THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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Inflammation Insights

NIEHS Science Days Celebration

BY ROBIN ARNETTE, NIEHS

Researchers at the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, North Carolina, have long faced the difficulty of traveling en masse from their labs to participate in the NIH Research Festival at the Bethesda, Maryland, campus. But since 2002, NIEHS has held its own festival—called NIEHS Science Days—at its own campus so scientists could share their work, explore collaborations, and have their excellence recognized.

The 2015 event, which took place on November 5 and 6, included a minisymposium on inflammation, a poster session with more than 90 posters by scientists from all divisions of the institute, and recognitions for trainee and mentor of the year as well as for the best trainee poster and talk.

"Science Days is, in part, a training exercise. It gives trainees a forum to develop their techniques in giving poster and oral presentations," said **Joel Abramowitz**, special assistant to the NIEHS scientific director. "No other institute has the breadth of the types of science that we do here, so the trainees have to explain themselves to a broad audience."

The minisymposium on the connections between inflammation and disease featured presentations by

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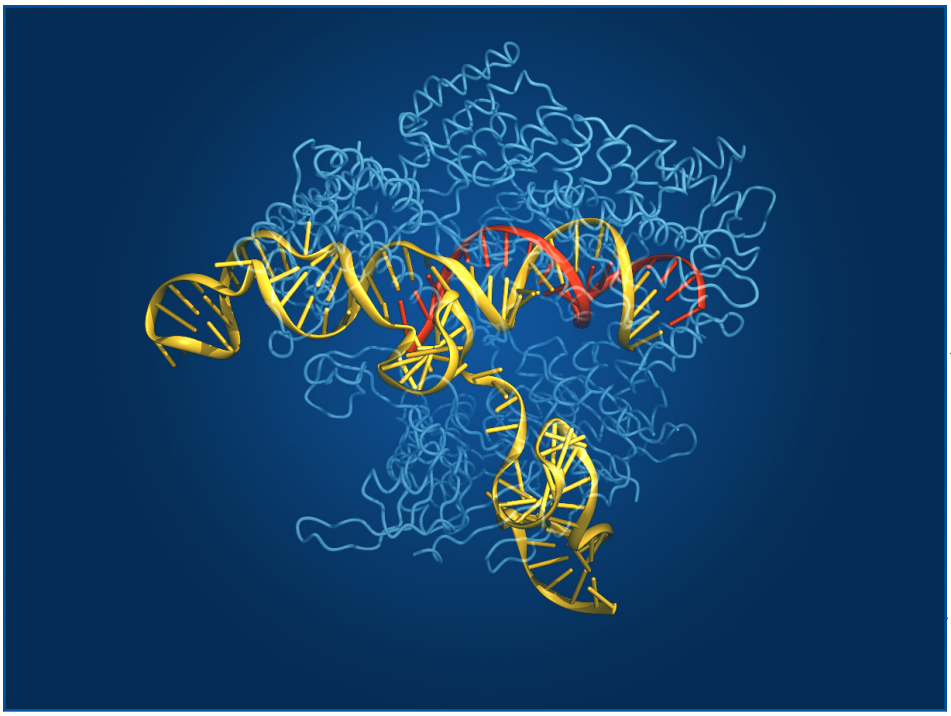
Genome Editing

Eugene Koonin's Continued Role in CRISPR, By Way of Yogurt

BY CHRISTOPHER WANJEK, OD



BANG WONG, BROAD INSTITUTE OF HARVARD AND MIT

Crystal structure of the CRISPR/Cas9 system, which enables DNA to be edited with unprecedented precision. Researchers use RNA guides called CRISPRs (red) to steer the Cas9 gene-editing enzyme (light blue) to a specific site on a DNA strand (yellow) that they wish to modify.

If *Streptococcus thermophilus* could erect statues, they'd do so to **Eugene Koonin**, a man responsible for saving untold trillions of their yogurt-making kind.

An evolutionary biologist and senior investigator in the National Library of Medicine's National Center for Biotechnology Information (NCBI), Koonin hypothesized in 2005 that "spacer DNA" in the clustered regularly interspaced short palindromic repeats (CRISPR) loci of bacteria and archaea, which matched sequences of bacteriophages,

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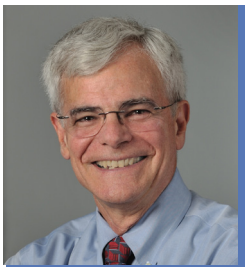


A Rising Tide Lifts All Shipshape Boats

BY MICHAEL GOTTESMAN, DDIR

The omnibus budget bill signed by President Obama on December 18, 2015, included a $2 billion increase for the NIH. Although close to $1 billion was specified for programs such as the Precision Medicine Initiative, Alzheimer disease, and antibiotic-resistant microorganisms, over $1 billion (a 3.92 percent increase) remains to support a broad array of biomedical initiatives. Approximately 10 percent of this $1 billion, based on individual institutes' and centers' (ICs') decisions, will be used in the intramural research program to sustain innovative and productive research and support infrastructure (including some salary increases).

In our long-term planning process, just completed, there are several new initiatives in genomic medicine, chronic inflammation, the microbiome and drug resistance, RNA biology and therapeutics, neurobiology including compulsive brain disorders, vaccines, cell-based therapies, and new animal models that will undoubtedly benefit from the increased availability of funds (http://1.usa.gov/1L5fIhQ; http://1.usa.gov/1NUsVMs). We are optimistic that efforts to enhance the diversity of our workforce and encourage trans-NIH projects and intramural-extramural collaboration will also get a boost from this year's budget.

This largest increase in the NIH budget in 12 years signals bipartisan support for the overall biomedical-research effort and a growing trust in NIH leadership and NIH-supported scientists to manage these funds effectively and efficiently. But to paraphrase an old saying, "With great budgets, comes great responsibility."

A new NIH five-year strategic plan, the result of a Congressional prerogative to ask NIH to specify how future funds would be allocated, emphasizes not only areas of great scientific opportunity in fundamental science, treatments and cures, and health-promotion and disease prevention, but also the central role that NIH plays in stewardship of these funds by setting trans-NIH priorities, improving oversight, and managing for results (http://1.usa.gov/1QMyq3W). These requirements include both extramural research activities and those conducted in the intramural research program. We will be closely watched for adherence to the principles outlined in the strategic plan and must continue to earn the trust of the American people in how we spend taxpayer dollars.

> The $2 billion increase in the NIH budget signals bipartisan support for the overall biomedical-research effort.

One area of increased scrutiny has been the care with which we conduct human-subjects research. After considerable effort by our clinical researchers, the American Association of Human Research Protection Programs accredited us in 2014. This accreditation reflects attention to details associated with the design, management, and execution of research on human subjects.

Despite our successes, we can always do better. Our recent experience with serious problems that caused the closing of the Clinical Center's Pharmaceutical Development Section illustrates the need for even closer attention to the important details of preparation of sterile materials for human use at the NIH.

Because it is critical to adhere precisely to the many laws, regulations, and policies that govern the conduct of biomedical research at the NIH, my office will be creating a regulatory affairs and compliance section to assist in and coordinate the many activities already ongoing in your ICs. Although the scope and functions of this entity are still being decided, the goal is to create a rigorous program of research compliance and quality assurance to ensure that research conducted by NIH adheres to the highest legal, professional, and ethical standards. In some cases, we will need to change the way we conduct business; in others, we will need to be even more vigilant to ensure that we follow procedures already in force. In these and many other aspects of the way we conduct business in the intramural research program, we will continue to earn the trust of Congress and the American people.

We are grateful to the leadership at NIH and in the Congress for this increased funding to support the biomedical research enterprise and sustain excellence in the NIH intramural research program. I am sure we will work together to ensure the most careful stewardship of these new investments. ●

An Intramural Gem

BEPS: Technical Help When and Where You Need It

BY CHRISTOPHER WANJEK, OD

Beset by poorly quantified analyte concentrations in your micro-immunoaffinity capillary electrophoresis results? Annoyed by what should have been passive microwave thermometry? Has your Quansys enzyme-linked immunosorbent assay (ELISA) array gone awry?

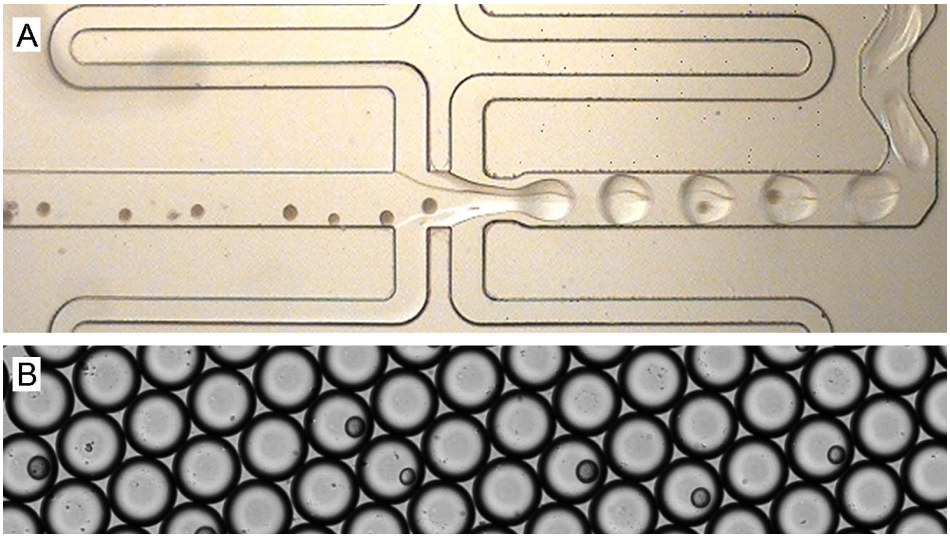
Relax. BEPS has got your back.

BEPS—an abbreviation far easier to pronounce than the many technical services this trans-NIH shared resource can provide—stands for Biomedical Engineering and Physical Science. Housed in Building 13, the group supports NIH's intramural basic and clinical scientists on applications of engineering, physics, imaging, measurement, and analysis. BEPS specializes in atomic-force microscopy; electron microscopy; microfabrication; microfluidics; analytical ultracentrifugation; surface plasmon resonance; microanalytical immunochemistry; thermal imaging; matrix-assisted laser desorption and ionization; inductively coupled plasma optical-emission spectrometry for trace analysis of metals in tissues; and many other techniques. And BEPS's offerings are available to any NIH intramural researcher.

"Our expertise ranges over length scales from the near-atomic to [the] whole organisms," said BEPS chief **Hank Eden**.

BEPS is a gem for those who discover it, said Eden, who also serves as deputy scientific director of intramural research programs at the National Institute of Biomedical Imaging and Bioengineering (NIBIB). Comprising six units, BEPS assists with numerous research projects each year, but NIH researchers often know of it only by word of mouth. BEPS hopes to take a more proactive role to ensure no NIH intramural scientist is left behind.

Consider microfabrication. BEPS has an in-house, multi-user facility for low-cost construction of microstructures for a variety of biomedical-research applications, particularly those requiring confinement of cells or the control of cellular environments. BEPS has trained researchers from nine institutes in microfabrication techniques and has recently started working with researchers to get the Drop-seq technology up and running on campus. The method uses microfluidic devices for co-encapsulation of single cells and bar-coded beads to generate high-throughput, low-cost, single-cell gene-expression data.



(A) MICHAEL KELLY, NIDCD; (B) NICOLE MORGAN, NIBIB

BEPS is helping NIH researchers implement Drop-seq technology for low-cost parallel RNA sequencing of single cells. The technology uses microfluidic devices for co-encapsulation of single cells and bar-coded beads. Shown: (A) the nozzle of a co-encapsulation device showing droplet generation and bead encapsulation; (B) a collection of uniform 100-micrometer-diameter droplets with beads encapsulated.

In the realm of immunochemistry, BEPS can assemble novel immunoassays to quantify concentrations of cytokines, chemokines, neuropeptides, hormones, and other analytes in submicroliter samples.

BEPS goes bench to bedside with thermometry, video microcapillaroscopy, and assessment of peripheral microcirculation. The group has aided in high-resolution infrared imaging to assess blood flow in organs as diverse as rat kidneys and human brains, and it has performed intraoperative and bedside optical imaging of tissue perfusion, oxygenation, and temperature. This same group also has ventured into wireless electronic patches and cellular phone technology for longitudinal monitoring in clinical research.

Many NIHers associate BEPS with microscopy, for good reason. BEPS can help with atomic-force microscopy for submillimeter-resolution imaging of macromolecular complexes, and lipid bilayers, cells, and tissues under physiological conditions. BEPS also specializes in cryoelectron microscopy and energy-dispersive X-ray spectroscopy.

"This is a fabulous resource at your fingertips," said **Michael Gottesman**, deputy director for intramural research. It "allows you to reach your utmost research potential that's simply not available at most research institutions." ●

For more information, go to http://www.nibib.nih.gov/beps or contact Hank Eden directly at edenh@mail.nih.gov.

FROM THE FELLOWS COMMITTEE

FARE Awards Recognize IRP Research Excellence

BY CRAIG MYRUM, NIA

The results are in and more than 200 NIH trainees will be receiving $1,000 travel grants. They are winners of the Fellows' Award for Research Excellence (FARE), awarded annually to recognize the outstanding scientific research performed by graduate students, postdocs, and clinical fellows in NIH intramural research program (IRP) groups.

The FelCom FARE subcommittee is run by postdocs. Organizers recruit more than 350 judges to evaluate over 900 abstracts.

"As scientists, we all have to write and critically review manuscripts, grants, etc.," said 2016 FARE committee member **Emily Vogtmann** (National Cancer Institute). "I was able to be a part of the whole process from abstract solicitation to review. This [experience] will be very helpful going forward as a reviewer of all types of work."

Because Vogtmann works at the Shady Grove Campus in Rockville, Maryland, she found participation useful for networking with people on the main campus in Bethesda. "Now when I get some e-mails on the NIH-Fellows LISTSERV, I actually know some of the people!" she said.

The top 25 percent of abstracts are chosen for FARE awards. One of the 2016 FARE recipients was **John Gallagher** (National Institute of Allergy and Infectious Diseases), whose mentor is Stadtman Investigator **Audray Harris**. Gallagher's work examines self-assembling protein nanoparticles, which are revolutionizing the design of vaccines. "Nanoparticles like these are proving to be among the best candidates to build a universal flu vaccine," he explained. "By efficiently activating B-cell receptors, they can guide the immune system towards conserved epitopes on hemagglutinin."

Using cryoelectron microscopy, Gallagher and colleagues described the molecular organization and epitope disposition of the nanoparticle. "It's amazing to zoom in to about 100,000-times magnification and see what they're doing," he said.

FARE recipients each receive $1,000 to attend a scientific meeting, where they will present their research either as a poster or as a seminar. Although Gallagher typically attends Biophysical Society meetings, he is considering presenting his work at a meeting more geared toward vaccines this year. ●

To find out how to be on the FARE subcommittee, e-mail FARE@mail.nih.gov. To see who won for 2016 and to apply for 2017, see https://www.training.nih.gov/felcom/fare. Applications will be accepted in February and March 2016.

SPECIAL REPORT FROM FORMER FELLOWS

So You Want to Be a Science Policy Wonk?

BY SARAH RHODES AND KRISTOFOR LANGLAIS, OD

Considering making the jump from the lab to a career in science policy? For many it is a tough decision to make (and may seem even harder to execute). For others it seems like a natural career progression. As two NIH postdocs who successfully made this leap of faith, we wanted to share a few tips we learned along the way.

When people start to think about science policy as a potential career path, one of the biggest questions that they often grapple with is, "What is science policy?" What you hear by chatting with people in the field makes it sound both interesting and exhilarating, but they often give very different answers about what they do on a daily basis. Science policy is often rather vaguely described as filling that space at the intersection of scientists, policymakers, and the public—a reflection of how nebulous a field it is.

In reality, *what* science policy actually is depends on which door you are looking through. In other words, it depends on *where* it is being done. There are many doorways into the science policy world—too many to cover here—but five of the key sectors are the government, the advocacy community (including professional societies), the Hill, academia, and think tanks. They all play different, but vital, roles in the science-policy arena, and what is the best fit for you will depend on many factors, including your personality, your skill set, and the reasons driving your desire to transition into this field.

For example, if you have a strong desire to draw attention to the need to increase funding for a particular research field or disease, then working for an advocacy organization in that field would be a good fit for you.

So what makes a great science-policy wonk? The good news is that science policy draws on many of the skills honed in the lab, one being scientific literacy. We say "literacy" rather than "knowledge base" because you are likely to work on areas

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The NIH Global Health Interest Group

How Climate Change Affects Health

BY HEBA DIAB (NHLBI) AND AMY KULLAS (NIGMS AND NIAID)

Climate change affects general and mental health, the spread of infectious diseases, and health security. To address these issues, the NIH Global Health Interest Group (GHIG) gathered climate-change experts for a symposium on October 15, 2015, in the Natcher Conference Center (Building 45).

The experts included National Institute of Environmental Health Sciences Director **Linda Birnbaum** and her senior advisor, **John Balbus**; ophthalmologist Sheila West from Johns Hopkins University (Baltimore); public-health physician-epidemiologist Jean-Paul Chretien from the Armed Forces Health Surveillance Center; global mental-health expert Inka Weissbecker from the International Medical Corps; and Mike Gremillion, chief of the Weather Strategic Plans and Interagency Integration Division of the United States Air Force.

General health: Climate change can make people more vulnerable to damaging pollutants and diseases, especially in developing countries that have poor health-care systems or in which people lack access to health care. In one example, Sheila West explained her work in Africa battling trachoma, an eye infection that is the world's leading cause of preventable blindness. It occurs where people live in overcrowded conditions with limited access to water and health care.

Infectious diseases: Jean-Paul Chretien discussed how global climate anomalies change the habits of infectious-disease vectors (such as mosquitoes, ticks, and rodents), increasing the potential for infectious diseases including dengue, cholera, and malaria. Given that most of these diseases affect the poorest populations around the world, it is no surprise that lack of medical facilities, increasingly severe weather challenges, and dwindling food and water resources not only lower survival rates but also affect the overall quality of life.

Mental health: Climate change can affect mental health, too. Millions of people will be displaced due to coastal flooding that stems from rising sea levels; millions more will migrate from expanding desert regions with reduced agricultural output and water shortages. Inka Weissbecker described how the loss of loved ones or population displacement resulting in loss of work, belongings, social networks, and identity are among the multiple stressors that undermine mental health. Unfortunately, people in such underserved areas are particularly vulnerable because their countries have the fewest resources for mental-health care, particularly those countries in Africa that have only one psychiatrist for the entire country.

Security: Mike Gremillion stressed how climate change influences economic security and security of the food and water supply. Flooding, droughts, tsunamis, heat waves, and other disasters kill thousands of people each year in developing and developed nations. As seen by bread shortages in Egypt, lost crops due to droughts in Central America, and food and water shortages due to unseasonable monsoons and droughts in India, the world's livelihood is becoming increasingly compromised. Consequently, these events have led to humanitarian crises, economic hardships, and stressed national and international security.

Solutions: Although climate change threatens human well-being, many consider it an opportunity to change global health. John Balbus quoted Margaret Chan, World Health Organization Director-General, who said, "The evidence is overwhelming: Climate change endangers human health. Solutions exist, and we need to act decisively to change this trajectory." It is the health-care sector, more than the technological and economic sectors, that has the potential to educate the public about the connection between climate change and their own health and well-being. ●

For more information, visit http://sigs.nih.gov/globalhealth/Pages/default.aspx or contact Gyan "John" Prakash (prakashg@mail.nih.gov) or Amy L. Kullas (amy.kullas@nih.gov).

NEW: VIRTUAL AND AUGMENTED REALITY INTEREST GROUP (VARIG)

VARIG will examine the role of virtual and augmented reality (VAR) in medical research and discuss technical aspects of VAR along with software (such as Unity) and hardware (such as Oculus Rift, Samsung Gear VR, and Google Cardboard viewers). VARIG will have a strong training component, too. To join the LISTSERV and receive notifications of the monthly meetings, go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=VARIG&A=1.

For more information, contact John Ostuni (ostunij@ninds.nih.gov). ●

CRISPR

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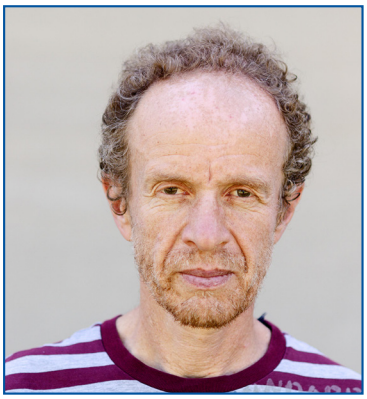


YURI WOLF, NLM

Eugene Koonin

could be a key part of a sort of adaptive immune system.

He didn't know at the time that his hypothesis, which has since led to phage-resilient strains of *S. thermophilus* for the yogurt industry, would be a major step in creating a precision technique for editing genes in species as diverse as humans, whelk, and whales. But more on that later.

Koonin, then as now, was simply interested in "patterns, rules, and trends in the evolution of genomes," he said. He and his colleagues were examining the genes adjacent to the CRISPR loci in bacteria and archaea as early as 2002 to identify partially conserved gene neighborhoods.

The CRISPR, with their spacers, were discovered in the late 1980s, but "no one knew what they were, and no one really cared," Koonin said. Koonin figured the gene neighborhoods of CRISPR must have some important purpose from an evolutionary viewpoint, or they wouldn't be so prominent. And so he probed.

Building on years of his own research on the concept of clusters of orthologous groups of proteins, Koonin and members of his NCBI lab, the Evolutionary Genomics Research Group, predicted that the functions of many of the proteins encoded by the genes in the CRISPR neighborhoods—known as CRISPR-associated proteins (Cas)—were to bind, cut, join, and unwind DNA and RNA.

That much would prove correct, as shown by extensive research over the following decade. To Koonin's regret, however, his central hypothesis was off the mark. He had thought that the spacers were a novel system of DNA repair. He missed the fact that these genes were almost always adjacent to strange batteries of repeats . . . which would be so important to the discovery of the CRISPR method for editing genomes.

Nevertheless, the group published a paper about this in 2002 that garnered some attention.

It would take three years and three independent laboratories (two in France and one in Spain) to discover that some of the CRISPR spacers were homologous to bits of foreign DNA from bacteriophages or plasmid DNA. Those researchers suggested, in general terms, that the spaces might serve as a defense mechanism against infections.

Koonin and a senior member of his lab, **Kira Makarova**, read these studies in late 2005 and quickly connected all the dots. They developed a hypothetical scheme analogous to that for the system of RNA interference in eukaryotes—a premise both simple and radical—that prokaryote organisms could usurp fragments of enemy viruses by means of self-inoculation, to ensure that their progeny could recognize a future viral attack and dismantle it.

In short, it was adaptive immunity at a Lamarckian level (the heritability of acquired characteristics).

The paper Koonin's group published in March 2006, with Makarova as the lead author, caught the attention of researchers at Danisco, an international company now owned by DuPont that provides enzymes and other biologics to food companies. The connection? *S. thermophilus*, the bacterium that can turn milk into yogurt, is something Danisco needs to thrive. Yet phages routinely infect and kill the bacteria.

Danisco wanted to test Koonin's hypothesis. The scientists there exposed *S. thermophilus* to a phage; sure enough, while many perished, a few bacteria managed to inoculate themselves and lived and then passed that immunity on. The result has been a healthier strain of *S. thermophilus*, saving the company millions of dollars.

Danisco scientists, led by Rodolphe Barrangou and Philippe Horvath, published their results in the journal *Science* in March 2007. They had no idea that this natural inoculation, which has played out for eons, had any connection to gene editing. But other scientists soon would, and the result has been the development of the DNA-editing tool CRISPR-Cas.

How did bacteria and archaea pull off this feat of self-inoculation? That was the central question asked by the scientists who went on to establish the CRISPR-Cas gene-editing system, among them Emmanuelle Charpentier (currently at Max Planck Institute of Infection Biology in Berlin) and Jennifer Doudna (University of California, Berkeley), working together and separately, and also Feng Zhang (Massachusetts Institute of Technology, Cambridge, Massachusetts).

A Charpentier-led paper published in *Nature* in 2011, in particular, proposed that the enzyme Cas9 works with a stretch of RNA called trans-activating CRISPR RNA (tracrRNA) and other spacer-derived RNA called CRISPR RNA (crRNA) to snip the invading phage DNA and incorporate it into its own. By 2012, Charpentier and Doudna's group published a paper in *Science* that described the method to use these RNA elements with Cas9 as the cleaving enzyme to find and cut DNA targets with unprecedented precision.

"The principle is very simple and extremely powerful," Koonin said. It involves using "a piece of RNA to recognize in a

highly specific manner a particular place in a DNA molecule and [cutting] the DNA in that place. If you think about that for a moment, this is the impossible dream of a genomic engineer."

The CRISPR-Cas method was named one of the *Science's* Top 10 Breakthroughs of 2013, just behind immunotherapy, another advance developed within the NIH intramural program.

> "The principle is very simple and extremely powerful. This is the impossible dream of a genomic engineer."

Having instigated two milestones in the development of practical uses of CRISPR-Cas—prediction first of the functions of the Cas proteins and second of the mechanism of CRISPR-mediated adaptive immunity—and having saved some yogurt bacteria on the way, Koonin is back for what he, only half-jokingly, calls part three, noting that the Cas9 enzyme is just the tip of the iceberg.

In the past four years, he has published dozens of articles further defining CRISPR-Cas with lab colleagues Makarova, **Yuri Wolf**, **Sergey Shmakov**, and others. Key to their discoveries has been the creation of a pipeline to explore protein function computationally.

Koonin's group identifies novel CRISPR-Cas loci and predicts protein function, and Zhang's MIT lab tests these predictions experimentally, a hand-in-glove collaboration.

In October 2015, with MIT's Zhang; Konstantin Severinov at Rutgers University in New Brunswick, New Jersey, and the Skolkovo Institute of Science and Technology in Moscow Oblast, Russia; and others, Koonin's group published a paper in *Molecular Cell* detailing three more naturally occurring systems that show potential for genome editing. The proteins are provisionally termed class 2 candidates 1, 2, and 3 (C2c1, C2c2, and C2c3). Although they share properties with Cas9 and centromere and promotor factor–1 (Cpf1, another CRISPR nuclease that Koonin's and Zhang's groups discovered earlier in 2015), they have unique characteristics that may be exploited for novel genome-editing applications.

The situation "recapitulates what happened to restriction enzymes in the early days of genetic engineering in the 1970s," Koonin said; then, the number of gene-editing tools grew dramatically. Koonin predicts that there are likely "a couple dozen" enzymes akin to Cas9 awaiting discovery, and his lab continues to hunt for them.

True to their research goals, Koonin and his colleagues have been able to infer an intricate evolutionary pathway for each of these adaptive defense systems.

Koonin doesn't much care for yogurt, truth be told. He said vinification bacteria are more his speed, and indeed he was studying bacterial cultures of fine California wine at about the same time the CRISPR research was taking root. Still all in all, he is impressed by the impact of his work on bacteria.

"The most remarkable aspect of the story is how evolution has achieved a broad repertoire of biological activities, a feat we can take advantage of for new genome manipulation tools," Koonin said. ●

CRISPR-Cas Timeline

Research in the NCBI Computational Biology Branch focuses on theoretical, analytical, and applied computational approaches to a broad range of fundamental problems in molecular biology and medicine. The branch provides tools for computational biology and information science to the entire scientific community. As such, NCBI has been both directly and indirectly involved in the establishment of CRISPR-Cas gene-editing technology. Below are a few milestones.

1997: A paper in *Science* by Koonin, led by David Lipman, established the concept of clusters of orthologous groups of proteins, which laid the foundations for the discovery of the CRISPR-Cas system. (*Science* **278**:631–6317, 1997)

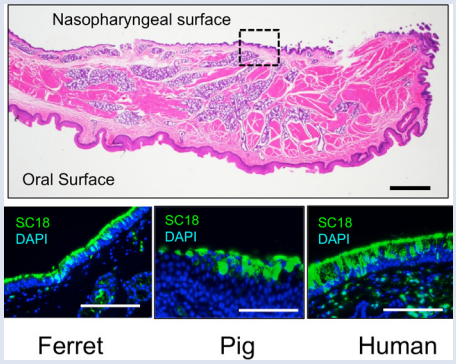
2002: A Koonin-led NCBI team predicted that many of the proteins encoded by the genes in the CRISPR neighborhoods—known as Cas, or CRISPR-associated proteins—were to bind, cut, join, and unwind DNA and RNA. (*Nucleic Acids Res* **30**:482–496, 2002)

2006: Koonin's team developed a hypothetical scheme in which spacer DNA in bacteria and archaea was a form of adaptive immunity that allowed prokaryote organisms to usurp fragments of enemy viruses by means of self-inoculation. The paper gave way to the yogurt bacteria study that launched the craze for modifying genes with CRISPR. (*Biol Direct* **1**:7, 2006)

2009: Koonin and Yuri Wolf published a paper stating that the CRISPR-Cas system of defense against mobile elements seemed to function via a genuine Lamarckian mechanism. (*Biol Direct* **4**:42, 2009)

2015: NCBI scientists and collaborators discover the first four new enzymes akin to Cas9. (*Cell* **163**:759–771, 2015 and *Mol Cell* **60**:385–397, 2015)

Intramural Research Briefs



NIAID

Flu viruses enter cells by binding to sialic acids on surface glycoproteins. In ferrets, pigs, and people, the nasopharyngeal surface of the soft palate contains regions of densely packed long-chain alpha 2,6 sialic acid molecules (shown in green) where influenza viruses with airborne transmissibility can outcompete less transmissible viruses.

NIAID: SOFT PALATE MAY BE KEY BREEDING GROUND FOR INFECTIOUS FLU

A collaboration between NIAID and MIT scientists has revealed that the soft palate, the soft tissue at the back of the roof of the mammalian mouth, may be important for flu transmission in humans. Historically, the soft palate has not been examined in animal models of influenza.

Flu infection starts when hemagglutinin proteins (which cause red blood cells to clump) on an influenza virus bind to sialic acid (SA) molecules on the tops of chainlike proteins that thickly line tissue throughout the respiratory tract. Forms of the flu that infect birds bind to a type of SA called alpha 2,3 SA, whereas those that infect humans and other mammals bind to a type of SA called alpha 2,6 SA.

The scientists made four mutations in the hemagglutinin of the 2009 influenza pandemic strain, which was good at spreading from person to person. The intent of the mutations was to make the virus preferentially bind to bird-type SA and, presumably, be less transmissible via air than the original virus. The engineered virus was used to infect a group of ferrets, which serve as a model of human influenza infection. The researchers were surprised that the engineered flu virus was transmitted by the airborne route to uninfected ferrets.

The researchers concluded that certain characteristics of the soft palate might provide a competitive advantage to more-contagious varieties of the flu. This information could aid efforts to define the properties governing flu-virus transmissibility and predict which viruses are most likely to spark pandemics. (NIH authors: S.S. Lakdawaka, E.W. Lamirande, A.R. Shih, C.T. Hanson, L. Vogel, M. Paskel, M. Minai, I. Moore, M. Orandle, and K. Subbarao, *Nature* **526**:122–125, 2015)

OD: NEW METHOD FOR MEASURING THE IMPACT OF SCIENTIFIC PUBLICATIONS

A working group in the NIH Office of the Director has created a new method for assessing the impact of scientific journal articles. The quality of a paper is commonly judged by examining the journal impact factor (JIF) of the journal in which it was published. The JIF reflects the average number of citations to all papers published in the previous two years in a journal, a measure of the journal's importance that has many weaknesses and obviously, when used as a proxy for a specific article's impact, underestimates the influence of a journal's most important papers.

The working group's alternative measure, called the relative citation ratio (RCR), compares the number of times a paper has been referenced with the number of citations received by a set of related papers. The team conducted an analysis of thousands of journal articles and determined that their RCRs were strongly associated with experts' assessments of their quality. Moreover, the group found that only 11 percent of papers with a high RCR appear in journals with a high JIF, suggesting that the JIF misjudges the impact of 89 percent of influential papers.

Although the RCR metric will require further testing and fine-tuning, it has the potential to help scientists, funding agencies, and policymakers more meaningfully evaluate scientific research. (NIH authors: B.I. Hutchins, X. Yuan, J.M. Anderson, and G.M. Santangelo, bioRxiv DOI10.1101/029629)

NCI, NIAMS, NHLBI, CC: NEW WAY FOR KILLER T CELLS TO COMMUNICATE

NIH researchers described for the first time an entirely new way in which anticancer killer T white-blood cells can directly communicate with one another to synchronize and coordinate their behavior. This behavior, which is reminiscent of quorum behavior observed in bees, ants, and microorganisms, allows T cells to function not as single actors but as an organized army moving in unison. The research is influencing current T-cell-therapy clinical trials (NCT02062359) being conducted at the Clinical Center. (NIH authors: C.A. Klebanoff, C.D. Scott, A.J. Leonardi, T.N. Yamamotoa, A.C. Cruz, R.M. Siegel, N.P. Restifo, and many others, *J Clin Invest* DOI:10.1172/JC181217; article: http://www.jci.org/articles/view/81217; commentary: https://www.jci.org/articles/view/85631)

NIDDK: PROTEIN SHUFFLES DNA

Many bacteria and microorganisms have an adaptive immune system known as the "clustered regularly interspaced short palindromic repeat" system, or CRISPR. This system allows for the recognition and destruction of invading viral DNA. NIDDK researchers have discovered that a protein related to one that enables CRISPR can relocate fragments of DNA.

The findings could have implications for genetic engineering of multicellular organisms. (NIH authors: A.B. Hickman and F. Dyda, *Nucl Acid Res* **43**:10576–10587, 2015)

CONTRIBUTORS: K. CARRERA (NIDDK), L.H. HUYNH (NICHD), K. LENOX (NIEHS), B. LEVY (NIMH), R. MACKAR (NIEHS), G. PIAZZA (NIDCR)

NICHD, NCI: IMPROVING GENE THERAPY BY STUDYING HIV

NICHD and NCI researchers and outside colleagues have clarified how the human immunodeficiency virus (HIV) targets specific genes as the virus integrates into the human genome, the process that allows the virus to replicate. The team found that HIV integrates most often into genes that have a high density of introns—intervening sequences that are removed, or spliced, as genetic information is processed into readable instructions. After identifying nearly one million integration sites to find the virus's preferred genes, the team discovered that many of these genes also have known roles in cancer progression. The findings have important implications for gene therapy. (NICHD authors: Parmit K. Singh, James R. Iben, and Henry L. Levin; NCI authors: Andrea L. Ferris and Stephen H. Hughes, *Genes Dev* **29:**2287–2297, 2015)

NIEHS: LIN28 IS A KEY PROTEIN AT WORK IN BREAST CANCER

The RNA-binding protein protein lin-28 (LIN28) plays a critical role in development timing and in cancer, but the molecular mechanisms underlying its role in promoting cancer has been poorly understood until now. A study by NIEHS scientists found that LIN28 uses diverse gene-regulatory mechanisms and functions as a master regulator of gene networks that modulate specific hallmarks of cancer. As a master regulator, LIN28 is a potential therapeutic target. (NIEHS authors: J. Yang, B.D. Bennett, S. Luo, K. Inoue, S.A. Grimm, P.R. Bushel, H.K. Kinyamu, and T.K. Archer, *Mol Cell Biol* **35:**3225–3243, 2015)

NIEHS: RGS2 PROTEIN HELPS PREPARE HEALTHY EGG-SPERM UNION

NIEHS researchers, collaborating with colleagues at three universities, have discovered that the RGS2 protein functions as a brake to suppress premature calcium release in eggs that are poised on the brink of development.

MARCI GLUCK, NIDDK

NIDDK scientists found that stimulating a part of the brain can reduce appetite and promote weight loss. Pictured: The study's computerized vending machine tracked the quantity and type of foods participants consumed.

While other researchers have shown that RGS2 plays an important role in regulating heart function and blood pressure, this is the first demonstration of the protein's significant role in fertilization. (NIH authors: M.L. Bernhardt, E. Padilla-Banks, C.E. McDonough, and C.J. Williams. *Development*; doi: 10.1242/dev.121707)

NIDCR: SWEET AND BITTER TASTE

An NIDCR intramural neuroscientist and colleagues at Columbia College of Physicians and Surgeons and Howard Hughes Medical Institute have demonstrated that stimulating defined regions of the brain's cortex can drive taste behavioral responses in the absence of bitter or sweet substances in the oral cavity. By using optogenetics to activate specific regions of the taste cortex, the neuroscientists fooled mice into thinking that bitter or sweet substances were tickling their taste buds. Stimulating the bitter brain field provoked gagging and attempts to clean the mouth of a nonexistent bitter substance. In contrast, stimulating the sweet brain field elicited compulsive licking. The study also showed that activating the bitter brain field could mask attraction to a sweet substance, and stimulating the sweet brain field could mask aversion to a bitter substance. (NIH author: Nicholas J.P. Ryba, *Nature* **527:**512–515, 2015)

Read more online at http://irp.nih.gov/catalyst/v24i1/research-briefs.

NCI, NIDDK: NEW COMPOUND REDUCES WEIGHT OF OBESE MICE

NCI and NIDDK researchers and colleagues created a new compound that reduces the weight of obese mice by acting on their intestinal cells. The new compound may contribute to the development of new therapeutic approaches for obesity-related metabolic disorders. (NIH authors: F. Gonzalez, C. Jiang, C. Xie, K.W. Krausz, J. Shi, C.N. Brocker, and O. Gavrilova, *Nature Commun* DOI:10.1038/ncomms10166)

NIDDK: BOOSTING ACTIVITY IN BRAIN REGION MAY AID WEIGHT LOSS

NIDDK researchers have demonstrated that applying transcranial direct current stimulation to the brain's dorsolateral prefrontal cortex can reduce appetite and promote weight loss. The results will next need to be replicated in a larger group of subjects. (NIH authors: M.E. Gluck, P. Piaggi, C.M. Weise, R.J. Schwartzenberg, M. Reinhardt, E.M. Wasserman, C.A. Venti, S.B. Votruba, and J. Krakoff; *Obesity* **23:**2149–2156, 2015)

NIDDK, NHLBI: NATURAL COMPOUND PREVENTS OBESITY IN MICE

A team of NIDDK and NHLBI researchers has found that treatment with the natural compound celastrol enabled normal-weight male mice to avoid obesity and metabolic dysfunction despite being fed a high-fat diet. (NIH authors: M.A. Xinran, X. Lingyan, A.T. Alberobello, O. Gavrilova, A. Bagattin, M. Skarulis, J. Liu, T. Finkel, and E. Mueller, *Cell Metab* **22:**695–708, 2015) ●

Inflammation Insights

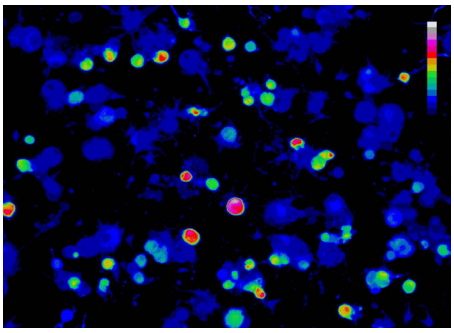
CONTINUED FROM PAGE 1

COURTESY OF NIEHS

Autumn leaves adorn the NIEHS campus in Research Triangle Park, North Carolina. Colleagues there can't always get to the NIH Research Festival on the main campus in Bethesda, so they hold their own NIEHS Science Days event every year. Their 2015 festival featured a minisymposium on inflammation, a poster session, and more.

an intramural scientist, a grantee, a researcher with NIEHS's National Toxicology Program (NTP), and a former postdoc. Their research confirms that although inflammation is the body's way of responding to injury and fighting off infection, it can lead to illness if it persists and can be a major player in the origins of certain human diseases.

The first speaker was senior investigator **Michael Fessler**, deputy chief of the NIEHS Immunity, Inflammation, and Disease Laboratory and head of the Clinical Investigation of Host Defense Group. Fessler discussed how oxysterols help clear inflammation in the lungs. He made the case that oxysterols may be important in acute respiratory distress syndrome, a lung condition with a mortality rate of 25 to 40 percent.



BRET BESSAC, DUKE UNIVERSITY

Exposure to chlorine gas stimulates TRPs in human trigeminal nerves, activating the neurons. In this image, shading from blue to pink corresponds to increasing amounts of calcium uptake, an indicator of cellular activity.

Fessler said cells, including macrophages, avoid cholesterol overload by relying on a transporter, ATP-binding cassette subfamily G member 1 (ABCG1), to export cholesterol from the cell. The absence of functioning ABCG1 leads to the inability to remove cholesterol, driving macrophages into a hyperinflammatory state and toward cell death.

Fessler's group found that 25-hydroxycholesterol activates anti-inflammatory properties of the liver X receptor (LXR), which is involved in clearing lung inflammation and promoting cholesterol export from cells.

NIEHS grantee Sven-Eric Jordt, an associate professor in anesthesiology at Duke University School of Medicine (Durham, North Carolina), described how sensory neurons become sensitized during injury and chronic-pain conditions, such as inflammation. He studies transient receptor potential (TRP) channels, a superfamily of proteins involved in the senses of sight, smell, taste, touch, and hearing.

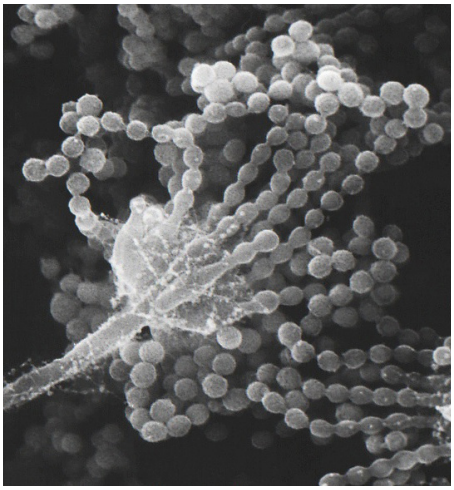
TRPs exist in the trigeminal nerves of the head and connect to the eyes, nose, and mouth. Airborne irritants such as smoke excite these nerve endings. TRPs also exist in the dorsal nerves connecting to the skin, where heat and chemical stimuli are sensed.

Jordt said that during chemically induced inflammation, TRPA1 and sensory nerves promote an inflammatory response. His work has demonstrated that the lungs make peptides that rely on sensory nerves to provide biochemical cues.

"Our hypothesis is that inflammation activates pulmonary neuroepithelial cells so that they produce neural peptides," Jordt said. "The sensory neurons become more sensitive to these peptides, inducing coughing and other symptoms during a pulmonary infection from a

pathogen that produces the endotoxin lipopolysaccharide."

According to NTP researcher **Dori Germolec**, head of the Systems Toxicology Group, mold spores are ubiquitous and are not a concern in healthy individuals unless they reach extremely high concentrations. Germolec studies the inflammatory responses that occur after long-term exposure to the mold *Aspergillus fumigatus*.



ROBERT SIMMONS, CDC

NIEHS researcher Dori Germolec studies the inflammatory responses that occur after long-term exposure to the mold *Aspergillus fumigatus* (pictured in a scanning electron micrograph). Aspergillus, normally harmless, is common in the environment and found in soil, on plants, and in decaying plant matter. It is also found in household dust, building materials, and even in spices and some food items.

To evaluate potential health effects after mold exposure, Germolec used an enclosed exposure system that provides a real-life inhalation exposure scenario. The system was developed by colleagues at the National Institute for Occupational Safety and Health in Morgantown, West Virginia.

The researchers exposed mice to either viable spores from *A. fumigatus* or heat-inactivated spores, which are considered nonviable. The nonviable spores generated some inflammatory responses, but the viable spores produced a much more potent inflammatory response that appeared to be related to spore germination in the lungs.

Germolec explained that the life stages of mold depend on temperature and humidity, and spore germination can occur when conditions are optimum for growth. "Everything we've looked at indicates that germination is critical to the development of the allergic response in mice," he said.

Next, former NIEHS trainee **Michelle Block**, now an associate professor in the Department of Anatomy and Cell Biology at Indiana University School of Medicine (Indianapolis), talked about her research on inflammation. She explained that microglia, the primary immune cells in the brain, sometimes stop being a neuronal police force and become instead a source of chronic inflammation and oxidative stress. The switch is an important one, according to Block, because neuroinflammation is a common denominator in several central nervous system (CNS) disorders, such as autism, Parkinson and Alzheimer diseases, stroke, multiple sclerosis, and traumatic brain injury.

"My obsession with understanding how and why microglia damage brain neurons started when I was at NIEHS," Block said. "We call the process neurotoxic reactive microgliosis, and we believe it underlies the chronic nature of CNS diseases, particularly many of those associated with aging."

For NIEHS scientists, getting up to the Bethesda campus to share their work is always special, but the "local" Science Days can be equally rewarding. ●

A Fitting Surprise

BY KELLY LENOX, NIEHS

The NIEHS Office of Fellows Career Development selects a fellow of the year based on nominations evaluated by a panel of scientists. The 2015 winner was **Miranda Bernhardt**, an Intramural Research Training Award fellow in the Reproductive Medicine Group, headed by **Carmen Williams**.

"Miranda has a passion for reproductive biology," said Williams. "And she's an intellectual powerhouse." She cited Bernhardt's successful demonstration of a novel calcium channel involved in egg fertilization (*Development* 142:2633–2640, 2015). Williams also noted Bernhardt's commitment to service, especially science education, among her qualifications for the prize.

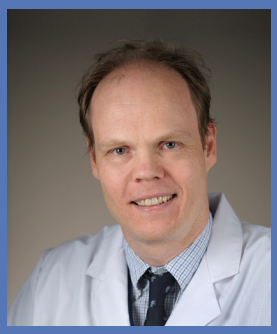
The NIEHS Trainees Assembly (NTA) names a mentor of the year based on nominations from trainees and researchers alike, and in a fitting surprise, the NTA choice was Williams. "I've been able to accomplish so much more than I would have without her leadership and guidance," Bernhardt said. Other nominators cited Williams's commitment to training the next generation of reproductive scientists and clinicians. One letter noted the possible key to Williams's success. "She listens to all ideas, no matter how outside the box they are." ●

STEVE MCCAW, NIEHS

Fellow of the Year Miranda Bernhardt (left) works for Mentor of the Year Carmen Williams (right).

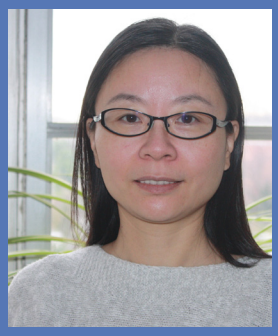
Recently Tenured

DEBORAH CITRIN, NCI-CCR



TIM F. GRETEN, NCI-CCR

RAJA JOTHI, NIEHS



ZHENG LI, NIMH

IRINI SERETI, NIAID

DEBORAH CITRIN, M.D., NCI-CCR

Senior Investigator, Radiation Oncology Branch, Center for Cancer Research, National Cancer Institute

Education: North Carolina State University, Raleigh, N.C. (B.S. in biology); Duke University School of Medicine, Durham, N.C. (M.D.)

Training: Residency in general internal medicine, Washington Hospital Center (Washington, D.C.); residency in radiation oncology, National Cancer Institute and the National Cancer Consortium

Came to NIH: In 2001 for residency training; became a staff clinician (2005–2007), an associate clinical investigator (2006–2007), and an investigator (2007)

Selected professional activities: Co-chair of the Biology Track Abstract Review Committee and member of the Scientific Program Committee, American Society for Therapeutic Radiology and Oncology

Outside interests: Entertaining her three children

Website: http://irp.nih.gov/pi/deborah-citrin

Research interests: My clinical and laboratory work focuses on improving radiation treatments to eradicate cancer cells while minimizing damage to normal tissue. A portion of my work involves understanding mechanisms of radiation resistance in tumor tissue. A small subset of tumors will never be cured by radiation, and we can't always predict which patients have these resistant tumors. By understanding these mechanisms, we can better determine which patients will need more-aggressive treatment and target the specific pathways that lead to radiation resistance. In addition, by understanding the pathways active in recurrent tumors, we can better develop such regimens as salvage therapy for patients with tumors that recur after irradiation.

On the other hand, aggressive radiation treatments can cause injury to the normal tissue that surrounds the tumor. Radiation therapy has changed drastically over the past 30 years as newer techniques allow improved sparing of normal tissue adjacent to or surrounding the tumor. Serious side effects do continue to occur in some patients, however. Understanding the causes of this injury and ways to prevent or treat it is another major area of my laboratory research and my clinical trials. In the laboratory, we are trying to develop therapies that exploit the differences between tumor and normal tissues in an effort to sensitize the tumor to irradiation while preventing radiation injury. Ultimately, this selective radiation will improve tumor cure while minimizing late injury from treatment. I am involved in the clinical care of patients with genitourinary cancers (prostate and bladder), gastrointestinal cancers, and a variety of other solid and liquid malignancies.

TIM F. GRETEN, M.D., NCI-CCR

Senior Investigator and Head, Gastrointestinal Malignancy Section, Thoracic and Gastrointestinal Oncology Branch, National Cancer Institute–Center for Cancer Research

Education: University of Kiel, in Kiel, Germany (M.D.)

Training: Internship in internal medicine, Ludwig Maximilian University of Munich (Munich); 3-year postdoctoral fellowship in tumor immunology at Johns Hopkins University (Baltimore); training in internal medicine, medical oncology, and gastroenterology at Hannover Medical School (Hannover, Germany)

Before coming to NIH: Associate professor in the Department of Gastroenterology, Hepatology, and Endocrinology at Hannover Medical School

Came to NIH: In 2010

Selected professional activities: Editor of *United European Gastroenterology Journal*; associate editor of *Clinical Cancer Research* and *Journal of Hepatology*

Outside interests: Spending quality time with his family

Website: http://irp.nih.gov/pi/tim-greten

Research interests: My research is focused on the liver, cancer, and immunology. I have projects in basic tumor immunology and translational research studies in hepatocellular carcinoma (HCC) and liver metastasis. In addition, I am doing

SWEE LAY THEIN, NHLBI

clinical trials in different gastrointestinal malignancies, including HCC. My lab and I are trying to better understand tumor immune interactions and immunological responses to anticancer treatment. I am convinced that a combined effort using different antitumor approaches will result in the best possible outcome for our patients.

Currently we are studying different aspects of the local tumor microenvironment, including the microbiome, metabolic changes, and innate immune cells. I am trying to translate our findings into the clinic. In addition, we are studying how ablative therapies including radiofrequency ablation, cryoablation, transarterial chemoembolization, and radiation can be combined with immune-based treatments in patients with hepatobiliary tumors and patients with colon cancer and liver metastasis.

RAJA JOTHI, PH.D., NIEHS

Senior Investigator, Systems Biology Group, Epigenetics and Stem Cell Biology Laboratory, National Institute of Environmental Health Sciences

Education: University of Madras, Chennai, India (B.E. in computer science and engineering); University of Texas at Dallas in Richardson, Texas (M.S. and Ph.D. in computer science)

Training: Postdoctoral research fellow in the Computational Biology Branch at NCBI/NLM and the Laboratory of Molecular Immunology at NHLBI

Came to NIH: In 2004 for training; became a tenure-track investigator in 2009

Selected professional activities: Editorial boards for *PLOS ONE* and *Frontiers in Bioinformatics and Computational Biology*; member of the International Society for Computational Biology

Outside Interests: Spending time with family; following the Dallas Cowboys

Website: http://irp.nih.gov/pi/raja-jothi

Research Interests: My laboratory seeks to understand how transcription regulators control gene-expression programs during cellular development, differentiation, and pathogenesis. We use embryonic stem cells as a model system to study the gene networks controlling key cell-fate decisions.

We use integrative interdisciplinary approaches, merging computational biology, biochemistry, and functional genomics, to map and characterize gene networks that define cell states during development, differentiation, and homeostasis. Research within the group is largely data-driven, through computational analyses of published and in-house-generated high-throughput genomic and proteomic datasets, with the goal of generating testable hypotheses. The laboratory component provides the means not only to test some of the hypotheses that come out of computational analyses but also to perform biochemical experiments to gain mechanistic insights.

We have successfully identified and characterized many genes and pathways with previously unknown roles in embryonic stem-cell biology. Our current efforts include understanding how signaling cascades instruct epigenetic and transcription networks regulating cell-fate decisions.

ZHENG LI, PH.D., NIMH

Senior Investigator, Section on Synapse Development and Plasticity, National Institute of Mental Health

Education: Jilin University, Chang Chun, China (B.S. in biochemistry and molecular biology); Peking University, Beijing, China (M.S. in biochemistry); State University of New York at Stony Brook, Stony Brook, N.Y. (Ph.D. in neuroscience)

Training: Postdoctoral training on synapse development and plasticity at the Massachusetts Institute of Technology (Cambridge, Mass.)

Came to NIH: In 2006 s

Website: http://irp.nih.gov/pi/zheng-li

Research interests: I am interested in the molecular and cellular mechanisms of synapse development and plasticity in normal and schizophrenic brains. My group uses a combination of optical imaging (two-photon and confocal), electrophysiology, and behavioral and genomic approaches to identify molecules and signaling pathways that control the function, structure, plasticity, and pathology of synapses.

Currently my research focuses on two areas: (1) the induction of the mechanism of long-term depression of synaptic transmission (LTD, a form of synaptic plasticity that leads to the weakening of synaptic response and synapse loss and is important for brain development and cognition); and (2) the function of schizophrenia risk genes in regulating synapse development and plasticity. We mainly conduct experiments with hippocampal neurons. The hippocampus is a brain structure essential for cognitive functions (such as learning and memory) and has been implicated in the pathophysiology of schizophrenia.

My group has uncovered a novel mechanism, mediated by cysteine-aspartic proteases or cysteine-dependent aspartate-directed proteases (caspases), for LTD

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Recently Tenured

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induction in hippocampal neurons. Caspases have well-known functions in aprogrammed cell death. However, the findings from my lab suggest that in the normal hippocampal neuron, caspases activate the key cellular process that is responsible for reducing synaptic strength without causing cell death.

We also demonstrated that micro RNAs (miRNAs) are required for long-lasting maintenance of synaptic plasticity, identified "plasticity miRNAs," and delineated the mechanisms by which they regulate synaptic plasticity.

Work from my group also indicates that the schizophrenia risk gene *DTNBP1* modulates synapse maturation during adolescence, the typical age of onset for schizophrenia. This finding provides insights into the neuronal basis of reduced mental performance associated with schizophrenia.

IRINI SERETI, M.D., NIAID

Senior Investigator and Chief, HIV Pathogenesis Section, Laboratory of Immunoregulation, National Institute of Allergy and Infectious Diseases

Education: University of Athens, Zografou, Greece (M.D.); Duke University School of Medicine, Durham, N.C. (M.H.S. in clinical research training)

Training: Research for one year in human immunodeficiency virus immunology at Rush Presbyterian Hospital (Chicago); internship, residency, and chief residency in medicine at Northwestern University Feinberg School of Medicine (Chicago)

Came to NIH: In 1997 as a clinical associate in the Laboratory of Immunoregulation; became a staff clinician in 2003; appointed to a clinical tenure-track position in 2009

Selected professional activities: Editorial boards of *Virus Eradication-Mediscript*, *Open Forum Infectious Diseases*, and *AIDS Research and Therapy*; mentoring students

Outside interests: Traveling; running; going to the movies; spending time with family and friends

Website: http://irp.nih.gov/pi/irini-sereti

Research interests: My group studies inflammatory complications in human immunodeficiency virus (HIV) including immune reconstitution inflammatory syndrome (IRIS). IRIS is an aberrant immune response—which frequently includes an intense inflammatory component—that can occur after the initiation of antiretroviral therapy (ART) in patients with HIV infection and severe CD4 lymphopenia.

Chronically ART-treated patients on the other hand may experience noninfectious complications of HIV, including cardiovascular disease that seem to be driven by chronic residual immune activation and inflammation. A better understanding of the pathogenesis of acute and chronic inflammation after ART in HIV-infected people will help us identify appropriate therapeutic targets so we can improve the clinical management of these patients.

Our second interest is the study of etiology, pathogenesis, and possible therapeutic interventions of idiopathic CD4 lymphopenia (ICL). ICL is a rare, likely heterogeneous condition characterized by low CD4 T-cell counts in the absence of HIV or other known infection or disease that can cause lymphopenia.

RECENTLY TENURED?

If you have been tenured in the past few months, the *NIH Catalyst* will be in touch with you soon to invite you to be included on these pages. We will ask for your CV and a recent photo, and then we will draft an article for your review.

SWEE LAY THEIN, M.D., D.SC., NHLBI

Senior Investigator and Chief, Sickle Cell Branch, National Heart, Lung, and Blood Institute

Education: University of Malaya in Kuala Lumpur, Malaysia (B.S. and M.B. in medicine/surgery; D.Sc. in medicine); Royal College of Physicians in London (M.R.C.P., F.R.C.P. in medicine); Royal College of Pathologists in London (M.R.C.P. and F.R.C.P.. in hematology)

Training: Clinical and laboratory training in hematology at the U.K. Royal Postgraduate Medical School, Hammersmith Hospital (London), and at the Royal Free Hospital (London); research training at the Weatherall Institute of Molecular Medicine, University of Oxford (Oxford, U.K.)

Before coming to NIH: Professor of molecular hematology and consultant hematologist at King's College London School of Medicine and King's College Hospital NHS Foundation Trust (London); clinical director of the Red Cell Centre in King's College Hospital

Came to NIH: In 2015

Selected professional activities: Associate editor of *Haematologica*; editorial board of *Blood*; and feature editor for the digital *Blood Hub* on sickle cell anemia

Outside interests: Attending and listening to opera; hiking; and cooking

Website: http://irp.nih.gov/pi/swee-lay-thein

Research interests: My research team is examining the genetic factors underlying the phenotypic variability of beta-thalassemia disorders and sickle-cell disease. Both of these conditions are caused by mutations affecting the beta-globin gene.

People with beta thalassemia have reduced production of red blood cells; people with sickle-cell disease have abnormal "sickled" hemoglobin (HbS). HbS makes red blood cells rigid and sickle-shaped, and the cells then block the blood vessels,

interrupt the oxygen supply to vital organs, and cause acute, intermittent pain. The rigid red blood cells are also fragile and easily destroyed, causing a life-long anemia.

Fetal hemoglobin (HbF) is the blood component primarily responsible for fetal oxygen transport and is present in infants until they are about six months old. The persistence of HbF beyond infancy is highly variable. High concentrations of HbF minimize many complications of sickle-cell disease and can increase life expectancy. Drug therapy can reactivate HbF production in both children and adults, reducing the severity of sickle-cell and beta-thalassemia symptoms.

By studying identical twins, my lab demonstrated that HbF concentrations are predominantly genetically controlled and that almost 90 percent of the difference in HbF concentrations from person to person can be accounted for by differences in genetic background. I have identified segments of DNA, called quantitative trait loci, on chromosome 11p (where the beta-globin gene is located), chromosome 6q, and the BCL11A gene on chromosome 2p. The loci, which have a beneficial clinical effect, stimulate HbF production in adults with and without sickle-cell disease or beta thalassemia.

My group is currently working on how the locus on chromosome 6q modifies HbF and how this process may provide a new genomic approach to increase HbF production therapeutically. By using new genome technologies and deep phenotyping, my research team hopes to identify and validate genetic biomarkers that will allow for early detection and monitoring of severe sickle-cell complications. We plan to contribute to the discovery and development of drugs—including those that promote HbF synthesis and inhibit HbS polymerization—to treat sickle-cell disease. ●

Policy Wonks

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that are foreign to your background, and you will need to able to rapidly become versed in those unfamiliar areas. That skill mirrors a more general ability to pick up new concepts quickly.

Two other key skill sets that the lab provides a training ground for are project management and analytical ability. For instance, the critical thinking involved in analyzing large datasets and evaluating others' work translates well into such day-to-day tasks as assessing the potential impact of new policies on the research endeavor. Experience gained planning and coordinating experiments prepares you for a role in managing large projects, often on a short deadline, and often juggling several projects at once.

As hinted above, organizational skills are vital to this field, and because a large aspect of the science-policy arena is bringing in experts in the field to inform policy decisions, chances are that you will be involved in organizing conferences as well as in running committees or working groups. These interactive functions segue nicely into one of the key differences between the lab and science policy: Whereas research is essentially a lone endeavor (you might collaborate with others but at the end of the day the research is yours and yours alone), policy is a team affair. Those who succeed in this career path are almost invariably good team players, well versed in the art of diplomacy. Last, and by no means least, you have to be a good oral and written communicator to a variety of different audiences from the general public to Congress.

As we mentioned, many of the skills developed as part of your training are translatable to a career in science policy. However, take a look at any science-policy job listing, and you will find that you lack several areas of experience for the job. Let these gaps guide you in the activities you choose to engage in to boost your resume.

Many of the additional experiences and skills needed to succeed in a science-policy career can be developed through extracurricular activities while completing your research training. For example, build a writing portfolio of accessible articles through writing for the *NIH Catalyst*, and join the NIH Fellows Committee (FelCom) to get a taste of policy development through committee work.

However, there is no substitute for work experience in the policy field. It will help you to make a fully informed decision about whether this transition is right for you and also make you a more-attractive candidate to prospective employers. Fellowships are a tried-and-tested route to gaining first-hand experience and can last from as little as three months to as long as two years.

Alternatively, you can gain work experience through volunteering or detailing in an institute's policy shop. (Read the *NIH Catalyst* article on details at http://irp.nih.gov/catalyst/v21i2/details-details-details.)

Developing professional relationships through networking is also key to your career success, and most people (including us) will tell you that they got their job through networking. You can make connections through science-policy forums and meet-up groups, LinkedIn, and informational interviews.

Finally, as you proceed, be clear on why you have chosen a science-policy career path. If you have just three minutes to explain your passion for a career in policy, be prepared to make an impact; you never know where it will lead! ●

Read more at http://irp.nih.gov/catalyst/v24i1/the-training-page-policy-wonks.

IN 2014 (NOT INCLUDED IN 2014 LIST)

William C. Hardy, Sr. (died March 25, 2014, age 98) was an NCI research technician for 25 years.

William R. Lynn (died November 18, 2014, age 68) was a federal health officer who helped manage antismoking efforts for NIH and the Office of the Surgeon General. He was a health officer in Indiana and Massachusetts before joining NCI in 1979. He edited Surgeon General **C. Everett Koop's** report on the effects of secondhand smoke and helped hire celebrities, including Brooke Shields and Mia Hamm, as antismoking spokespersons.

J. Frederic "Fred" Mushinski (died December 18, 2014, age 76) was the head of the Molecular Genetics Section in the NCI Laboratory of Genetics and the Laboratory of Cancer Biology and Genetics from the late 1960s until 2009.

Vinson "Vinse" Romero Oviatt (died December 13, 2014, age 88) was chief of the Environmental Safety Branch in the Division of Research Services (1969–1979); then joined the World Health Organization; returned to NIH in 1987 to become assistant director of the Division of Safety; and retired a few years later.

William J. Zukel (died July 10, 2014, age 92), who served in several capacities at NHLBI including as deputy director, retired from the Public Health Service in 1988.

IN 2015

Sam Baron (died June 22, 2015, age 86), a leader in the field of interferon research, was a scientist at NIH from 1955 to 1975. He was chairman of the Microbiology Department at the University of Texas Medical Branch in Galveston until 1997 and retired as professor of microbiology emeritus in 2007. He continued his research in his own lab and as a volunteer scientist at FDA's Center for Biologics Evaluation (2002–2003), at NCI's Center for Cancer Research (2003–2004), and in NIAID's Cytokine Biology Section (2004–2015).

Linda Brown (died October 25, 2015, age 73) worked in NIH's Medical Arts Department for 48 years, first as a general illustrator, then as chief of the Design Section, and for the past 17 years as creative services director. She ensured that NIH's world-class science was represented by world-class art.

Allen W. Cheever (died August 29, 2015, age 83), a leading expert in schistosomiasis, devoted his 35-year career in the Public Health Service to conducting research at NIH. He joined the Laboratory of Parasitic Diseases at the National Institute of Allergy and Infectious Diseases in 1964.

Joseph A. DiPaolo (died November 3, 2015, age 91), a renowned cancer researcher at NCI (1963–2008) and scientist emeritus, was chief of NCI's biology laboratory from 1976 to 1999.

Joel Elkes (died October 30, 2015, age 101), considered the father of modern neuropsychopharmacology, was chief of NIMH's neuropharmacology research center from 1957 to 1963. After leaving NIH, he held positions at several universities including as chairman of psychiatry at Johns Hopkins University sfrom 1963 to 1974.

Willis "Bill" R. Foster (died December 21, 2015, age 87) was a senior staff physician in NIDDK's Office of Scientific Program and Policy Analysis. Before coming to NIH in 1983, he worked for 17 years in medical information analysis at the Smithsonian Science Information Exchange. He was a co-author of the fourth edition of *Human Nutrition* and received a number of awards including the NIH Director's Award in 1995. He retired from NIH in 2001.

Alfred G. Gilman (died December 23, 2015, age 74) shared the 1994 Nobel Prize in Physiology or Medicine with former NIEHS Director Martin Rodbell for the discovery of G-proteins and their role in signal transduction in cells. Gilman was a postdoctoral fellow (1969-1971) in NIH's Laboratory of Biochemical Genetics run by Marshall Nirenberg who had shared the 1968 Nobel Prize in Physiology or Medicine for his work on deciphering the genetic code.

David B. Gray (died February 12, 2015, age 71), former deputy director of NICHD's National Center for Medical Rehabilitation Research, worked at NICHD from 1981 to 1986 and from 1987 to 1995, served on NICHD's advisory council, and was a professor of occupational therapy and neurology at Washington University School of Medicine in St. Louis. Gray became a quadriplegic after he fell from his roof in 1976, and his own experience with medical rehabilitation led to his professional interest in the field.

William J. "Bill" Hadlow (died June 20, 2015, age 94) was a veterinary pathologist and spent most of his career at NIAID's Rocky Mountain Laboratories in Hamilton, Montana (1952–1958; 1961–1987). In 1961, he started what has become a world-renowned prion-disease research program.

Joseph Handler (died December 21, 2015, age 86), who first arrived at the NIH as a Public Health Service fellow in 1957, was a former section chief in NHLBI's Laboratory of Kidney and Electrolyte Metabolism. He made major contributions to our understanding of kidney function during his tenure at NIH from 1960 to 1988. He then moved to the Johns Hopkins School of Medicine in Baltimore, where he was the director of nephrology in the Department of Medicine from 1988 to 2003.

Pauline Hardy (died October 27, 2015, age 81) was a long-time dishwasher in NIDDK's Laboratory of Molecular Biology (1974–2002).

Eileen G. Hasselmeyer (died June 6, 2015, age 91), a former assistant surgeon general, retired in 1989 after more than 29 years of active duty with the Commissioned Corps—26 of which were spent with NICHD. She helped develop the sudden infant death syndrome (SIDS) research initiative in the Department of Health, Education, and Welfare and was recognized for her contributions to SIDS research.

Gordon Blackistone Hughes (died February 15, 2015, at 66) was clinical trials coordinator for the NIDCD (2008–2015) in the areas of hearing, balance, taste, smell, voice, speech, and language. He was most well-known for his hallmark textbook, *Clinical Otology*.

Richard M. Krause (died January 6, 2015, age 90) was the director of NIAID from 1975 to 1984. In 1984, he retired from the U.S. Public Health Service and became dean of medicine at Emory University in Atlanta. In 1989, he returned to NIH to become a senior scientific advisor at the Fogarty International Center. He worked into his late 80s, both at Fogarty and as an investigator emeritus in the NIAID Laboratory of Human Bacterial Pathogenesis, where he led an ongoing joint Indo-U.S. effort examining the incidence of streptococcal pharyngitis and rheumatic fever in schoolchildren in India.

Marion G. Lawrence (died September 28, 2015, age 86) was a biochemist in the Clinical Center's Critical Care Medicine Department (1985-2009).

Frederick P. Li (died June 10, 2015, age 75), a pioneer in establishing genetic risk factors for cancer, was a long-time researcher in NCI's Division of Cancer Epidemiology and Genetics (1967–1991). He is widely known for his contribution to the discovery in the 1960s of the cancer-predisposition syndrome later named for him and his collaborator, former DCEG Division Director Joseph F. Fraumeni, Jr. The two identified what came to be known as Li-Fraumeni Syndrome from the study of a group of families with an unexpected constellation of tumors occurring at very young ages.

Guy W. Moore (died November 13, 2015, age 93) retired from NIH in 1979 as chief of the News Branch in the Office of the Director. He came to NIH in 1960 as deputy director of the information office in the Division of General Medical Sciences after having served as the first information officer of the Medical Research and Development Command of the Army's Office of the Surgeon General.

Gayle Mundell (died March 2, 2015, age 56), a human-resources liaison and ethics-program coordinator in NIDCD, retired in January 2015 after having been at NIH for nearly 25 years.

Betty Murgolo (died October 8, 2015, age 69) was in the document-delivery department of the NIH Library and helped many people throughout NIH during her 32 years there.

David Orloff (died September 13, 2015, age 58) was the director of FDA's Division of Metabolism and Endocrinology Products and oversaw the approval of a new class of statin drugs. After achieving the rank of captain in the Public Health Service in 2005, he joined Medpace Inc., where he was regarded as an industry opinion leader in the study of metabolic diseases and drug development.

Joanne Panza (died July 12, 2015, age 69) was a former executive officer of NEI.

William E. Paul (died September 19, 2015, age 79) was a giant in the field of immunology; served as chief of NIAID's Laboratory of Immunology starting in 1970, as director of the NIH Office of AIDS Research, and as NIH Associate Director for AIDS Research (1994–1997). He was best known for his groundbreaking work on T-cell and cytokine biology, including the discovery of interleukin-4 and his extensive body of research on this cytokine that established it as a critical regulator of allergic and inflammatory diseases.

Donald C. Rau (died December 11, 2015), the head of NICHD's Section on Macromolecular Recognition and Assembly, joined NIH in 1980 and retired in 2015. His research focused on elucidating the physical forces between molecules and the coupling of these to structure and dynamics of biologically important macromolecules.

Lee Rosen (died October 22, 2015, age 68) was a scientific-review officer in the Center for Scientific Review's biomedical imaging and technology study section for 26 years.

Padman Sarma (died June 24, 2015, age 83), who began his career at NCI in the 1960s, pioneered methods to test for cancer-causing viruses and enabled advancements in sciences including leukemia, sarcoma, influenza, rubella, testicular cancer, and HIV/AIDS. In 1983, he became a program director in NCI's extramural program and continued until he retired in 1995.

John F. Sherman (died June 28, 2015, age 95) served as NIH deputy director (1968–1974), including four months as acting NIH director in early 1973. He came to NIH as an officer in the Public Health Service Commissioned Corps in January 1953; he was a research pharmacologist in the Laboratory of Tropical Diseases, National

CONTINUED ON PAGE 18

Obituaries

CONTINUED FROM PAGE 17

Microbiological Institute, which became NIAID in 1955. In 1956, he began a series of extramural leadership positions, and in 1964 he was named NIH associate director for extramural programs. He was the first Ph.D. to attain the rank of assistant surgeon general.

Louis Sokoloff (died July 30, 2015, age 93), who spent more than 40 years at NIH starting in the 1950s, pioneered the use of the positron-emission tomography scan to measure human brain function and diagnose disorders. He headed NIMH's brain metabolism laboratory and received the Albert Lasker Clinical Medical Research Award in 1981 for his role in developing color images that map brain function.

Cliff Sonnenbrot (died October 21, 2015, age 59) was a chemist lab manager in NHLBI's Laboratory of Developmental Systems Biology.

Kenneth (Ken) Stith (died August 8, 2015, age 67), who joined NIH in 2000, was the director of the Office of Financial Management and deputy chief financial officer.

Louis Stokes (died October 18, 2015, age 90), a United States congressman (D-Ohio) for whom NIH's Building 50 is named, served throughout his career as a strong, reliable supporter of federal funding for medical research in general and for NIH in particular.

Richard M. Suzman (died April 1, 2015, age 72) was the director of NIA's Division of Behavioral and Social Research. He made important contributions to the science of demography and promoted the development of new subfields, including the demography of disability and the bio-demography of aging. He joined NIA in 1983 and became division director in 1998.

Norman Talal (died April 25, 2015, age 80) was a preeminent authority on Sjögren syndrome whose research offered new perspectives on autoimmune diseases. He began his NIH career as a research associate and became a senior investigator at NIAMS. He left NIH in 1971 to join the University of California at San Francisco.

Arthur Upton (died February 14, 2015, age 92), a renowned pathologist and expert in radiation biology, was the former director of NCI (1977–1980). Using his knowledge of environmental carcinogenesis, he made environmental issues one of his first initiatives.

Sholom Wacholder (died October 4, 2015, age 60), an expert in cancer epidemiology and biostatistics in NCI's Division of Cancer Epidemiology and Genetics (1986-2015), was the lead statistician for the NCI study of the natural history of human papillomavirus and cancer.

Belle Waring (died January 31, 2015, age 63) was a science writer who enjoyed doing stories on NIH scientists and their achievements. She started her NIH career in 2002 as a prints and photographs technician in NLM's History of Medicine Division; in 2006, she became a writer-editor for the *NIH Record*. ●

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

NATIONAL ACADEMY OF SCIENCES WORKSHOP

Environment and Health: What's the Human Microbiome Have to Do with It?
January 14–15, 2016, 9:00 a.m.–5:00 p.m.
NAS Keck Center, Room 100
500 5th Street NW, Washington, D.C.
On-site and webcast registration is required:
http://nas-sites.org/emergingscience/meetings/microbiome2/

The microbiome—the collection of bacteria, viruses, and fungi living on and inside our bodies—affects health in many ways and can even influence our responses to environmental chemicals. Explore the intersection of the environment, the microbiome, and human health at this workshop, sponsored by NIEHS.

PI DAY 2016 CALL FOR PARTICIPATION

March 14, 2016, 10:00 a.m.–4:30 p.m.
Lipsett Auditorium & FAES Terrace (Bldg. 10)
Register early to present talk/poster/demo (no later than January 29)
Website: https://datascience.nih.gov/PiDay2016

The goal of the NIH Pi Day Celebration is to increase awareness across the biomedical-science community of the role that the quantitative sciences play in biomedical science. As part of the Pi Day Celebration, NIH staff will have the opportunity to give short presentations called "PiCo Talks," display posters, or do demonstrations. Other events include a keynote address by Carlos Bustamante, the chair of Stanford's new Biomedical Data Science Department. If you/your institute or center would like to organize a new Pi Day event for the NIH community, contact Michelle Dunn (michelle.dunn@nih.gov or 301-402-9827).

THE INFLAMMATORY DISEASE INTEREST GROUP SEMINAR SERIES AND SYMPOSIUM

Every other Tuesday, 12:00–1:30 p.m.
Lipsett Amphitheater (Building 10)

In addition to the regular meetings, the first IDIG minisymposium will be held on May 2, 2016, and is being organized in collaboration with the Inflammation Research Association and MedImmune/AstraZeneca. The theme of this one-day meeting is "Tissue Homeostasis, Repair, Regeneration, and Fibrosis." Events will include keynote presentations, invited speakers, and a poster session. Save the date.

To join the IDIG LISTSERV (INFLAM-DIS-L), visit https://list.nih.gov/cgi-bin/wa.exe?SUBED1=INFLAM-DIS-L&A=1 or contact Thomas A. Wynn at twynn@niaid.nih.gov.

Schedule for 2016:

March 22: "Chemokines and Chemokine Receptors in IL-17A Mediated Inflammation" (Josh Farber, NIAID)

April 5: "T-cell Subsets in Autoimmune inflammation" (Vanja Lazarevic, NCI)

April 26: "Anti-inflammatory Activity of Ubiquitin Binding Proteins and Ubiquitin Modifying Enzymes in Autoimmunity" (Averil Ma, University of California at San Francisco, UCSF)

May 10: "Mechanisms and Treatment Strategies for Chronic Inflammatory and Fibrotic Disease" (Tom Wynn, NIAID)

May 24: "Endogenous Signals Driving Sterile Injury Induced Inflammation" (Ken Rock, University of Massachusetts Medical School)

June 7: "Neurovascular Regulation of Inflammation and Tissue Repair" (Katerina Akassoglou, UCSF)

TRANS-NIH BIOMARKERS IN PEDIATRIC THERAPEUTICS

Day varies each month; 12:00–1:00 p.m.
Locations vary

The Trans-NIH Biomarkers in Pediatric Therapeutics SIG has been formed to promote information exchange and professional interactions; to collect and disseminate information; to promote initiatives to address knowledge gaps; and to address issues preventing the implementation of research in the application of biomarkers to diagnosis, prognostication, evaluation of disease progression, response to therapy, and toxicity in the different pediatric subpopulations. In addition, the SIG also addresses preclinical biomarkers related to the development of new molecular entities or toxicity evaluation of new drugs tested or developed at NIH. This special interest group is launching a series of monthly didactic lectures in January (below). All are welcome to attend either in person or via webinar. If you are interested in attending, contact Maurice Koo at koom@mail.nih.gov for more information. If you are interested in joining this SIG, please contact George Giacoia at giacoiag@exchange.nih.gov.

January 12: "Application of Metabolomics to Provide Pediatric Biomarkers" (Susan Sumner, RTI International), Rockledge II, Room 9100/9104

February 23: "Harmonization of Terminology for Biomarkers and Endpoints to Strengthen Quality and Improve Efficiency of Translational Science" (Lisa McShane, NCI), Building 45, Room D

March TBD: "Pediatric Biomarkers and the Convergence of Academic and Regulatory Sciences" (Lynne Yao, FDA)

April TBD: "Biomarkers in Pediatrics: Children as Biomarker Orphans" (Allen Everett, Johns Hopkins University)

KUDOS

Congratulations to John Hardy, former chief of the NIA Laboratory of Neurogenetics, who is the winner of a 2016 Breakthrough Prize in Life Sciences for "discovering mutations in the Amyloid Precursor Protein gene (APP) that cause early onset Alzheimer's disease." See Hardy, who was an NIH PI from 2001 to 2007 explain this award-winning work in an HBO video from 2005. http://www.alz.org/research/video/alzheimers_videos_and_media_genetics.asp

NIH UNVEILS NEW STRATEGIC PLAN

On December 16, 2015, NIH released the "NIH-Wide Strategic Plan, Fiscal Years 2016-2020: Turning Discovery Into Health." To read the plan, go to http://1.usa.gov/1QMyq3W.

Read more announcements online at http://irp.nih.gov/catalyst/v24i1/announcements.

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CATALYTIC REACTIONS?

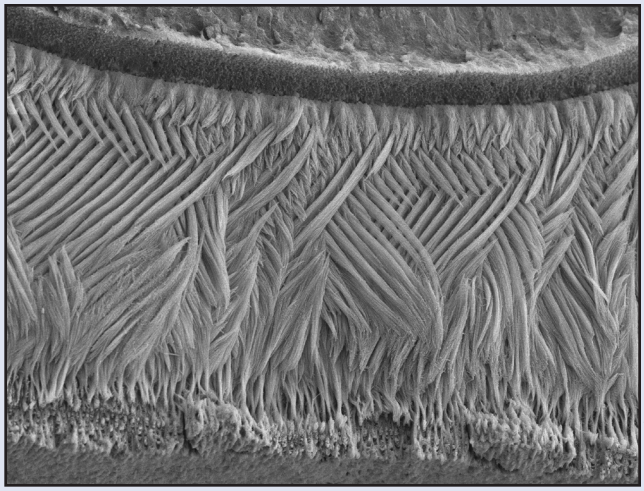
If you have a photo or other graphic that reflects an aspect of life at NIH (including laboratory life) or a quotation or confession that scientists might appreciate and that would be fit to print in the space to the right, why not send it via e-mail: catalyst@nih.gov; fax: 301-402-4303; or mail: *The 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
http://irp.nih.gov/catalyst/v24i1

PHOTOGRAPHIC MOMENT

Lattice Pattern in Tooth Enamel



OLIVIER DUVERGER AND MARIA MORASSO, NIAMS

Enamel is the hardest substance in the body and protects the surface of teeth. This scanning-electron-microscopy image shows the lattice pattern formed by enamel rods, an arrangement that confers strength and flexibility. Genetic mutations affecting enamel formation can result in defects in the thickness, mineralization, and the lattice pattern of the enamel. The defects can produce weak teeth prone to decay, which in turn can increase the risk of other health problems such as systemic infections and heart disease. National Institute of Arthritis and Musculoskeletal and Skin Diseases investigators **Olivier Duverger** and **Maria I. Morasso** are using mouse models to study how genetic variation affects enamel development and health. This image was selected as a 2015 winner of the BioArt competition of the Federation of American Societies for Experimental Biology (http://www.faseb.org/Resources-for-the-Public/Scientific-Contests/BioArt/2015-BioArt-Winners.aspx). ●

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