

## Big Secrets in Small Genes

The Work of Gisela Storz, Ph.D.

BY JENNIFER PATTERSON-WEST, NIDDK

HER COLLEAGUES LAUGHED AT HER “crazy idea” when she was a graduate student at the University of California, Berkeley, in the 1980s. **Gisela Storz** had predicted that a single protein (OxyR) could sense a destructive oxidant, hydrogen peroxide, bind to DNA, and turn on genes that would neutralize the threat. But Storz has gotten the last laugh. Turns out that her hypothesis was correct.

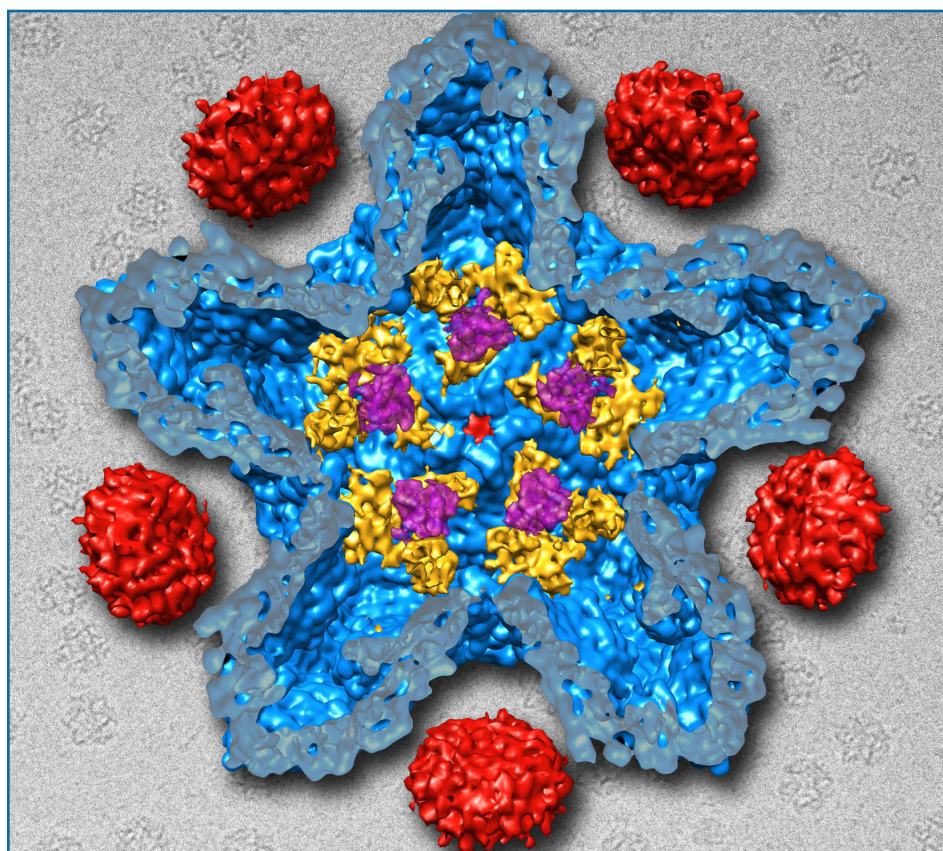
Storz, now a distinguished investigator at the National Institute of Child Health and Human Development and a member of the National Academy of Sciences, continued to study OxyR throughout her training and later as an investigator at NIH. For many years, her lab studied redox-sensitive transcription factors and the bacterial and yeast responses to oxidative stress. Her group discovered that the activity of the *Escherichia coli* transcription factor OxyR is regulated by a reversible disulfide-bond formation (*Science* **279**:1718–1721, 1998). Her group also serendipitously found one of the first small regulatory RNAs—the OxyS RNA (*Cell* **90**:43–53, 1997). Today, her lab focuses on the identification and characterization of small, noncoding RNAs (sRNAs) and of small proteins with 50 amino acids or fewer.

Storz highlighted her lab’s many contributions to the field of sRNAs and small proteins at this year’s Anita Roberts lecture held in May 2017. During nearly 20

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## The Brain, Inflammation, Cancer, and More

Report from the 2017 NIH Research Festival



D. NEMECEK, J.B. HEYMANN, A.C. STEVEN, NIAMS

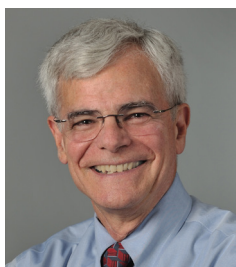
You guessed right: The bacteriophage Phi-6, which serves as a model system for rotavirus, the most common cause of diarrheal disease among infants and young children. Shown here, a cryo-electron microscopy image of Phi-6’s protein shell, or procapsid, cut open to show the different types of protein: P1 (blue), P4 (red), P7, yellow, and P2 (purple).

THE ANNUAL RESEARCH FESTIVAL IS “ABOUT THE SCIENCE WE DO HERE, BUT ALSO ABOUT the people who do that science,” said Deputy Director for Intramural Research **Michael Gottesman** at the festival’s opening on September 13. The intent of the festival is for

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## Taking Stock of the NIH Research Festival

Don't Miss the Very Best that NIH Has to Offer

BY MICHAEL GOTTESMAN, DDIR

THE 2017 NIH INTRAMURAL RESEARCH Festival, co-chaired by scientific directors **Susan Amara** (NIMH) and **Steve Chanock** (NCI's Division of Cancer Epidemiology and Genetics), was by most accounts an amazing scientific potpourri of innovative research and new biotechnology as well as an opportunity to showcase the work of our trainees and fellows in the context of the long-term goals for intramural research.

Yet attendance was at best modest for most of the sessions. What should we do to encourage all of our scientific staff to participate more fully?

Let's take a step back to review the purpose and history of the festival. It had its beginnings in 1986 when then-Scientific Director **Abner Notkins** (NIDCR) dreamed up the idea for the first NIH Intramural Research Day. His goal was to bring our scientific staff out of their laboratories and clinics to meet each other in an informal setting to share research and receive constructive feedback and to enhance opportunities for collaboration. There were anecdotes then that NIH intramural scientists were meeting for the first time at national and international scientific meetings. So Research Day was intended as a way to get NIH scientists to meet each other on campus.

The Research Festival has evolved into a multiday event. We have added a mix of plenary sessions focusing on themes developed by the scientific directors who lead each year's festival program committee,

and workshops reflecting the interests of our scientific interest groups. (Every year two different scientific directors with complementary interests are asked to manage the festival.) Plenary-session themes this year included the BRAIN Initiative, inflammatory diseases, and the Cancer Moonshot.

Other popular events included the

### If research conferences are an essential element of our discipline, more of us should attend our Research Festival.

Technical Sales Association tent show of scientific equipment and services and poster sessions featuring posters from our postdoctoral fellows, NIH leadership, and "future leaders" who are being recruited for positions at the NIH. And there was more: special exhibits on resources for intramural research; a Green Labs Fair featuring the latest in "green" tools and techniques; virtual-reality demonstrations; and an animal-tribute ceremony acknowledging the important role animals play in research. Since a "festival" should be festive, we had food provided by local vendors and refreshments at the workshops and poster sessions. One year we even had a "battle of the bands" featuring NIH directors.

For scientists who argue convincingly and consistently that research conferences are an essential element of their discipline,

why don't more of us attend our Research Festival? In a survey we conducted several years ago, we found that the major reason given by our fellows for not attending NIH lectures and scientific events, such as the Research Festival and the NIH Director's Wednesday Afternoon Lecture Series, was conflicting activities (the research itself, deadlines involving publication and other administrative requirements, and other events, of which there are many at the NIH). So in setting priorities, NIH communal research activities, most of which are not spot-on focused on the lab or clinical work of the scientist, get less attention. Why is not giving the Research Festival a higher

priority a strategic mistake? Most of the truly paradigm-shifting science in modern biology has come from interactions among people in multiple different fields. Given the rich intellectual environment at the NIH, with over 1,000 principal investigators and nearly 3,000 postdoctoral fellows, we are in a prime position to generate truly exciting collaborations just within the NIH. This is precisely the same reason for the Wednesday Afternoon Lectures, which are designed to stimulate trans-disciplinary approaches across the more thematic lines of institutes and centers (ICs). We have tried to encourage collaborations in many ways including providing funding for trans-NIH collaborations through the new Innovation Awards program, through the established Bench-to-Bedside program, through IC-based grants for this purpose,



and via shared resources and shared core facilities (<https://nih.scientist.com>). Our newly renovated IRP website (<https://irp.nih.gov>) communicates the excitement and the diversity of NIH science, and the NIH Intramural Database (<https://intramural.nih.gov>) allows anyone to find a colleague with a resource or interest that would lead to fruitful collaboration.

But nothing replaces the one-on-one interactions and conversations that occur at the Research Festival, and the chance for anyone who attends to be guided through what is most exciting currently in NIH intramural research even if it does not coincide with their current research program.

We have set the dates for next year's Research Festival (September 12–14, 2018) and want to encourage all of you to participate more fully. We will remind you through the year about the event in hopes that you will not schedule other activities during this time. I will continue to remind you, in forums such as this, how important it is for career development and enhancement to think outside the box. And we will ensure that the NIH Research Festival continues to highlight our best and most exciting science.

If you tend to pass on such events, you may be missing the very best of what NIH has to offer—a chance to learn new things from experts within our midst. We craft the Research Festival to highlight scientific trends and to provide you with insight into where the IRP is heading and who is doing what.

As always, I welcome your ideas. ●



Norman E. "Ned" Sharpless is the new director of NCI.

## Norman Sharpless Sworn in as New NCI Director

**NORMAN E. "NED" SHARPLESS** TOOK the oath of office on October 17, 2017, to become the 15th director of the National Cancer Institute (NCI). He succeeded **Harold E. Varmus**, who stepped down as director in March 2015. **Douglas R. Lowy** was NCI's acting director since April 2015.

Sharpless comes to NCI from the University of North Carolina School of Medicine (Chapel Hill, North Carolina), where he served as director of the NCI-Designated Lineberger Comprehensive Cancer Center and as the Wellcome Distinguished Professor in Cancer Research. As a practicing oncologist at the North Carolina Cancer Hospital (Chapel Hill), the clinical arm of Lineberger, he specialized in the care of patients with hematologic cancers. He is the author of more than 150 original scientific papers, reviews, and book chapters and is an inventor on 10 patents. His research has focused on the molecular biology of cancer and aging.

Lowy will resume his role as a deputy director at NCI and will continue his work as chief of the Laboratory of Cellular Oncology in NCI's Center for Cancer Research. ●

## NIH Partners with 11 Biopharmaceutical Companies

ON THURSDAY, OCTOBER 12, 2017, THE NIH and 11 leading biopharmaceutical companies launched the Partnership for Accelerating Cancer Therapies (PACT), a five-year public-private research collaboration totaling \$215 million as part of the Cancer Moonshot. PACT will initially focus on identifying, developing, and validating robust biomarkers to advance new immunotherapy treatments for cancer. The partnership will be managed by the Foundation for the National Institutes of Health, with the Food and Drug Administration serving in an advisory role.

New immunotherapies have resulted in dramatic responses in certain cancer cases. They have also been the focus of intense investment by biopharmaceutical companies seeking to provide new options for patients who do not respond to other cancer therapies, but they don't work for all patients. Development and standardization of biomarkers to understand how immunotherapies work in some patients, and to predict their response to treatment, are urgently needed.

PACT will facilitate information sharing by all stakeholders to better coordinate clinical efforts, align investigative approaches, reduce duplication, and enable more high-quality trials to be conducted. ●

For more information about PACT, visit [bit.ly/2gqGCyu](http://bit.ly/2gqGCyu).

Read more online at <https://irp.nih.gov/catalyst/v25i6/news-briefs>.

**Gisela Storz**

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years of studying sRNAs primarily in *E. coli*, the Storz lab has shown that sRNAs are part of many response pathways in bacterial cells. More recent work in the lab has indicated that small proteins also play an important regulatory function.

The sRNAs and proteins are often not detected by genetic screens or biochemical assays. Storz noted that many of the sRNAs and small proteins that laid the foundation for this field were discovered by serendipity. It has since been recognized that sRNAs regulate bacterial adaptation to various environmental conditions including cell-envelope stress, iron availability, and carbon metabolism. Adaptation to these environments is often essential for bacterial survival and virulence. Regulatory sRNAs can function in primarily two ways: 1) as protein-binding sRNAs that titrate the activity of proteins and 2) as antisense sRNAs, the more common type, that bind to a target messenger RNA (mRNA), thereby affecting transcription, stability, or translation of the mRNA. In her lecture, Storz focused on the latter class of regulatory sRNAs.

She described how her lab, with the help of then-postdoc **Taylor Updegrave** (now in the National Cancer Institute, NCI), collaborated with researchers at the University of California at San Francisco to show that an sRNA called MicL was regulating the outer-membrane lipoprotein lipoma-preferred partner, the most abundant protein in *E. coli* (*Genes Dev* **28**:1620–1634, 2014).

Most of the sRNA-mRNA systems studied to date were discovered at the level of each individual sRNA, but the Storz lab and others have moved to more-global genomic approaches for identifying sRNAs and their mRNA targets. **Sahar Melamed**, a postdoctoral fellow in the Storz lab, is using a deep-sequencing approach termed RIL-seq that he developed at the Hebrew University of Jerusalem (Jerusalem). He has



BILL BRANSON

Gisela Storz, a distinguished investigator at the National Institute of Child Health and Human Development and a member of the National Academy of Sciences, does research on the identification and characterization of small, noncoding RNAs and of small proteins made up of 50 amino acids or less.

identified four sRNAs and showed that the overexpression of one of them results in cells with significantly more flagella.

While studying sRNAs, the Storz lab kept stumbling across small proteins and started to characterize their function. For example, a former postdoc in the Storz lab, **Lauren Waters** (now at the University of Wisconsin-Oshkosh), showed that a short open-reading frame in the sRNA RybA encoded a small protein. It is currently hypothesized that the small protein regulates the activity of the manganese exporter.

The small protein that has been most characterized by the Storz lab is AcrZ, which co-purifies with a component of a multidrug efflux pump that confers resistance to a variety of antibiotics and other compounds in *E. coli*. Interestingly, cells lacking AcrZ are only sensitive to a subset of these drugs, suggesting that AcrZ affects the specificity of drug export (*Proc Natl Acad Sci U S A* **109**:16696–16701, 2012).

Storz also explained how she is developing more systematic approaches to find small proteins. One of her postdocs, **Jeremy Weaver**, is working on a mass-spectrometry approach for identifying small proteins in bacterial cells.

At the end of her lecture, Storz mentioned the pioneering women who were her mentors: the late biochemists **Thressa Stadtman** (National Heart, Lung, and Blood Institute) and **Claude Klee** (NCI), and her ongoing collaborator, microbiologist **Susan Gottesman** (NCI). Stadtman was known for her work on anaerobic electron transport and selenium biochemistry. Klee is remembered for her pioneering work on the biochemistry of calcium-dependent signaling and calcium-binding proteins. And Gottesman is well known for her work in the area of regulated proteolysis and the co-discovery and characterization of many bacterial sRNAs.

Their support was subtle, Storz said, but their assistance with some early experiments and invitations to give seminars had a positive impact. They also served as role models for achieving balance between career and family life. Storz noted that these role models all had spouses at NIH and how the recruitment of two-career couples at the NIH provides a unique mechanism for improving the retention of women in science. ●

To watch a videocast of Storz's Anita Roberts lecture, "The Hidden Secrets of Small Genes," held on May 16, 2017, go to <https://videocast.nih.gov/launch.asp?23286>.

Read more online at <https://irp.nih.gov/catalyst/v25i6/gisela-storz-phd-discovering-big-secrets-in-small-genes>.

## Insights from Former Surgeon General Vivek Murthy

### Rising Stress: Causes and Remedies

BY SUSAN CHACKO, CIT



Former U.S. Surgeon General Vivek Murthy (2014-2017) visited NIH on September 7, 2017, to talk about the public-health consequences of psychological stress.

AS THE 19TH SURGEON GENERAL OF THE United States between 2014 and 2017, Vivek Murthy worked to address many public-health challenges such as the Ebola and Zika viruses, the Flint water crisis, the opioid crisis, obesity, mental illness, and tobacco-related disease. He issued the first-ever Surgeon General's report to address substance-use disorders and the wider range of health problems and consequences related to alcohol and drug misuse in the United States. Murthy visited NIH recently to share his concerns about another growing health problem: the increase in psychological stress across America.

In September 2017, Murthy, the invited speaker for the Stephen Strauss lecture, and NIH Director **Francis Collins** discussed the public-health consequences of psychological stress and fielded questions submitted in advance by NIH staff as well as by viewers watching the conversation on Facebook Live.

Murthy talked about the cross-country listening tour he took soon after he became Surgeon General to understand how communities were addressing public-health issues. He saw families in pain because they had lost children to the opioid crisis and then were shunned by their community afterward. In Flint, Michigan, he met parents worried that they had allowed their

children to drink lead-tainted water. He met students and discovered that 95 percent of them had suffered unbearable stress in the previous month. Everywhere, he saw people experience severe emotional pressures that they often did not know how to handle.

Reported stress levels are on the rise, Murthy said. In a 2015 survey, 24 percent of adults reported extreme psychological stress, an increase from 18 percent just one year earlier. A third of Americans said that they were more stressed than in the previous year.

“Not all stress is bad,” Murthy said. He differentiated short-term adaptive stress that enhances performance from long-term chronic stress that increases the risk of chronic diseases such as heart disease, cancer, anxiety, and depression.

Money, work, relationships, and health: Murthy and Collins agreed that these were the main contributors to stress. The “always-on” workplaces, the “relentless 24/7 work culture,” and continuously available technology make for overextended people.

Strong social connections are one powerful antidote to stress, said Murthy. Social support can be helpful in alleviating psychological stress caused by illness. But social media can sometimes provide only the illusion of connections and not support.

Other stress antidotes include exercise, sleep, meditation, and even music. Exercise can function as an acute antidepressant, said Murthy. Sleep allows the brain to regenerate and body tissues to heal; improves decision-making, learning, and creative abilities; and is connected to reduced rates of obesity, diabetes, hypertension, and heart disease.

There are many kinds of meditation that can have a powerful calming response, said Murthy. He described how transcendental meditation helped a California middle school that had high suspension rates and incidence

of violence. The students were skeptical at first but as they practiced meditation over a year, the school became noticeably calmer and had a drastically reduced suspension rate and lower teacher absenteeism. Students were enthusiastically and voluntarily participating in the meditation program.

“Music [also] has a powerful ability to change how we perceive the world and activate a relaxation response,” said Murthy, citing a McGill University study that indicated music can be better than drugs at reducing anxiety.

Health-care providers are rarely prepared to help patients with stress and are not even trained to address stress in their own lives. “What’s valued in medicine is medical knowledge,” Murthy observed, but clinicians need to lead by example. Collins and Murthy reminisced gloomily about their own medical training in which stress management was rarely, if ever, mentioned, and doctors were admired for their ability to carry on without sleep.

“We need to go beyond addressing stress in our own lives to reaching out to reduce stress in others’ lives, via social connections, compassion, kindness,” Murthy concluded. “We need to create a culture that values and supports everyone.” ●

To watch a videocast of the conversation, “A Nation Under Pressure: The Public Health Consequences of Stress in America,” held on Thursday, September 7, 2017, go to <https://videocast.nih.gov/launch.asp?23443>.

Read more online at <https://irp.nih.gov/catalyst/v25i6/insights-from-former-surgeon-general-vivek-murthy>.

## Newest Lasker Clinical Research Scholar: Anish Thomas, M.D.

BY LAURA STEPHENSON CARTER

**MEET THE NEWEST NIH LASKER Clinical Research Scholar: Anish Thomas** whose clinical research focuses on small-cell lung cancer (SCLC), one of the most aggressive human cancers.

The Lasker Clinical Research Scholars Program, an “intramural–extramural” NIH program in partnership with the Albert and Mary Lasker Foundation, aims to grow the diminishing pool of talented physician-scientists by providing the necessary financial support to establish their careers. Lasker Scholars receive a unique combination of NIH funding for clinical research for up to 10 years. In the first phase of the program, Scholars receive appointments for five to seven years as tenure-track investigators within the NIH Intramural Research Program with independent budgets. In the second phase, successful Scholars will receive up to three years of NIH support for their research at an extramural research facility; or the Scholar can be considered to remain as an investigator within the intramural program. To learn more, go to <https://www.nih.gov/research-training/lasker-clinical-research-scholars>.

The following is a lightly edited version of the interview with Anish Thomas who joins 14 others in the NIH Lasker Clinical Research Scholar program.

### **ANISH THOMAS, M.B.B.S., M.D.**

*Lasker Clinical Research Scholar, Developmental Therapeutics Branch, Center for Cancer Research, National Cancer Institute*

**EDUCATION:** St. John’s Medical College, Bangalore, India (M.B.B.S. and M.D.)

**TRAINING:** Postgraduate training, St. John’s Medical College; internal medicine residency, State University of New York Upstate Medical University (Syracuse, N.Y.); training in medical oncology at NCI and in hematology at NHLBI



CHIA-CHI CHARLIE CHANG

The newest Lasker Clinical Research Scholar, Anish Thomas, conducts clinical research on small-cell lung cancer (SCLC), the most lethal form of lung cancer.

**CAME TO NIH:** In 2013 as a fellow for training; was a staff clinician in NCI’s Thoracic and GI Oncology Branch (2013–2016); in 2016 became a staff clinician in the NCI’s Developmental Therapeutics Branch; became a Lasker Scholar in September 2017

**WEBSITE:** <https://www.irp.nih.gov/pi/anish-thomas>

**Research Focus:** I focus on small-cell lung cancer (SCLC), one of the most aggressive human cancers. The goal of my research is to systematically develop more-effective therapies for patients with SCLC and similar chemotherapy-refractory tumors by targeting key pathways involved in DNA replication, repair, and chromatin remodeling. I design and conduct phase 1 and phase 2 clinical trials.

### **How did you get interested in your field?**

For about a year after coming to the United States and during my residency at SUNY Upstate Medical University, I worked in

the lab of former NCI researcher **Bernard Poiesz**. (In 1980, the year before the first cases of AIDS were reported, Poiesz, **Frank Ruscetti**, **Robert Gallo**, and colleagues at NCI discovered and characterized the first human cancer-causing retrovirus—human T-cell lymphotropic virus–type 1, HTLV-1—in a patient with leukemia/lymphoma, and they later identified HTLV-2.) It was my first time working in a lab, and the experience gave me an opportunity to learn its language.

My decision to go into thoracic oncology was influenced by the high human cost of SCLC (more people die from lung cancer annually than from colon, breast, and prostate cancers combined) and by my work with **Giuseppe Giaccone**, then chief of NCI’s Medical Oncology Branch. There have been no major changes in the treatment of SCLC. I am hoping our work can make a difference.

### **What discoveries have you made?**

I have been involved in the design and conduct of some practice-changing clinical trials. One was a study of sunitinib in people with thymic cancers, which are generally fatal with no standard treatment options after chemotherapy fails. In our trial, sunitinib showed unprecedented responses in thymic-carcinoma patients. Based on these results, the National Comprehensive Cancer Network guidelines now recommend sunitinib for recurrent thymic carcinoma. I was also involved with one of the first reported basket trials (for thoracic malignancies), which concentrate on a specific mutation rather than a specific cancer. Basket trials are now used extensively in evaluating the personalized-medicine hypothesis. ●

Read more online at <https://irp.nih.gov/catalyst/v25i6/newest-lasker-clinical-research-scholar-anish-thomas-md>.



# History of the National Library of Medicine

## A Photographic Recollection

BY ALIA SAJANI, NIAID

**HISTORY AS TOLD FROM THE PERSPECTIVE** of an institution's leaders provides an important but incomplete picture of that institution's contributions to society. But a history drawn from stories of the people who are integral to the day-to-day running of that institution can offer a fresh perspective and a more holistic understanding of the past. There have been many books and articles documenting the history of the National Library of Medicine (NLM). The latest one—*Images of America: US National Library of Medicine* (Arcadia Publishing)—actually draws on the stories of the people who have worked there and helped to shape its 180 years of service to the nation and the world.

The NLM traces its origins to the early 19th century, when it was a few dozen books in what was then the Library of the Surgeon General's Office of the U.S. Army, and is now the world's largest medical library and is located at the NIH in Bethesda, Maryland.

The book's co-editors, **Jeffrey S. Reznick** and **Kenneth M. Koyle**, chief and deputy chief of NLM's History of Medicine Division, and their colleagues in the division researched and wrote the chapters. Curator **Ginny Roth** guided the selection of the archival photographs that appear in the book.



NLM staff complete their work using the current technology of the period including index cards, mimeograph machines, and manual typewriters (circa 1948).

The book documents NLM's significant contributions to American culture and history and demonstrates the "NLM's story as part of the fabric of U.S. history," said Reznick. The entire book and all of the images in it are freely available through the NLM digital-collections repository. The NLM's "Circulating Now" blog also serialized the book. Reznick and Koyle hope this open access, as well as the narrative of the book itself, will make the history of the NLM more accessible to the general public.

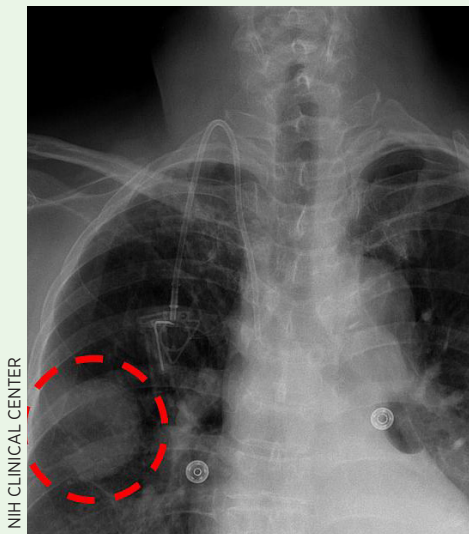
The 18-month-long process of collecting material and organizing stories resulted in a chronological telling of the library's history spanning the early 19th century to the late 20th century. The photographs represent only a small portion of the nearly 150,000 prints and photographs held by the library (about half of which are digitized and freely available via the NLM Digital Collections). Other images were obtained from the National Archives, the Smithsonian Institution Archives, the National Museum of Health and Medicine, and the Tulane University Rudolph Matas Library of the Health Sciences.

"Researching, selecting, and synthesizing material for this new, publicly available history of the [NLM] was like discovering and documenting a family tree," said Reznick. "In this case, it was the very large NLM family tree consisting of generations of public servants who helped to conceive, build, and lead what has become the world's largest biomedical library." ●

To read more and to link to the "Circulating Now," blog, digital copies of the book and photos, and a videocast of the event announcing the new book, go to <https://irp.nih.gov/catalyst/v25i6/history-of-the-national-library-of-medicine>.

- 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
- 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
- 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

## Intramural Research Briefs



A chest X-ray identifies a lung mass.

### CC, NCBI (NLM): CHEST X-RAY DATASETS PROVIDED TO SCIENTIFIC COMMUNITY

The NIH Clinical Center recently released over 100,000 anonymized chest X-ray images and their corresponding data to the scientific community. The release will allow researchers across the country and around the world to freely access the datasets and increase their ability to teach computers how to detect and diagnose disease. Ultimately, this artificial intelligence mechanism can lead to clinicians making better diagnostic decisions for patients. The dataset of scans, which was rigorously screened to remove all personally identifiable information, is from more than 30,000 patients, including many with advanced lung disease.

Reading and diagnosing chest X-ray images may seem a relatively simple task for radiologists, but in fact, it is a complex reasoning problem that often requires careful observation and knowledge of anatomical principles, physiology, and pathology. Such factors increase the difficulty of developing a consistent and automated technique for reading chest X-ray images while simultaneously considering all common thoracic diseases.

The hope is that computers will be taught to read and process extremely large numbers of scans, to confirm the results radiologists

have found, and to potentially identify other findings that may have been overlooked.

“The international demand for the dataset has been nothing short of astounding,” said Senior Investigator **Ronald Summers**, who led the initiative. “We are seeing downloads occurring 24 hours a day, seven days a week, already numbering in excess of 1,000 downloads to date.” (NIH authors: X. Wang, Y. Peng, L. Lu, Z. Lu, M. Bagheri, and R.M. Summers, *IEEE CVPR* 2097–2106, 2017)

### NIEHS: DNA DAMAGE CAUSED BY CANCER TREATMENT REVERSED BY ZATT PROTEIN

An international team led by scientists at NIEHS is the first to discover a new way that cells fix an important and dangerous type of DNA damage known as a DNA-protein cross-link (DPC). The researchers found that a protein named zinc finger protein 451 (ZATT) can eliminate DPCs with the help of another protein, tyrosyl-DNA phosphodiesterase 2 (TDP2). Because DPCs form when individuals receive some types of cancer treatments, understanding how TDP2 and ZATT work together to repair the damage may improve the health outcomes of cancer patients. Chemotherapeutic drugs can induce DPCs and so can many antibiotics. (NIH authors: M.J. Schellenberg, L.R. Butler, J.G. Williams, G.A. Mueller, R.E. London, and R.S. Williams, *Science* 357:1412–1416; 2017. DOI:10.1126/science.aam6468.)

### NINDS: DRAIN PIPES IN OUR BRAINS

By scanning the brains of healthy volunteers, NINDS researchers saw the first, long-sought evidence that our brains may drain some waste out through lymphatic vessels, the body’s sewer system. The results further suggest the vessels could act as a pipeline between the brain and the immune system. To look for the vessels, the team used magnetic-resonance imaging to scan the brains of five healthy volunteers who had been injected with gadobutrol, a magnetic dye typically used to visualize brain blood vessels damaged by diseases, such

as multiple sclerosis or cancer. The dye molecules are small enough to leak out of blood vessels in the dura but too big to pass through the blood-brain barrier and enter other parts of the brain.

The researchers also found evidence for blood and lymph vessels in the dura of autopsied human brain tissue. Moreover, scans and autopsies of brains from nonhuman primates confirmed the results seen in humans, suggesting the lymphatic system is a common feature of mammalian brains. The team plans to investigate whether the lymphatic system works differently in patients who have multiple sclerosis or other neuroinflammatory disorders. (NINDS authors: M. Absinta, S.-K. Ha, G. Nair, P. Sati, N.J. Luciano, M. Palisoc, A. Louveau, K.A. Zaghloul, S. Pittaluga, J. Kipnis, and D.S. Reich, *eLife* 2017;6:e29738; DOI:10.7554/eLife.29738) ●

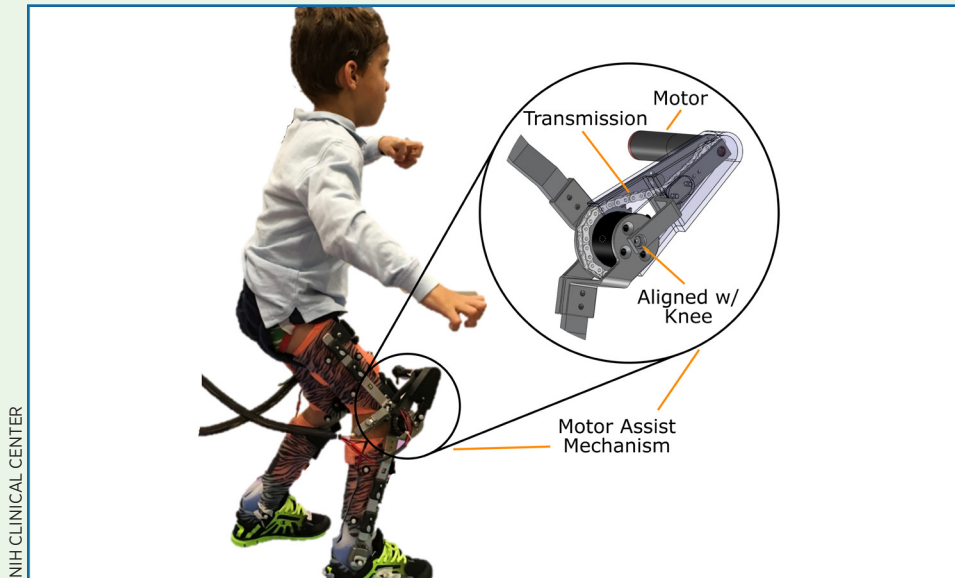
Read more online at <https://irp.nih.gov/catalyst/v25i6/research-briefs>:

- **NCI: DNA Linking Number Paradox Solved**
- **NICHD: Healthy Lifestyle Reduces Heart Attack, Stroke Risk after Gestational Diabetes**
- **NIAID: Multiple Research Approaches Are Key to Pandemic Preparedness**
- **NIAID: Three-in-One Antibody Protects Monkeys from HIV-Like Virus**
- **NIEHS: Gulf-Spill Oil Dispersants Associated with Health Symptoms in Cleanup Workers**
- **NIMH: Life-Saving Post-ER Suicide Prevention Strategies Are Cost Effective**
- **NHGRI: Sequencing All 24 Human Chromosomes May Help Improve Prenatal Genetic Screening**
- **NIAID: Mechanism of Increased Cardiovascular Risks with HIV**



## Robotic Exoskeleton Helps Children with Cerebral Palsy

BY MOLLY H. FREIMUTH, CC



NIH CLINICAL CENTER

The pediatric exoskeleton, seen above, shows the custom-designed motorized assembly for providing knee-extension assistance during walking.

WITH MOTORS, SENSORS, AND electronic-technology-powered braces wrapped around their legs, several pediatric patients participating in a Rehabilitation Medicine clinical trial looked like characters from the *Iron Man* or *Transformers* movies—and more importantly, they felt like the superheroes they resembled. The patients, all of whom have cerebral palsy, walked with crouch gait, or excessive bending of the knees. To improve their walking, researchers led by staff scientist **Thomas Bulea** (in the Clinical Center’s Rehabilitation Medicine Department) created the first robotic exoskeleton specifically designed to treat crouch gait in children with cerebral palsy by providing powered knee-extension assistance at key points during walking.

Cerebral palsy is the most prevalent childhood movement disorder in the United States, with approximately 10,000 new cases diagnosed each year. It is caused by a brain injury or abnormality in infancy or early childhood that disrupts the control of movement, posture, and balance. Crouch gait is a

common and debilitating condition in children with this disorder. Despite conventional treatments (including muscle injections, surgery, physical therapy, and orthotics), crouch gait can lead to a progressive degeneration of walking function, ultimately resulting in the loss of walking ability in roughly half of adults with the disorder.

Bulea and his team are among the first to create a device like this for children. Most wearable exoskeletons are intended for adults with paralysis and replace the lost function of the user’s muscles to restore walking ability. Bulea’s team designed their exoskeleton “to change the way children with crouch gait from cerebral palsy walk.”

The exoskeleton helps children with crouch gait by tracking the natural movement patterns of their limbs and supplying motorized assistance for knee extension at the appropriate times of the walking cycle.

The majority of the children, ages 5 to 19, were able to improve their knee extension by up to 37 degrees while wearing the brace. According to Bulea, it was the first time in their life some of the parents had seen their

children walk while standing that tall.

“Our results show that the exoskeleton can safely and effectively change the posture of a child while they wear it,” said Bulea. “The exciting part is that the children’s muscle activity was preserved when they walked in this new way with the exoskeleton, suggesting that long-term use of this device might be a viable way to train a new walking pattern.”

The team hopes that after proper validation of the science, the technology will move out of the lab and into clinics.

“Ultimately, our goal is to have this device reach as many children who can benefit as possible,” Bulea concluded.

The team is also planning studies in children with more-severe gait deficits from cerebral palsy as well as in those with other disorders such as spina bifida or muscular dystrophy. ●

This article is adapted from one that appeared in the September 2017 issue of the *Clinical Center News*. (Reference to journal article: CC authors: Z.F. Lerner, D.L. Damiano, and T.C. Bulea, *Sci Transl Med* 9:eaam9145, 2017; DOI:10.1126/scitranslmed.aam9145)



A child with cerebral palsy, assisted by the NIH pediatric exoskeleton, walks across a surface.

NIH CLINICAL CENTER

## NIH Research Festival

CONTINUED FROM PAGE 1

people from different institutes and centers (ICs) to meet each other and “to get new ideas, talk about their research, and hear about other people’s research so collaborations [can] start.”

The festival, which was held September 13 to 15 in the NIH Clinical Center, featured three plenary sessions: one on the BRAIN initiative, one on inflammatory diseases, and one on the Cancer Moonshot. Those as well as the concurrent symposia and poster sessions covered some of “the hottest topics at NIH,” said Gottesman. In addition, there were special exhibits on intramural resources; the Green Labs Fair; the FARE Awards ceremony; virtual-reality demos; the Technical Sales Association Exhibit Tent; a ceremony to recognize the contributions of research animals; and more.

This year’s event was co-chaired by scientific directors **Susan Amara** (National Institute of Mental Health) and **Stephen Chanock** (National Cancer Institute’s Division of Cancer Epidemiology and Genetics).

“It was natural for Susan and [me] to think about neurology and cancer as it was a natural reflection of what we do,” said Chanock. And “inflammatory diseases... was a best reflection of [research] that cuts across NIH.”

Other scientific directors got into the act and presented posters and delicious baked goods. NCI Scientific Director **Tom Misteli** took first place for his poster on “High-Throughput 3D Imaging of the Human Genome.” Two of the baked-goods submissions tied for first place: **Darryl Zeldin’s** (NIEHS) “Spice Cake with Buttercream Frosting” and **Luigi Ferrucci’s** (NIA) “Little Crostatas.”

Following are articles on the plenary sessions and some of the concurrent symposia. The plenary sessions were also videocast and are archived online.



PHONLAMA PHOTO/THINKSTOCKPHOTOS.COM

The BRAIN Initiative funds intramural and extramural scientists who create new technologies to change the way neuroscience studies the brain.

## PLENARY SESSIONS

### BRAIN INITIATIVE: BRIDGING GAPS IN NEURO KNOWLEDGE

BY EMILY PETRUS, NINDS

**THE BRAIN RESEARCH THROUGH** Advancing Innovative Neurotechnologies (BRAIN) Initiative was launched in 2013 to develop new methods and to bridge the knowledge gaps for diagnosing and treating mental-health diseases and neurological disorders. It funds scientists who create new technologies to change the way neuroscience studies the brain, explained **Gregory Farber** (NIMH), co-leader of the BRAIN initiative coordination team and one of the presenters at the first plenary session held on September 13 at the 2017 NIH Research Festival.

Through the BRAIN Initiative, NIH is providing grants to both extramural and intramural researchers and widening its net to draw in mathematicians, physicists, and computer scientists. These investigators are first-time NIH applicants from outside of the traditional neuroscience field, and they will change the way biomedical research is conducted. The long-term goal

is to “make circuit abnormalities the basis of diagnostics, and normalization of circuit function the target of intervention,” according to the BRAIN Initiative website (<https://www.braininitiative.nih.gov>). Three grant awardees presented their work at the plenary session.

BRAIN-grantee **Dietmar Plenz** (NIMH) described his studies of how neurons fire together in specific patterns, called “neuronal avalanches,” which can be described with computer modeling and mathematical algorithms. The activity of neurons and the earth’s seismic eruptions follow similar mathematical equations; Plenz’s group first described how these neuronal avalanches can be detected in a manner similar to how we use the Richter scale to measure earthquakes. His group hypothesizes that neuronal avalanches are a new type of brain activity that can be distinguished from network oscillations and may provide a means for the brain’s ability to optimize information processing while maintaining network stability.

Another BRAIN-funded investigator, Patrick Kanold (University of Maryland, College Park), and Plenz are collaborating to describe how groups of neurons fire



together. They have discovered that small-sound stimuli evoke neuronal avalanches in the auditory part of the brain, complete with “aftershocks” of activity that carry stimulus information for many seconds. Kanold’s group focuses on the circuit interactions between cells in the rodent auditory system. His studies show that the auditory cortex organizes as a tonotopic map (arranged by pitch or sound frequencies) at large scale. However, this map becomes much more intermingled at the single-neuron level, indicating that our understanding of the brain’s organization may require precise measures at single-cell resolution, a major aim of the BRAIN Initiative.

Neuroscience “needs a collaborative effort of many kinds of people,” said Kanold. “We need some traditional neuroscientists. We need tool builders, people who build microscopes and genetic tools, computational neuroscientists and theorists,” he continued. “What it means is there’s a change in the way we do neuroscience: You have team science.”

**Peter Basser** (NICHD) described advances his group has made, using axon-diameter measurements, in detecting connectivity in the brain. Basser is best known for the development of diffusion tensor imaging, which allows for noninvasive imaging of brain connectivity by measuring white-matter tracts in both the clinic and the lab. White matter (myelin) wraps neurons and forms a type of insulation to make sure signals get where they’re going quickly, and it also reduces alterations in the signals’ strength and timing. Using his BRAIN grant, Basser’s group is developing a latency map to measure how long it takes to send “packets of information” from one place to another. Disruptions in white matter can cause problems in how the brain talks within itself and to the rest of the body. These problems can result in paralysis, cognitive and motor dysfunction, and sometimes death. Scanning for myelin

health is a new tool that clinicians can use to diagnose demyelinating diseases such as multiple sclerosis.

“There is this enormous mystery waiting to be unlocked,” said President Barak Obama when announcing the initiative in 2013. “The BRAIN Initiative will change that by giving scientists the tools they need to get a dynamic picture of the brain in action and better understand how we think and how we learn and how we remember. And that knowledge could be, will be, transformative.”

**The Plenary Session “The BRAIN Initiative,” held on September 13, 2017, was moderated by Dietmar Plentz (NIMH). To watch a video-cast, go to <https://videocast.nih.gov/launch.asp?23456>. Intramural researchers wishing to find out more about how to apply for BRAIN grants can visit <https://www.braininitiative.nih.gov/funding/index.htm>.**

#### **INFLAMMATORY DISEASES: FIXING THINGS WHEN THE IMMUNE SYSTEM GOES AWRY**

BY LESLEY EARL, NCI

**AT THE TURN OF THE 21ST CENTURY**, the immune system, while complicated, seemed fairly straightforward: Immune cells, both innate and adaptive, fought off infections, and non-immune cells had non-immune functions. But in the past 17 years, our understanding of the immune system has radically changed. For inflammatory diseases, diseases in which the regulation of the immune system is fundamentally altered, we have come to see that non-immune cells—and the microbiota as well—have critical influence on the course of disease.

“We see now that on many levels, all cells are immune cells,” said **Susan Amara** (NIMH), co-chair of the 2017 NIH Research Festival. In the festival’s second plenary session, the speakers highlighted how unexpected regulation and functions

of the immune system have led to a new understanding of immune deficiencies, autoimmune diseases, and cancer therapeutics.

In the first presentation, given by **William Comrie** (NIAID), a postdoctoral fellow in **Michael Lenardo’s** lab, the lab’s research into rare, congenital disorders of the immune system was discussed. Using next-generation sequencing, “you can learn the genetic cause of an unknown disease and potentially target that biological pathway,” said Comrie. “Along the way, we sometimes gain insight into key human biology.”

In one example, the researchers found that a congenital autoimmune disorder was caused by mutations in *CTLA4*, which codes for cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), a receptor critical for controlling T-cell activation; the mutations triggered runaway activation of T cells. A clinical trial that uses a CTLA-4 mimic to replace the missing signal is currently underway at the NIH Clinical Center. In a second example, Comrie described a new primary immune deficiency characterized by early-onset protein-losing enteropathy, gastrointestinal inflammation, and deadly vascular thrombosis. Screening of 11 patients in eight families revealed that the disorder was caused by mutations in both copies of the gene encoding cluster of differentiation 55 (CD55), which prevents complement-mediated attack of human cells. The elevated complement activation and elevated terminal membrane-attack-complex formation in patients appear to be the root cause of much of the intestinal and vascular damage, because treatment with complement inhibitors in CD55-deficient patients greatly reduces the symptoms of disease.

In the second presentation, **Romina Goldszmid** (NCI) explored the role of inflammation and the tumor microenvironment in cancer—and not only on the development of cancer, but also on a patient’s

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**Research Festival**  
CONTINUED FROM PAGE 11

response to standard chemotherapies. Tumors, Goldszmid said, can be classified immunologically as “hot” (inflamed, with high numbers of infiltrating effector immune cells), “cold” (not inflamed, with few infiltrating effector immune cells and more cells with immunosuppressive activity), or somewhere in-between. Hot tumors with a high concentration of CD8+ T cells are more likely to respond to immunotherapies (therapies based not on small-molecule drugs, but on antibodies or specially adjusted immune cells).

Surprisingly, hot tumors are also more likely to respond better to standard chemotherapy treatments. But the mechanism of the chemotherapy response is different: It requires the action of innate myeloid cells. Goldszmid found that, if primed by the proper microbiota, neutrophils can release reactive oxygen species after encountering preliminary damage from certain chemotherapeutic agents, thus intensifying the anticancer effect of the therapy. The key, said Goldszmid, is “thinking about how the therapies work” and understanding whether they need help from cells like neutrophils and the microbiota to be effective. Getting

the right balance of signals to harness the power of the immune system may be the key to cancer treatment, whether the treatment is chemotherapy or immunotherapy.

**Mariana Kaplan** (NIAMS), the third speaker in the plenary session, also found neutrophils to be unexpectedly critical in her study of autoimmune disorders such as systemic lupus erythematosus (SLE, or lupus). While SLE is generally thought to be mediated by antibodies reactive to autoantigens (abnormal self-antigens) such as DNA, Kaplan sought to answer questions such as how the autoantigens were being released and what was causing complications such as atherosclerosis, which is also common in people with SLE. She found a key role for neutrophils in this process: When activated by certain danger signals, neutrophils undergo a process known as NETosis (NET stands for “nuclear extracellular traps”) in which the neutrophils extrude their nuclear material along with molecules present in their granules, making them available to antigen-presenting cells and activating a variety of inflammatory pathways and vascular damage. SLE patients, she found, have a high concentration of neutrophils predisposed to undergoing NETosis. “This gives us some hope

that if we target some of these deleterious pathways mediated by these neutrophils, we may be able to prevent or mitigate some of the organ damage” in SLE patients, said Kaplan.

“No matter what disease you are working on,” said session moderator **John J. O’Shea** (NIAMS), “you may not think of yourself as an immunologist or an inflammatory pathologist, but in fact you are.” As shown by the speakers in the plenary session, the interplay between immune cells, non-immune cells, and the microbiota affects the body in unexpected ways. “Every cell,” O’Shea emphasized, “is an immune cell.”

To watch a videocast of the 2017 Research Festival’s “Inflammatory Diseases” plenary session, held on September 14, 2017, go to <https://videocast.nih.gov/launch.asp?23459>.

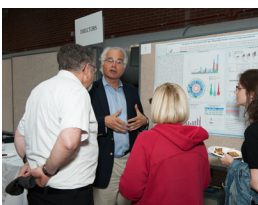
**THE CANCER MOONSHOT**

BY ZOE SHANCER, NCI

**THE CANCER MOONSHOT**, ANNOUNCED BY former President Barack Obama in his last State of the Union Address in January 2016, aims to double the rate of progress in our understanding of cancer and achieve in five years what would otherwise take a decade. Plenary session moderator **Dinah Singer** (NCI-CCR) outlined the main goals of the initiative:

- Accelerate our understanding of cancer across the cancer continuum from basic to translational and clinical, including prevention and screening.
- Encourage more collaboration and cooperation across the entire cancer-research community, not just NIH-funded research.
- Improve and enhance data sharing.

What does the initiative mean for intramural researchers? Plenty. Singer explained how a blue-ribbon panel of 28 scientific experts (with the help of 150 working-group members) developed 10



The 2017 Research Festival featured scientific lectures, poster sessions, special exhibits on intramural resources, and more. Clockwise from top left: Festival co-chair Steve Chanock explained his research at the scientific directors poster session; people were eager to see the “green” resources showcased at the Green Labs Fair; Festival co-chair Susan Amara introduced some of the scientific sessions; scientists gave talks and took part in panel discussions; Festival goers sampled delicious treats prepared by scientific directors; and flowers were placed on a commemorative plaque at the ceremony to honor research animals.



ALL: MARLEEN VAN DEN NESTE

scientific recommendations, which are already being implemented. Several new extramural and intramural initiatives will be funded, including three intramural projects being launched as part of the Cancer Moonshot and described at this plenary session: a formal evaluation of single-dose regimens of the human papillomavirus (HPV) vaccines; population screening for cancer-predisposition genes; and a rare-tumor initiative.

**HPV vaccines.** Some types of the sexually transmitted HPV cause about 300,000 deaths from cervical and other cancers per year worldwide. The HPV vaccine—usually administered in two to three doses to adolescents and three doses to young adults—can provide protection, yet many people go unvaccinated, especially in low-income countries. **Aimée Kreimer** (NCI-DCEG) is testing one-dose vaccines versus two-dose vaccines to prevent HPV. A one-dose vaccine could dramatically lower the barriers to vaccination.

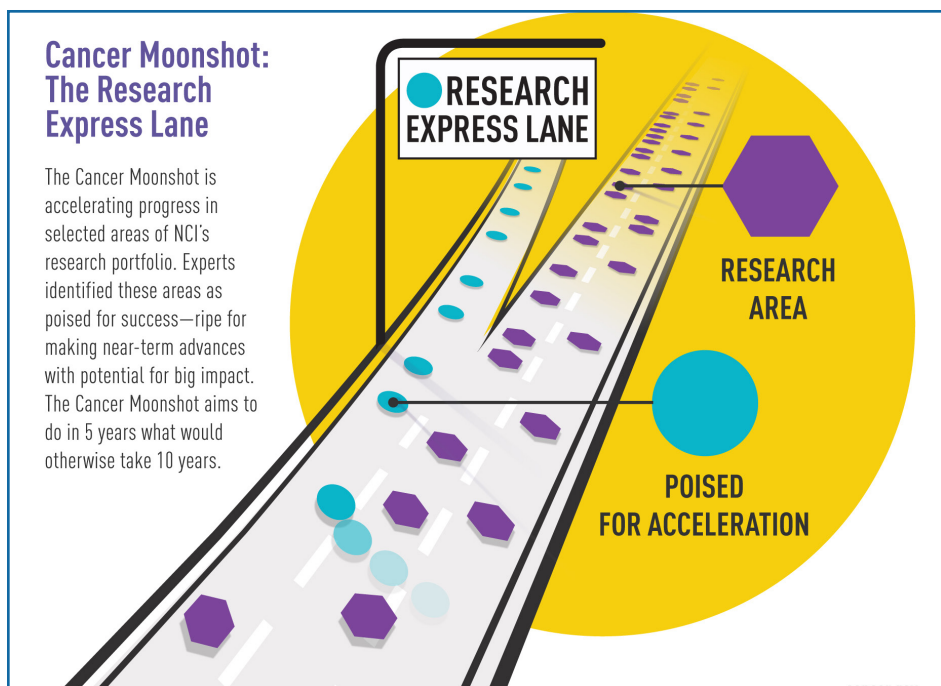
Kreimer described a new NCI HPV-vaccine trial that will be conducted in Costa Rica. The evidence to date suggests that although this subunit vaccine typically requires a multidose regimen, a single dose may produce durable protection against HPV infections. Subunit vaccines only contain antigens to and not live particles of the pathogen. The new trial will definitively answer the question whether one dose of the HPV vaccine is sufficient, and if so, it raises the potential for other subunit vaccines to be administered in single-dose regimens.

“[W]e know how many vaccine doses our children get in the first five years,” Kreimer said. “This is not even possible in developing countries, so think how we can revolutionize vaccinology if we demonstrate that a single-dose platform can work.”

**Population screening for cancer-predisposition genes.** There are more than 120 cancer-predisposition genes (CPG). Carriers of germ-line pathogenic variants in CPG

## Cancer Moonshot: The Research Express Lane

The Cancer Moonshot is accelerating progress in selected areas of NCI's research portfolio. Experts identified these areas as poised for success—ripe for making near-term advances with potential for big impact. The Cancer Moonshot aims to do in 5 years what would otherwise take 10 years.



are at a high risk for cancer, and preventive strategies may be implemented. **Maria Isabel Achatz** (NCI-DCEG) discussed her group's previous experience in discovering the high occurrence of a founder mutation in the *TP53* gene in Brazil involved in Li-Fraumeni syndrome, a rare inherited disorder that leads to a higher than normal risk of developing certain cancers. Defining the prevalence of the founder mutation in 0.3 percent of the population of southern Brazil's population has public-health implications. Achatz's group will be also measuring the population prevalence and cancer penetrance of germ-line pathogenic mutations in CPG in an unbiased cohort of newborn screening samples from Michigan. She hopes to identify the contribution of germ-line variants in CPG to childhood and young-adult cancer etiology and to understand how germ-line variants affect underrepresented minorities. All information they collect will be available in public databases for data queries, hypothesis generation, and future testing.

**The Rare Tumors Initiative.** Rare tumors lead to a quarter of cancer deaths and contribute greatly to our understanding of cancer mechanisms, explained **Brigitte**

**Widemann** (NCI-CCR), who presented a proposal for the Rare Tumors Initiative and Rare Tumor Patient Engagement Network. She provided an overview of examples of NCI's Center for Cancer Research's intramural research in rare tumors. She highlighted research on chimeric antigen-receptor therapies for acute myeloid leukemia (a type of blood cancer), the development of the first therapy for plexiform neurofibroma (a benign tumor of the sheaths of peripheral nerves), clinical trials for targeted therapies for gastrointestinal stromal tumors (uncommon tumors of connective tissue in the gastrointestinal tract), and clinical data and tissue analysis for ependymoma (a rare tumor of epithelial lining of ventricles in the brain or spinal cord or, rarely, the pelvis).

The Rare Tumors Initiative will develop a shared infrastructure to study rare tumors; connect patients and investigators through advocacy groups; and develop a biorepository available to researchers worldwide. ●

To view a videocast of the 2017 Research Festival Plenary Session III, “The Cancer Moonshot,” go to <https://videocast.nih.gov/launch.asp?23462>.

## 2017 Research Festival: Selected Concurrent Symposia

### CELL-BASED THERAPIES TO THE RESCUE

BY ALEXIS CARTER, NCI

CELL-BASED THERAPIES HAVE BEEN USED in clinical trials for more than 25 years with limited effectiveness...until now. Several intramural scientists shared their stories about how cell therapies are contributing to advances in cancer immunotherapy, gene therapy, and regenerative medicine and how the Clinical Center's Cell Processing Section is playing a critical role.

In cancer immunotherapy, T cells can be genetically engineered to treat lymphoma and other blood cancers. **James Kochenderfer's** (NCI-CCR) explained how he developed an anti-cluster of differentiation 19 chimeric antigen receptor (CAR)-engineered T-cell therapy that causes lasting remission in advanced lymphoma. Also in the gene-therapy realm, **Suk See De Ravin** (NIAID) described how she and **Harry Malech** (NIAID) used CRISPR/Cas9 gene editing to correct a genetic mutation in hematopoietic stem cells that causes a rare inherited immunodeficiency disease called chronic granulomatous disease.

Cell-based therapies are also being used to regenerate parts of the eye that are damaged in age-related macular degeneration (AMD). **Kapil Bharti** (NEI) has developed an autologous induced pluripotent stem cell (iPS) technology-based cell therapy to treat AMD. He described preclinical studies for which he developed an iPS-cell-derived patch that protects against AMD-related vision loss. His team is currently manufacturing the patch and hopes that by 2018, it can be transplanted into people with AMD.

And FARE Award winner **Defne Bayik** (NCI-CCR) is doing research that may have implications for the treatment of autoimmune and inflammatory diseases.

It's the NIH Clinical Center's Cell

Processing Section that produces the cellular therapies used in clinical trials. Section Director **David Stroncek** (CC) talked about the complexities of producing, analyzing, and developing high-quality cellular therapies. One of the products the section manufactures is CAR T cells, recently FDA-approved for the treatment of children with acute lymphoblastic leukemia. Until recently, CAR T-cell therapy was used only in small clinical trials in people with advanced blood cancers.

The "Cell-Based Therapies: Transitioning from the Research Laboratory to the Clinic" concurrent symposium was chaired by **David F. Stroncek** (CC).

### SEARCHING FOR WHAT CAUSES DISEASES

BY HUSSAIN ATHER, NIDDK

THE GENOMICS ERA HAS LED TO EXCITING discoveries in human genetics that have greatly improved the understanding of the causes of rare and common diseases.

**Kenneth Fischbeck** (NINDS), whose group has identified genes and helped in the development of treatments for hereditary neuromuscular diseases, described how oligonucleotides have been used in mice and patients to correct for the disease-causing genetic mutations. **Douglas Stewart** (NCI), who is investigating the genetics and clinical aspects of the rare pediatric lung cancer pleuropulmonary blastoma (PPB), explained how PPB was caused by germ-line mutations in *DICER1*. *DICER1* syndrome increases the risk of a variety of cancerous and noncancerous (benign) tumors. Some mutation carriers, however, develop cancer while others remain healthy.

In her talk on uncovering etiology and improving patient care through characterization of cancer-predisposition syndromes,

**Sharon Savage** (NCI-DCEG) spoke about her work on the phenotype of dyskeratosis congenita (DC), a disorder that can increase the risk of developing leukemia and other cancers. **Daniel Kastner** (NHGRI) talked about the expanding spectrum of autoimmune-inflammatory diseases and the role of next-generation sequencing in discovering new human diseases. As an example, he discussed how exome sequencing in two unrelated children with unexplained recurrent fevers and early-onset stroke led to his lab's discovery of mutations in a previously poorly characterized gene called *CECR1*. With the benefit of genetic testing, many more patients have been recognized with this condition.

Genomics is showing that the phenotypes associated with neurological diseases are much broader than we previously appreciated. "Genetics is already leading to a reclassification of neurological diseases," said **Bryan Traynor** (NIA). "In the longer term, machine learning applied to genomic data will further enhance our ability to recognize and diagnose diseases and to identify individuals within the population at greater risk of disease so that they can benefit from early intervention."

FARE Award winner **Michael Leney-Greene** (NIAID), a graduate student in **Helen Su's** and **Michael Lenardo's** lab, described research on patients suffering from an autoimmune disease caused by mutations in a gene that is a member of the mammalian target of rapamycin complex 1 (mTORC1) regulatory complex that controls protein synthesis.

The "Genotyping and Phenotyping" concurrent symposium was chaired by **Kenneth Fischbeck** (NINDS) and **Sharon A. Savage** (NCI-DCEG).



## NEUROSCIENCE AND COMPULSIVE DISORDERS

BY CLARISSA JAMES, NIMH

WHETHER IT BE COMPULSIVE EATING, excessive alcohol consumption, or substance abuse, such behaviors are driven by shared neurocircuitry that we struggle to understand. The NIH Center on Compulsive Behaviors (CCB), a collaboration of researchers from seven institutes, is advancing scientific discovery in the field of compulsive disorders. Several CCB members presented their research at the 2017 Research Festival.

**Michael Krashes** (NIDDK), who is deciphering the neural wiring that underlies hunger, described his work on hunger-driven motivation in rodents. To understand the neural circuitry underlying alcoholism, **Veronica Alvarez** (NIAAA) has focused on dopamine D2 receptors (D2R) in the striatum area of the brain. **Yavin Shaham** (NIDA) wants to understand the cellular and neuroanatomical mechanisms that underlie drug relapse in addicts who've been abstinent. He found that neuronal ensembles in certain parts of the brain play an important role in relapse to methamphetamine seeking after voluntary abstinence.

**Philip Shaw** (NHGRI) explores the similarities and differences in the neural bases of impulsive and compulsive behavioral disorders. Both these disorders share deficits in the ability to inhibit responses. This deficit is traced to hypoactivity in the brain's right inferior frontal gyrus.

FARE Award winner **Andrew Kesner** (NIDA), a graduate student in **Satoshi Ike-moto's** lab, used optogenetics to determine how an understudied region in the posterior hypothalamus may play an important role in motivational processes and in driving reward-seeking behavior.

The concurrent symposium "Neuroscience and Compulsive Disorders" was co-chaired by **Veronica Alvarez** (NIAAA) and **Philip Shaw** (NHGRI).

## SINGLE-CELL ANALYSIS: AN OLD IDEA WITH NEW TRICKS

BY EMILY PETRUS, NINDS

SINGLE-CELL ANALYSIS MEANS FIGURING out how every cell is different and then using the unique characteristics of each to solve bigger problems. Until now this technology was difficult to manage, but the marriage of biology, computer science, and bioinformatics has transformed this field.

Immune-system researcher **John Tsang** (NIAID) is interested in how the human body's environment and age can modify the heterogeneity of macrophages. Older people have more homogenous cell populations than younger people do; the homogenous cell populations may underlie changes in the immune function as people age.

**Jamie Diemer** (NHGRI), a biologist in **Paul Liu's** lab, uses single-cell analysis to detect abnormal myeloid progenitors as a biomarker in transgenic mice before they develop leukemia. In a similar vein, HIV researcher **Eli Boritz** (NIAID) uses single-cell analysis of infected T cells in an attempt to identify HIV patients' viral reservoirs. If the reservoirs had a marker, clinicians could wipe out that small, but specific, cell population in an effort to cure HIV.

Other researchers' work had a basic-science spin. FARE winner **Yihan Wan** (NCI), a postdoc in **Daniel Larson's** lab, presented her research visualizing active transcription of genes in single cells in real time. **Michael Kelly** (NIDCD), a research fellow in **Matthew Kelley's** lab, described the lab's use of high-throughput single-cell transcriptional-profiling methods to map how hair cells in the cochlea differentiate through developmental time.

The concurrent symposium "A Diversity of Biological Insights from Single-Cell Analysis across Multiple Diseases" was chaired by **Mark Cookson** (NIA) and **Yong-Chen William Lu** (NCI-CCR).

## THE MICROBIOME: A KEY PRIMER OF THE IMMUNE SYSTEM

BY JENNIFER PATTERSON WEST, NIDDK

THE IMPORTANCE OF THE MICROBIOME in human health and in disease progression has revolutionized how we think about disease. **Yasmine Belkaid** (NIAID) discussed the interplay between the skin microbiota and the immune system. She described how she and postdoc **Jonathan L. Linehan** (NIGMS) observed that the commensal bacterium *Staphylococcus epidermidis* induced commensal-specific CD8+ T cells in the skin without causing inflammation or tissue damage. The cells protected against subsequent infections from pathogenic bacteria and promoted tissue repair.

The microbiome plays a role in boosting cancer immunotherapy. Visiting postdoctoral fellow **Marie A. Vetizou** (NCI-CCR), in **Giorgio Trinchieri's** lab, is trying to improve the efficacy of the monoclonal antibody ipilimumab, used to treat melanoma, without increasing its toxicity. The drug's efficacy is lost in a germ-free environment but certain bacteria normally found in the gut can restore efficacy and protect against colitis associated with anti-cancer treatment.

**Julie A. Segre** (NHGRI) recently found that eukaryotic viruses made up less than four percent of the skin microbiome of healthy volunteers, but 90 percent of the microbiome of people who had a rare immune disorder called DOCK8 immunodeficiency syndrome. **Jason Brenchley** (NIAID) is exploring whether gastrointestinal microbial dysbiosis increases the chances of developing an HIV infection. ●

The "Microbiome" session was chaired by **Yasmine Belkaid** (NIAID).

Read more online at <https://irp.nih.gov/catalyst/v25i6/2017-research-festival-selected-concurrent-symposia>.

## Recently Tenured



NIHAL ALTAN-BONNET, NHLBI



SONJA BEST, NIAID



MELISSA FRIESEN, NCI-DCEG



GRETCHEN GIERACH, NCI-DCEG



HONG XU, NHLBI

### NIHAL ALTAN-BONNET PH.D., NHLBI

*Senior Investigator and Head, Laboratory of Host-Pathogen Dynamics, National Heart, Lung, and Blood Institute*

**Education:** Hunter College, City University of New York, New York (B.A. in biology and chemistry); The Rockefeller University, New York (Ph.D. in cellular biophysics)

**Training:** Postdoctoral research fellow, NICHD's Cell Biology and Metabolism Branch

**Before coming to NIH:** Assistant Professor, Federated Department of Biological Sciences, Rutgers University (Newark, N.J.)

**Came to NIH:** In 1999–2005 for training; returned in 2013 as a Stadtman investigator in NHLBI

**Selected professional activities:** Serving on NIH and NSF study sections; mentoring K-12 and college students; serving as reviewer for scientific journals and on editorial boards

**Outside interests:** Taking road trips with family (for example, to national parks); discovering roadside diners; hiking; swimming; reading

**Website:** <https://irp.nih.gov/pi/nihal-altan-bonnet>

**Research interests:** By combining cutting-edge imaging technologies with lipidomic and proteomic approaches, my lab has discovered novel replication and transmission mechanisms that are surprisingly shared by many different human, animal, and

plant viruses. Focusing on shared attributes among viruses has led to a deeper understanding of what it means to be a virus. Our investigations have revealed that although there are many significant differences among viruses—in genomes, capsid structures, and replication mechanisms—surprisingly there are also many common critical features of their lifecycles that enhance their infectivity. For example, we have found that many viruses exploit certain lipid-enriched membranes, such as phosphatidylinositol-4-phosphate and cholesterol, to dock and assemble their enzymes, which in turn we have shown leads to greater efficiency in replicating their genomes. More recently we have discovered that many different viruses transport themselves to the next host as populations inside vesicles, rather than as individuals. We showed that this ability enhances their genetic diversity and transmission efficiency. Discovering these and other common viral attributes we believe will not only provide insight into the virus-host interface but will also provide opportunities for novel types of panviral therapeutic interventions.

If you have been recently tenured, *The NIH Catalyst* will be in touch with you soon to do an article about you on these pages.

### SONJA M. BEST, PH.D., NIAID

*Senior Investigator and Chief, Innate Immunity and Pathogenesis Section, Laboratory of Virology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases*

**Education:** University of Adelaide, Adelaide, SA, Australia (B.S. with majors in immunology and microbiology, second major in zoology); Australian National University, Canberra, Australia (Ph.D. in biochemistry and molecular biology)

**Training:** IRTA visiting fellow and later a research fellow in NIAID's Laboratory of Persistent Viral Diseases

**Came to NIH:** In 1999 for training; in 2007 became a staff scientist; in 2009 became a tenure-track investigator

**Selected professional activities:** Editorial board member, *Journal of Biological Chemistry*, *Journal of Virology*, and *Journal of Interferon and Cytokine Research*; board of reviewing editors, *Science Translational Medicine*; invented monoclonal antibody specific for the extracellular domain of human protein interferon-alpha and -beta receptor subunit 1

**Outside interests:** Hiking with the dog; entertaining friends; pencil drawing and sketching; traveling

**Website:** <https://irp.nih.gov/pi/sonja-best>





**Research interests:** The world has witnessed several major emerging viral diseases in the past 20 years, including West Nile virus, Zika virus, and Ebola virus. I am interested in understanding the mechanisms underpinning early immune activation after infection with RNA viruses and how emerging viruses evade these early responses to cause disease. The innate immune response is rapidly engaged after virus infection and functions to limit virus replication and mobilize adaptive immune responses, in large part through the production of type I interferons (IFN). The molecular interactions between this critical IFN response and the infecting virus (specifically, the ability of the virus to antagonize the response) can determine host tropism and the potential of a virus to emerge from an animal source into humans. These viral evasion strategies are not always functional in mice and can be a significant limitation in developing animal models of disease for testing of vaccines and other countermeasures.

We are using the insight from these virus-host interactions to develop better mouse models of disease by engineering mice with targeted gene deletions or gene knock-ins in key molecules involved in innate signaling and virus restriction. Our current virus models include emerging flaviviruses (such as Zika virus and tick-borne encephalitis virus) and filoviruses (Ebola virus). Specific topics currently being explored in the laboratory include the mechanisms used by these viruses to modulate host innate immunity, the role of novel IFN-stimulated genes in host-specific resistance to virus infection, and the importance of macrophage and dendritic-cell function to antiviral innate and adaptive immune responses. Understanding key events at this virus-host interface will help us to understand virus emergence, and engineering better mouse models will facilitate design of vaccines and therapeutics.

**MELISSA C. FRIESEN, PH.D., NCI-DCEG**

*Senior Investigator, Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute*

**Education:** University of British Columbia, Vancouver, B.C., Canada (B.Sc. in chemistry); School of Occupational and Environmental Health, University of British Columbia, Vancouver (M.Sc. and Ph.D.)

**Training:** Research fellow, Population Health Learning Observatory (Vancouver); research fellow, Centre for Occupational and Environmental Health, Monash University (Melbourne, Australia); postdoctoral research fellow, Environmental Health Sciences, University of California at Berkeley, (Berkeley, Calif.)

**Came to NIH:** In 2009

**Selected professional activities:** Member of editorial review board of the *Journal of Occupational and Environmental Hygiene*; member of the international advisory board of the *Annals of Occupational Hygiene*

**Outside interests:** Traveling; bicycling

**Website:** <https://irp.nih.gov/pi/melissa-friesen>

**Research interests:** I am developing quantitative-assessment strategies and tools to accurately calculate lifetime occupational exposures to various substances among men and women. These exposure estimates are used to identify causes of increased cancer risk. By using more-refined and more-proximal exposure measures, I have identified and quantified exposure-response relationships for several exposure-disease associations that have not previously been published: straight metalworking fluid and bladder cancer; lead and meningioma; pentachlorophenol (organochlorine compound used as a pesticide and a disinfectant) and non-Hodgkin lymphoma; and wood dust and hospitalization for chronic lung diseases.

To improve the transparency and efficiency of exposure-assessment efforts in

case-control studies of cancer, I developed a framework to apply exposure decision rules that link occupational information from study subjects to estimates of occupational exposure. I used this approach to evaluate occupational exposure to metalworking fluids and the risk of bladder cancer. I demonstrated for the first time that quantitative estimates from population-based studies are comparable to the high-quality assessment efforts in industry-based studies. Both methods yield similar and consistent exposure-response associations.

I have extended the use of statistical models—to predict historical exposure—commonly used in industry-based studies to population-based studies. For example, I have developed a framework to combine subjective ratings of exposure from job-exposure matrices and exposure measurements to better discriminate between time and job differences in exposure levels in population-based studies. I have also extended the use of meta-regression models to determinants of exposure concentrations from occupational and environmental exposure scenarios reported in the published literature.

I have also created exposure-assessment tools by efficiently transforming participants' verbatim responses in occupational questionnaires into usable data. I led the development of an algorithm to automatically code job descriptions into standardized occupation classification codes. I also generated keyword-based approaches to use the verbatim responses to systematically extract variables representing exposure scenarios that can be used in decision rules and to assign more-detailed questionnaires to subsets of study participants.

I have found that the accuracy of exposure-assessment tools may differ by sex. By pooling occupational responses from three studies, I found gender differences

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## Recently Tenured

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in the prevalence and frequency of work tasks. In addition, there are several factors that may explain why women's physiologic responses to exposure may be different from men's including hormonal influences and physiologic differences that can influence internal exposure dose. Failure to at least consider gender differences may result in biased estimates of risk.

### **GRETCHEN L. GIERACH, M.P.H., PH.D., NCI-DCEG**

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

**Education:** Pennsylvania State University, University Park, Pa. (B.S. in behavioral health); University of Pittsburgh Graduate School of Public Health, Pittsburgh (M.P.H. and Ph.D. in epidemiology)

**Training:** Cancer Prevention Fellow, Cancer Prevention Fellowship Program, Office of Preventive Oncology, NCI

**Came to NIH:** In 2006 for training; in 2010 appointed as a tenure-track investigator

**Selected professional activities:** Chair of NCI-DCEG's Breast Cancer Working Group; co-chair of NCI-DCEG's Hormone Laboratory Advisory Committee

**Outside interests:** Enjoys spending time with her husband, two sons, and yellow Labrador retriever; cooking; traveling

**Website:** <https://irp.nih.gov/pi/gretchen-gierach>

**Research interests:** I conduct integrative molecular epidemiologic research aimed at advancing our understanding of breast-cancer etiology and progression. My research focuses on breast density and hormones, two of the strongest risk factors for sporadic breast cancer among women.

My work on breast density uses a range of technologies and approaches to improve

the measurement of density, delineate risk factors for elevated density, and understand mechanisms that mediate its relationship to breast-cancer risk and progression. I lead the BREAST Stamp Project, which aims to characterize the radiologic, histologic, and molecular features of dense breast tissue and to understand how the microenvironment of dense breasts promotes neoplastic transformation of the breast epithelium. I am also investigating whether standardized microscopic (terminal duct lobular involution) and macroscopic (mammographic breast density) measures of breast-tissue architecture could represent clinically useful intermediate endpoints of risk in a nested case-control study of 1,000 women diagnosed with benign breast disease, among whom 500 subsequently developed breast cancer. Findings from these efforts could improve risk-assessment strategies for the increasing number of women undergoing breast biopsies after a mammogram.

In light of growing evidence indicating that reductions in mammographic density, specifically among tamoxifen users, may predict reduced risk of breast-cancer development and progression, my colleagues and I are integrating serial measures of mammographic breast density into a cohort study of patients with invasive breast cancer diagnosed within a general community health-care plan. In the Ultrasound Study of Tamoxifen, we are using novel 3-D whole-breast ultrasound-tomography methods to assess changes in breast sound speed, a surrogate for volumetric breast density, within the first year of clinically indicated tamoxifen use. These studies may provide support for future investigations evaluating change in mammographic density as a "biosensor" of factors that increase or decrease breast-cancer risk.

To study hormonal carcinogenesis, I conduct epidemiologic studies to evaluate

the influence of endogenous and exogenous hormones on both radiologic and histologic measures of breast-tissue composition and risk. The ultimate goal of my research is to facilitate the development of improved strategies for risk stratification, prevention, early detection, and treatment by better understanding breast carcinogenesis and the basic mechanisms underlying established risk factors.

### **HONG XU, PH.D., NHLBI**

*Senior Investigator, Laboratory of Molecular Genetics, National Heart, Lung, and Blood Institute*

**Education:** Nankai University, Tianjin, China (B.S. in biology); Peking University, Beijing, China (M.S. in molecular biology); Johns Hopkins University School of Medicine, Baltimore (Ph.D. in genetics)

**Training:** Postdoctoral fellow, Department of Biochemistry and Biophysics, University of California, San Francisco (San Francisco); Research area was genetics and developmental biology

**Came to NIH:** In 2010

**Outside interests:** Hiking; working in the yard

**Website:** <https://irp.nih.gov/pi/hong-xu>

**Interview:** <https://youtu.be/YewksTvhVTs>

**Research interests:** My research focuses on several of the most important but unresolved issues related to our second genome—our mitochondrial DNA (mtDNA)—which is transmitted through the maternal lineage. Mutations in mtDNA are associated with many inherited and age-related disorders including neurodegeneration, muscular atrophy, and diabetes. My colleagues and I want to understand how a mother can provide healthy mitochondria, without harmful mtDNA mutations, to her children.

I previously developed a genetic approach to select for inheritable mtDNA



mutations in fruit flies of the genus *Drosophila*, which paved the way for studying mtDNA genetics and modeling human mtDNA diseases. My lab reported that the ectopic expression of an alternative repository enzyme can fully rescue a lethal mtDNA mutation, suggesting a potential therapy for currently incurable mtDNA diseases.

We also discovered that the selective proliferation of healthy mitochondria containing wild-type mtDNA would increase the proportion of the wild-type genome in oocytes. The greater number of healthy mitochondria would outcompete the unhealthy mitochondria and consequently limit the transmission of deleterious mtDNA variants to the next generation. Our model of selective inheritance explains the strong purifying selection observed in animal studies and challenges the existing dogma known as bottleneck inheritance as an effective way to weed out the mtDNA mutations.

We also revealed a translational boost on the mitochondrial outer membrane that promotes the synthesis of nuclear-encoded mitochondrial proteins. This boost supports the prodigious mtDNA replication during oogenesis and explains how a single nuclear genome within a germ cell can support the biogenesis of millions of mitochondria to power the early embryonic development. We are now combining our new techniques in mtDNA genetics with powerful manipulations of the nuclear genome in *Drosophila* to investigate the cellular processes that regulate mitochondrial genome organization, segregation, and expression. We are exploring how these regulations affect mtDNA inheritance. We are also undertaking a high-risk endeavor to develop new methods for mtDNA transformation. This process would help to generate cell and animal models of human mtDNA diseases and facilitate the development of effective therapies. ●

### NEW: BIOMEDICAL INSTRUMENTATION DEVELOPMENT

Across the NIH intramural community, researchers and engineers develop novel hardware and software solutions that enable cutting-edge laboratory and clinical biomedical research. These researchers and engineers contribute to a wide variety of fields using research tools such as magnetic resonance imaging, positron-emission tomography, optical imaging, behavioral assays, animal studies, and clinical trials. Despite the diversity of applications, common threads exist in the technologies and methods used to develop novel systems, such as electronics, embedded and desktop programming, mechanical design and fabrication, optical design and assembly, automation, and algorithms.

The Biomedical Instrumentation Development SIG provides a forum for NIH's intramural research program engineers and scientists who are developing custom biomedical instrumentation and related software solutions. Through meetings and a mailing list, the SIG facilitates collaborations and provides a mechanism for members to share expertise to solve emerging challenges in laboratory- and clinical-research applications. Meetings provide a venue for researchers to share their work and seek assistance in resolving problems as well as provide tutorials on methods, equipment, and best practices. For more information on the SIG, notices of meetings, and to join the LISTSERV, go to <https://oir.nih.gov/sigs/biomedical-instrumentation-development-scientific-interest-group> or contact **John Kakareka** ([kakareka@nih.gov](mailto:kakareka@nih.gov)) or **Randy Pursley** ([pursley@nih.gov](mailto:pursley@nih.gov)).

### NEW: SEX AND GENDER IN HEALTH AND DISEASE

The purpose of SGHD group is to explore the influences of sex (as a biological variable) and gender (as a social construct) on health and disease across the lifespan; to promote the

dissemination of research and foster potential interdisciplinary collaborations among NIH scientists who work on, or are interested in, aspects of sex-based research across the research continuum or in sex-differences research relevant to health and disease; and to serve as a platform for cross-disciplinary connections to inform biomedical and social and behavioral research efforts.

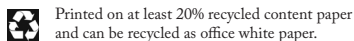
The SGHD SIG also aims to catalyze new collaborations by leveraging the scientific expertise and acumen at NIH and neighboring research institutions. The SIG co-chairs are **Inna Belfer** ([inna.belfer@nih.gov](mailto:inna.belfer@nih.gov)) and **Katrina Serrano** ([katrina.serrano@nih.gov](mailto:katrina.serrano@nih.gov)), both in the Office of Research on Women's Health. For more information about meetings and resources and how to join the SGHD LISTSERV, contact the co-chairs.

### SCIENTIFIC INTEREST GROUPS

NIH Scientific Interest Groups (SIGs) are assemblies of scientists with common research interests. These groups engage with their members via a LISTSERV; sponsor symposia, poster sessions, and lectures; offer mentoring and career guidance for junior scientists; help researchers share the latest techniques and information; act as informal advisors to the Deputy Director for Intramural Research; provide advice for the annual NIH Research Festival; and serve as hosts for the Wednesday Afternoon Lecture Series. Most of these groups welcome interested non-NIH scientists.

SIGs form and evolve regularly as new scientific trends arise. Information about group activities or new groups is published in *The NIH Catalyst*, and on the DDIR Web Board (NIH-only). Central coordination for the groups is provided by the Office of Intramural Research. The NIH also hosts scientific LISTSERVs and intramural organizations. For a list of the SIGs and other information, go to <https://oir.nih.gov/sigs>. ●

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## CATALYTIC REACTIONS?

IF YOU HAVE A PHOTO OR other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via e-mail: [catalyst@nih.gov](mailto:catalyst@nih.gov); fax: 301-402-4303; or mail: *The NIH Catalyst*, Building 1, Room 333.

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

**READ MORE ARTICLES, AND EXPANDED VERSIONS OF THE ONES IN THIS ISSUE, ONLINE AT**  
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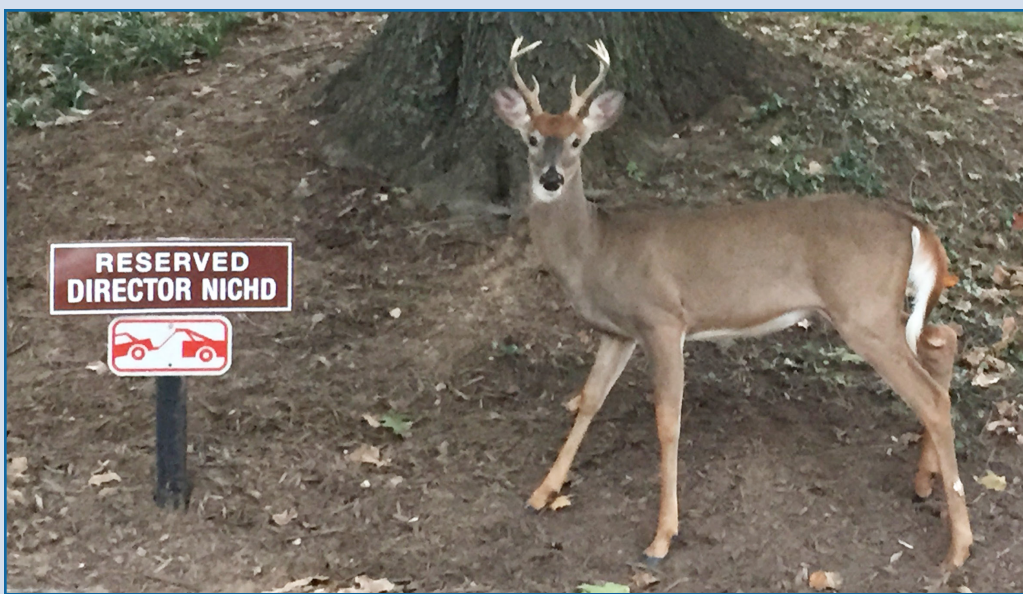
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## PHOTOGRAPHIC MOMENT



### Bucking Protocol!



MARTIN PLAYFORD, NHLBI

Buck Whitetail, the acting director of the National Institute for Cervidae, Hydropotinae, and other Deer, pauses before meeting with the NIH Director about the controversial deer-neutering program.

**Staff scientist Martin Playford snapped this photo using his iPhone 6 one fall evening. Playford works in the Section of Inflammation and Cardiometabolic Diseases in the National Heart, Lung, and Blood Institute.**

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