine what triggers graft-versus-host disease (GVHD). a process in which transplanted cells sometimes attack the transplant patient's tissues.

"Although we have doubled the annual number of Clinical Center patients that we care for, the Dental Clinic has room for growth," Lee said. "It's time that we tell the NIH intramural program that we are here to care for patients and collaborate." ●

CLINICAL CASE CONFERENCES

NIDCR Clinical Director Janice Lee invites NIH clinical staff and investigators to participate in the weekly NIDCR Clinical Case Conference, a forum to discuss rare conditions that have dental, oral, or craniofacial manifestations. These case conferences are held on Fridays at 11:00 a.m. in the Clinical Center (Building 10), Conference Room 5-2550. For more information, contact Janice Lee at janice.lee@mail.gov or check her website: http://www.nidcr.nih.gov/research/NIDCRLaboratories/OfficeoftheClinicalDirector.

DENTAL CLINIC CONTACTS

For research collaborations

- Janice Lee: Craniofacial anomalies
- Michael Collins: Metabolic skeletal disease
- Ilias Alevizos: Salivary gland dysfunction
- Niki Moutsopoulos: Periodontal disease and immunodeficiency
- Jacqueline Mays: Oral chronic graft-versus-host disease

For dental consults

- Pamela Gardner*: Oral medicine specialist
- Bob Range*: Hospital dentist
- Kal Shastri: Oral and maxillofacial surgeon
- Bonnie Gitman: Oral and maxillofacial surgeon

* Main contacts for dental consults

Cajal

CONTINUED FROM PAGE 1

Cajal, known as the father of modern neuroscience, was a prolific medical artist and produced hundreds of drawings depicting the organization of nerve cells in the brain. Seven of those original drawings had been displayed at the PNRC since 2014. The symposium marked the installation of seven new drawings to replace the first set and the beginning of a new scientific partnership between NIH and Spanish neuroscientists.

"Ramón y Cajal showed how the nervous system is connected," said **Jeffrey Diamond**, symposium organizer and a senior investigator in the National Institute of Neurological Disorders and Stroke (NINDS). "We hope to strengthen our connections with neuroscientists in Spain."

In 2013, Diamond visited the Cajal Institute in Madrid to study Ramón y Cajal's drawings. While he was there, he proposed that NIH borrow some of them to be exhibited in the newly finished PNRC. The Cajal Institute directors agreed, and the first set of drawings was unveiled at NIH on November 6, 2014, , in an exhibit created by **Hank Grasso** of the Office of NIH History and Museum. They included drawings of neuronal circuits in the retina, spinal cord, and cerebellum.

The experience was so successful that the Cajal Institute agreed to loan a second set of drawings, which were put on display in conjunction with the symposium. In addition, the event marked the beginning of a scientific partnership that features joint talks given by NIH and Cajal Institute scientists.

"We want neuroscientists here and in Spain to share their ideas [that] are ultimately rooted in the drawings of Santiago Ramón y Cajal," said Diamond.

The first set of drawings was returned to Spain in September 2015. The current set arrived on October 26 and was installed at the PNRC on October 27. They include drawings of brain cells called astrocytes, drawings of growing neurons, and a circuit diagram of the olfactory bulb, the part of the brain that detects odors.

During the symposium, pairs of NIH and Spanish neuroscientists who had similar research interests gave talks matched to the drawings. NINDS senior investigator **Leonardo Belluscio** and Spanish neuroscientist Laura Lopez-Mascaraque described the development of the olfactory bulb. **Heather Cameron** (National Institute of Mental Health) was paired with Jose Luis Trejo to talk about their work on newborn neurons in the hippocampus, a part of the brain associated with learning and memory. NINDS investigator **Bibi Bielekova** and Fernando de Castro discussed their studies on multiple sclerosis, a disorder in which the myelin that insulates neurons is destroyed. **Christopher McBain** (National Institute of Child Health and Human Development) and Juan de Carlos described the development of circuits in the brain's cortical regions.

In addition, two artists—**Dawn Hunter** from the University of South Carolina (Columbia, South Carolina) and former NINDS artist-in-residence **Rebecca Kamen**—spoke about how Santiago Ramón y Cajal inspired their work. Hunter's drawings and Kamen's sculptures are on display in the PNRC.

The final keynote lecture was given by neuroscientist Rafael Yuste, a professor at Columbia University (New York). Yuste was born and raised in Madrid and later moved to the United States to start his own laboratory.

"Santiago Ramón y Cajal is why I became a neuroscientist," Yuste said. "After reading his book *Advice for a Young Investigator*, I started my career at Instituto Cajal. I'm proud to represent Spanish science in the [United States] and abroad."

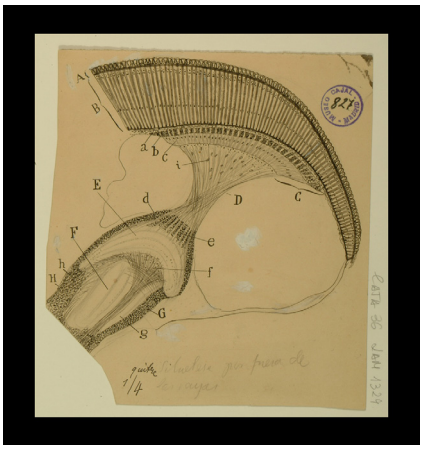
Yuste also discussed the importance of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) initiative, which was launched by President Barack Obama in April 2013. In 2011, Yuste was one of six authors of a white paper that became the foundation for the initiative.

"To fix neurological disorders, we need to understand the circuitry behind them," said Yuste. "Just as Ramón y Cajal used new methods to resolve the neuron theory, we need to use and develop new technologies to take the next step towards understanding the brain."

After the symposium, the speakers attended a reception at the residence of the Spanish ambassador.

"Today's celebration was a truly unique moment for the NIH, Instituto Cajal, and the global neuroscience community," said NINDS Director **Walter Koroshetz**. ●

The current installment of drawings will be on display on the first floor of the PNRC (Building 35) through early fall. For more information, visit http://www.ninds.nih.gov/news_and_events/events/Cajal_Symposium_2015.htm.



COURTESY OF CSIC INSTITUTO CAJAL, MADRID, SPAIN

Cajal's drawing above details the many ommatidia (small unit eyes) present in a single fly eye, as well as the neural circuitry relaying visual signals toward the brain.

Up Close and Personal with Diane Rehm

A Conversation with NPR's Renowned Talk-Show Host

BY SOMA CHOWDHURY, NIGMS

BILL BRANSON

NIH Director Francis Collins had fun interviewing NPR radio host Diane Rehm at the J. Edward Rall Cultural Lecture, part of the Wednesday Afternoon Lecture Series.

NATIONALLY ACCLAIMED PUBLIC-RADIO talk-show host Diane Rehm is used to asking all the questions. *The Diane Rehm Show* features thoughtful and lively conversations with newsmakers, authors, and experts of all kinds. Even NIH Director **Francis Collins** has been on her show a few times. But the tables were turned recently when she was invited to be the guest at NIH's J. Edward Rall Cultural Lecture. Collins played host and asked all the questions—his own as well as ones that other NIHers had sent him in advance. During their conversation, Rehm talked about her public-radio career, her struggles with her voice, some deep personal conflicts relating to her husband's death, and her views on "death with dignity."

Rehm began her radio career in 1973 as a volunteer producer for WAMU-FM 88.5, the National Public Radio (NPR) member station in Washington, D.C. She was soon hired as an assistant producer and later became the host and producer of two health-oriented programs. In 1979, she began hosting WAMU's local morning talk show *Kaleidoscope*, which was renamed *The Diane Rehm Show* in 1984. In 2009, she won the prestigious George Foster Peabody Personal Award in recognition of her "wide-ranging [show] covering politics, the arts, science, cultural trends, literature, and world affairs [that is] an exemplar of thoughtful, civil discourse about public affairs."

She is also the author of several books. Her most recent, *On My Own*, is about the long, drawn-out death (from Parkinson disease) of her husband of 54 years and her struggle to reconstruct her life without him.

Following is an edited transcript of the conversation that took place between Collins and Rehm on April 7, 2016, in Masur Auditorium (Building 10).

To read the full interview online, go to http://irp.nih.gov/catalyst/v24i3/up-close-and-personal-with-diane-rehm.

COLLINS: You did not have a traditional pathway toward becoming a journalist of such wide repute. How did it all start?

REHM: I began as a secretary at the Washington, D.C., Department of Highways. My boss would drive to work and see all the potholes in the roads, and when he arrived at the office, he'd say, "Diane, get on the two-way and tell the workers where the potholes are." That's what I did. I was recruited to other jobs and ended up as secretary at the U.S. Department of State. One day a brash young man [John Rehm] with a crew cut, blond hair, and broad shoulders walked in. [He later became my husband.]

COLLINS: But how did that lead into WAMU and radio?

REHM: After staying at home for 14 years raising two wonderful children, I realized they would soon be gone. My husband had his career, but what was I going to do? So I took a course called "Developing New Horizons for Women" at George Washington University [Washington, D.C.]. There were about 20 of us, and for some reason they all said to me, "You really ought to be in broadcasting." Well it was the craziest thing I had ever heard because although I had grown up with radio all my life, I had never thought about broadcasting. Within two weeks of finishing that course, I decided to volunteer at WAMU on the campus of American University [Washington, D.C.]. On my very first day, the talk-show host was out sick. The manager was going to do the program and invited me into the studio to help. For 90 minutes we interviewed a representative of the Dairy Council. When I got home, John Rehm looked at me and said, "Someday you're going be the host of that show."

COLLINS: Do you specifically try to emphasize medical research on your program?
REHM: Death and illness and medicine have always been things I had great interest in. My mother died from liver cancer when I was 19, and my father died of a broken heart 11 months after my mother passed away. I wanted to know why, and there were no answers. When John's father got diabetes and later diabetic retinopathy, he took his own life. A couple of years later, John's 92-year-old mother felt she could no longer function or walk and took her own life, too.

COLLINS: Give us some pointers on how scientists can be great interviewees.
REHM: By being concise. By knowing their subject so well that it comes out not as a scientist talking to a scientist but rather a scientist who knows his or her subject so well that it's conversational. That's the kind of message that reaches people.

COLLINS: You had your own medical challenge. Your career as a radio host depends on your voice, which was afflicted by a rare condition called spasmodic dysphonia. How did you deal with that?
REHM: From 1992 to 1998, I felt my voice clutching, clamping. It started with a cough, a tiny little cough. I went from doctor to doctor to doctor, all of whom kept putting tubes down my throat. I think the insertion of those tubes did not help my condition. The last doctor who did that said, okay, I'm putting a camera on the end of this tube to see what's going on with your vocal cords. He called me the next day and said, "Sorry, the camera didn't work." Not good. The last day I was on the air was in February 1998. I told my boss that I had to find out what was wrong with my voice. I sat at home for four months, not answering the phones, not speaking to anyone except my husband. Wouldn't go to the door, wouldn't go out of the house for fear of having to speak with someone. Then my wonderful internist referred me to neurologist Dr. Stephen Reich and otolaryngologist Dr. Paul Flint at Johns Hopkins [Baltimore]. Within one hour they said I had spasmodic dysphonia and gave me a botulinum toxin (Botox) injection in my vocal chords. The Botox paralyzes the vocal cords so they don't come together for a little while. Then slowly, slowly they begin to vibrate and I could speak again. Dr. Flint is now at Oregon Health and Science University Hospital [Portland, Oregon], and I go there every four months to get my Botox injections from him.

COLLINS: You wrote an intensely personal book, *On My Own*, after your husband's death from Parkinson disease. Tell us your thoughts about what we as scientists or as a nation could have done that wasn't done. What could have been different?
REHM: In the end, John could no longer care for himself in any way. One day our family gathered around his bed at the assisted-living facility where he was staying, and he said, "I'm ready to die." He asked his physician to help him. But his physician said that he understood John's wishes, yet he couldn't legally, morally, or ethically help John because Maryland did not yet have a "Right-to-Die" law. The doctor suggested that if John was absolutely determined, he could help himself by stopping food, water, and medication. So John stopped eating, drinking, and taking his medicines. He said he felt great, and I know why—he felt as though he had taken his life back into his own hands. For the next two days, he was fine. His face looked pink, he looked wonderful, and then at the end of the second day he fell asleep and he never woke again. For 10 days I saw that man lying there helplessly.

I think this country had been death averse until Oregon passed its Death with Dignity law, then Washington State, then Vermont, and now California. We have to talk more openly about death and about what we want at the end of life. I think there is so much to talk about and so much for the doctors to learn about listening to the patient about what the patient wants and how best you can make that happen.

I will be talking a great deal about the Right to Die after I step away from the microphone [when I retire at the end of the year] without crossing any lines.

COLLINS: Why have you decided to step away?
REHM: Because in September I will be 80 years old. I thought 80 was a good time to make the change. ●

The J. Edward Rall Cultural Lecture, part of the Wednesday Afternoon Lecture Series, honors Joseph Edward Rall, who helped to define NIH's modern intramural research program and, in the 1950s, to establish a stable academic-like community within a rapidly expanding government agency. The videocast of the April 7, 2016, lecture featuring Diane Rehm can be viewed at http://videocast.nih.gov/launch.asp?19606.

Recently Tenured

VERONICA A. ALVAREZ, NIAAA

YOGITA CHUDASAMA, NIMH

MICHAEL T. COLLINS, NIDCR

NEAL FREEDMAN, NCI-DCEG

JANET E. HALL, NIEHS

VERONICA A. ALVAREZ, PH.D., NIAAA

Senior Investigator; Chief, Section on Neuronal Structure, Laboratory for Integrative Neuroscience, National Institute on Alcohol Abuse and Alcoholism

Education: University of Buenos Aires, Buenos Aires, Argentina (B.S. in biology; Ph.D. in neuroscience)

Training: Postdoctoral training in neurobiology at Harvard Medical School (Boston) and the Vollum Institute, Oregon Health and Science University (Portland, Ore.)

Came to NIH: In 2008

Outside interests: Running; hiking; spending time with family

Website: http://irp.nih.gov/pi/veronica-alvarez

Research interests: I am interested in the neurobiology of addiction and am trying to understand the cellular mechanisms that control reward-motivated and compulsive behaviors. The goal of my lab is to find out how cocaine and alcohol affect synapses and neuronal connectivity to drive the development of compulsive drug-seeking behaviors that characterize individuals suffering from cocaine abuse or alcohol-use disorder. In my laboratory, we combine multiple techniques ranging from cellular and synaptic approaches all the way to behavioral analysis and in vivo manipulations in wild-type and genetically engineered mouse models. We expect that our studies will provide information about the short-term and long-term effects of stimulant drugs and alcohol on synapses and on the way that different brain regions talk to each other and integrate information. In addition, we hope our findings will lead to the identification of neuronal markers associated with higher vulnerability to addiction and aid in the development of new therapies to treat drug abuse and dependence.

YOGITA CHUDASAMA, PH.D., NIMH

Senior Investigator; Chief of the Section on Behavioral Neuroscience and Director of the Rodent Behavioral Core, National Institute of Mental Health

Education: Cardiff University, Cardiff, Wales, United Kingdom (B.Sc. in applied psychology; Ph.D. in behavioral neuroscience)

Training: Postdoctoral fellowship at the Department of Experimental Psychology, University of Cambridge (Cambridge, England); postdoctoral fellowship at NIMH's Laboratory of Neuropsychology

Before returning to NIH: Associate professor, Department of Psychology at McGill University (Montreal)

Came to NIH: In 2003 for training in NIMH (2003–2006); visiting professor (2013–2014) in the National Institute on Drug Abuse; joined NIMH in 2015

Outside interests: Hiking; traveling; exploring

Research interests: I am interested in the neural circuits underlying the control of executive functions (control of attention and inhibition, working memory, reasoning, problem solving, and planning). Impairments in executive function, which are characteristic of people with neuropsychiatric disorders such as schizophrenia, persist long after acute symptoms subside and severely compromise the patients' psychosocial function and quality of life. My lab uses rodent models to dissect complex executive behavior into its cognitive components and to examine how large-scale neural circuits contribute to each component. In recent years, we have demonstrated that executive behaviors are not restricted to the prefrontal cortex but depend heavily on a broad network of interconnected structures that include the hippocampus, basal ganglia, and midline thalamic nuclei. We are particularly interested in the complex interplay among these structures in cognition and their related pharmacology.

My lab is also trying to understand the functional anatomy of social and emotional development. There is significant overlap in the brain structures that govern executive and social behavior. For these studies, we use the common marmoset (*Callithrix jacchus*), a New World monkey. Marmosets provide many opportunities for studying the same circuitry and have well-developed social

MITCHELL HO, NCI-CCR

LINDSAY MORTON, NCI-DCEG

JUNG-HYUN PARK, NCI-CCR

behaviors that cannot be well modeled in rodents. One major interest is in how marmosets solve problems through social cooperation.

Using a combined approach in rodents and primates provides us with a unique perspective on the detailed circuits that support executive behaviors that often go awry in people who suffer from poor control over their decisions, memories, and actions.

MICHAEL T. COLLINS, M.D., NIDCR

Senior Investigator and Chief, Skeletal Clinical Studies Section, Craniofacial and Skeletal Diseases Branch, National Institute of Dental and Craniofacial Research

Education: Catholic University of America, Washington, D.C. (music); University of Maryland at College Park (B.G.S. in premedical general studies); University of Maryland at Baltimore (M.D.)

Training: Internal medicine residency and chief resident in medicine, University of Maryland at Baltimore; Endocrine Fellowship Training, NIH Inter-institute Endocrine Training Program, National Institute of Child Health and Human Development

Came to NIH: In 1986 as a biologist in the National Institute of Mental Health (as an undergraduate); returned in 1995 for endocrine fellowship training in NICHD; in 1998, joined the NIDCR as a clinical associate; became a NIDCR staff clinician in 1999 and a tenure-track investigator in 2006

Selected professional activities: Associate program director, NIH Inter-institute Endocrine Training Program; chair, Medical Advisory Committee, Fibrous Dysplasia Foundation; advisory boards MAGIC Foundation and Yale Center for X-Linked Hypophosphatemia; FDA Advisory Committee for Reproductive Health Drugs; consultant to U.S. Department of Justice

Outside interests: Spending time with family and friends; enjoying food, music, and nature

Website: http://irp.nih.gov/pi/michael-collins

Research interests: My group is trying to understand the spectrum, natural history, and underlying pathophysiology of diseases of mineral homeostasis and the skeleton, improve the care of patients with these diseases, and mentor the next generation of clinician-scientists to do the same. We are focusing on pathophysiologically and mechanistically related human diseases, natural-history studies, translational investigation, and clinical trials. We are investigating fibrous dysplasia of bone and McCune-Albright syndrome (FD/MAS), a multisystem disease caused by somatic activating mutations of the cAMP-regulating protein Gs alpha subunit. It is defined by a combination of a skeletal dysplasia, café-au-lait skin macules, and endocrine dysfunction, which can include an excess of the recently discovered phosphate- and vitamin D-regulating hormone fibroblast growth factor 23 (FGF23).

One of the major thrusts of my research is to identify molecules with inhibitory and stimulatory activity at the mutations in Gs alpha subunit that cause FD/MAS and identify compounds from which to develop drugs to treat it. I also have an active research program on mineral metabolism. In particular, we are looking at diseases of FGF23 excess; osteomalacic disorders such as tumor-induced osteomalacia and X-linked hypophosphatemic rickets; and FGF23 deficiency, such as familial tumoral calcinosis (a condition characterized by abnormal deposition of calcium phosphate crystals in tissue). We are also seeking to identify new disorders of FGF23, the cellular and molecular pathophysiology of disorders of FGF23, and novel mechanistically related treatments.

NEAL FREEDMAN, PH.D., M.P.H., NCI-DCEG

Senior Investigator, Metabolic Epidemiology Branch, National Cancer Institute–Division of Cancer Epidemiology and Genetics

Education: Brown University, Providence, R.I. (Sc.B. in biochemistry and colonial American history); University of California, San Francisco (Ph.D. in biomedical sciences); Harvard School of Public Health, Boston (M.P.H. in quantitative methods)

Training: Cancer Prevention Fellow, Nutritional Epidemiology Branch, NCI-DCEG

Came to NIH: In 2005 for training; became a tenure-track investigator in DCEG in 2009

Selected professional activities: Associate editor for *American Journal of Epidemiology and Tobacco Regulatory Science*; NCI-DCEG principal investigator for the Prostate, Lung, Colon, and Ovary (PLCO) Cohort Study

CONTINUED ON PAGE 16

Recently Tenured

CONTINUED FROM PAGE 15

Outside interests: Spending time with family; hiking and being outside; reading; doing photography; baking; and enjoying delicious food
Website: http://irp.nih.gov/pi/neal-freedman

Research interests: I am interested in the role of diet and lifestyle in cancer with a particular focus on tobacco products and on liver cancer.

In my tobacco research, my research group and I seek to understand how long-term trends in tobacco use affect disease risks. For example, we have chronicled the impact of historically different cigarette smoking patterns in men and women. In the past, men in the United States smoked more than women, started smoking at a younger age, and tended to have higher smoking-associated disease risks. But today, U.S. women smoke at a similar rate—and start at a similar age—as men. Our work has shown that these changes have resulted in now-similar disease risks among U.S. men and women who smoke cigarettes.

Although the prevalence of cigarette smoking has declined substantially in the United States over the past 50 years, cigarettes continue to be responsible for nearly a third of cancer mortality. Yet other tobacco products are also commonplace including smokeless tobacco, cigars, and emerging products such as electronic cigarettes and water pipes. In our studies, we aim to understand the health risks of using each of these types of tobacco products and of using multiple products.

We are also investigating how diet and lifestyle are associated with liver cancer. Liver cancer is the second leading cause of cancer death in the world. Strong risk factors have been identified including aflatoxin (toxins produces by certain fungi found on agricultural crops), alcohol, chronic hepatitis B and C infections, and diabetes. My work has suggested an important role for diet in liver cancer, and we are currently following up one of the most promising leads—coffee. There is an inverse relationship between coffee intake and the incidence of liver cancer and other liver diseases, suggesting that drinking coffee may have benefits for the liver. We are using a broad range of classical and molecular epidemiologic approaches to better understand the potential impact of coffee drinking on liver disease and on health.

JANET E. HALL, M.D., M.SC., NIEHS

Senior Investigator; Head of the Reproductive Physiology and Pathophysiology Group, Neuroendocrinology of Reproduction and Aging, National Institute of Environmental Health Sciences

Education: McMaster University, Hamilton, Ontario, Canada (B.A./B.P.E in English and physical education; M.Sc.; M.D.)
Training: Residency in internal medicine and chief resident at McMaster University; clinical and research fellowships in endocrinology and metabolism at Massachusetts General Hospital (Boston)
Before coming to NIH: Professor of medicine, Harvard Medical School (Boston); associate chief of the Reproductive Endocrine Unit and associate physician at Massachusetts General Hospital
Came to NIH: In 2015
Selected professional activities: Extramural funding from NICHD and NIA; former president of the Endocrine Society; associate editor, *Endocrine Reviews*
Outside interests: Boston HealthCare for the Homeless and the Carroll School of Lincoln, which serves children with language-based learning disabilities
Website: http://www.niehs.nih.gov/research/atniehs/labs/crb/pi/rpp/index.cfm

Research interests: I study human reproductive physiology and pathophysiology with a view to translating this information so it can benefit women who have reproductive disorders. The focus of my research is on the neuroendocrine interactions that govern normal reproduction and the changes that occur with aging. We have used this information as a backdrop to provide insights into the pathophysiology of clinical reproductive endocrine disorders. At Harvard, I studied the mechanisms underlying the critical events of the menstrual cycle, how sleep and circadian factors influence these processes, and how signals from the ovary contribute to repeated cycles of follicle development and ovulation. In addition, we investigated the neuroendocrine underpinnings of reproductive disorders including congenital gonadotropin-releasing hormone (GnRH) deficiency, hypothalamic amenorrhea, polycystic ovarian syndrome, and premature ovarian insufficiency. My group investigated the integrated changes that occur with reproductive aging and is finalizing the analysis of neuroimaging studies that investigate how aging influences the way estrogen affects cognitive processes.

Since moving to NIEHS, I am continuing several longstanding collaborations as well as developing new studies. I am maintaining my Massachusetts General Hospital (MGH) program—and working to move it to NIH—in which I use pulsatile GnRH for ovulation induction in patients with GnRH deficiency. I continue to be involved in genotype and phenotype studies in collaboration with colleagues from MGH and the National Institute of Child Health and Human Development. Within this collaborative group I lead the genotype-phenotype studies in women with hypothalamic amenorrhea (a condition in which hypothalamic signaling to other parts of the reproductive system is interrupted because of physiologic stresses such as nutritional imbalance). At NIEHS, my group has established a protocol to investigate factors leading to the variability in

neuroendocrine responsiveness to physiologic environmental stresses in normal women that will provide critical insights into the pathophysiology of hypothalamic amenorrhea. I am also collaborating with investigators in NIEHS's Epidemiology Branch to determine the impact of environmental toxins on reproductive function. In the next year, my group will re-establish our neuroimaging program, which seeks to understand the effects of endocrine disruptors on cortical and hypothalamic function.

MITCHELL HO, PH.D., NCI-CCR

Senior Investigator; Chief, Antibody Therapy Section, Laboratory of Molecular Biology, National Cancer Institute–Center for Cancer Research

Education: East China Normal University, Shanghai, China (B.S. in biology); San Francisco State University, San Francisco, Calif. (M.A. in cellular and molecular biology); University of Illinois at Urbana-Champaign, Champaign, Ill. (Ph.D. in immunology)

Training: Postdoctoral training at NCI's Laboratory of Molecular Biology

Came to NIH: In 2002 for training; in 2008 became tenure-track investigator in NCI's Center for Cancer Research

Selected professional activities: Founding chair of the NIH Antibody Interest Group; member of the Board of Distinguished Advisors for the Antibody Society; chair of the Department of Biochemistry for the FAES Graduate School at the NIH

Outside interests: Swimming; hiking; aquariums

Website: http://irp.nih.gov/pi/mitchell-ho

Research interests: I am a protein biochemist and my research focuses on the use of antibody-engineering technology to advance the development of cancer therapeutics. By combining cutting-edge antibody technology with cellular functional assays, my laboratory has pioneered the production of inhibitory antibodies that attack tumor-specific glypicans. These glypicans are cell-surface heparan sulfate proteoglycans that modulate multiple signaling pathways known to be fundamental in cancer development. We have generated human monoclonal antibodies that have the unique ability to inactivate the wingless-related integration site (Wnt)–yes-associated protein (Yap) signaling pathways by binding to cryptic Wnt binding sites on glypican-3 (GPC3). Our Wnt-inhibitory antibodies not only serve as research tools to investigate the biological interaction of Wnt and GPC3 but also exhibit significant inhibition of GPC3-positive liver-tumor growth in mice. To further enhance the antitumor efficacy, we have constructed chimeric proteins composed of an antibody fragment fused to an immunotoxin. Our immunotoxin causes the regression of liver cancer in mice via dual inhibition of both Wnt-Yap signaling and protein synthesis. Our work established GPC3 as a therapeutic target for immunotoxins and other antibody-toxin/drug conjugates in liver cancer. Furthermore, we are also evaluating additional glypicans as new targets in antibody-based cancer therapies.

Our lab also focuses on the protein mesothelin because of its high expression in mesothelioma and other solid tumors. The molecular interaction between mesothelin and the protein mucin 16 (MUC16, also known as cancer antigen 125) may facilitate the implantation and spread of tumors. We experimentally identified the functional binding domain (named IAB) in mesothelin for MUC16. Moreover, we have generated the anti-mesothelin antibodies that target poorly immunogenic epitopes close to the cell membrane. Our anti-mesothelin antibodies show promising potential for the treatment and diagnostics of mesothelioma and other cancers.

LINDSAY M. MORTON, PH.D., NCI-DCEG

Senior Investigator, Radiation Epidemiology Branch, National Cancer Institute–Division of Cancer Epidemiology and Genetics

Education: Dartmouth College, Hanover, N.H. (B.A., Senior Fellow with Honors, concentration in biology); Yale School of Public Health, New Haven, Conn. (Ph.D. in epidemiology with a focus on cancer epidemiology)

Training: Postdoctoral fellow in NCI-DCEG; research fellow in NCI-DCEG

Came to NIH: In 2004 for training; became tenure-track investigator in Radiation Epidemiology Branch in 2008

Selected professional activities: Childhood Cancer Survivor Study Steering Committee; Lymphoma Research Foundation Scientific Advisory Board; *Cancer Research* editorial board member

Outside interests: Swimming; playing outside (hiking, kayaking, and more); cooking; spending time with friends and family

Website: http://irp.nih.gov/pi/lindsay-morton

Research interests: I am studying multiple primary cancers to evaluate the carcinogenic effects of radiotherapy and chemotherapy as well as to identify other environmental and genetic risk factors for second cancers. Second cancers are a leading cause of morbidity and mortality among cancer survivors. Treatments for first primary cancers are an important cause of subsequent malignancy. There is still much to learn about treatment-related second cancers, particularly whether inherited susceptibility could modify risks and the magnitude of risks associated with current treatment approaches. Beyond the consideration of treatments, many second cancers are likely caused by shared environmental and inherited risk factors, but few studies in the past have collected data on additional risk factors.

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Recently Tenured

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I lead a multicenter study of gastrointestinal (GI) cancers (stomach, pancreas, esophagus) among survivors of Hodgkin lymphoma and cancers of the testis, breast, and cervix. The study represents the first comprehensive effort beyond the atomic bomb survivor studies in Japan to quantify the radiation dose–response relationship for upper-GI cancers. Additionally, it is one of just a few studies to quantify chemotherapy-related risks for solid tumors. We have found that the radiation-related risks for all three GI organs increase linearly with increasing dose. We also identified that radiation-related stomach cancer risk after Hodgkin lymphoma was particularly high for patients who also received the chemotherapy drug procarbazine. The increased risks of GI cancer often persist 25 years or more after the first-cancer diagnosis.

In the arena of second-cancer risk among childhood-cancer survivors, I have partnered with the Childhood Cancer Survivor Study to conduct the first large-scale studies of genetic susceptibility to treatment-related second cancers, a major cause of morbidity and mortality in childhood-cancer survivors. We have completed genotyping of over 5,000 childhood-cancer survivors and are combining these data with long-term follow-up and detailed treatment information. Individuals with certain hereditary disorders, such as ataxia telangiectasia (a rare inherited disorder that affects the nervous system, immune system, and other body systems and is characterized by progressive difficulty with coordinating movement), have increased sensitivity to the effects of radiation. But less is known about genetic susceptibility to radiation-related carcinogenesis beyond these rare disorders, and very little is known about genetic susceptibility to chemotherapy-related carcinogenesis. Data from this study will be shared through the Childhood Cancer Survivor Study and the database of Genotypes and Phenotypes (dbGaP) to create a resource to investigate genetic susceptibility to a range of adverse effects in childhood-cancer survivors. These studies hold promise for informing decisions regarding front-line therapy and/or post-treatment surveillance, as well as providing insight into mechanisms of treatment-related carcinogenesis.

JUNG-HYUN PARK, PH.D., NCI-CCR

Senior Investigator, Experimental Immunology Branch, National Cancer Institute–Center for Cancer Research

Education: University of Cologne, Cologne, Germany (B.S. in biology); Julius Maximilian University of Würzburg, Würzburg, Germany (M.S. in biology; Ph.D. in immunology)

Training: Postdoctoral training at the Korea Research Institute of Bioscience and Biotechnology (Daejeon, South Korea); research fellow at NCI-CCR's Experimental Immunology Branch

Before coming to NIH: Research associate at the Korea Research Institute of Bioscience and Biotechnology

Came to NIH: In 2001 as a research fellow; became a tenure-track investigator in 2008

Selected professional activities: Deputy editor, *ImmuneNetwork*; co-chair, NIH–Cytokine Interest Group; faculty, NIH–University of Pennsylvania Immunology Graduate Partnership Program

Outside interests: Playing the violin; reading and trying to understand books on philosophy

Website: http://irp.nih.gov/pi/jung-hyun-park

Research interests: My research focuses on understanding the mechanisms of cytokine-receptor regulation and signaling in immune cells. Specifically, I am interested in interrogating the molecular pathways that control cytokine-receptor signaling in T cells, which are key players in immune surveillance and immune activation. Multiple developmental and environmental cues control cytokine signaling in parallel to cytokine-receptor expression. T cells can show variations in their cytokine responsiveness, resulting in distinct cell-fate choice and effector T-cell generation. Why some T cells choose to respond to a cytokine but other T cells in the same environment remain unresponsive is a fundamental question in immunology that fascinates the members of my lab.

Recently, we discovered a transcriptional basis for such distinct cytokine responsiveness during T-cell development in the thymus. We reported that the zinc finger protein ThPOK induces the expression of suppressor of cytokine signaling molecules to desensitize cytokine-receptor signaling. We also identified another mechanism to desensitize cytokine receptors: a soluble form of the common gamma-chain cytokine receptor (gc), which was generated by alternative splicing and was expressed by activated T cells. We found that soluble gc (sgc) proteins bind to interleukin (IL)–7 and IL-2 receptors even in the absence of cytokines, and they inhibit gc cytokine signaling but promote pro-inflammatory IL-17 expression. Thus, sgc is a novel immunomodulatory molecule that controls cytokine responsiveness in activated T cells. As we continue to investigate the mechanisms that control cytokine responsiveness, we hope to gain a better understanding of the molecular basis for distinct cytokine signaling in T-cell development, differentiation, and homeostasis. ●

ANITA ROBERTS LECTURE
"Functional Architecture of Face Processing in the Primate Brain"
Tuesday May 10, 1:00–2:00 p.m.
Wilson Hall (Building 1)

The presentation will be by NIMH senior investigator **Leslie Ungerleider**, member of the Laboratory on Brain and Cognition and chief of the Section on Neurocircuitry. She examines the neural mechanisms for the processing of facial identity and facial expression in the brains of human and nonhuman primates. She is an NIH Distinguished Investigator and member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the National Academy of Medicine. To arrange for sign-language interpretation, contact Margaret McBurney at mmcburney@od.nih.gov or 301-496-1921.

NATIONAL WOMEN'S HEALTH WEEK: INAUGURAL VIVIAN W. PINN SEMINAR
Tuesday, May 10, 2:00–3:30 p.m.
Cloisters Hall (Building 60)
Free and open to the public

The seminar—which honors **Vivian W. Pinn**, the first and former director of the Office of Research on Women's Health—will feature a keynote address from NCI senior clinical investigator **Lauren V. Wood.** For more information, visit http://nih.gov/women.

JSPS POSTDOCTORAL FELLOWSHIPS
Deadline: Friday, May 27, at 5:00 p.m.
For information and application forms: http://jspsusa.org/wp/fellowship/kaitoku-nih

NIH and the Japan Society for the Promotion of Science (JSPS) are accepting applications for JSPS Postdoctoral Fellowships at NIH for 2017. The NIH-JSPS Intramural Fellowship, which is awarded to about 15 postdocs annually, provides a two-year stipend to Japanese postdocs to work in NIH intramural labs. Applicants must meet all the requirements (see website for details). For more information, contact Tina Chung (301-496-1653 or chungt@mail.nih.gov).

POINT-OF-CARE TECHNOLOGY RESEARCH NETWORK SCIENCE SYMPOSIUM
"Co-inventing the Future through Collaboration"
Thursday, June 9, 8:00 a.m.–4:00 p.m.
Natcher Conference Center (Building 45)
For information: 1.usa.gov/1T2A8vk
To register: bit.ly/24hZIVt

This NIBIB-sponsored symposium will focus on point-of-care technologies and their clinical translation. NIBIB created POCTRN in 2007 to drive the development of appropriate point-of-care diagnostic technologies through collaborative efforts that merge scientific and technological capabilities with clinical needs. The event will include posters, presentations by guest speakers and POCTRN centers' scientists, and 30 electronic poster presentations and demonstrations. The keynote speaker is Stefanie Akselrod, who will deliver the talk "Bringing a POC Test to the U.S. Market—FDA Perspective."

ANNUAL NIH AND FDA GLYCOSCIENCE RESEARCH DAY
Wednesday, June 29, 8:50 a.m.–5:00 p.m.
Natcher Conference Center (Building 45)
Poster abstract deadline: May 25
Register/more info: http://1.usa.gov/1VUQ2OX

This event will explore a broad range of aspects of the glycosciences; promote communication and interaction among intramural laboratories, as well as with researchers from local universities; and facilitate collaboration. There will be morning and afternoon platform sessions; poster sessions; and an FAES-sponsored mentoring and networking luncheon that will afford students and postdoctoral fellows an opportunity to speak one-on-one with invited speakers, researchers from the NIH and FDA intramural laboratories, and NIH extramural program directors who handle glycosciences-related grant portfolios. For more information, contact Donna Krasnewich (dkras@mail.nih.gov or 301-594-0943) or Pamela Marino (marinop@nigms.nih.gov or 301-594-3827).

GRADUATE & PROFESSIONAL SCHOOL FAIR
Thursday, July 14, 8:45 a.m.–3:30 p.m.
Exhibits will be open: 9:45 a.m.–2:15 p.m.
Natcher Conference Center (Building 45)
Registration; list of institutions attending: https://www.training.nih.gov/gp_fair

NIH summer interns (especially those in college) and postbacs, as well as other college students in the Washington, D.C., area, can prepare for the next step in their careers by exploring educational programs leading to graduate and professional degrees. Representatives—of graduate schools, medical and dental schools, schools of public health, and other biomedical programs—from more than 150 outstanding U.S. colleges and universities will be at the fair in the hopes of recruiting NIH trainees. The day will also include workshops on getting to graduate and professional school, M.D.-Ph.D. programs, interviewing, careers in public health, computational biology/bioinformatics, psychology, and dentistry.

M.H.S. IN CLINICAL RESEARCH
Classes begin on August 29, 2016
Application deadline: May 15, 2016
Website: bit.ly/1pCgSgQ

Consider earning a Master of Health Science degree in clinical research by applying to the NIH-Duke Training Program. You will earn a master's degree from Duke University School of Medicine (Durham, N.C.) while attending classes part-time on the NIH campus. The tuition-based program is designed primarily for clinical fellows, physicians, and dentists already in staff positions as well as for other health professionals who desire formal training in the quantitative and methodological principles of clinical research. For questions, contact Nicole Garner (Nicole.Garner@nih.gov) or Gail Ladd (gail.ladd@duke.edu). Enrollment in this program is limited to 30 individuals at the NIH. ●

Read more online at http://irp.nih.gov/catalyst/v24i3/announcements.

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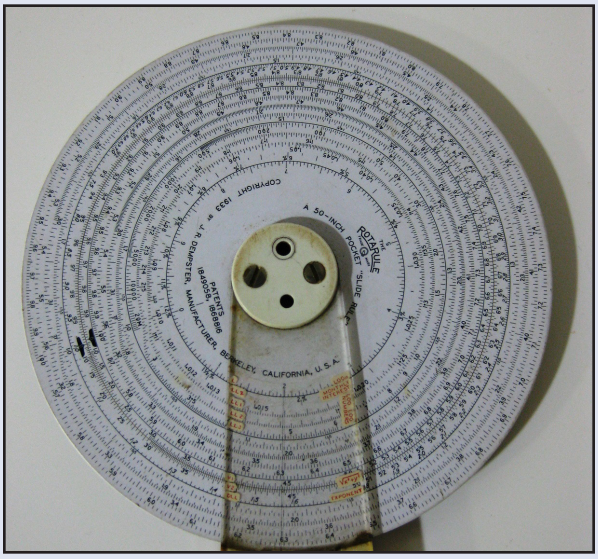
Also, we welcome "letters to the editor" for publication and your reactions to anything on the *Catalyst* pages.

READ LONGER VERSIONS OF THESE ARTICLES ONLINE (IN COLOR) AT http://irp.nih.gov/catalyst/v24i3

FROM THE ANNALS OF NIH HISTORY

When the Slide Rule Ruled

BY MICHELE LYONS, OFFICE OF NIH HISTORY



OFFICE OF NIH HISTORY

What do Isaac Newton, Thomas Jefferson, Albert Einstein, and the Apollo astronauts have in common? They all used slide rules! Slide rules were invented in the early 1600s to do complicated calculations, and they ruled the scientific world until 1972, when Hewlett-Packard came out with its first handheld electronic calculator. The circular slide rule shown here eliminated the problem of calculations running off the scale because this scale had no end. John R. Dempster patented the design for the J.R. Dempster RotaRule Pocket Slide Rule No. AA in 1932. This rule belonged to **Wallace P. Rowe**, chief of the Laboratory of Viral Diseases in the National Institute of Allergy and Infectious Diseases, who was the first to isolate an adenovirus from patients and helped to clarify its role in respiratory disease. To read about some of the slide rules in the Office of NIH History's collection, go to https://history.nih.gov/exhibits/computers/abacussliderules.html. And, in May 2016, check out the social media links for posts that feature more slide rules used by NIH scientists in their quest to improve human health. ●

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