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Medicine Rocks

Minerals in Medicine Exhibit

FROM THE *CLINICAL CENTER NEWS*

The NIH Clinical Center (CC), in partnership with the Smithsonian Institution, held a ribbon-cutting ceremony September 12, for a new "Minerals in Medicine" exhibition showcasing more than 40 minerals crucial to human health and biomedicine. The minerals will be on display for 18 months.

On loan from the National Museum of Natural History, the exhibit's crystals and minerals, are not only interesting to admire but also educational in that they allow spectators to learn about their important roles in keeping the human body healthy. The minerals enable the creation of life-saving medicines and cutting-edge medical equipment used in the CC and health-care facilities worldwide.

"This exhibit is a product of a great partnership between Jeffrey Post and his colleagues at the Smithsonian's Museum of Natural History and the NIH Clinical Center," said CC Director **John Gallin**. "It is really a treat to be able to display the natural beauty of these magnificent crystals that contain elements vital to human health. We hope our staff, visitors, and patients smile when looking at these miracles of nature."

The exhibit, prominently placed near Admissions on the first floor, is seen by hundreds of people each day. **Bob Range**, a hospital dentist with the National Institute of Dental and Craniofacial Research who works in the Clinical Center, recently

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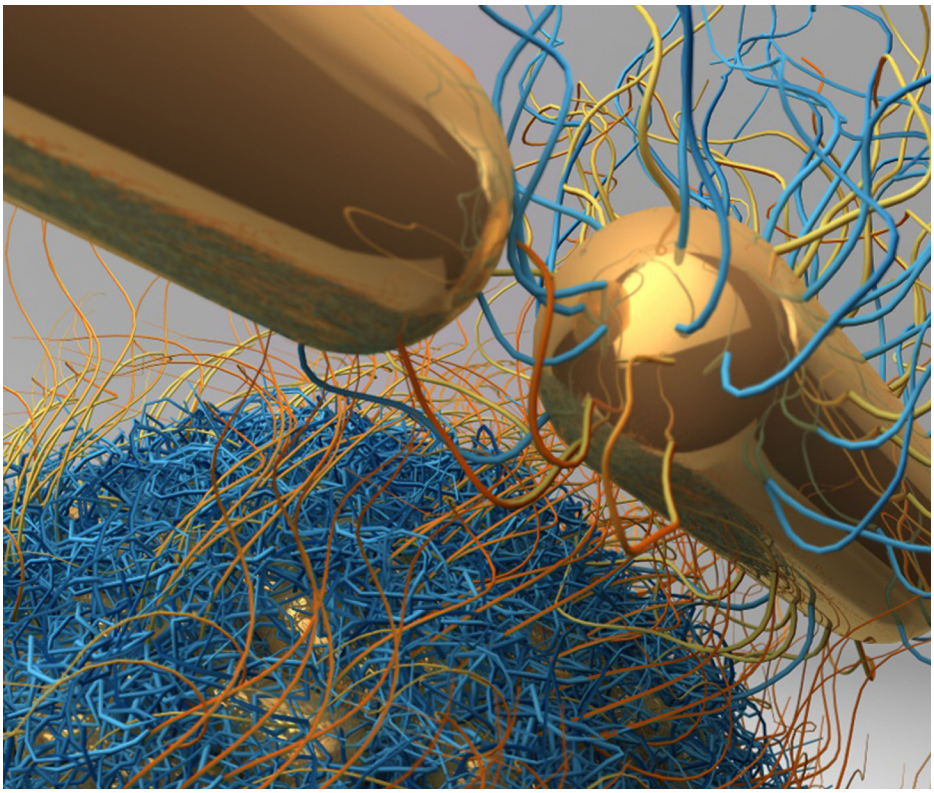
Celebrating 30 Years

Report from the 2016 NIH Research Festival

BY NIH CATALYST WRITERS



SHAWN CHEN AND JIBIN SONG, NIBIB

Shawn Chen's lab is engineering nanoparticles to carry drugs to tumors. When targeted with a laser, the vesicles release their payload. Shown: A nanovesicle assembled from individual gold nanorods; the hairy-looking material is a polymer coating on the surface of the vesicle. Chen talked about his work in the plenary session on imaging (page 11).

A taste of NIH research. That's what the Research Festival is all about. And for the past 30 years, the festival has provided a lively venue for intramural scientists to share their work with their peers.

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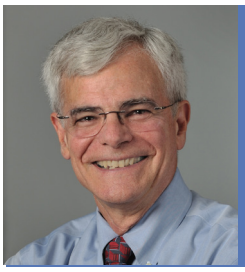


Transparency in Clinical Research: Improving Safety and Quality by Working in Partnership

BY MICHAEL GOTTESMAN, DDIR; ANDREW GRIFFITH, BRUCE BURNETT, AND VALERIE BONHAM

Clinical research is a team effort. The team includes patients and other research volunteers, our colleagues on institutional review boards (IRBs), agencies such as the Food and Drug Administration (FDA), Congress and other public and private entities that support the work that we do, and the broader public. Without all members of the team working together, we cannot accomplish our mission to improve the lives of those we serve.

Teamwork requires clear and effective communication among all members of the team. For many years, NIH has been charting new ground to expand access to information about clinical research and research results. In September, a series of reforms were announced to further these goals and ensure that NIH-funded research meets the highest performance standards. These policies, known generally as the "NIH Clinical Trial Stewardship Reforms," include requirements that all NIH-funded clinical trials, including Intramural Research Program (IRP) activities, must register and report results at ClinicalTrials.gov, a public database maintained by the National Library of Medicine.

Increased transparency on clinical-trial availability, enrollment criteria, and outcome measures and results, both positive and negative, will strengthen the design of future trials, deepen public understanding of the work we do, and reduce the possibility that patients and other volunteers will be exposed to unnecessary risk.

Another important advance will be the development of a new electronic system to collect information about NIH's entire intramural clinical-trial portfolio. Once completed, this initiative will enable better monitoring and a more comprehensive analysis of intramural clinical research. This comprehensive database will protect the integrity of our science and the safety of the research participants.

> Increased transparency on clinical trial availability, enrollment criteria, and positive and negative outcome measures will deepen public understanding of the work we do.

The newly formed Office of Research Support and Compliance (ORSC) within the Office of Intramural Research is working to improve communication among our team members by facilitating the access and sharing of information across the IRP. As a central office, ORSC is positioned as both a service provider and an expert resource for all researchers and research programs within the IRP. It will serve as a nexus to collect, aggregate, and compare data about IRP clinical-research activities. Through data review, the ORSC will enable us to detect trends and gaps so that we can accurately and efficiently target training and other resources to improve safety and quality.

For example, we recently learned about troubling delays in reporting serious adverse events (SAEs) and unanticipated problems (UPs)—to the IRB, study sponsor, and FDA—in an NCI-sponsored and -conducted phase I study. SAEs and UPs often occur in clinical research, especially when patients are seriously ill. To learn effectively from these situations and to ensure patient safety, it is absolutely required that SAEs and UPs be reported in a timely manner.

Intramural investigators across NIH have now been asked to audit their clinical-research studies and especially their reporting of SAEs and UPs. When this data collection is complete, the ORSC will help us to understand and correct possible weak points or misunderstandings in reporting duties in specific programs or for specific types of events. This is a forward-looking effort to raise our oversight of clinical research to even higher levels.

The ORSC is also reaching out to all NIH IRBs to identify and understand instances of delayed reporting of UPs and SAEs to the IRBs. The ORSC will also use an experienced contractor to initiate a detailed audit of a sample of clinical protocols in all NIH institutes and centers (ICs), focusing on protocols that are regulated by the FDA. This audit is expected to begin early next year. The ORSC will work closely with the Office of Human Subjects Research Protection, the NIH IRBs, and IC compliance staff and leadership. The office welcomes and encourages comments from investigators and other staff across the IRP. It is an important first step toward our goal

of clear communication among the entire team.

Another important component of our goal to reach the highest levels of clinical care in the Clinical Center is the ongoing series of discussion groups involving members of our patient-care staff. The groups are facilitated by **Stewart Simonson**, who is a lawyer dedicated to public-health issues and a former director of emergency preparedness in the Department of Health and Human Services. More than 500 staff members are participating in these meetings, which include frank discussions of areas in which NIH clinical care, already of high quality, can be further improved. These discussions will inform practice in the Clinical Center and the discussions will be communicated to NIH staff through a regular newsletter.

The ORSC can be contacted directly by e-mailing or calling Acting Director **Bruce Burnett** or Deputy Director **Valerie Bonham** or by e-mailing orsccontact@mail.nih.gov. To report concerns or issues anonymously, you may call the NIH Clinical Center Anonymous Safety Hotline at 1-866-444-8811.

Our first responsibility is always the safety and compassionate care of all our patients and NIH research volunteers. They are the most important members of our clinical-research team. As with all successful teams, all of us need to communicate freely and clearly to achieve our goals of advancing foundational knowledge and improving the lives of the people we serve.

Andrew Griffith is the scientific director for the National Institute of Deafness and Other Communications Disorders and the deputy director for Intramural Clinical Research; Bruce Burnett is the acting director of ORSC; and Valerie Bonham is the deputy director of ORSC. To read more about the "NIH Clinical Trial Stewardship Reforms," go to https://www.nih.gov/news-events/summary-hhs-nih-initiatives-enhance-availability-clinical-trial-information.

New Freezer Policy

In an ongoing effort to phase out older, non-energy-efficient freezers that use an overwhelming amount of energy, NIH's Division of Environmental Protection (DEP) in the Office of Research Facilities Development and Operations (ORFDO) has issued a new policy—and manual chapter—that covers the selection, placement, maintenance, and inspection of ultralow-temperature (ULT) freezers.

Selection: This policy encourages ICs to use the New Equipment Sales and Rental Program through the Division of Scientific Equipment and Instrumentation Services (DSEIS), Office of Research Services, to acquire energy-efficient ULT freezers. Advantages to using DSEIS for these acquisitions include competitive pricing and options such as monthly rentals and rent-to-purchase agreements. For more information, contact **Anju Vergheese** (Branch Chief) at anju.vergheese@nih.gov or **Mary McKeehan** at rental@ors.od.nih.gov. The DEP will develop and annually update a list of energy-efficient ULT-freezers. This list is available on the NIH Energy Management Systems (NEMS) website (https://nems.nih.gov/programs/Pages/NIH-Ultra-Low-Temperature-Freezer-Policy.aspx) or by request to the DEP director.

Inventory: All ULT freezers are accountable property and therefore must have a barcode decal affixed to the front and the information entered into NIH Business System within five working days of receipt of equipment. When no longer needed, the freezers must be disposed of according to property-disposal requirements.

Placement: ULT freezers will be placed only in locations that are adequately ventilated, temperature controlled, and away from excessive foot traffic.

Maintenance: ICs shall perform regular preventative maintenance on all ULT freezers twice a year. Note: The Division of Scientific Equipment and Instrumentation Services in the Office of Research Services is available to provide this service. For information on pricing and contracts, contact **Glenn Simons** (simonsgd@mail.nih.gov) or **Jerry Tyus** (jerry.tyus@nih.gov).

Inspections and Compliance: ORFDO personnel will inspect the freezers to ensure compliance with the new policy, note deficiencies, and remedy noncompliant occurrences.

To review the chapter, go to https://oma1.od.nih.gov/manualchapters/acquisitions/26101-16/. For further information, contact Susan Hinton (hintons@mail.nih.gov).

NIAID Announces Redesign of ClinRegs Website

ClinRegs, an online database that helps researchers sort through country-specific clinical-research regulatory information, is making it even easier for researchers to conduct clinical trials around the world. The National Institute of Allergy and Infectious Diseases (NIAID), which launched the website in 2014, has released a new version, which now covers 17 countries. New or improved features include:

- An interactive homepage map of the countries included
- A table of contents on each country page for easier navigation
- Drop-down menus to switch among countries for comparison
- A Quick Facts table for each country
- In-context links for users to submit updates or comments

To visit the site, go to http://clinregs.niaid.nih.gov. To read an article on the same topic that appeared in the January–February 2015 issue of the *NIH Catalyst*, go to http://irp.nih.gov/catalyst/v23i1/news-you-can-use.

FROM THE FELLOWS COMMITTEE

The Synergistic Role of Secondary Mentoring

BY JENNIFER PATTERSON-WEST (NIDDK), JESSICA PIERCE (NIDDK), AFROUZ ANDERSON (NICHD), COURTNEY KURTYKA (NICHD), TERESA RAMIREZ (NHGRI)

Scientists at all levels need mentoring to acquire expertise for their field of research, develop communication and other skills, and expand their network. Typically, the principal investigator (PI) is thought of as the mentor in most scientific relationships. However, PIs usually have multiple mentees and a wide range of responsibilities that limit their availability to focus on all aspects of each person's scientific and career development. For this reason, trainees may benefit from additional or secondary mentors who can provide training in their chosen career path and expand their professional network.

Several institutes have successful secondary mentoring—sometimes called co-mentoring—programsincluding the National Cancer Institute (NCI), which has four; the National Institute of Diabetes, Digestive, and Kidney Disease (NIDDK); the National Institute of Drug Abuse (NIDA); and the National Human Genome Research Institute (NHGRI).

We conducted a survey of these programs, interviewed some of the participants, and learned that having multiple mentors provides critical opportunities for trainees to increase their self-awareness and develop their professional identity. Secondary mentors represent different areas of expertise that complement the expertise of the trainee's PI, provide insight into the trainees' career paths, and help trainees assess their skills.

Read more about these programs in the online edition of the *NIH Catalyst* at irp.nih.gov/catalyst/v24i6/the-training-page.

Independent Programs

For trainees interested in establishing secondary mentoring relationships on their own, here are some tips:

- **Define your goals:** Determine whether you want to acquire experience with a new technique; access expertise in a related field; want insight into a specific career path; or learn how to improve or optimize your work-life balance. It may help to complete a self-assessment and career-development plan to pinpoint those issues that require additional training or mentoring.
- **Evaluate** whether it's your PI or other mentors who can best provide mentoring for the skills you want to build.
- **Identify potential mentors:** Look for collaborators, members of affinity groups, professionals in your field of interest, or the National Research Mentoring Network (https://nrmnet.net/) to identify potential mentors who have expertise in your area of interest.
- **Establish contact:** Ask a colleague or your PI for an introduction, introduce yourself at a conference or after a seminar, or send a cold-call e-mail. A cold-call e-mail should take less than a minute to read and have three parts: a brief introduction; a short explanation of why you are contacting them; and a request for a meeting or phone call (include potential dates and times).
- **The first meeting** should be an informational interview. Research your contact's background beforehand so that you can ask targeted questions. Prepare questions related to your goal or intended career path. You will be expected to drive the conversation, so the more prepared you are before the meeting, the more you will gain from it.
- **After the first meeting:** Determine whether all of your questions were answered and/or if you would benefit from additional meetings, what else you would like to learn from your contact, whether you feel inspired, and how comfortable you felt discussing your career and goals with your contact. Write a thank-you note or an e-mail and ask for a second meeting if appropriate.
- **Decide if you want an informal or formal mentoring relationship:** Before your second meeting, you need to decide whether you want an informal or formal mentoring relationship. For informal relationships, you do not need to broach the topic of mentoring and can set up meetings as needed. For formal mentoring relationships, you should ask whether the potential mentor could advise you in a specific area and lay out your needs (frequency of meetings, accessibility of mentor, etc.). Do not be discouraged if a potential mentor does not have sufficient time to put toward such a relationship or redirects you to someone else who may be better suited to mentor you.
- **After you find a mentor:** Make sure to keep in touch and set up meetings as needed. Typically, the mentee drives the relationship, especially at the beginning. At each meeting, have plenty of questions and be prepared to discuss your progress, problems you are facing in reaching your goal, and trepidations you may have about your future prospects or ability to reach your career or science goal. As you continue to develop your mentoring relationship, try to give back by sharing your skills and expertise with your mentor. Something as simple as sharing a journal article or notes from a conference or seminar can show that you are paying attention to what interests them.

We are confident that trainees would benefit from having additional mentors. If institutes and centers could either either start formal programs or add a mentoring section to individual-development plans, trainees would have a framework for incorporating these experiences into their training at the NIH. ●

Achieving the Cancer Moonshot Goals

BY LAURIE-ANNE SAYLES, NCI

National Cancer Institute (NCI) Acting Director **Douglas Lowy** accepted the recommendations of a Blue Ribbon Panel (BRP) on 10 recommendations most likely to make a decade's worth of progress against cancer in five years, a key goal of the White House Cancer Moonshot. The report was presented by the BRP and approved by the National Cancer Advisory Board. With this road map in hand, NCI is poised to move forward in investing in these critical areas of research.

Along with the 10 scientific recommendations, the road map has additional specific, special projects. These include a demonstration project to test for Lynch syndrome, a heritable genetic condition that increases risk of several types of cancer, to improve early detection and prevention; the establishment of a nationwide pediatric-immunotherapy clinical-trials network to enhance the speed with which new immunotherapies can be tested in children; the exploration of patient-derived organoids; and the use of "microdosing" devices to test drug responses in living tumors.

Lowy will share these recommendations with the Cancer Moonshot Task Force. "I am deeply indebted to the 28 outstanding individuals who have served on the Blue Ribbon Panel and to the 150 working group members who put aside business as usual to contribute their years of expertise to this once-in-a-lifetime opportunity," said Lowy. "NCI is also greatly appreciative of Vice President [Joe] Biden's leadership and passion for the Cancer Moonshot and for motivating all who have been working so hard to make it a reality." ●

To view the 10 recommendations and read the full report, visit http://www.cancer.gov/BRP.

NASA astronaut Kate Rubins, who is aboard the International Space Station, chatted recently with NIH Director Francis Collins.

Space Station, This is Bethesda Calling

BY LAURA STEPHENSON CARTER

More than 58,000 people from all over the United States and at least 53 countries watched Facebook-Live on October 18 as Earth-bound NIH Director **Francis Collins** engaged in a lively conversation with NASA astronaut–scientist Kate Rubins, who was aboard the International Space Station (ISS). Rubins was the first person to sequence DNA in space. She answered questions about the challenges of doing research at the station.

Many of the ISS experiments will determine how space radiation and the microgravity environment would affect astronauts on long-duration space journeys. Rubins described several experiments including one that is looking at the effects of radiation on human heart cells; another that is using identical twins—one on the space station and one on Earth—to see how humans respond to the microgravity environment; and still another that is exploring differences in how heart cells develop and interact in a microgravity environment. ●

To view the space chat on the NIH YouTube channel, go to http://bit.ly/2ekYNo0.

Clinical Center Update: Coming Into Focus

BY MICHAEL GOTTESMAN

At the Clinical Center (CC) Town Hall meeting held on September 7, NIH staff and contractors were invited to sign up for focus groups to discuss patient care and safety in the CC and ways to improve both the practice and the process of carrying out NIH's research mission.

So far, there have some 30 focus groups, each with 15 to 20 participants, and many more are planned. The meetings have brought together a diverse group of NIHers. The idea is to hear from all staffing levels, particularly those in and about the CC who interact directly with patients (principal investigators, staff clinicians, clinical fellows, admission staff, hospitality, nurses, social workers, technicians, etc.) and even indirectly (facility crews, unit clerks, medical records staff, and so on). People outside the CC are encouraged to participate, too, as they may also have insight into how to improve clinical services.

The new Hospital Board met on October 21 to hear the recommendations and concerns raised in the focus groups. Several themes have emerged including the need to improve communications, improve infrastructure, provide more resources, develop a better-defined system of identifying people responsible for key tasks, and ensure consistency in patient-care practices and procedures.

If you haven't already participated in a focus group, there is still time. These groups will continue for the foreseeable future in order to give as many people as possible the chance to share their ideas and concerns. ●

To sign up for a focus group, go to http://intranet.cc.nih.gov/focusgroups.html.

Read longer versions online at http://irp.nih.gov/catalyst/v24i6/news-briefs.

Minerals in Medicine Exhibit

CONTINUED FROM PAGE 1

ANDREW PROPP

The "Minerals in Medicine" exhibit opened at the NIH Clinical Center in September, with a ribbon-cutting ceremony by John Gallin, director of the CC, and Jeffrey Post, chair of the Department of Mineral Sciences and curator of the National Gem and Mineral Collection at the Smithsonian Institution National Museum of Natural History.

visited the exhibit and was particularly interested in the minerals used in dentistry, including gypsum, calcite with marcasite, and fluorapatite with calcite.

"Naturally occurring stones and minerals have long been an essential staple of dental materials—allowing providers to clean and strengthen teeth, create anatomical restorations, and pour impressions in stone to fabricate removable and fixed prostheses," said Range. "It is quite remarkable to see some of these materials on display in their unprocessed organic form. The stones are stunning."

Similarly, **Dennis Johnson**, a computerized tomography (CT) technologist in the CC Radiology and Imaging Sciences Department, enjoyed viewing the hübnerite with quartz (from Pasto Bueno, Peru), which is used in CT imaging. ●

Some of the Minerals on Display

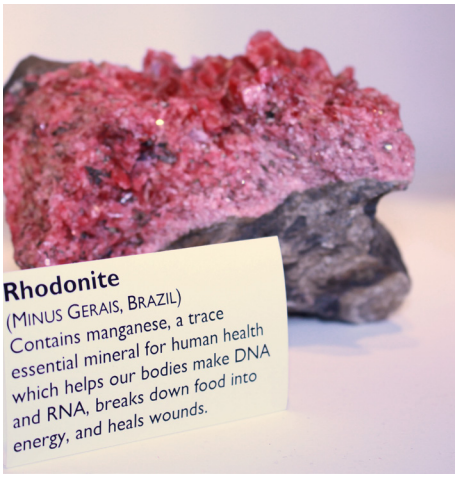
ANDREW PROPP

Cinnabar with Quartz (Kyrgyzstan)

The common bright scarlet to brick-red form of mercury sulfide. Mercury amalgam is used in glass thermometers and has been used for over 150 years in tooth fillings.

Quartz (Arkansas)

Due to its ability to generate an electric charge, to rotate the plane of light polarization, and to be transparent in ultraviolet rays, it is used to make precision medical instruments.



Rhodonite (Brazil)

Contains manganese, a trace essential mineral for human health. It helps our bodies make DNA and RNA, breaks down food into energy, and heals wounds.

Into the Future and Out of the Past

Special Treats at the 2016 NIH Research Festival

BY LESLEY EARL, NCI

A Walk in the Future: Virtual Reality and Innovative Technologies

We're not talking just three-dimensional (3-D) glasses anymore, folks. Yes, okay, you still have to wear the glasses (and they're pretty hefty, too). But with new features such as accelerometers to track your speed, gyroscopes to adjust to changes in your head tilt, and infrared trackers to catch your movement, the experience of virtual reality can be immersive, vibrant, and even interactive, letting you enter fanciful worlds or directly interact with scientific data in 3-D.

Members of the Virtual and Augmented Reality Interest Group (VARIG) brought their virtual reality setups to the NIH Library, allowing visitors to try out the experience and imagine what the technology could bring to their research. One group, the National Human Genome Research Institute's Immersive Virtual Environment Testing Area, led by **Susan Persky,** is exploring ways to apply these technologies to behavioral research, using virtual avatars to study how people interact in various health-relevant situations.

But the applications of this technology—whether they be studying and evaluating movement or simply interacting with a 3-D model of an organism, cell, or protein in virtual space—offer possibilities limited only by what you can dream up.

On the other hand, if you'd rather hold your model in not-so-virtual reality, you can always have the NIH Library print it out, in 3-D, ready to bring to your next presentation or to share with colleagues! ●

Read longer versions online at http://irp.nih.gov/catalyst/v24i6/nih-research-festival-into-the-future-and-out-of-the-past.

A Walk in the Past: NLM's History of Medicine Collections

Located in the southeast corner of the NIH campus, the National Library of Medicine (NLM) serves the world's medical-research community in many ways. Most visible is its role indexing peer-reviewed biomedical research.

But the NLM also archives historical biomedical documents, a task that includes not only preserving a variety of materials from centuries past but also collecting and preserving modern records and "born digital" materials, such as websites and blogs, for future research.

During the Research Festival, the NLM hosted tours of the History of Medicine collections, guiding visitors through its current exhibition (documents relating to the history of domestic violence) to the incunabula room, where the oldest and most precious of NLM's collections are housed.

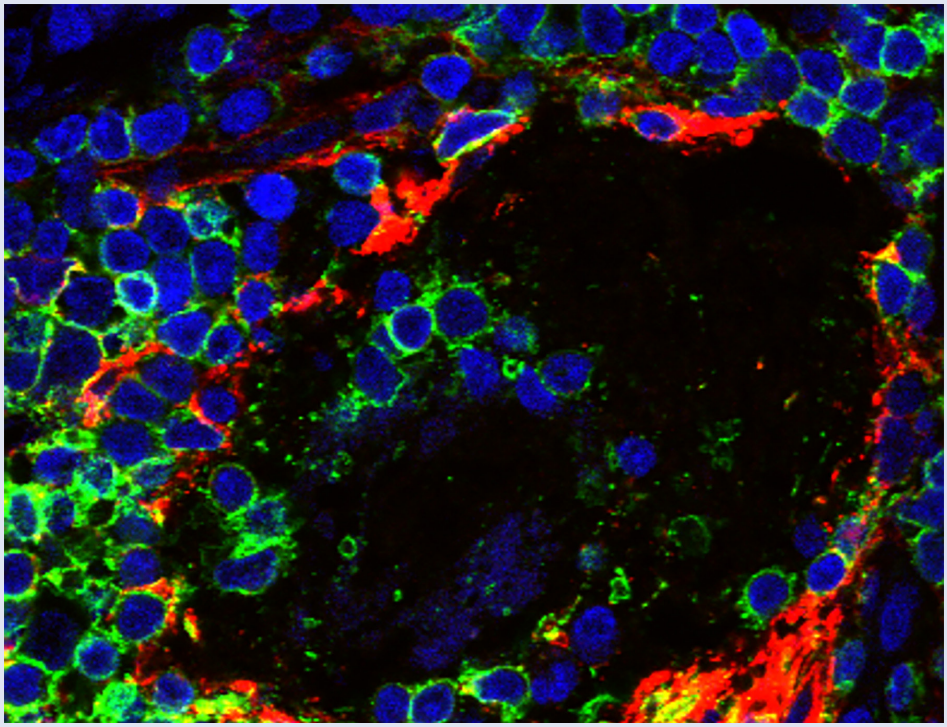
Some of the rare books held there include hand-written medical documents dating back nearly 1,000 years and more modern works such as first editions of Charles Darwin's *On the Origin of Species* and Florence Nightingale's *Notes on Nursing*.

And what about the latest in research, with some journals online-only? As file types and computing standards change, the NLM is actively preserving these documents for centuries to come. Visit the NLM to learn more about its work. You will be warmly welcomed. ●

For more information about NLM, go to https://www.nlm.nih.gov/. For more on the History of Medicine Division and its online exhibitions and digital collections, go to https://www.nlm.nih.gov/hmd/.

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



ILIAS ALEVIZOS, NIDCR

NIDCR: B lymphocytes line the rim of a salivary duct in salivary gland tissue from a Sjögren syndrome patient.

NIDCR: SPOTLIGHT ON SJÖGREN SYNDROME AQUAPORIN GENE THERAPY

A team led by NIDCR researchers has demonstrated that gene therapy with *AQP1*, the gene that codes for the protein aquaporin 1, restored saliva and tear flow in mice that were suffering from symptoms of Sjögren syndrome—dry mouth and dry eyes and inflamed salivary and tear glands. The syndrome is a chronic autoimmune disease that affects some 35 million people worldwide, mostly older women. Currently, there is no effective treatment for Sjögren syndrome.

Aquaporins are proteins that serve as water channels in cell membranes. In this study, the investigators introduced *AQP1* into the salivary gland of mice bred to have Sjögren syndrome. The *AQP1* increased water permeability of the salivary gland and enabled fluid to move constantly through ducts into the mouth, improving saliva flow in mice with dry mouth. Surprisingly, the expression of *AQP1* in salivary glands also enhanced tear secretion and reduced inflammation. According to the authors, these results support the possibility of testing *AQP1* gene therapy to restore saliva and tear flow in people with the syndrome. (NIH authors: Z. Lai, H. Yin, J. Cabrera-Pérez, M.C. Guimaro, S. Afione, D.G. Michael, A. Patel, W.D. Swaim, C. Zheng, and J.A. Chiorini, *Proc Natl Acad Sci USA* **113**:5694–5699, 2016)

NIDCR: SPOTLIGHT ON SJÖGREN SYNDROME ROLE OF VIRAL INFECTIONS

The causes of Sjögren syndrome have been elusive, but viral infections have long been suspected to be involved. Two studies by NIDCR researchers provide evidence for a causal relationship between infection with Epstein-Barr virus (EBV) or hepatitis delta virus (HDV) and Sjögren syndrome. These studies reveal new details on viral mechanisms at work in salivary glands and lay the foundation for developing novel therapeutic strategies.

In the first study, the researchers focused on an EBV microRNA, *ebv-miR-BART13-3p*, which had been found at concentrations more than 20 times as high in Sjögren patients' salivary glands as in the salivary glands of healthy control subjects. Suspecting a role for microRNA, the investigators examined its effect on the activity of salivary gland genes in cultured cells and found that it suppresses the activity of two genes, *STIM1* and *AQP5*. (NIH authors: A. Gallo, S.I. Jang, H.L. Ong, P. Perez, M. Tandon, I. Ambudkar, G. Illei, and I. Alevizos, *EBioMedicine* **10**:216–226, 2016; http://www.ebiomedicine.com/article/S2352-3964(16)30298-5/fulltext)

In the second study, another team of NIDCR scientists observed replicating HDV in the salivary glands of 50 percent of Sjögren syndrome patients tested. When HDV proteins were expressed in the salivary glands of mice, there was a reduction in saliva production and accumulation of lymphocytes in the glands, hallmarks of the syndrome. (NIH authors: M.L. Weller, M.R. Gardener, Z.C. Bogus, M.A. Smith, E. Astorri, D.G. Michael, D.A. Michael, C. Zheng, P.D. Burbelo, Z. Lai, P.A. Wilson, W. Swaim, B. Handelman, S.A. Afione, M. Bombardieri, and J.A. Chiorini, *Pathog Immun* **1**:12–40, 2016)

NIEHS: DIFFERENCES BETWEEN ALLERGIC AND NONALLERGIC DUST-MITE PROTEINS

NIEHS scientists and others have determined what differentiates dust-mite allergens from the nonallergen proteins that dust mites produce. According to the researchers, dust-mite allergens are more chemically stable and produced in larger quantities than other dust-mite proteins. The finding that dust-mite allergens are more durable and more abundant than other dust-mite proteins supports two hypotheses about how allergenic compounds stimulate an immune response in the body.

One theory is that proteins that are more stable do not break down during the journey from the source—such as dust mites, cockroaches, and ragweed—to a person. Another possible explanation is that more-stable

NIDCR BRIEFS PREPARED BY LORENA BRITO DE SOUZA (NIDCR) AND DAVE VANNIER (NIDCR)

proteins are harder for the immune system to digest, therefore initiating signals in the body that indicate they are dangerous particles. (NIH authors: T.A. Randall, G.E. Kissling, R.E. London, and G.A. Mueller, *J Allergy Clin Immunol* DOI:10.1016/j.jaci.2016.08.016)

NIAID, NHGRI, NIMH: GENETIC EXPLANATION FOR A FRUSTRATING SYNDROME

A team led by NIAID scientists has identified a genetic explanation for a syndrome characterized by multiple frustrating and difficult-to-treat symptoms, including dizziness and lightheadedness, skin flushing and itching, gastrointestinal complaints, chronic pain, and bone and joint problems. Some people who experience these diverse symptoms have elevated concentrations of tryptase, a protein in the blood often associated with allergic reactions. Multiple copies of *TPSAB1,* the gene for alpha tryptase, drive these tryptase elevations and may contribute to the symptoms, according to the study. Although more research is needed, this study sets the stage for advances in diagnosis and treatment. (NIAID authors: J.J. Lyons, X. Yu, A. Jamil, Y. Bai, Y. Liu, M.P. O'Connell, C. Nelson, T. DiMaggio, R.J. Carlson, S. Agama, T.M. Wilson, S. Tucker, K.D. Stone, D.D. Metcalfe, J.D. Milner, M. Zhao, R.J. Hohman, H. Matthews, A.J. Oler, and Y. Zhang; NHGRI authors: K.L. Lewis, C. Hong, and L.G. Biesecker; NIMH author: M. Pao; *Nat Genet* DOI:10.1038/ng.3696, 2016)

NIDDK: WEIGHT LOSS LEADS TO STRONG INCREASE IN APPETITE

Analysis of a trial that used the drug canagliflozin found that as people lost weight, their appetite increased proportionately, leading to the consumption of more calories and a leveling off of weight loss. The findings provide the first measurement in people of how strongly appetite counters weight loss as part of the body's feedback-control system regulating weight. NIDDK investigators analyzed data from a year-long, placebo-controlled, double-blind trial in 242 people (153 received canagliflozin) with type 2 diabetes who could eat and drink without restriction. (NIH authors: A. Sanghvi and K.D. Hall, *Obesity* DOI:http://dx.doi.org/10.1101/051045)

NIAID: ZMAPP HOLDS PROMISE AS EBOLA TREATMENT

A randomized, controlled clinical trial to evaluate the experimental Ebola treatment ZMapp found it to be safe and well-tolerated, according to NIAID investigators. The trial enrolled 72 participants with confirmed Ebola virus infection. The participants came from Sierra Leone (54), Guinea (12), Liberia (five), and the United States (one, a health-care worker evacuated from Sierra Leone). (NIH authors: R.T. Davey, Jr., L. Dodd, M.A. Proschan, J. Tierney, H.C. Lane, and A.S. Fauci, *N Engl J Med* **375**:1448–1456, 2016)

NICHD: MORNING SICKNESS LINKED TO LOWER RISK OF PREGNANCY LOSS

Nausea and vomiting during pregnancy is associated with a lower risk of miscarriage in pregnant women, according to a new analysis by NICHD researchers and others. The cause of morning sickness is not known, but scientists have proposed that it protects the fetus against toxins and disease-causing organisms in foods and beverages. For their study, the researchers analyzed data from 797 women who had positive pregnancy tests, with 188 pregnancies ending in loss. By the eighth week of pregnancy, 57.3 percent of the women reported experiencing nausea, and 26.6 percent reported nausea with vomiting. The researchers found that these women were 50 to 75 percent less likely to experience a pregnancy loss than those who had not experienced nausea alone or nausea accompanied by vomiting. (NIH authors: S.N. Hinkle, S.L. Mumford, K.L. Grantz, E.M. Mitchell, L.A. Sjaarda, R.G. Radin, N.J. Perkins, and E.F. Schisterman, *JAMA Intern Med* DOI:10.1001/jamainternmed.2016.5641)

Read more online at http://irp.nih.gov/catalyst/v24i6/research-briefs.

NINDS, NCCIH, CC: "SIXTH SENSE" MAY BE MORE THAN JUST A FEELING

With the help of two young patients—one nine and the other 19—with a unique neurological disorder, an initial study by NIH scientists suggests that a gene called *PIEZO2* controls specific aspects of human touch and proprioception, a "sixth sense" describing the awareness of one's body in space. Mutations in the gene caused the two to have movement and balance problems and the loss of some forms of touch. Despite their difficulties, they both appeared to cope with these challenges by relying heavily on vision and other senses. (NCCIH authors: A.T. Chesler, M. Szczot, M. Čeko, and C. Laubacher; NINDS authors: D. Bharucha-Goebel, S. Donkervoort, L. H. Hayes, D. Nguyen, A.R. Foley, C.E. Le Pichon, and C.G. Bönnemann; CC authors: K. Alter, C. Zampieri, and C. Stanley; *N Engl J Med* **375**:1355–1364, 2016)

NICHD: DEPRESSION IN EARLY PREGNANCY LINKED TO GESTATIONAL DIABETES

Researchers at NICHD have discovered a two-way link between depression and gestational diabetes. Women who reported feeling depressed during the first two trimesters of pregnancy were nearly twice as likely to develop gestational diabetes. Conversely, women who developed gestational diabetes were more likely to report postpartum depression six weeks after giving birth than a similar group of women who did not develop gestational diabetes. The researchers analyzed pregnancy records from the NICHD Fetal Growth Studies-Singleton Cohort, which tracked the progress of thousands of pregnancies. The study was not able to prove a cause-and-effect relationship between symptoms of depression and gestational diabetes, according to the researchers. (NICHD authors: S.N. Hinkle, G.M. Buck Louis, S. Rawal, Y. Zhu, P.S. Albert, and C. Zhang; *Diabetologia* DOI:10.1007/s00125-016-4086-1) ●

Research Festival

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"We had a lot of enthusiasm from scientists in organizing the sessions," said festival co-chair **Andrew Griffith**, the scientific director of the National Institute on Deafness and Other Communication Disorders.

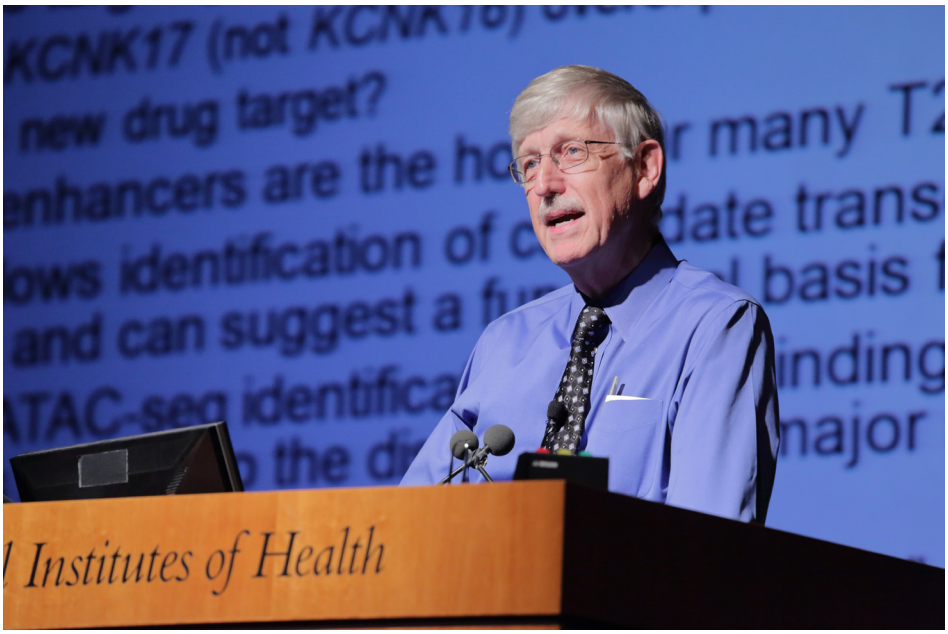
The festival, which was held on September 14–16 in the Clinical Center, featured three plenary sessions on some of NIH's cutting-edge research—on superenhancers, clinical imaging, and cell-based immune therapies. The three days were also filled with concurrent symposia, poster sessions (including one for institute directors and scientific directors), special exhibits on intramural resources, the Green Labs Fair, the FARE Awards ceremony, demonstrations on three-dimensional printing and virtual reality, tours of the National Library of Medicine and the Clinical Center, the Technical Sales Association exhibit tent show, and more.

"A highlight was having [NIH Director **Francis] Collins** speak and present on his science," said festival co-chair **Ann Cashion**, who's the scientific director of the National Institute of Nursing Research. Collins spoke at the superenhancer plenary.

The poster sessions were another highlight and gave trainees a chance to shine. "Our trainees and fellows do exceptional work," said Cashion. "It's wonderful to see those who are going to replace me showing such promise and such unique new ways of thinking."

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

Longer articles about the Research Festival and more photos are in the online edition of the *NIH Catalyst* at http://irp.nih.gov/catalyst/v24i6/nih-research-festival-celebrating-30-years.



ERNIE BRANSON

NIH Director Francis Collins kicked off the 2016 Research Festival with a talk on his research on stretch enhancers, non-coding regions of the genome that enhance gene expression from a distance.

PLENARY SESSIONS

FIRST ON THE SCENE: INTRAMURAL RESEARCHERS TALK SUPERENHANCERS

Research Festival Plenary Session I

BY LESLEY EARL, NCI

Although the Research Festival itself is celebrating its 30th year, the topic for the opening plenary session of 2016 has only just celebrated its 3rd birthday! With a potential role in helping conditions ranging from diabetes to cancer to infectious diseases, the newborn field of superenhancer research seems to have a great big future in front of it.

In 2013, two different groups investigating epigenetics discovered that certain multi-kilobase non-codiong regions of the genome seemed not only to be able to enhance gene expression from a distance but also to powerfully act on genes in specific cell types. One of these groups was led by **Francis Collins**, NIH director and head of the molecular genetics section in the National Human Genome Research Institute.

Collins described how his group discovered "stretch enhancers," a slightly broader category of strong enhancers that includes superenhancers. While looking for the mechanism for how genetic risk factors influence type 2 diabetes, his team found that the majority of risk-producing single-nucleotide polymorphisms (SNPs) fell in noncoding regions of the genome. "If you really want to understand type 2 diabetes on a functional basis, and how genetic risks play out," he said, "you have to roll up your sleeves and say, 'We're going to get into epigenetics.'"

And so they did. Using ChromHMM software to analyze epigenetic data, Collins's group found that many of their diabetes-associated SNPs fell in certain long stretches of non-coding DNA with the histone marks characteristic of enhancers. Then they used a method called ATAC-seq to identify transcription-factor binding sites, within those regions, that are altered

in the presence of a genetic risk variant. In so doing, they discovered multiple examples of motifs for the RFX (regulatory factor X) family of transcription factors. RFX "is much more of a master transcription factor than we had realized," said Collins. In fact, this search led them to RFX6, which seems to be closely tied to the special functions of pancreatic islet beta cells (which store and release insulin) that are critical to the prevention of diabetes.

In the second talk, **Rafael Casellas** (National Institute of Arthritis and Musculoskeletal and Skin Diseases), joined by Erez Lieberman-Aiden from Baylor College of Medicine (Houston), laid out how a particular feature—specifically, the formation of long loops in the genome—is critical for superenhancers to do their work. When circulating B cells are activated by antigens, Casellas said, the process that leads to the production of antibodies involves a massive amplification of the transcriptome (the set of all messenger RNA molecules in a cell or population of cells). While examining the genome of these cells with super-resolution stochastic optical-reconstruction microscopy, Casellas noted that clusters of nucleosomes rapidly decompacted into monocucleosome fibers. This observation got him looking at how the architecture of chromatin changes when superenhancers go to work.

Using a technique called chromosome conformation capture using high-throughput sequencing (Hi-C), which detects chromatin interactions in the mammalian nucleus, Casellas and Lieberman-Aiden could spot long-range patterns in chromatin. These patterns "have become associated with many magic powers," said Lieberman-Aiden.

In Hi-C maps, bright spots or stripes on the edges of squares indicate loops that form between flanking CTCF-binding sites, which act as insulators between domains of gene activiation.

"I love superenhancers because they're the most striking examples of stripes we find in the genome," said Casellas.

But how does the presence of these regions translate into changes in expression? In the final presentation of the session, **Keiko Ozato** (National Institute of Child Health and Human Development) discussed bromodomain-containing protein 4 (BRD4), a protein that binds acetylated histones such as those at superenhancer sites. BRD4 "is at the center of superenhancer research," said Ozato. In macrophages, she explained, entire categories of expression programs that are activated after stimulation—such as inflammatory proteins, responses to injury, and other immune responses—are governed by superenhancers and most require BRD4, making proteins such as BRD4 master controllers for whole-gene expression programs.

"Superenhancers are diverse and fluid" and can potentially regulate a vast array of cellular programs, said Ozato. For a field still in its infancy, research on superenhancers seems to be quickly narrowing the gap between genome, gene expression, and cellular identity and function.

To view a videocast of the 2016 Research Festival's Plenary Session I, "Super Enhancers in Cell Identity and Disease," held on September 14, go to https://videocast.nih.gov/launch.asp?19852.

CLINICAL IMAGING

Research Festival Plenary Session II

BY EMILY PETRUS, NINDS

The NIH intramural program has helped to pioneer the field of clinical imaging, from the earliest development of magnetic-resonance imaging (MRI) technology and **Louis Sokoloff**'s now-classic positron emission tomography (PET) scan techniques to map and measure brain function, to recent breakthroughs such as MRI-guided closed-chest heart repair.

This plenary session highlighted the latest research of three NIH scientists who are extending this tradition of clinical-imaging advances: **Xiaoyuan (Shawn) Chen** (National Institute of Biomedical Imaging and Biomedical Engineering), who discussed his work with nanotheranostics; **Jessica Gill** (National Institute of Nursing Research), who presented her discoveries of mechanisms underlying differential responses to traumatic brain injury; and PET expert **Robert Innis** (National Institute of Mental Health), who talked about his most recent method for imaging proteins as a biomarker for neuroinflammation.

Chen's lab is developing molecular-imaging tools that can help with the early diagnosis of disease, monitor response to therapy, and guide drug discovery and development. His nanotheranostics work—the integration of diagnostic and therapeutic function using nanotechnology—involves packaging drugs inside tiny, gold, star-shaped nanoparticles called AuNanostars and delivering them straight to where they're needed in a patient. These AuNanostars can be engineered to accumulate within a tumor and then, when targeted with a laser, release their drugs. Within hours of delivering their payload, they collapse and are secreted from the body. Chen is hoping to collaborate with the FDA and pharmaceutical companies to get his lab's inventions into mainstream medicine.

Neuronal imaging is one of the tools that Gill is using to improve methods for identifying and helping patients at high risk for psychological and neurological impairments after a concussion or other kind of traumatic brain injury. She is using the presence of tau proteins, commonly associated with Alzheimer disease (AD), as a biomarker

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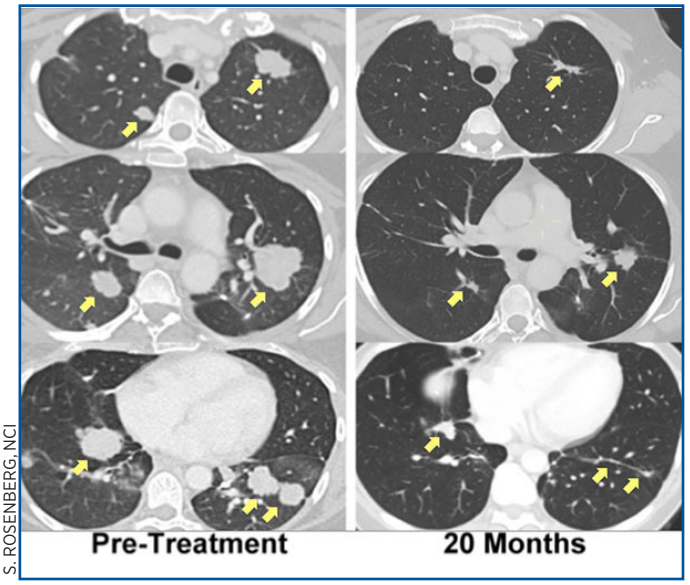

S. ROSENBERG, NCI

A patient with metastatic bile duct cancer, treated with immunotherapy using her own mutation-specific T cells, has experienced regression of her metastatic lung and liver tumors that had been ongoing for more than two years.

for brain injury. The amount of the protein found in blood or sweat is positively correlated with the severity of the injury.

Although the tau proteins are present in such small concentrations that they are nearly undetectable, Gill's group has tweaked the single-molecule arrays method to amplify the protein's detection up to 300-fold. This method for detecting tau can be used outside the clinic, for example, on a football field or a battlefield, and enables clinicians to predict which patients can resume their activities safely after a head injury and which are at increased risk of developing chronic neurological deficits and will need additional interventions.

PET imaging to detect inflammation biomarkers may help physicians more accurately diagnose and treat patients with such neuroinflammatory disorders as depression and AD, according to Innis. Until now, diagnosing and treating neurological disorders was based on trial and error, but Innis's imaging method would eliminate the guesswork. He has identified several biomarkers including a new line of radioligands that can be detected with PET. Innis is currently collaborating with pharmaceutical companies to bring this technology to the clinic.

The videocast of the "New Insights through Clinical Imaging" plenary session, held on September 15, is at https://videocast.nih.gov/launch.asp?19854.

HARNESSING THE IMMUNE SYSTEM

Research Festival Plenary Session III

BY MANJU BHASKAR, NINDS

Immunotherapy has become a viable treatment thanks to the pioneering work of National Cancer Institute (NCI) researchers, that of **Michael Potter** on monoclonal antibodies in the 1960s and **Robert Gallo** on interleukin-2 (IL-2) in the 1970s. This plenary session featured three NIH scientists who built on these advances and have been able to harness the immune system to fight cancer and other chronic, noninfectious diseases: **Steven Rosenberg** (NCI), who was the first to recognize the potential of IL-2 and apply it as a novel anti-cancer agent in 1984; **Nicholas Restifo** (NCI), who discussed new immunotherapies for patients with advanced cancer; and **John Tisdale** (National Heart, Lung, and Blood Institute), who presented his research on combining hematopoietic stem-cell methods with immunotherapy for the treatment of the genetic-based sickle-cell disease.

Rosenberg, widely regarded as the father of immunotherapy, developed the first effective immunotherapies in patients with advanced cancer and was the first to successfully import genes into humans. In his talk, he emphasized the ability of human lymphocytes to recognize unique cancer antigens and how antitumor T-cell receptors can be exploited to develop new cell-transfer immunotherapy treatments for cancer.

The identification and targeting of mutations unique to each cancer has the potential to extend cell therapy to patients with epithelial cancers. Rosenberg's studies on cell-transfer immunotherapies has resulted in durable, complete remission in patients with metastatic melanoma.

Restifo, one of Rosenberg's former postdocs and a pioneer in the use of T-cell–based immunotherapies, was the first to identify myeloid-derived cell substances that impair antitumor T-cell responses in humans. He discussed the immunology of oxygen and potassium and how they can be used to destroy cancer. His lab is currently working on reprogramming T cells to induce curative responses in patients with metastatic cancer.

Cell-based immune therapy is also being explored as a way to treat sickle-cell disease. Tisdale described his work combining hematopoietic stem-cell transplant methods with immunotherapy. Usually, a patient's immune system must be suppressed so transplanted cells and tissue aren't rejected, and preventing rejection can mean a lifetime of taking immunosuppressant drugs. But Tisdale found that, in adult patients, hematopoietic stem cells from matched sibling donors could be successfully transplanted without having to destroy the patient's immune system. ●

To watch a videocast of the 2016 Research Festival's "Cell-based Immune Therapy" plenary session, held on September 16, go to https://videocast.nih.gov/launch.asp?19862.

Concurrent Symposia

BENCH-TO-BEDSIDE HOMERUNS

BY OMOZUSI ANDREWS, NIAID

The NIH Clinical Center (CC) has been home to transformative stories of researchers who successfully took an idea from the bench to the bedside. Some of the NIH researchers who were beneficiaries of the CC's Bench-to-Bedside and Back Awards were on hand to retell their homerun stories.

Peter Pinto's team (National Cancer Institute, NCI) hit a homerun when they used high-resolution magnetic-resonance imaging transrectal ultrasound to diagnosis advanced prostate cancer and to distinguish aggressive high-grade prostate lesions from indolent tumors, which can be watched rather than requiring aggressive surgery.

National Human Genome Research Institute researchers **Charles Venditti** and **Irini Manoli** scored homeruns with their work on methylmalonic acidemia (MMA), an inherited disorder in which the body is unable to process certain proteins and fats properly. Venditti described how, in knockout and transgenic mice with MMA, the team could use a breath test to predict the severity of the disease and then use a variety of gene-delivery approaches to rescue the unstable metabolic symptoms. The team developed a similar breath test for humans with MMA.

Yet another homerun was hit by **Katherine Meilleur** (National Institute of Nursing Research), who is studying common skeletal myopathies caused by mutations in the *RYR1* gene. In a clinical trial, she discovered that patients suffering from *RYR1*-related myopathies showed increased "oxidative stress." And the homeruns kept coming. **Jack A. Yanovski** (National Institute of Child Health and Human Development, NICHD), who pointed out that several genes "confer the potential for obesity," hit a homerun with his discovery that mutations in the *mc3r* gene predisposed children to obesity.

FARE Award winner **Reema Railkar**'s (NCI) homerun resulted from her use of quantitative high-throughput screening to identify novel therapies for bladder cancer. She described how the candidate drug flavopiridol was "highly effective" at inhibiting aggressive bladder cancer cells.

The "From Insight to Therapy: Bench-to-bedside Homeruns" session was co-chaired by John I. Gallin (Clinical Center) and Constantine A. Stratakis (NICHD).

THE MIGHTY MICROBIOME

BY JENNIFER PATTERSON WEST, NIDDK

In the past, microbes were considered enemies to human health. Recent discoveries, however, have highlighted the key role that the human-associated microbiome plays in promoting health. Several intramural investigators discussed how their explorations of microbial communities have shed light on the etiology of disease and have helped them design interventions to promote health and treat disease.

Julie Segre (National Human Genome Research Institute, NHGRI) investigates how bacteria and other microbes that constitute the skin microbiome contribute to health and how changes in them can lead to chronic skin disorders such as eczema and psoriasis. Surprisingly, she found that the skin microbiome differs less among individuals than among microenvironments in the same person: dry, moist, and sebaceous.

The lung microbiome is the focus of **Curtis Harris**'s research (National Cancer Institute). He examined nearly 400 samples—frozen lung-cancer tumor samples and controls—and found an increase in Variovorax and Streptococcus bacteria in the tumors. He said that mechanistic studies must be performed to determine the role of the two taxa in cancer.

The oral cavity is second only to the gastrointestinal tract in the diversity of the microbial community. **Niki Moutsopoulos** (National Institute of Dental and Craniofacial Research) studies periodontitis, a microbial-stimulated disease that leads to the destruction of tooth-supporting structures. She examined the oral microbiome of patients with leukocyte-adhesion deficiency 1 (LAD1) and severe periodontitis, and she showed that the dysbiotic microbial communities in LAD1 may stimulate a local inflammatory response.

FARE Award winner **Dennise A. de Jesus-Diaz** (National Institute of Allergy and Infectious Diseases, NIAID), who is characterizing the microbiota of pediatric patients during a norovirus episode and recovery, observed an increase in proteobacteria in the intestinal microbiota of patients during norovirus infection. She is currently working on a new intestinal enteroid cell-culture system to incorporate secondary metabolites produced by bacteria.

Multidrug-resistant microbes are also being investigated by intramural researchers. In 2011, a strain of carbapenem-resistant *Klebsiella pneumonia* colonized 18 patients at the NIH Clinical Center, with seven deaths attributed to the infections. **Tara N. Palmore** (NIAID) described how she collaborated with Segre's team of researchers, who used advanced genomic technologies to hunt down and contain the bacteria. She even did a study to determine whether health-care workers had been colonized by the microbes and were possibly spreading them. Fortunately, she found no evidence of colonization.

The "Zen of Microbiota" session was chaired by Julie Segre (NHGRI).

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TELL ME YOUR EXPOSURES AND I'LL TELL YOU WHO YOU ARE

BY LORENA BRITO DE SOUZA, NIDCR

Exposure to toxic environmental chemicals and agents while in utero and other developmentally sensitive times can have negative effects on later health outcomes in children, adults, and even future generations. Several intramural scientists are exploring this field of developmental origins of health and disease (DOHaD).

Using data from epidemiologic studies, **Edwina Yeung** (National Institute of Child Health and Human Development, NICHD) showed that obesity during pregnancy affects not only the mother's health but also the early development of her child.

In another epidemiological study, **Martha Linet** (National Cancer Institute) showed that repeated diagnostic X-ray exams during childhood and adolescence could result in a higher risk of breast cancer in adulthood. Moreover, children and teenagers who were exposed to radiation from atomic bombs or the catastrophic Chernobyl nuclear power plant accident in 1986 are more susceptible to the development of solid tumors and thyroid cancers, respectively.

Epigeneticists are also conducting studies in an attempt to understand the molecular drivers of DOHaD. **Bruce Howard** (NICHD) discussed how defects in the maintenance of epigenetic structures may underlie common developmental disorders and age-related diseases. He pointed out that certain genomic regions are more susceptible to altered epigenetic states that can lead to neurodegenerative diseases.

FARE Award winner **Katryn Harwood** (National Institute of Diabetes and Digestive and Kidney Diseases) is trying to understand the role of the O-linked beta-N-acetylglucosamine (O-GlcNAc) cycling enzymes in the epigenome. O-GlcNAc is an intracellular carbohydrate that modifies proteins in the nucleus and cytoplasm. Harwood proposes that the balance between the cycling enzymes O-GlcNAc transferase and O-GlcNAcase plays an important role in turning on and off transcription processes that control germ-line maintenance and embryo viability.

The timing of exposures can have different effects, according to **Carmen Williams** (National Institute of Environmental Health Sciences, NIEHS), who talked about how estrogenic endocrine disruptors alter the ability of the female reproductive-tract environment to support fertilization and embryo development.

The "Lasting Legacies: Long-term Effects of Early Developmental Exposures" session was chaired by Carmen Williams (NIEHS).

INFLAMMATION AND CHRONIC DISEASE

BY STEPHANIE COOPERSTEIN

NIH scientists are deciphering the mechanisms that trigger inflammation, which, when dysregulated, can lead to chronic disease.

Skin: Many types of bacteria colonize healthy skin, but this diversity is lost in atopic dermatitis patients' skin, which is dominated by *Staphylococcus aureus*. Using mouse models, **Keisuke (Chris) Nagao** (National Cancer Institute, NCI) discovered that *S. aureus* was the driving force behind the atopic inflammation and that the absence of the enzyme ADAM-17 impaired normal regulatory signaling.

Eyes: Inflammation plays a role in the development of age-related and other degenerative eye diseases. **Kapil Bharti** (National Eye Institute) is investigating how damage to the outer blood-retina barrier causes macular edema. He has created a novel model of macular edema and is looking for the signaling pathways that cause the condition. Bharti's team hopes their research will be useful for both preclinical and clinical studies related to inflammatory diseases that affect the human retina.

Liver cancer: Metabolic events control T-cell immunity and inflammation in liver cancer, according to **Tim Greten** (NCI). He compared risk factors for viral hepatitis and nonalcoholic liver disease–related inflammation and found commonalities in T-cell infiltration, immune signature, and natural-killer-cell function. He also found that a fatty diet induced fatty-liver buildup.

Rebound inflammation: Few therapies exist for fibrotic disease such as asthma, liver cirrhosis, cardiovascular disease, idiopathic pulmonary fibrosis, Crohn disease, and ulcerative colitis. **Thomas Wynn** (National Institute of Allergy and Infectious Diseases, NIAID) discussed ways to improve antifibrotic therapy by fighting rebound inflammation (inflammation that develops in response to antifibrotic drugs). His group was the first to demonstrate a central and indispensable role for interleukin-13 (IL-13) in the development of fibrosis and has hypothesized that any intervention that disrupts critical steps in the IL-13 response might emerge as a viable therapeutic strategy for fibrosis.

Lung: Second-time FARE Award winner **Seddon Thomas** (National Institute of Environmental Health Sciences) is doing research to better correlate inflammatory asthmatic reactions with environmental causes. She summarized her research on the gene *MYD88* which codes for a protein that helps orchestrate the lung's immune responses to inhaled allergens.

The "Rings of Fire: Inflammation at the Intersection of Chronic Diseases" session was chaired by Thomas Wynn (NIAID).

PRECISION MEDICINE NOW

BY ANTHONY DIBELLO, NIDDK

PRECISION MEDICINE—AN ARENA THAT takes into account individual variability in genes, environment, and lifestyle—is the focus of much NIH research these days.

Richard Siegel (National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIAMS) explained how genetic variants that alter the expression of tumor necrosis factor (TNF)-pathway components can affect the risk of developing autoimmune and autoinflammatory diseases such as Behçet disease, Crohn disease, multiple sclerosis, primary biliary cirrhosis, rheumatoid arthritis, and ulcerative colitis.

Leslie Biesecker (National Human Genome Research Institute, NHGRI) directs ClinSeq, an NHGRI clinical study launched in 2007, that explores how genetics can inform patient health and medical diagnosis and improve genetic-data management and utilization. He described case studies and highlighted projects aimed at improving genomic-data analysis and data sharing.

Ivona Aksentijevich's (NHGRI) use of genomic sequencing led to the discovery of two autoinflammatory diseases—haploinsufficiency of A20 and otulipenia—and the identification of a promising therapeutic approach that involves inhibiting TNF-cytokine signaling.

Javed Khan's (NCI) work also points to the clinical feasibility of using DNA sequencing to inform therapeutic approaches for treating relapsed and refractory tumors in children. He identified many genetic mutations in a clinical genomics study of pediatric cancer patients. In addition, he described NCI's new "ClinOmics" program that enables genome-guided precision therapies for adults and children with cancer.

The session was concluded by FARE Award winner **Ngoc-Han Ha** (NCI), who presented her discovery of the role played by the circadian rhythm gene *Arntl2* in determining metastatic susceptibility and progression in breast-cancer patients.

NIH expects personalized precision medicine to play a significant role in the tailoring of treatments for human disease in the future.

The "Precision Medicine Now: The Power of NIH Patient Cohorts to Wed Genotype with Phenotype" session was chaired by Richard M. Siegel (NIAMS).

BIG DATA AND BIG QUESTIONS

BY ADAM THOMAS, NCI

WITH THE DECREASING COSTS AND increasing speeds of sequencing technology, scientists are rapidly generating large volumes of data. Advances in computational biology may be able to help us interpret this overwhelming wealth of information. Several NIH investigators spoke at the Research Festival about using "big data" in their work.

José Faraldo-Gómez (National Heart, Lung, and Blood Institute) uses computer modeling to study membrane-associated proteins. In a simulated membrane environment, a computer can calculate the force on every single atom to determine the movements of each. A supercomputing infrastructure enables scientists to calculate in seconds what would have once taken a single processor decades to complete. Faraldo-Gómez has used supercomputing modeling to show that the enzyme that creates ATP drives the membrane perturbations that give the mitochondrion its distinct folded appearance. The folds increase the organelle's surface area, enabling the cell to generate more ATP in a smaller volume.

Jianxin Shi (NCI) and colleagues performed an integrative genomic analysis for lung adenocarcinoma (LUAD) patients in the NCI EAGLE (Environment And Genetics in Lung Cancer Etiology) study. This study identified several driver genes in LUAD including two novel ones. The study also showed that the number of somatic mutations and certain other mutation types was associated with increased risk of distant metastasis.

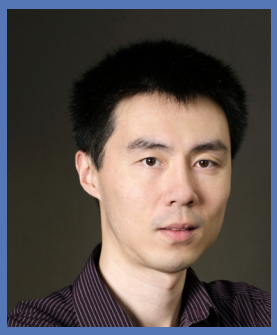
Can big data help us determine the optimal dose, timing, or drug combination for treating cancer patients? To answer this question, **Orit Lavi** (NCI) is exploring how redundancy causes problems in chemotherapy. Redundant elements are those that act in the same biologic or dynamic manner and can compensate for each other if necessary. For example, targeting an oncogene by inhibiting one of its transcriptional activators is useless if there are other activators that can take over. She argues that the integrated computational approaches of mathematical modeling and statistical analysis of information—on tumor heterogeneity, drug resistance, and redundant functions—may enable us to determine the optimal course of treatment.

FARE Award winner **Jessica Petrick** (NCI) studies the relationship between weight changes during a person's lifetime and two types of cancer that have been increasing: esophageal and gastric cardia adenocarcinoma. Using data from two large cancer cohort studies, Petrick found that individuals who were overweight as young adults and obese later in life were at the highest risk for these cancers. Future work may look into whether weight gain between childhood and young adulthood has any effect on cancer risk. ●

The "Making Sense of Greek Letters and Too Many Numbers in the Age of Big Data" session was chaired by Stephen Chanock (NCI).

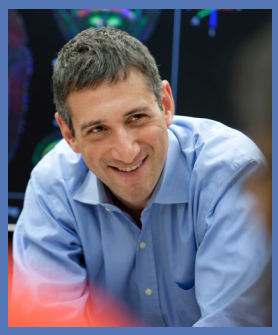
Recently Tenured

DIANE L. DAMIANO, CC



GUANG HU, NIEHS

YINLING HU, NCI-CCR



DANIEL S. REICH, NINDS

R. SCOTT WILLIAMS, NIEHS

DIANE L. DAMIANO, PH.D., P.T., CC

Senior Investigator and Chief, Functional and Applied Biomechanics Section, Rehabilitation Medicine Department, NIH Clinical Center

Education: Catholic University of America, Washington, D.C. (B.A. in biological sciences); Duke University, Durham, N.C. (M.S. in physical therapy); University of Virginia, Charlottesville, Va. (Ph.D. in biomechanics and research design)

Before coming to NIH: Associate professor of orthopedics on tenure track, University of Virginia; research associate professor of neurology and adjunct professor of physical therapy, Washington University (St. Louis)

Came to NIH: In 2008

Selected professional activities: Past president of the American Academy of Cerebral Palsy and Developmental Medicine; member of editorial boards of *Neurorehabilitation and Neural Repair*, *Developmental Medicine and Child Neurology*, and the *Journal of Pediatric Rehabilitation*

Outside interests: Hiking; jogging; playing tennis; traveling

Website: http://irp.nih.gov/pi/diane-damiano

Research interests: My scientific career path has been somewhat unusual in that I was in my late 30s when I started my Ph.D. and never did a postdoctoral fellowship. Before that, I was a pediatric physical therapist for 12 years and worked with children who had cerebral palsy (CP) and other physical disabilities. The prevailing clinical wisdom at the time (1980s) was that anyone with a brain injury—such as CP or stroke—should not strengthen their muscles because it would increase their spasticity. However, it was obvious to me that these children had poor muscle development and were weak. They seemed to worsen with age because their muscles could not keep up with their increased physical growth.

So for my Ph.D. thesis I decided to challenge the prevailing dogma and conducted a small clinical trial of progressive-resistance weight training in children with CP. It worked. The children all had marked increases in leg strength, and even after a few weeks several were starting to demonstrate improvements in their ability to walk; one child was able to run for the first time (running requires more strength than walking). Because I was one of the first researchers to recognize and quantify that muscles in patients with spasticity were, in fact, weak and needed strengthening, my research attracted a lot of attention in the rehabilitation field. Immediately after the University of Virginia awarded me my Ph.D., they hired me as an assistant professor of orthopedics and as the research director of UVA's Motion Analysis and Motor Performance Laboratory.

Today at NIH, I am continuing my work on the role of physical activity in enhancing motor coordination and promoting muscle and neural recovery in those with brain injuries. We are also pioneering the use of noninvasive mobile brain-imaging technologies such as electroencephalography and near-infrared spectroscopy to compare the brain mechanisms underlying motor coordination in children with CP with those of children who are developing normally.

More recently, my laboratory has been developing and testing novel training devices, such as a powered (either with an external motor or by electrical muscle stimulation) exoskeleton, to improve functional mobility in people with CP. Our short-term goal is to enhance their movement capabilities by providing only a small amount of assistance. Our long-term goal is to exploit the inherent plasticity in the brain and in muscles for more permanent and sustainable functional gains.

If you have been recently tenured, the *NIH Catalyst* will be contacting you soon about including you on these pages. It's a great way for your colleagues to get to know about you and your work.

GUANG HU, PH.D., NIEHS

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

Education: Fudan University, Shanghai, People's Republic of China (B.S. in biochemistry); Baylor College of Medicine, Houston (Ph.D. in biochemistry and molecular biology)

Training: Postdoctoral fellowship at Brigham and Women's Hospital (Boston)

Came to NIH: In 2009

Selected professional activities: NIEHS Epigenomics Core Governance Committee

Outside Interests: Doing photography; reading science-fiction novels; playing table tennis

Website: http://irp.nih.gov/pi/guang-hu

Research interests: We study embryonic stem cells (ESCs), which are cells derived from the inner mass of the blastocyst-stage embryo. ESCs have two defining characteristics: self-renewal and pluripotency. Self-renewal describes ESCs' capability to go through cycles of cell division and maintain the undifferentiated state. Pluripotency describes their capability to differentiate into all cell types found in the adult body. Due to these unique properties, ESCs hold great promises for both basic and translational research. In addition, ESCs may also provide new tools and insights for environmental health sciences.

The long-term goal of our research is to better understand the molecular mechanisms that regulate ESC self-renewal and pluripotency. We have previously carried out a genome-wide genetic screen in mouse ESCs and identified a list of novel regulators of ESC self-renewal. We have since investigated the function of several of the identified factors in ESCs, cell reprogramming, and mouse embryonic development. We found that these factors regulate which genes are turned on in pluripotent cells through transcriptional and post-transcriptional mechanisms.

In future research, we will use a combination of genetic, genomic, and biochemical approaches to continue to investigate ESC self-renewal and pluripotency. By understanding how pluripotent stem cells differentiate into various cell types, we hope to provide new insights into how mammals develop and to advance the field of regenerative medicine. Our findings may also aid the establishment of novel cell-based models for developmental toxicology and environmental-health sciences studies.

YINLING HU, PH.D., NCI-CCR

Senior Investigator and Head, Inflammation and Tumorigenesis Section, Cancer Inflammation Program; National Cancer Institute-Center for Cancer Research

Education: Institute of Epidemiology and Microbiology, Chinese Academy of Medical Sciences, Beijing (B.S. in biology); Peking Union Medical College, Institute of Virology, Beijing (M.S. in medicine); Melbourne University, Ludwig Institute for Cancer Research, Melbourne, Australia (Ph.D. in molecular biology)

Training: Postdoctoral fellow, Peter MacCallum Cancer Institute (Melbourne); postdoctoral fellow in pharmacology, University of California (San Diego)

Before coming to NIH: Assistant professor, University of Texas MD Anderson Cancer Center Science Park (Smithville, Texas)

Came to NIH: In 2008

Selected professional activities: Member of editorial boards for *Journal of Genetic Syndromes* and *Gene Therapy and Journal of Inflammation and Cancer*; training students

Outside interests: Hiking and engaging in other outdoor activities; enjoys playing with her dogs

Website: http://irp.nih.gov/pi/yinling-hu

Research interests: My lab is trying to understand the physiological activities of I-kappa-B kinase alpha (IKK-alpha) in skin, lung, and esophageal tumorigenesis and inflammation and reveal the mechanisms by which IKK-alpha regulates these functions. We use molecular biology approaches and genetic animal models, including *Ikk-alpha* conditional knockout, *Ikk-alpha* kinase inactive knockin, and *Ikk-alpha* transgenic mice.

Decreased expression of IKK-alpha has been reported in a large percentage of human squamous-cell carcinomas (SCC). The Cancer Genome Atlas genomic sequencing data show many mutations and deletions in a high proportion of human skin SCCs and melanomas and in a broad spectrum of other human cancers. In our experiments with mice, we demonstrated that IKK-alpha is a tumor suppressor in these cancers.

We revealed the molecular mechanisms underlying IKK-alpha-mediated pathways in tumorigenesis. We reported that, in the epithelial cells, IKK-alpha induces a cell-cycle arrest and upregulates the expression of a cell-cycle checkpoint protein in response to DNA damage and represses epidermal growth factor receptor activity in a cell-differentiation and proliferation program. Moreover, we have demonstrated that a reduction in IKK-alpha elevates tumor-microenvironmental inflammation.

Recently, we found that IKK-alpha plays a critical role in infection-associated skin and esophageal carcinogenesis. We are trying to figure out how environmental microbiota become pathogenic for human carcinogenesis when the host immune system is impaired. Our goal is to help the prevention, diagnosis, and therapeutic treatment of these human cancers.

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Recently Tenured

CONTINUED FROM PAGE 17

DANIEL S. REICH, M.D., PH.D., NINDS

Senior Investigator and Chief, Translational Neuroradiology Section, National Institute of Neurological Disorders and Stroke

Education: Yale University, New Haven, Conn. (B.S. in mathematics and physics); The Rockefeller University and Weill Medical College of Cornell University, New York (M.D. and Ph.D. in visual neurophysiology)

Training: Residency in neurology/diagnostic radiology/neuroradiology at Johns Hopkins Hospital (Baltimore)

Came to NIH: In 2009

Selected professional activities: Elected member of the American Society for Clinical Investigation; serving as federal liaison to several nonprofit-foundation advisory boards; hosting congressional and cabinet-level visitors to NIH; co-organized a meeting celebrating 40 years of neuroimmunology at NINDS (2015); established the North American Imaging in Multiple Sclerosis cooperative (2012); participated in the NIH Celebration of Science (2012); was awarded the National Multiple Sclerosis Society's Barancik Prize for Innovation in Multiple Sclerosis Research (2016)

Outside interests: Playing chamber music (violin and viola); traveling with his family; running; biking

Website: http://irp.nih.gov/pi/daniel-reich

Research interests: Our lab's major goal is to understand the pathobiology of multiple sclerosis (MS) through the use of advanced magnetic-resonance imaging (MRI) methods and correlative histopathological techniques. We focus on methods that can be translated to patient care and used as outcome measures in clinical trials of new drugs to treat aspects of MS, for which there is currently no therapy, such as demyelination and neurodegeneration.

Over the past few years, we have been interested in the spatiotemporal dynamics of lesion formation and repair in the white matter, which we study using ultra-high-field (7 tesla) MRI both in people with MS and in animals induced to have a disease that very much resembles MS. We have elucidated the timing and conditions required for the failure of early repair of inflammatory demyelination in the brain and have proposed several trial designs to test therapies that might enhance that repair. We are currently focused on ways to detect and treat chronic inflammation in both gray and white matter.

To translate the discoveries made in the lab, we partner with the NINDS Neuroimmunology Clinic, the trans-NIH Nuclear Magnetic Resonance Center, and the Clinical Center Department of Radiology and Imaging Sciences. We also collaborate with other research groups on campus that study diseases involving inflammation of the central nervous system, for which our imaging methods might prove helpful.

R. SCOTT WILLIAMS PH.D., NIEHS

Senior Investigator, Genome Stability Structural Biology Group, Genome Integrity and Structural Biology Laboratory, National Institute of Environmental Health Sciences

Education: University of Calgary, Calgary, Alberta, Canada (B.Sc. in cellular, molecular, and microbial biology); University of Alberta, Edmonton, Alberta, Canada (Ph.D. in biochemistry)

Training: Postdoctoral fellowship at the University of Alberta; postdoctoral fellowship at The Scripps Research Institute (La Jolla, Calif.)

Came to NIH: In 2009

Selected professional activities: Member, American Chemical Society; member, Faculty of 1000 Medicine

Outside Interests: Playing tennis; mountain biking

Website: http://irp.nih.gov/pi/robert-williams

Research Interests: My group and I examine how cells recognize and repair DNA-strand breaks. The failure to resolve damage at DNA ends that occurs in inherited human diseases is linked to accumulation of mutations in our DNA, neurological disease, aging, and cancer. We use a multipronged approach that integrates biochemical, mutational, and structural analyses of proteins and protein-DNA complexes. In particular, molecular-structural studies involving X-ray crystallography form the bedrock of our work. We aim to identify and characterize the cellular DNA-damage recognition, signaling, and reversal processes that act as the first line of defense against chemicals, radiation, and other environmental factors that result in DNA breakage.

Current work in the laboratory is aimed at deciphering the functions of DNA end-processing factors tyrosyl-DNA phosphodiesterase 2 (TDP2), aprataxin (APTX), and CtIP/Ctp1 tumor suppressor. Defects in processes we study destabilize the genome and alter organismal functions and susceptibility to genotoxic stressors. They are also linked to human diseases that progress over a lifespan. For example, *TDP2* mutations are found in individuals who have intellectual disabilities, seizures, and lack of muscle coordination known as ataxia. Deficiencies in APTX cause difficulty in walking and in controlling eye movements seen in ataxia with oculomotor apraxia 1. *CtIP* mutations are linked to Seckel syndrome, a rare disease characterized by extremely short stature, small brain, and other birth defects. We envision that a detailed molecular understanding of genome-repair mechanisms will lead to the development of novel cancer treatments and other DNA-targeted chemotherapeutics. ●

National Academy of Medicine: New NIH Members

Karen Faith Berman, M.D., senior investigator and chief of the Section on Integrative Neuroimaging, the Psychosis and Cognitive Studies Section, and the Clinical and Translational Neuroscience Branch, National Institute of Mental Health. Her group uses neuroimaging to map brain activity and neurochemical mechanisms associated with normal higher-cognitive function as well as dysfunction in neuropsychiatric illnesses such as schizophrenia, illnesses having genetic sources of cognitive dysfunction such as Williams syndrome, and other conditions affecting cognition such as normal aging. She also studies the effects of gonadal steroid hormones on brain function.

Leslie Glenn Biesecker, M.D., chief of the Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute. His laboratory is engaged in studies in two main areas: clinical genomics and rare malformation syndromes, with a focus on disorders of mosaic overgrowth. His group is the first to launch therapeutic trials for Proteus syndrome, a congenital condition characterized by the overgrowth of bones, skin, and other tissues, and often accompanied by tumors.

Antonello Bonci, M.D., scientific director, National Institute on Drug Abuse, and chief, Synaptic Plasticity Section, Cellular Neurobiology Research Branch. His goal is to understand the synaptic properties and plasticity of neurons in brain areas relevant to stress and substance-use disorders. His laboratory was the first to demonstrate that cocaine produces a form of long-term cellular memory called long-term potentiation. His team is also developing novel optogenetic-based treatments against cocaine addiction.

Jake Liang, M.D., chief, Liver Diseases Branch, and deputy director of translational research, National Institute of Diabetes and Digestive and Kidney Diseases. His research focuses on understanding the mechanisms of disease and therapy, and improving treatment and prevention of hepatitis B virus and hepatitis C virus infections and viral hepatitis-associated hepatocellular carcinoma. ●

Artist and Neuroscientist: Bevil Conway, Ph.D.

BY KATHRYN DEMOTT, NEI

KATHRYN DEMOTT, NEI

Bevil Conway's glass and silk-thread sculptures are on semipermanent exhibit at NIH's John Edward Porter Neuroscience Research Center (Building 35). He created the untitled green silk-thread sculpture in 2014.

The Artist: When he is not in the lab, neuroscientist **Bevil Conway** (National Eye Institute) is a professional painter and sculptor who views his work as an artist as inextricably tied to his work as a neuroscientist. "The rules employed by artists have a strong basis in neural hardware," he said. "I am fascinated by how we can use our understanding of the brain in order to understand the choices artists make."

Our visual systems must constantly simplify the world around us because it is impossible for them to communicate everything about the visual world to the brain. As a result, "our visual systems extract what have turned out to be ecologically relevant cues—like edges and contrast—and don't bother with all the other stuff—like gradual changes in illumination or absolute levels of illumination," he said. "Artists learn how to perform an analogous task: to extract and represent what they consider to be relevant pieces of their conceptual and visual worlds."

Many of his works are displayed in private collections in Europe, Africa, and North America and are in the public collection of the Fogg Museum at Harvard University (Cambridge, Massachusetts) and the Boston Public Library, and some are on semipermanent exhibit at NIH's John Edward Porter Neuroscience Research Center (Building 35).

The Scientist

Current position: Investigator and chief of the Unit on Sensation, Cognition and Action Laboratory of Sensorimotor Research, National Eye Institute (jointly affiliated with National Institute of Neurological Disorders and Stroke, National Institute of Mental Health, and National Institute on Drug Abuse)

Education: McGill University, Montreal (B.S. in biology); Harvard Medical School, Boston (M.M.S.); Harvard University, Cambridge, Massachusetts (Ph.D. in neurobiology)

Training: Postdoctoral fellowships at Harvard Medical School and Bremen University (Bremen, Germany); elected a junior fellow in the Harvard Society of Fellows to pursue his combined interest in visual art and visual neuroscience

Before coming to NIH: Associate professor, Neuroscience, Wellesley College (Wellesley, Massachusetts); principal research scientist, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology (Cambridge, Massachusetts)

Came to NIH: In 2016

Interesting activities: After graduate school, he moved to Nepal to help develop the curriculum for a new medical school—the Kathmandu University Medical School

Research interests: Investigates the neural basis for visual perception; uses color perception as a model system for exploring how the brain processes physical stimuli from the retina. He uses functional magnetic-resonance imaging to study humans and macaques to better understand the architecture involved in how brains recognize faces, color, objects, and places. ●

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

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FROM THE ANNALS OF NIH HISTORY

Probing Metabolic Mysteries in the 1950s

FROM THE *NIH RECORD*, SEPTEMBER 9, 1957

COURTESY OF NIH

To penetrate into the deeper mysteries of metabolism, [NIH] scientists…have begun using a [temperature- and humidity-controlled] sealed chamber to collect metabolic and physiologic data related to the energy expenditure of research patients. This "metabolic chamber" makes possible the study of the body's utilization of air, food, and water under a variety of controlled living conditions. The patient…can comfortably remain in the chamber for several days [and] eats and drinks precisely measured amounts of food and liquids. By the use of a plastic hood [shown on the patient volunteer], the composition of the air breathed is controlled, and the expired air, as well as other body wastes, is captured and analyzed. A light, flexible cable, which includes a two-way communication system, is attached to the helmet and transmits minute-to-minute changes in the patterns of metabolism. This information is recorded by complex instruments in another room. While in the chamber, the patient has all the comforts of home except for his confinement to a space of 9 by 13 feet [while] every breath and heartbeat is being recorded and measured electronically. ●

To learn about the current-day Metabolic Clinical Research Unit at NIH, go to bit.ly/2fsDfkg.

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