THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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Brain Injuries

Detecting Them on the Battlefield

BY ALICIA EVANGELISTA, NHLBI

Imagine a handheld scanner that could be used in the battlefield to detect whether an injured soldier has suffered a traumatic brain injury (TBI). NICHD 's senior investigator **Amir Gandjbakhche** and research fellow **Jason Riley** led a team of NIH scientists to perfect an imaging technology that would make such a device possible.

The idea was straightforward: Create a device that could detect a TBI and make it simple enough for any soldier to grab out of a truck and use it in the heat of battle. The device needed to be portable, able to withstand the chaos of the battlefield, and use an imaging technology that could measure bleeding in the brain, an emergency that requires immediate medical attention.

Current imaging technology is sophisticated but limited. Magnetic resonance imaging and computed tomography scanners are large and unwieldy and therefore not very useful in the field. Near-infrared scanners, which use infrared light to detect hematomas, are portable, but the detection device must be held still to get accurate readings. Traditional imaging systems are based on mathematical models in which both the machine's and the patient's locations are fixed, but in the real world, things move, said Riley, a mathematician and engineer and the lead author of the paper that described a prototype hematoma detector (*Biomed Opt Express* **3**:192–205, 2012).

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The Epidemic That Just Won't Quit

NIH Obesity Researchers to the Rescue

BY MATT WENHAM, NIDDK, AND OTHERS

Obesity has become an epidemic in the United States that affects approximately one-third of adults and nearly 17 percent of children and teens. People who are obese are at increased risk for developing many serious health problems including diabetes, fatty liver disease, cardiovascular disease, and a reduced life expectancy. And obesity disproportionately affects racial- and ethnic-minority populations as well as those who are socioeconomically disadvantaged. The high prevalence of obesity is thought to result from the interaction of genetic susceptibility with behaviors and environmental factors that promote increased calorie intake and sedentary lifestyles. NIH funds and does research on all aspects of obesity. Here, we share highlights of a few of the NIH intramural researchers who are tackling the epidemic.

GUSTOIMAGES/PHOTO RESEARCHERS, INC

Obese woman, colored magnetic resonance imaging (MRI) scan. This coronal scan, vertically through the body, has revealed the internal organs and tissues, including the bones, muscles, and layers of fat. The brain is seen in the head, and in the torso the intestines, liver, heart and lungs are seen. Here, the liver (triangular, upper left) is enlarged and the lungs are compressed in comparison to the organs of a woman who is not overweight (not shown). The extra body weight present in obese patients puts a strain on the heart and lungs.

NIDDK Experts Tackle Obesity

BY MATT WENHAM, NIDDK

The National Institute of Diabetes and Digestive and Kidney Diseases, as its name implies, is front and center in the battle against obesity, given it is a major cause of diabetes, digestive, and kidney diseases. NIDDK's obesity researchers include Kevin Hall, Monica Skarulis, Kong Chen, William Knowler, Leslie Baier, and many others.

Kevin Hall, for one, never expected his Ph.D. in physics and his expertise in mathematics modeling would lead to a career as an obesity researcher. He went from studying nonlinear dynamics in graduate school to building computer models of type 2 diabetes at

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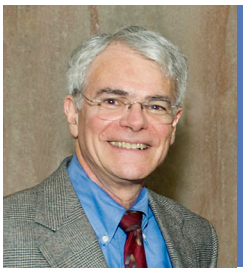


Recognizing Our Senior Faculty

BY MICHAEL GOTTESMAN, DDIR

Many of NIH's senior scientists and scientific support staff have spent most, if not all, of their careers in the intramural research program. Scientists who have received NIH support during the most productive phases of their careers often feel a strong obligation to contribute to the general welfare of this unique organization. NIH, in turn, makes every effort to recognize the lifetime contributions of senior faculty. We may hold symposia to honor the scientific contributions of our most outstanding scientists; grant emeritus status to senior investigators who retire but wish to continue a productive relationship with the NIH; or present individual awards that recognize specific contributions.

I am struck by our senior faculty's impact on the conduct of science, the mentoring of a new generation of scientists, the management of scientific programs, and their important advisory function. I would like to provide some examples, by no means exclusive, of the enormous role that our senior faculty plays in making the NIH a jewel in the crown of the federal government and to suggest that more recognition of contributions by all dedicated scientific staff would be well-deserved.

Ruth Kirschstein, who died in October 2009 at 83, was a luminary in the field of polio vaccine development and oversight of vaccine production. She was the first woman director of an NIH institute (NIGMS), an NIH deputy director, and acting director of the NIH on two occasions. She was a mentor to many NIH scientists and science administrators, a trusted senior advisor to many NIH directors, and one of the most dedicated public servants in the federal government. To learn more about her amazing contributions, you can download a free copy of *Always There: The Remarkable Life of Ruth Lillian Kirschstein, M.D.*, by Alison F. Davis at http://www.nih.gov/about/kirschstein/index.htm (see article on facing page).

I would also like to single out **Henry Metzger**, a renowned expert on the biology and biochemistry of immunoglobulin E (an antibody that causes acute allergic reactions) and former scientific director of NIAMS. He has been a scientist emeritus and senior advisor to the Board of Scientific Directors for several years. Dr. Metzger continues to play an active role as a senior advisor and chair of NIH's Dual Use Committee. In his advice and deliberations, Dr. Metzger provides insight, wisdom, a vast store of knowledge, and common sense to help NIH tackle very difficult issues that may have a profound effect on the conduct of science here.

Another exemplary NIH citizen is neuroscientist **Richard Nakamura**, former deputy director and scientific director of NIMH and now the acting director of the Center for Scientific Review. Dr. Nakamura never shied away from taking on the most difficult problems and always suggested solutions that were both humane and practical. We are grateful for his continuing service to the NIH and for being a trusted advisor to the intramural program.

Finally, I would like to mention **Paul Plotz**, an internationally recognized rheumatologist and expert on myositis (a rare autoimmune disease that destroys muscles). He has served NIH in many capacities including the establishment of the "Great Teachers" series in the Clinical Center. Dr. Plotz has been an acting deputy director in NIAMS, a senior advisor to my office, and a mentor to many at NIH. Even after his recent retirement and appointment as scientist emeritus, Dr. Plotz has returned to take on some clinical responsibilities in NIAMS.

Obviously, there are many, many more people at NIH who could be mentioned here. I hope this essay will encourage you to say "Thank you" to our senior faculty who have contributed so much to NIH over their years as active scientists and administrators, some of whom continue to make contributions even after their formal retirement.

It is also obvious that there are many senior scientific staff—staff scientists and clinicians, research technicians, and other support personnel in our labs—who go out of their way every day to make NIH a better place in which to work. Some of these support staff may be considering retirement in the near future. The scientific directors have endorsed a program that allows emeritus status for people other than senior investigators, with the possibility of continued involvement at NIH in an advisory and/or mentoring capacity and with access to NIH e-mail and library facilities. Such a program goes a small way toward the recognition due many of our dedicated workforce. ●

Our Strength Is in Cultural Diversity

BY THE EDITORS

Here at the "United Nations" of the NIH, we have scientists representing approximately 100 countries, from Albania to Zimbabwe. More than 3,000 of our scientists are visiting from, or were born in, a so-called "foreign" country—an odd term given the collegiality we cherish and expect at NIH.

Countries with the highest representation here include China, India, Japan, and South Korea. Such diversity in cultural background and scientific training is crucial to our mission to conduct high-impact laboratory, clinical, and population-based research and to facilitate new approaches to improve health though prevention, diagnosis, and treatment. In short, success in biomedical and behavioral research depends on a culturally diverse workplace. The contributions of diverse backgrounds to generating new and varied ideas is why the NIH is committed to preserving, strengthening, and celebrating cultural and ethnic diversity and why it strives to protect this diversity from any sexual, racial, or ethnic prejudice.

Mind you, featuring scientists from 100 countries in a newsletter that comes out bimonthly could take some time. Nevertheless, in forthcoming issues, *The NIH Catalyst* plans to highlight some of the stellar international elements of the intramural program. ●

New Face for NIH Clinical Trials

BY MICHAEL GOTTESMAN

I get a mix of feelings when I see non-NIHers whom I know in the NIH Clinical Center. Sometimes they are here for a serious reason: Either they or someone they know is sick and participating in a research protocol. I'm happy, of course, that they have an opportunity to come to one of the best places in the world. I'm not happy that they need our care.

Not every visitor to the Clinical Center, however, is deathly ill. The vast majority come as healthy individuals or with a manageable disease or disorder, volunteering their time—and a few bodily fluids along the way—in the name of clinical research. Actually, these volunteers represent the NIH Clinical Center's bread and butter. We have about 1,500 active clinical trials, and most of these would fall apart without a steady stream of volunteers.

This is why I'm pleased to help announce a new Web site for NIH clinical trials at http://clinicalresearchtrials.nih.gov. This is a bright, friendly site filled with faces of volunteers, meant to help attract more people to the NIH Clinical Center. It is filled with personal volunteer stories and researcher stories, and serves as a gateway to our Bethesda-based trials and the national clinical trials site at http://Clinicaltrials.gov.

Now, most of you have "volunteered" your career to support the Clinical Center in some way, either as a member of the Clinical Center staff or as part of a research team providing scientific insights that someday may lead to cures and treatments. Nevertheless, do remember that you can volunteer more directly in as many trials as you like, from asthma to Zollinger–Ellison syndrome. Many need healthy individuals.

Thanks must go to the NIH Office of Communications and Public Liaison and the trans-NIH team that put this site together. ●

Ruth Kirschstein Featured in E-Biography

BY HEATHER DOLAN

BILL BRANSON

Always There: The Remarkable Life of Ruth Lillian Kirschstein, M.D., by Alison F. Davis tells the story of a rare woman who was a medical scientist, classical pianist, physician, art lover, humanitarian, and research administrator. Kirschstein, who died in October 2009 at the age of 83, dedicated her career at NIH to public health.

As a researcher, she led the development of safety tests for the vaccines for polio, measles, and rubella. While serving as the first female director of an NIH institute (NIGMS), she launched a structural biology program that contributed significantly to the development of human immunodeficiency virus antiretroviral drugs. She was also acting director of NIH twice (in 1993 and from 2000 to 2002) and deputy director for six years. The biography commemorates her life, personally and professionally, and the many roles she served as wife, mother, scientist, administrator, advisor, and mentor.

The biography is available for download, free, in several digital formats, including for Kindle, Nook, and iPad at http://www.nih.gov/about/kirschstein/index.htm.

To hear a NIH Radio podcast interview with author Davis, go to http://www.nih.gov/news/radio/podcast/2012/archiveindex.htm and click on episode 1053 (February 24, 2012).

FROM THE FELLOWS COMMITTEE

LGBT Fellows and Friends

BY ANDREW BROADBENT, NIAID

January marked not only the beginning of a new year, but also the birth of a new group: NIH LGBT Fellows and Friends.

LGBT stands for lesbian, gay, bisexual, and transgender. The organizers Julien Senac (NHGRI) and Christiane Kuschal (NCI) say this new group "aims to make LGBT [people] at NIH more visible by giving seminars on issues of interest to LGBT individuals and by having social and networking events." In addition, they point out that the group is open to anyone, and every event is all-inclusive, whether or not individuals identify as LGBT.

The group certainly is in line with the value NIH places on diversity. The first meeting took the form of a seminar and discussion in which the NIH LGBT Research Coordinating Committee co-chairs, Elizabeth Wehr (NICHD) and Meredith D. Temple-O'Connor (OD), presented an overview of the Institute of Medicine report on LGBT health.

Personally, I didn't even know there was any NIH LGBT research that would require a committee to coordinate it, so I learned something new right away. I was also pleasantly surprised to see that not only was there a decent turnout for the meeting, but that there were also all kinds of people there—people of various ages, ethnicities, and sexes, and from all walks of NIH life.

To find out about upcoming seminars, professional development activities, networking opportunities, and other LGBT events, join the NIH LGBT Fellows and Friends LISTSERV at http://list.nih.gov/cgi-bin/wa.exe?A0=NIH-LGBT-FF. ●

FROM THE OFFICE OF INTRAMURAL TRAINING AND EDUCATION

New Spoken English Course for Non-native Speakers

BY JULIE GOLD, OITE

"He asked me a question after my talk. I knew the answer, but I just couldn't explain it."

"I am so embarrassed in my lab. I have a lot of data, but no one knows I'm doing anything because I don't feel comfortable talking about it."

Understanding that some international trainees face these and other English-language challenges, OITE has for several years been offering programs geared toward helping non-native English-speaking scientists to feel more comfortable at work and in their social circles. Recently, OITE began exploring even better ways to help non-native speakers perfect their English.

In the summer of 2010, OITE connected with Mike Long, a professor of second-language acquisition at the University of Maryland (College Park, Md.). His team performed a needs analysis that identified trainees' most serious language difficulties: The greatest challenges arise during nonscripted scientific discussions, such as after presentations and during lab meetings.

In the fall of 2011, OITE piloted a new series of English classes designed to help international students improve their oral and listening fluency, particularly in areas related to their research. According to the program evaluations, both from those who completed the classes and those who dropped out, many students learned a great deal and became more proficient in English. Those who did not complete the class cited lack of time and scheduling challenges as the main problems.

To address the time issue, OITE will pilot a shorter, two-day course in March 2012. The course aims to increase trainees' comfort with English and help them understand how to continue practicing the language. In addition, within the next few months, OITE plans to dedicate a section of its Web site to English language learning. The site will feature helpful resources including "TalkShare," a LISTSERV aimed at helping NIH community members find language partners to practice with. To sign up for the TalkShare LISTSERV, go to https://list.nih.gov/cgi-bin/wa.exe?A0=oite-talkshare.

Moving to a foreign country to live and work, especially when one doesn't feel comfortable with the language, can be scary. OITE staff hopes that its resources will help trainees become more confident and successful in their labs and beyond. For more information and to sign up for a course, visit the OITE Web site at https://www.training.nih.gov. For questions, contact Julie Gold at goldje@mail.nih.gov. ●

Fluorescing Blobs Reveal Molecules

BY BELLE WARING

Seeing a lone molecule up close and personal just got faster and easier thanks to a new technique developed by scientists at NIDCD and NICHD.

"It's very practical and very accessible," said **Bechara Kachar**, head of the NIDCD Laboratory of Cell Structure and Dynamics and senior author on a study of the technique. "It doesn't require further technical development, and the software is freely available. We hope that more researchers will take advantage of it." (*Proc Natl Acad Sci USA* **108:**21081–21086, 2011)

Even the most powerful light microscopes have limitations, and so to discern very tiny structures, scientists label them with "probes." The fluorophore, a probe that absorbs and gives off light, works like a pedestrian wearing a reflective safety vest at night. If you see the vest, you can bet there's a person underneath. If you see the fluorophore, you can safely assume a molecule is occupying the same spot.

Over time, as fluorophores emit light, they blink and bleach (lose color) like fireworks fading in the night sky. Kachar's team wondered whether measuring these changes could help track individual molecules.

"Fluorescence images often look like blobs, since molecules overlap one another," said the paper's first author **Dylan T. Burnette** (NICHD).

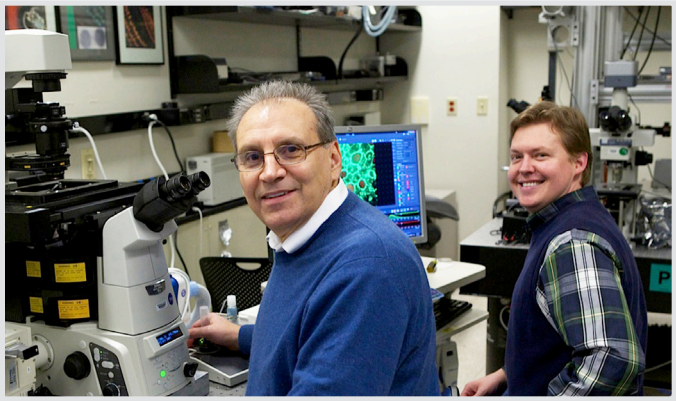
So they made a technical and conceptual leap. First, they videorecorded a sequence of images in real time. Then, using copyright-free software (ImageJ: http://rsbweb.nih.gov/ij/) developed at NIH, they digitally subtracted from each image the subsequent image overlapping it. This process left the earlier image intact and let them see precisely where each molecule had been.

"If you take a photograph of the foliage of a tree in the summer, you cannot clearly visualize each leaf, although you know they are there," said Kachar. "However, in autumn, when the leaves start falling individually, we can pinpoint the location of each leaf as it falls."

Once they had detected each "fallen" or bleached molecule, they could calculate precisely its original location coordinates to make a comprehensive molecule map within a cellular structure.

"Bleaching-blinking-assisted localization microscopy, or BaLM, is a relatively simple and accessible new technique," said Kachar. "Molecular information can now be attained where before there were only fluorescing blobs."

This technique may help find the molecular hallmarks of diseases. "We always knew that all the data [were] there," said Kachar. "We just had to reveal it." ●



URI MANOR, NICHD

Bechara Kachar, M.D. (left), head of the NIDCD Laboratory of Cell Structure and Dynamics and senior author on the study about a new imaging technique, with first author Dylan T. Burnette, Ph.D., an NIGMS Pharmacology Research Associate (PRAT) Fellow working in the laboratory of Jennifer Lippincott-Schwartz (NICHD).

Imaging at NIH

The NIH has pioneered many microscopic imaging techniques, such as the real-time picture processor, among the first computer hardware systems designed for imaging in the 1960s. Below are new techniques NIH researchers and colleagues at Howard Hughes Medical Institute's Janelia Farm Research Campus (Ashburn, Va.) are developing.

PALM: Photo-activated localization microscopy entails controlled activation of single, tagged molecules for composite images, providing resolution at about 20 nanometers; invented by H. Hess and E. Betzig, now at Janelia Farm, and further developed by J. Lippincott-Schwartz (NICHD) and others.

PALM applications: Two-color PALM, spt-PALM (single-particle tracking), iPALM (interferometric), and three-dimensional PALM have qualities beneficial for imaging certain cell types and depths; developed by NIH and HHMI.

iSPIM: The "i" is for "inverted," a spin on SPIM, single-plane illumination microscopy, used for noninvasive imaging of living samples, such as *Caenorhabditis elegans*; see Y. Wu (NIBIB) et al. (*Proc Natl Acad Sci USA* **108**:17708–17713, 2011)

MSIM: A multifocal pattern added to basic structured illumination microscopy probes to a depth of about 50 micrometers.

TED: Total-emission detection maximizes the probability of collecting scattered and ballistic light to optimize signal-to-noise ratio about 10-fold; a spinoff is epiTED for live in vivo imaging.

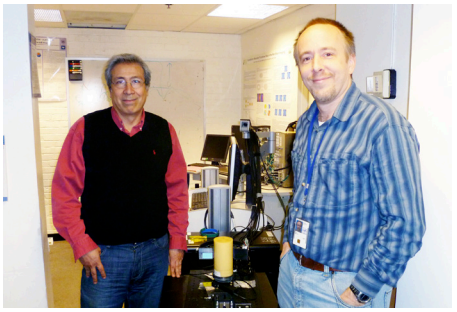
SPECIAL THANKS TO CATHERINE GALBRAITH (NICHD) AND HARI SHROFF (NIBIB) FOR HELPING TO COMPILE THIS LIST.

Brain Injuries

CONTINUED FROM PAGE 1

Researchers at NIH's Center for Neuroscience and Regenerative Medicine (CNRM), NINDS, NIBIB, CIT, and NICHD collaborated on a solution and figured out how to develop a motion-based sensor. The device employs a mathematical model that uses motion as a signal for detecting changes in blood volume in the head. Riley compared the technology to a global positioning system and the remote controls of gaming systems that track user motion. Inside the prototype, three motion lasers "talk" to one another, referencing their location in space compared with the other two sensors, thus tracking the movement of the device itself. Meanwhile, the device images the brain by using near-infrared light to penetrate the skull and characterizes the amount of blood pooling by measuring the changing light absorbance.

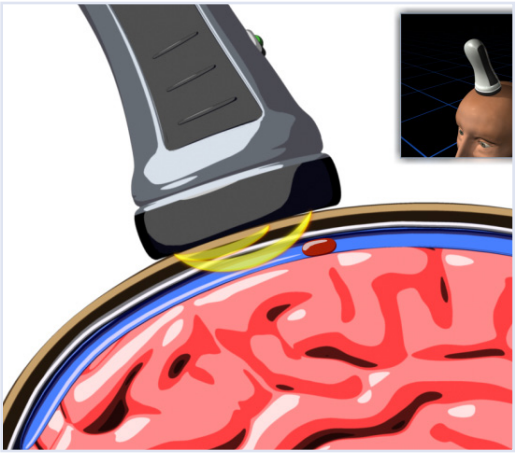
An existing handheld device called the InfraScanner—developed by the Office of Naval Research, approved recently by the Food and Drug Administration, and used in Europe—requires the user and patient to remain motionless. But the NIH device, a cross between a Star Trek tricorder and an electric razor, could move over the skull and use a motion signal to monitor light absorbance, pinpointing where the absorbance changes and identifying locations of pooled blood. In tests using optical phantoms (small objects mimicking the material properties of the skull), the prototype was able to successfully identify deposits of India ink that simulated hematomas.



ALICIA EVANGELISTA, NHLBI

Amir Gandjbakhche (left) and Jason Riley (right) invented a portable device that might one day be used to detect traumatic brain injuries at accident scenes or on the battlefield.

Riley and Gandjbakhche have submitted a proposal to the NIH Bench-to-Bedside program to build a prototype that will be tested at Suburban Hospital (Bethesda, Md.). It could take five years before this low-cost device is ready for the battlefield. The researchers also envision a variety of other uses: in hospital emergency rooms for diagnosing hematomas quickly and effectively; in developing nations, where expensive diagnostic equipment is not available; and as a wireless device that would allow a user in a remote location to send brain images for assessment at a hospital far away. ●



TIM MZOREK, NICHD

This prototype handheld near-infrared imaging device can be used at the scene of accidents to quickly detect traumatic brain injuries such as hematomas. To watch a video of the device in action, go to http://www.osa.org/About_Osa/Newsroom/News_Releases/Releases/12.2011/Monthly-Tip-Sheet-December-2011.aspx.

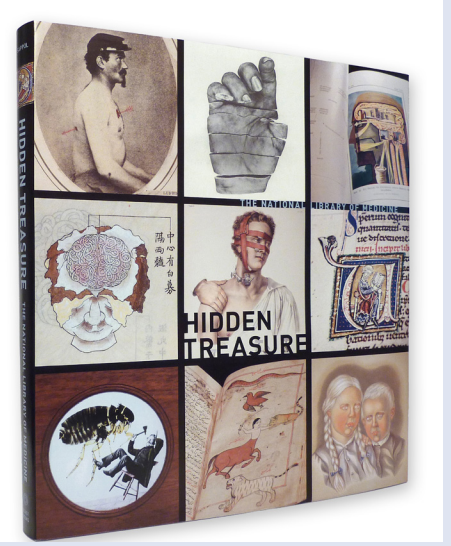
In addition to Gandjbakhche and Riley (NICHD), the collaborators on this project include Eric Wassermann (NINDS), Paul Smith (NIBIB), Tom Pohida (CIT), and James Smirniotopoulos (CNRM, a collaborative of NIH and the Department of Defense to address TBI.) For more information on CNRM, visit http://www.usuhs.mil/cnrm.

Hidden Treasures at NLM

BY HEATHER DOLAN

NIH's National Library of Medicine (NLM) has compiled a remarkably illustrated book edited by Michael Sappol, *Hidden Treasure*, which features rare, beautiful, idiosyncratic, and surprising works in the collection of the world's largest medical library. NLM selected extraordinary pieces largely unseen by the public from more than 17 million items dating from the eleventh century to the present. Each photograph of an object is accompanied by a brief, explanatory essay.

Among the treasures featured are charming hand-painted glass "magic lantern slides," which doctors used to entertain and help cure inmates at St. Elizabeth's Hospital for the Insane (in the 1800s in Washington, D.C.), to surreal views of mechanically sliced cadavers in the photographic anatomical atlas of France's notorious surgeon Eugène-Louis Doyen. Overall, the book encompasses a staggering variety of objects from around the world and seven centuries. The official publication date is in April, but you can place orders through all major online booksellers now.



Two Drosophila Interest Groups

BY KRISTINA MCLINDEN, NINDS

For nearly a decade, the **Drosophila Neurobiology Interest Group** (DNIG) has been serving as a forum and a community for Drosophilists and neuroscientists alike. DNIG—one of the many legacies left by NIMH senior investigator Howard Nash, who passed away in 2011—brings together scientists of different backgrounds to discuss issues related to Drosophila research. The core of this group is the Drosophila Neurobiology Colloquium (DNC), which meets biweekly and features high-quality talks given by NIH scientists and invited speakers. Research using fruit flies is relevant to many models of human health, as over 77 percent of human disease genes are conserved. And powerful genetic tools set Drosophila apart as a model system. DNC talks highlight Drosophila-specific and other genetic techniques. Colloquia are every other Friday at noon in building 40, room 1201/1203. To join the LISTSERV or find a meeting schedule, visit http://sigs.nih.gov/DNIG/Pages/default.aspx or contact Mihaela Serpe at serpemih@mail.nih.gov.

The general **Drosophila Interest Group** promotes convivial discussion for Drosophila enthusiasts of all backgrounds, interests, and disciplines. This group meets periodically and is open to all members of NIH as well as to scientists from local universities and research institutes. The LISTSERV provides an open community that discusses new findings, resolves research questions, and explores ideas. To join, go to http://sigs.nih.gov/drosophila/Pages/default.aspx. If you are interested in presenting your research or would like more information, contact the group leader, Jim Kennison, at kennisoj@dir6.nichd.nih.gov.

New Geroscience Interest Group

BY BARBARA CIRE, NIA

"Aging underlies everything. If we can understand what's happening in the aging cell, we will have a key to treating a host of chronic diseases that come with growing older."

So says Felipe Sierra, director of NIA's Division of Aging Biology and a moving force behind the new trans-NIH Geroscience Interest Group (GSIG). The goal of the group is to stimulate interest and involvement in the basic science of aging, and it has been launched with the blessing of several institute directors.

The group is sponsoring a seminar on Thursday, March 8: "Targeting Aging to Delay Multiple Chronic Diseases: A New Frontier," Masur Auditorium (Building 10), 11:30 a.m. to 12:30 p.m. Dr. James L. Kirkland, director of the Robert and Arlene Kogod Center on Aging at the Mayo Clinic (Rochester, Minn.), will discuss cell senescence and other aging topics and expand on his recent *Nature* article, which described a causal relationship between senescent cells and age-related diseases. Other activities planned for later this year include two more seminars and a workshop on inflammation and age-related diseases. The GSIG also sponsors a journal club that meets monthly.

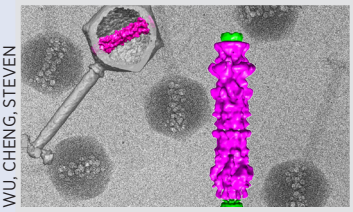
This research transcends institutes, says Sierra, and may be of broad interest to researchers in many areas. For more information about the GSIG, contact Sierra at sierraf@nia.nih.gov. Look for more information coming soon to http://sigs.nih.gov/geroscience. Join the Geroscience LISTSERV at https://list.nih.gov/cgi-bin/wa.exe?SUBED1=geroscience-l&A=1.

For a complete SIG list, go to http://www.nih.gov/sigs

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
DOE: Department of Energy
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
FDA: Food and Drug Administration
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCCAM: National Center for Complementary and Alternative Medicine
NCBI: National Center for Biotechnology Information
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

Research Briefs



WU, CHENG, STEVEN

Bubblegram imaging allows three-dimensional reconstructions of cryo-electron micrographs of viruses; (left) the virus's outer shell, tail, and inner structure; (right) blow-up of the inner viral structure.

NIAMS: "BUBBLEGRAM IMAGING" OF VIRUSES

Cryo-electron microscopy (cryo-EM) can image very small particles, but because of its radiation it doesn't image viruses very well. If the radiation dose is too low, it is not possible to see inside the virus; if it's too high, it damages the organism, destroying the very structures scientists want to see. But NIAMS researchers with colleagues from University of Maryland Medical School (Baltimore) developed a method they call "bubblegram imaging" that turns the problem into a solution.

Using low doses of radiation, they image the outer surface of a virus, and using high doses, they view the inner structure, which appears as "a cylinder of bubbles." They then superimpose low-dose and high-dose radiation images to get a clear visualization of the complete viral structure. Future applications for bubblegram imaging may include visualizing the differences between cancer and noncancer cells. (NIAMS authors: W. Wu, N. Cheng, A.C. Steven; *Science* **335**:182, 2012)

NICHD, NIDCD, NIMH: HIV-EXPOSED CHILDREN AT RISK OF LANGUAGE DELAY

Children exposed to the human immunodeficiency virus (HIV) before birth are at risk for language impairments, according to a study conducted by NIH researchers and collaborators from other institutions. The exposed children were twice as likely to have a language impairment as children in the general population. The 468 children in the study were 7 to 16 years old; 306 were HIV-infected; 162 were exposed to HIV during pregnancy but did not become HIV-infected. The researchers found that 35 percent of the participants had difficulty understanding spoken words and struggled to express themselves verbally. Future studies will determine whether the findings can be attributed to HIV exposure or to other unidentified factors, such as family status, maternal substance use, environment, or social or economic background. (NIH authors: G.K. Siberry, H.J. Hoffman, S.M. Allison; *J Dev Behav Pediatr* **33**:112–123, 2012)

NIAID, NHGRI: RESEARCHERS FIND CAUSE OF RARE IMMUNE DISEASE

NIH researchers and their collaborators have identified a genetic mutation that causes a rare immune disorder called "PLAID" (for PLCG2-associated antibody deficiency and immune dysregulation). The study included 27 people, from three unrelated families, who all suffered from an inherited form of cold urticaria, an allergic disease characterized by the formation of itchy, sometimes painful hives, fainting, and, in certain cases, life-threatening reactions in response to cold temperatures. The mutation causes the enzyme PLCG2 to function without shutting off. Inhibiting PLCG activity could be a therapeutic strategy to treat people with PLAID and other PLCG2-mutation disorders. (NIH authors: M. Ombrello, E.F. Remmers, I. Askentijevich, D.L. Kastner; G. Sun, S. Datta, H. Komarow, G. Cruse, M.-Y. Jung, A.M. Gilfillan, D.D. Metcalfe, C. Nelson, M. O'Brien, L. Wisch, K. Stone, J.D. Milner, A.F. Freeman, S.M. Holland, P. Torabi-Parizi, N. Subramanian, H.S. Kim, E.O. Long, J. Ho, S. Moir, D.C. Douek; *N Engl J Med* **366**:330–338, 2012)

NHLBI: HOW THE RED WINE CHEMICAL RESVERATROL MIGHT WORK

Resveratrol, a chemical found in the skin of red grapes and other plants, may confer health benefits, including prevention of diet-induced obesity, improved glucose tolerance, and increased physical endurance. But it's not clear how it works. NIH researchers and outside colleagues found that resveratrol inhibits phosphodiesterase (PDE) proteins, enzymes that help to regulate cell energy. Previous studies suggested that resveratrol directly activates sirtuin 1, a protein associated with aging. The researchers traced the metabolic activity in cells treated with resveratrol and identified PDE4, not sirtuin 1, as the primary target for the benefits of resveratrol. When PDE4 is inhibited by resveratrol, it triggers a series of events, one of which indirectly activates sirtuin 1. Further studies are needed to determine all of resveratrol's protein interactions. (NHLBI authors: S.-J. Park, F. Ahmad, A.L. Brown, M.K. Kim, M.A. Beaven, V. Manganiello, J.H. Chung; *Cell* **148**:421–433, 2012)

NIMH, NIDA: TRACKING DNA METHYLATION SHEDS LIGHT ON BRAIN DISORDERS

For the first time, scientists have tracked the activity, across the lifespan, of an environmentally responsive regulatory mechanism that turns genes on and off in the prefrontal cortex (PFC). NIH researchers and others tracked DNA methylation, which is known to affect gene activity and is influenced by environmental factors. Using postmortem brains of non–psychiatrically impaired individuals ages two weeks to 80 years old, the researchers examined methylation at 27,000 sites within PFC genes. Genes implicated in schizophrenia and autism DNA methylation abruptly switched from off to on during the critical transition from fetal to postnatal life.

The investigators suggest brain disorders may be traceable to altered methylation of genes early in life and observed that the overall amount of PFC methylation is low prenatally, when gene expression is highest, but increases as gene expression plummets in early childhood. It then levels off as we grow older. (NIH Authors: S. Numata, T. Ye, T.M. Hyde, X. Guitart-Navarro, R. Tao, M. Wininger, C. Colantuoni, D. Weinberger, J. Kleinman, B. Lipska; *Amer J Hum Genet* **90**:260–272, 2012) ●

From "Paper of the Week" to "Breast Cancer Treatment of the Year"?

How a Calcium-binding Protein Activates an Estrogen Receptor

BY HEATHER DOLAN

David B. Sacks is a celebrity . . . in the chemistry world, that is. One of his studies has been designated "Paper of the Week" in the March 16 issue of *Journal of Biological Chemistry*. Each year, only 50 to 100 papers are selected for this honor out of more than 6,600 published.

Sacks, along with research fellow **Zhigang Li** and University of California at Davis colleagues James B. Ames and Yonghong Zhang, are being recognized for their work on how the calcium-binding protein calmodulin (CaM) activates an estrogen receptor (ER) implicated in breast cancer. (*J Biol Chem* **287**:9336-9344, 2012)

About 70 percent of breast cancers depend on ERs for growth. The researchers described how the structure of CaM induces ER-alpha dimerization, the linkage of two molecules to form a single molecule, and prevents ER-alpha degradation.

These activities make CaM "unique among the known structures of calmodulin target complexes," said Sacks, who is chief of the NIH Clinical Center's Chemistry Service. Still, he was surprised that the study was highlighted in the journal. "I've previously published 35 papers in *JBC* and this is the first that was awarded 'Paper of the Week.'"

Prior work done by Sacks's group and others demonstrated that CaM inhibition reduces the growth of human breast-cancer cells. Sacks's findings suggest that CaM is an important component of ER-signaling pathways, and that the molecular interaction between CaM and ER has the potential to be a therapeutic target for treating breast-cancer patients.

Although Sacks is pleased with the *Journal of Biological Chemistry* recognition, he knows there's a lot of work ahead. "We continue to work on this exciting area of research," he said, "and hope to generate further understanding of ER function." ●

Our First AAAS Webinar

All Eyes on the NIH

BY CHRISTOPHER WANJEK

The NIH intramural research program hosted its first *Science*/American Association for the Advancement of Science (AAAS) Webinar on February 29, entitled "Applying New Imaging Techniques to Your Research: Advice from the Experts." This featured **Hari Shroff** (NIBIB), **Sriram Subramaniam** (NCI), and **Clare Waterman** (NHLBI).

The pre-event buzz was promising—nearly 2,400 researchers worldwide registered to participate, the largest number for any *Science*/AAAS Webinar—and, indeed, close to that many did watch, while hundreds more may view the archive.

The committee for promoting the IRP, the same group that has created the Web site at http://irp.nih.gov, had a pointed goal for producing this Webinar: to highlight homegrown NIH research, what we call intramural . . . and, hopefully, what the world will now understand as "intramural." In short,

Sriram Subramaniam (NCI) was one of three NIH scientists featured in a recent AAAS/Science webinar.

this event was as much a recruitment and publicity tool as it was an excellent training opportunity for scientists.

We have an identity crisis, as you know, with many scientists viewing the NIH primarily as a grant-allocating organization. The term "intramural," to the outsider, doesn't drive home the fact that we have approximately 8,000 scientists and a hospital devoted to clinical research. Anyone watching the February 29 Webinar, though, archived for free viewing at http://Webinar.sciencemag.org/Webinar/archive/applying-new-imaging-techniques-your-research, will clearly understand that Shroff, Subramaniam, and Waterman are leading experts working in NIH labs and loving it.

In these cash-strapped times, such alternate forms of publicity may prove to be a solid investment. For the price of a couple of full-page *Science* ads, we placed ourselves in front of a key target audience. Our three speakers—whether they were ready or not—have since been contacted by a range of researchers and potential collaborators with impassioned questions.

Funding permitting, the committee hopes to produce a few Webinars per year. We have many ideas for topics and we welcome your suggestions, too. Write to us at IRPinfo@mail.nih.gov. ●

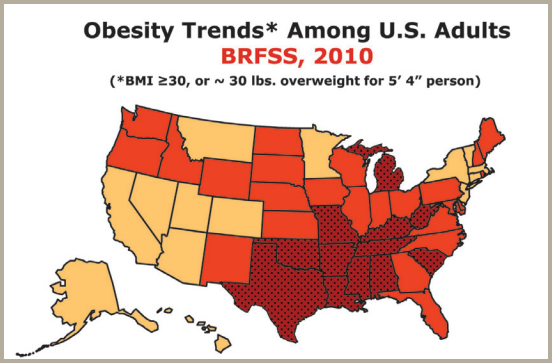
Special thanks to NIH Events Management for providing support to *Science*/AAAS.

a biotech company to constructing mathematical models of metabolism at NIDDK. Today, Hall is seeking to understand how changes in diet and exercise change the way a person metabolizes food. His findings may contribute to new approaches for tackling obesity.

Hall's group of computer-modeling experts works with clinical investigators to study one of the enduring questions in obesity research: Are all calories equal whether they come from carbohydrate, fat, or protein? Their study systematically addresses whether altering overall calorie intake, and the proportions of carbohydrates and fats, can change the way a body processes food. The researchers build complex models, based on previous research, to predict the outcome of dietary modifications. Then they collaborate with clinicians in NIDDK's Metabolic Clinical Research Unit (MCRU) in the NIH Clinical Center to test their predictions on normal weight and obese volunteers.

Results thus far have shown that reducing the proportion of fat in the diet has little effect on the rate of fat metabolism, whereas reducing carbohydrate intake leads to increased fat burning. (For more details on this research, see *Lancet* **378**: 826-847, 2011, featured in the "Research Briefs" section of the September-October 2011 *NIH Catalyst*). Hall is also collaborating with NIMH investigators to study the effect of dietary changes on brain chemistry.

The MCRU facility, led by clinical director **Monica Skarulis** and clinical investigator **Kong Chen**, features three state-of-the-art metabolic suites that are specially designed to accommodate morbidly obese people. Study subjects can be sealed inside the rooms for up to 24 hours, and their metabolic rates can be monitored by measuring oxygen consumption and carbon dioxide production. Room temperature and food intake can be altered and the effect on patient metabolism determined.



SOURCE: BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM CDC

LEFT More than one third of adults in the U.S. are obese (with a body mass index of 30 or greater). For an animated map showing obesity prevalence from 1985 through 2010, go to http://www.cdc.gov/obesity/data/trends.html.

20%–24% 25%–29% ≥30%

Meanwhile, more than 2,000 miles from Bethesda, researchers at NIDDK's Phoenix Epidemiology and Clinical Research Branch are also tackling obesity. **William Knowler** leads two longitudinal clinical trials to determine whether long-term intentional weight loss can help prevent or control type 2 diabetes. The notion that weight loss is beneficial for obese people with diabetes is an accepted "fact," according to Knowler. But, until now, there have been no long-term studies to validate that weight loss prevents diabetes and its resulting complications such as cardiovascular disease and reduced life expectancy. Although the studies will continue through 2014, preliminary analyses have shown that long-term weight loss is possible for diabetic patients, and those at risk for developing diabetes can reduce that risk by 58 percent if they lose weight.

Leslie Baier, Knowler's colleague in Phoenix, is trying to identify and characterize susceptibility genes for type 2 diabetes and obesity in Pima Indians. Pima Indians have the highest reported prevalence of type 2 diabetes of any population in the world, and many are obese. Baier uses molecular genetic approaches to look in the Pima population at genes already associated with obesity or diabetes in Caucasians, and she is conducting genome-wide searches for new genes associated with obesity and diabetes. She hopes what she learns will help clinicians identify people at risk for these diseases and provide more effective interventions.

With increasing numbers of Americans becoming overweight or obese and the incidence of these conditions also rising worldwide, the obesity research program at NIDDK is helping to shed light on the complex factors involved in this multifaceted disease. The unique facilities at NIH and the diverse nature of the intramural program are allowing investigators to study the problem from multiple angles. A physics degree may not seem a likely weapon in this fight, but NIH is hitting obesity with everything it's got.

Fat Cells Regulate Metabolism

BY KATHERINE BRICCENO, NINDS

HAIMING CAO MAY BE NEW TO NIH—he came to NHLBI in 2011 as a tenure-track investigator—but he's no stranger to fat. During his postdoctoral training, he studied the metabolomics of fat and found that palmitoleate, a hormone naturally produced by fat, enhances insulin action and reduces lipid accumulation in the liver. Palmitoleate may protect against diabetes and weight gain.

At NIH, Cao is identifying other fat- and liver-secreted proteins that signal the metabolic state of tissues. He is using proteomics, the study of the entire complement of proteins produced by an organism, to screen potential signaling proteins. So far, his laboratory has identified more than 200 targets. Next, he plans to measure concentrations of target proteins in obese mice under different feeding conditions.

Corresponding changes in the concentration of a target protein could indicate that it modulates the metabolic response of the obese mice. If any of the new target proteins show a metabolic effect, Cao would work with clinical collaborators to measure concentrations of those proteins in serum samples from obese patients.

RIGHT Kevin Hall participated in a press conference in conjunction with the Lancet series on obesity last summer. (Far right) Clinical Center nurse Cynthia Hahn is demonstrating how blood would be taken from a patient who is in one of the metabolic suites. The "patient" is really clinical investigator Francesco Celi who posed for the photo.

GLOBAL HEALTH TV/ELSEVIER

KONG CHEN, NIDDK

Cao would also like to generate a transgenic mouse that expresses the target protein, raise an antibody to that protein, and use it to suppress that protein in mice. Successful treatment of mice could indicate a potential therapy for humans.

Parkinson Disease Protein May Regulate Fat Metabolism

BY KATHERINE BRICCENO, NINDS

One of the NHLBI researchers studying obesity is **Michael Sack**, chief of the Laboratory of Mitochondrial Biology in Cardiometabolic Syndromes. He may have found a surprising connection between Parkinson disease and obesity. He led a team of NHLBI and NINDS scientists that found that Parkin, an important protein linked with some cases of early-onset Parkinson disease, regulates how cells take up and process dietary fats. Laboratory mice with a defective Parkin gene did not display obvious signs of Parkinson disease, nor did they gain weight even when fed a high-fat diet. The researchers saw a similar pattern in humans when they analyzed blood cells from patients enrolled at the NIH Parkinson Clinic. In lab tests, cells from people with the defective gene for Parkin were less able to absorb fat than were cells from people without the defective gene. (*J Clin Invest* **121**:3701–3712, 2011)

Sack is following up this initial finding with an in-depth clinical study. He plans to collect more data from Parkinson patients and matched control subjects to generate a metabolic profile that would include measures of insulin resistance and body fat.

Sack also plans to collect skin biopsies to obtain fibroblasts from Parkinson patients. The fibroblasts will be made into induced-pluripotent stem cells that can be converted into various cell types. Sack hopes to generate fat cells to further characterize their metabolic findings and dopaminergic neurons to study the neurons that are primarily affected in Parkinson disease.

In collaboration with the NIH Regenerative Medicine Center and the NINDS, Sack will use the dopaminergic neurons to investigate the effect of disrupted lipid metabolism on Parkinson susceptibility. The brain requires a relatively large amount of fat for normal function. Cholesterol and lipid species are needed for neurotransmission and membrane integrity. For mitochondria in particular, lipid content is key to proper function. Disruption of these lipids may make mitochondria less able to handle oxidative and free radical stress. Therefore, impaired mitochondria may contribute to the death of dopaminergic neurons that characterizes Parkinson disease.

Cancer Cells Need Fat to Survive

BY JASON STAGNO, NCI

Tumor cells require large amounts of energy, and one of the primary sources of energy resides in adipose (fat) tissue. Perhaps it was only a matter of time until a molecular target for treating cancer emerged with a distinct role in another highly relevant disease: obesity.

Deborah K. Morrison, chief of NCI-CCR's Laboratory of Cell and Developmental Signaling (Frederick, Md.), stumbled upon this discovery a couple of years ago. Her lab focuses on cellular growth mechanisms regulated by the rat sarcoma (Ras) guanine triphosphatase (GTPase) protein and its associated signal transduction pathways, particularly in relation to tumor growth and formation. Energy homeostasis, the body's balancing act of modulating immediate and long-term energy needs, is achieved through a complex system of regulatory cell-signaling pathways. The enzyme 5' adenosine monophosphate (AMP)–activated protein kinase (AMPK) serves as one of several master regulators by stimulating glycolysis and fatty-acid metabolism as well as by aiding in the insulin-dependent cellular uptake of glucose.

In 2009, Morrison and collaborators discovered that the multifunctional molecular scaffolding protein for Ras signaling, kinase suppressor of Ras 2 (KSR2), which is involved in cell growth and differentiation, also interacts with AMPK and is essential for AMPK-dependent regulation of energy metabolism. These findings provided new insight into the roles of these proteins in insulin pathways, demonstrating in mice that the deletion of KSR2 leads to obesity and insulin resistance and that these knockout mice conserve energy and store fat with high efficiency.

Shortly thereafter, Morrison and coworkers identified yet another family of scaffolding proteins, connector enhancers of KSR (CNK), that plays a similar dual role in both kinase signaling cascades and insulin regulation.

These discoveries came as a surprise. "We did not expect that these particular scaffolding proteins for Ras signaling would

CONTINUED ON PAGE 12

Obesity

CONTINUED FROM PAGE 11

be directly involved in these metabolic pathways," said Morrison. "We expected them to be primarily involved in cell proliferation and cell division."

The Morrison lab is also designing agents that can target specific domains of KSR2 and CNK1 scaffolding proteins in order to efficiently and selectively inhibit particular functions. "Targeting these scaffolding proteins can be difficult," said Morrison. "Our goal is to disrupt key protein-protein interactions by targeting specific protein domains without negatively affecting others." Discovering the novel role of certain scaffolding proteins in the regulation of energy metabolism is certainly a major contribution, not only to cancer research, but also to treating obesity.

Multifaceted Research Program

BY MICHELLE BOND, NIDDK

Understanding the relationship between obesity and its related medical complications—diabetes, heart disease, and other illnesses—is the basis of **Jack Yanovski**'s research at NICHD. Yanovski, senior investigator and chief of the Section on Growth and Obesity, has devoted his career to understanding the etiology of obesity. In a letter to the *New England Journal of Medicine*, he noted the need for interventions in early childhood to safely and effectively prevent obesity. He also emphasized the need for treatment to promote and sustain weight loss for obese individuals. (*N Engl J Med* **364**:987-989, 2011).

Yanovski's interest in the causes of childhood obesity began during his pediatric endocrinology fellowship at NICHD in 1989. While studying Cushing syndrome, a hormone disorder caused by high concentrations of cortisol in the blood, he observed that most individuals being evaluated for the syndrome had become obese not as a result of problems with adrenal steroid production but for other, unknown, reasons. This early work foreshadowed his research into other rare syndromes associated with hyperphagia (excessive intake of food) and obesity. Today his research elucidates the endophenotypes (different clusters of genetically based behavioral and/or metabolic signs, systems, and/or traits found together) that contribute to childhood obesity.

He uses a multifaceted approach to reach an understanding of the genetic antecedents of obesity. His work ranges from studies of molecular mechanisms that distribute the signal provided to the brain by leptin, a hormone that plays a key role in appetite and metabolism, to clinical studies that examine pharmacotherapeutic treatment of obese individuals.

Recently, Yanovski and coworkers studied the efficacy of metformin (an oral antidiabetic drug that suppresses liver glucose production) pharmacotherapy along with a dietician-administered weight-reduction program in children believed to be at high risk for developing type 2 diabetes. Metformin had a modest but favorable effect on body weight and composition and improved glucose homeostasis in obese, insulin-resistant children. Yanovski's group also showed that depressive symptoms in children correlate with the progression of insulin resistance. They plan to examine approaches for ameliorating depressive symptoms as a method to improve glucose metabolism.

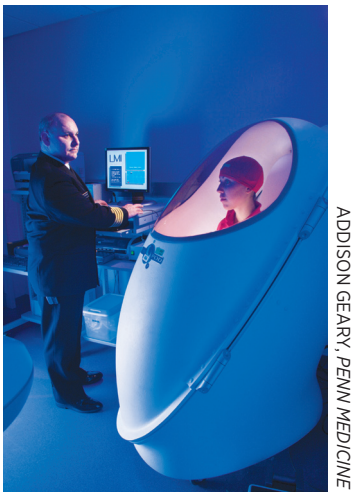
Although Yanovski has made progress in understanding both the genetic and physiological causes of obesity, he emphasizes the need for multidimensional research. We are "never going to be satisfied with what we know today," he said. "We always need to expand what we know . . . to help our patients."

An Epidemiological Approach: Obesity and Aging

BY RACHEL MURPHY, NIA

Two senior investigators in NIA's Laboratory of Epidemiology, Demography, and Biometry (LEDB) have taken an epidemiologic approach to studying relationships between obesity and aging. **Tamara Harris** has organized a multicomponent research program to understand how obesity and obesity-related health conditions contribute to disability and life expectancy in old age. **Lenore Launer**, LEDB's acting chief, is exploring how body weight contributes to outcomes of neurologic disease including dementia and Alzheimer disease.

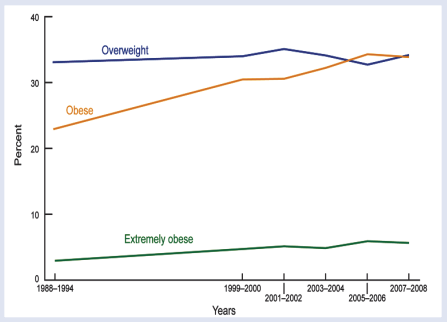
Harris became interested in studying weight in older people because she was intrigued by a paradox: People who are overweight or obese are likely to become disabled in old age; yet often overweight and obese people live longer. She established the Health, Aging, and Body Composition Study (Health ABC), a 14-year study of more than 3,000 older



ADDISON GEARY, *PENN MEDICINE*

As Jack Yanovski monitors the readings, former research associate Laura Wolkoff sits inside the Bod Pod. The machine measures body composition (fat mass and fat-free mass) non-invasively.

TRENDS IN OVERWEIGHT AND OBESITY



CDC

Trends in overweight, obesity, and extreme obesity among adults aged 20 years and older: United States, 1998–2008. Overweight is defined as a body mass index (BMI) of 25 or greater but less than 30; obesity is a BMI of 30 or greater; extreme obesity is a BMI of 40 or greater. (CDC, National Center for Health Statistics)

Americans to examine this paradox. Participants in the Health ABC study had dual-energy X-ray absorptiometry and computed tomography scans to measure muscle and adipose tissue. One of the study's findings was that people who are overweight or obese tend to have more fat in their muscle than lean people. Surprisingly, fat infiltration in muscle was a stronger predictor of disability in old age than was low muscle mass.

In old age, people who have been obese or overweight since earlier in life have more difficulty walking and climbing stairs than do people who gained weight only in old age, according to Harris. She and Launer established the Age, Gene/Environment Susceptibility–Reykjavik Study (AGES-Reykjavik) to examine risk factors, including genetic susceptibility and gene-environment interaction, in relation to disease and disability in old age. Midlife measures from the Reykjavik Study will be used to investigate the long-standing effects of obesity on health outcomes in old age.

There is intriguing new evidence that suggests obesity in middle age may increase the risk of developing memory problems and Alzheimer disease in old age, according to Launer. Launer is planning an investigation into the role of body weight on neurological outcomes in the AGES-Reykjavik Study. AGES-Reykjavik has one of the largest databases of brain magnetic resonance imaging (MRI) images in the world in addition to detailed health information on participants from mid-life to old age. Launer hypothesizes that linking data on body weight and weight-related conditions to brain structure, size, and MRI indicators of brain pathology may provide additional insight on the relationship between obesity and neurological outcomes in old age.

The investigator's research emphasizes the importance of earlier life behaviors and exposures in determining health in old age and suggests that maintaining a healthy body weight throughout adulthood helps to promote healthy aging. They hope their work will help identify key periods in life for intervention and treatment and define weight recommendations for healthy aging. ●

More Obesity Research

There are many other NIH intramural researchers doing obesity-related research in NCI, NHGRI, NHLBI, NIAAA, NICHD, NIDA, NIDDK, NIEHS, and other institutes and centers. The subjects of NIH obesity studies range from the molecular link between metabolic imbalance and breast cancer risk; to metabolic differences in people's reactions to cold temperatures; to sleep deprivation and weight gain; to food as addiction; to metabolic effects of non-nutritive sweeteners; to the rise in nonalcoholic fatty liver disease, which is linked to obesity; to imaging studies that identify patterns in weight gain and progression in obesity-related diseases; to the relationship between the increase in the food supply and obesity; to environmental chemicals and weight gain; and more.

HBO SERIES ON OBESITY TO DEBUT IN MAY

NIH RESEARCHERS PLAYED A BIG ROLE

The HBO series on the obesity epidemic, "The Weight of the Nation," will air in May and help launch one of the most far-reaching public health campaigns on the epidemic to date. To create the series, HBO partnered with NIH, the Institute of Medicine (IOM), Centers for Disease Control and Prevention (CDC), the Michael and Susan Dell Foundation, and Kaiser Permanente. Several NIH researchers were interviewed, but at press time, it is not known whether they will appear in the program.

The series comprises four documentary films, a three-part HBO Family series, 14 bonus shorts, a social media campaign, a book published by St. Martin's Press, and a nationwide community-based outreach campaign to support the initiative.

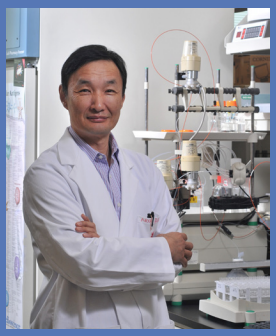
The four-documentary series debuts Monday, May 14, on HBO with two films airing back-to-back that night and two more the next night. The three-part HBO Family series debuts Wednesday, May 16.

"If we don't succeed in turning this epidemic around, we are going to face, for the first time in our history, a situation where our children are going to live shorter lives than we do," said NIH Director Francis S. Collins in the press release announcing the program.

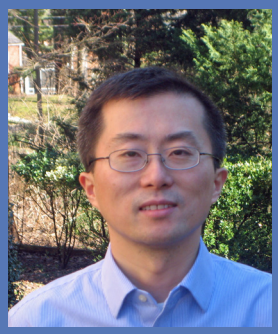
Recently Tenured

KAREN ADELMAN, NIEHS

AMY BERRINGTON DE GONZÁLEZ, NCI-DCEG



ARYA BIRAGYN (BIRA ARYA), NIA



KAI GE, NIDDK

DAVID LEOPOLD, NIMH

KAREN ADELMAN, PH.D., NIEHS

Senior Investigator; Head, Transcriptional Responses to the Environment Group, Laboratory of Molecular Carcinogenesis

Education: State University of New York, Buffalo, N.Y. (B.S. in biology); Génétique Cellulaire et Moléculaire, Université de Paris VI, Paris (Ph.D. in molecular and cellular genetics)

Training: Postdoctoral training in the Department of Microbiology and Immunology and the Department of Molecular Biology and Genetics at Cornell University (Ithaca, N.Y.)

Came to NIH: In August 2005

Selected professional activities: Member, American Society of Biological Chemists and co-organizer 2012 Thematic Session on Gene Regulation at Experimental Biology Meeting; co-organizer 2013 Federation of American Societies for Experimental Biology meeting

Outside interests: Spending time with her children (ages 4 and 1); photography; traveling; cooking

Research interests: We investigate the interplay between signals from the environment and transcription by RNA polymerase II (Pol II). The wrapping of DNA-containing genes around nucleosomes prevents access to the DNA. Although this wrapping may help keep stress-responsive genes silent under normal conditions, it poses a problem to the transcription machinery during times of stress. We seek to understand how cells modulate chromatin around stress-responsive promoters to respond to environmental insult or injury.

We use genomic approaches in Drosophila and murine models to quantify alterations in Pol II distribution and gene expression that occur when a cell receives specific stimuli from the environment. We recently found that many genes in signal-responsive pathways are preloaded with Pol II before full-scale gene activation. Pol II is engaged in early transcription elongation, but pauses after synthesizing a short (25 to 60 nucleotides) mRNA transcript. Surprisingly, we observed that this paused Pol II plays a critical role in establishing an accessible chromatin architecture around gene promoters that facilitate further gene activation. We are further investigating paused Pol II's role in other inducible gene systems.

AMY BERRINGTON DE GONZÁLEZ, PH.D., NCI-DCEG

Senior Investigator, Radiation Epidemiology Branch

Education: University of Manchester, Manchester, England (B.S. in mathematics); University of Kent, Canterbury, England (M.S. in applied statistics); University of Oxford, Oxford, England (Ph.D. in cancer epidemiology)

Training: Postdoctoral training in the Cancer Epidemiology Unit, University of Oxford

Before coming to NIH: Assistant professor of epidemiology at the Johns Hopkins Bloomberg School of Public Health (Baltimore); research lecturer in the Nuffield Department of Clinical Medicine, University of Oxford

Came to NIH: In February 2008

Selected professional activities: Member of two radiation research committees at the National Academy of Sciences and a U.K. Health Protection Agency committee

Outside interests: Literature and music

Research interests: Over the past three decades in the U.S., radiation exposure from medical sources has increased sixfold. My goal is to provide information for public health and clinical purposes by quantifying the potential cancer risks from both conventional and emerging medical technologies that involve ionizing radiation. I use theoretical risk-projection modeling and conduct epidemiological studies of medically exposed populations.

I have conducted a series of risk-projection studies to estimate the potential cancer risks from emerging technologies, including computed topography (CT) colonography and use of low-dose-radiation CT scanning to obtain an interior view of the colon; and lung CT screening. My collaborators and I developed the NCI Radiation Risk Assessment Tool (RadRAT),

KEVIN F. O'CONNELL, NIDDK

GEOFFREY SCHOENBAUM, NIDA

RACHAEL STOLZENBERG-SOLOMON, NCI-DCEG

computer software that estimates lifetime cancer risks from low-dose radiation exposures.

Examination of second-cancer (different cancer from original diagnosis) risks after radiotherapy provides insights into the long-term effects of high-dose fractionated radiation exposure. I conducted several studies using NCI's Surveillance Epidemiology and End Results cancer registries to evaluate second-cancer patterns and risks related to radiotherapy treatment. I am using medical records from Kaiser Permanente Health Plans to develop a cohort of breast cancer survivors and studying the late effects of various breast cancer treatments. I am also doing a pilot study to assess the feasibility of conducting the first multicenter study of second-cancer risks from proton therapy and intensity-modulated radiation therapy.

ARYA BIRAGYN (BIRA ARYA), PH.D., NIA

Senior Investigator; Chief, Immunotherapeutics Section, Laboratory of Molecular Biology and Immunology

Education: Lomonosov Moscow State University, Moscow, Russia (M.S. in genetics); Engelgardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow (Ph.D. in molecular biology)

Training: Postdoctoral training in the Department of Animal Sciences, University of Illinois at Urbana-Champaign and in NCI's Laboratory of Immuno-regulation and the Lymphoma Development Program

Before coming to NIH: After training at NIH, was a scientist at the Science Applications International Corporation (Frederick, Md.)

Came to NIH: In 1992 for training at NCI; returned in 2000 as NCI staff scientist; became NIA tenure track investigator in 2003

Selected professional activities: Adjunct associate professor, Johns Hopkins University, Baltimore; Editorial board member for the *Journal of Biological Chemistry*

Outside interests: Participating in charity activities to improve health care in Mongolia; member of Project C.U.R.E.; bicycling; skiing

Research interests: Our laboratory is studying the role and function of regulatory cells in cancer metastasis. We discovered a new subset of regulatory B cells, tBregs, which are induced by cancer to generate regulatory T cells (Tregs) and suppress immune responses. To control Tregs and tBregs, we developed a novel technology by fusing a chemokine and a toxin into what we call a "chemotoxin." Chemotoxins kill cells that express certain chemokine receptors. We demonstrated that C-C chemokine receptor type 4 (CCR4) is a key chemokine receptor that regulates trafficking of Tregs. Chemotoxin can also be used to control breast cancer metastasis to the lung as well as combat leukemia in mice, suggesting that it can be an effective treatment for human cancers and T-cell lymphoma and leukemia.

My laboratory also has expertise in vaccines. We successfully generated several potent cancer vaccines, such as chemokine-based simple vaccines for human use, by targeting an embryonic antigen that is expressed in several human malignancies. We recently created a novel Alzheimer disease (AD) vaccine that combats AD and significantly extends the life span of a mouse model used in AD research.

KAI GE, PH.D., NIDDK

Senior Investigator; Chief, Adipocyte Biology and Gene Regulation Section, Laboratory of Endocrinology and Receptor Biology

Education: Fudan University, Shanghai (B.S. in biochemistry); Shanghai Institute of Biochemistry, Chinese Academy of Sciences, Shanghai (Ph.D. in molecular biology)

Training: Postdoctoral training with Lasker Awardee Robert Roeder at Rockefeller University (New York); postdoctoral training in the Molecular Genetics Program at the Wistar Institute (Philadelphia)

Came to NIH: In September 2003

Outside interests: Visiting museums and zoos with his daughter; playing badminton and ping-pong; reading *National Geographic* and other educational publications

Research interests: Obesity is the single most important risk factor for type 2 diabetes, which accounts for 90 to 95 percent of all cases. A better understanding of the mechanisms that regulate adipogenesis—the generation of fat—may lead to novel approaches to the treatment of obesity and type 2 diabetes. My laboratory studies regulatory mechanisms of gene expression. We use adipogenesis as a model to study epigenetic regulation of gene expression and cell differentiation. Epigenetic mechanisms change these in a heritable way

CONTINUED ON PAGE 16

Recently Tenured

CONTINUED FROM PAGE 15

through pathways other than DNA sequence alteration.

We have identified novel epigenetic regulators including histone methyltransferases and demethylases with unique properties. We have also shown that histone methylation regulates the expression of both positive and negative master regulators of adipogenesis. Our current efforts include the investigation of adipogenesis regulation by these novel epigenetic factors and the use of adipogenesis as a model system to study the biological functions of many newly identified epigenetic regulators.

DAVID LEOPOLD, PH.D., NIMH

Senior Investigator; Chief, Section on Cognitive Neurophysiology and Imaging; Director, Neurophysiology Imaging Facility

Education: Duke University, Durham, N.C. (B.S.E. in biomedical engineering); Baylor College of Medicine, Houston (Ph.D. in neuroscience)

Training: Postdoctoral training in the Physiology of Cognitive Processes Department at the Max Planck Institute for Biological Cybernetics (Tübingen, Germany)

Came to NIH: In January 2004 to establish the Unit on Cognitive Neurophysiology and Imaging and to head the Neurophysiology Imaging Facility Core

Outside interests: Hiking; bird watching; reading about history

Research interests: My overarching research goal is to understand the large-scale organization of brain activity related to visual perception. In perception, stimuli of varying complexity—simple (color, brightness), intermediate (shape, geometric arrangement), and complex (identity, meaning)—are processed simultaneously. In the lab, we combine behavioral, neurophysiological, imaging, and neuropharmacological techniques to gain insights into how the brain interprets the visual world. We are particularly interested in the functional interactions between diverse brain areas.

In one series of studies, we trained monkeys to report how they perceived a visual stimulus by pressing response keys. We then presented them with a bi-stable visual illusion (in which a stimulus property, such as direction of movement or three-dimensional shape, appears to change spontaneously every few seconds) and measured whether, at each moment, neural responses were linked to the monkey's reported subjective perception. We found that neural responses in certain regions of the visual cortex and thalamus consistently reflected the perceived stimulus, even though the physical stimulus was always the same. These results illustrate that the visual brain actively interprets the images on the retina.

We also study how the brain processes faces and other high-level visual stimuli. In one study, we are determining how the brain responds during the observation of dynamic social behaviors. We measure brain activity in monkeys as they repeatedly view videos of other monkeys. Luckily for us, they are quite content to watch movies of their kin, even if the movies are "re-runs." We plan to use a similar method, using movies depicting complex human social situations, to study activity in the brains of patients with schizophrenia.

KEVIN F. O'CONNELL, PH.D., NIDDK

Senior Investigator, Genetics of Simple Eukaryotes Section, Laboratory of Biochemistry and Genetics

Education: University of New Hampshire, Durham, N.H. (B.A. in microbiology); University of Massachusetts, Worcester, Mass. (Ph.D. in molecular genetics and microbiology)

Training: Postdoctoral training in the Laboratory of Molecular Biology, University of Wisconsin (Madison)

Came to NIH: In February 2002

Selected professional activities: Member, American Society for Cell Biology; Editorial Board Member, *Prion*

Outside interests: Spending time with his wife and daughters

Research interests: My laboratory uses the worm *Caenorhabditis elegans* as a model system to address questions concerning the assembly and function of the centrosome. The centrosome is an organelle that serves as the cell's primary microtubule-organizing center (MTOC) and duplicates once per cell cycle. Through its ability to form polarized arrays of microtubules, the centrosome participates in critical cellular processes such as intracellular transport, the generation and maintenance of cellular polarity, cell motility, and cell division.

Because the mechanisms that govern centrosome duplication and behavior in *C. elegans* are likely to be highly conserved, our findings should prove valuable in understanding analogous processes in humans and diseases such as autosomal recessive primary microcephaly, cancer, infertility, and various ciliopathies that are linked to centrosome defects. Ciliopathies are caused by defects in the function or structure of cilia; examples include obesity, polycystic kidney, situs inversus (major internal organs in reversed positions), and Joubert syndrome (a rare brain malformation that affects the cerebellar vermis, an area of the cerebellum that controls balance and coordination).

By combining molecular genetics with biochemistry, my lab has identified several factors required for the centrosome duplication pathway. These factors include the master cell-cycle regulator ZYG-1, the protein spindle defective–2 (SPD-2), and the protein phosphatase 2A–suppressor of Ras-6 (PP2A-SUR-6). These factors and three other proteins form the core conserved machinery that drives centrosome duplication.

GEOFFREY SCHOENBAUM, M.D., PH.D., NIDA

Senior Investigator; Chief of the Behavioral Neurophysiology Neuroscience Section and of the Cellular Neurobiology Research Branch

Education: University of Georgia, Athens, Ga. (B.S. in biology); University of North Carolina, Chapel Hill, N.C. (M.D.; Ph.D. in neurobiology)

Training: Postdoctoral fellowship in the Department of Psychology at the University of North Carolina, Chapel Hill

Before coming to NIH: Professor of anatomy and neurobiology at the University of Maryland School of Medicine (Baltimore)

Came to NIH: In October 2011

Outside interests: Technical mountain biking; spending time with his family

Research interests: We are trying to better understand how neural circuits—particularly in the orbitofrontal cortex (OFC) of the brain—mediate simple associative learning and decision-making. By studying how neural circuits mediate simple behaviors in rats, we hope to understand how these circuits function in humans, how they are disrupted in clinical brain disorders, and develop treatments.

Using reinforcer devaluation (making a reinforcer undesirable through association with illness or satiation) and unit recordings that measure activity from OFC neurons, our laboratory was among the first to demonstrate a critical role for the OFC in goal-directed behavior. Recently, we have shown that the information supplied by the OFC both drives behavior and facilitates new learning.

We have also demonstrated that exposure to cocaine and other drugs of abuse induces long-lasting changes in the representation of information about expected outcomes in the OFC. These results suggest that features of addiction, such as loss of behavioral control and failed learning, may be partly due to drug-induced changes in OFC-dependent functions.

RACHAEL STOLZENBERG-SOLOMON, PH.D., M.P.H., R.D., NCI-DCEG

Senior Investigator, Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics

Education: University of California, Davis, Calif. (B.S. in dietetics); Vanderbilt University, Nashville, Tenn. (M.Ed. in health-science nutrition); Johns Hopkins University School of Hygiene and Public Health, Baltimore (M.P.H. in nutrition and epidemiology; Ph.D. in epidemiology)

Training: Dietetic internship at Vanderbilt University Medical Center (Nashville, Tenn.); predoctoral and postdoctoral training in NCI's Division of Cancer Prevention and Control; postdoctoral training in NCI's Division of Cancer Epidemiology and Genetics

Before coming to NIH: Research dietitian at VA Medical Center (Nashville, Tenn.); clinical dietitian and senior clinical dietitian at Johns Hopkins Hospital (Baltimore)

Came to NIH: In 1996 for training; in December 2002 as a tenure track investigator

Selected professional activities: Associate editor, *American Journal of Epidemiology*; editorial board member, *Cancer Biomarkers Epidemiology and Genetics*; adjunct associate professor, Yale University School of Hygiene and Public Health (New Haven, Conn.)

Outside interests: Spending time with family and two children; cooking international foods; jogging

Research interests: The principal focus of my research has been the etiology of pancreatic cancer. Using epidemiologic approaches, I have made several original observations into the nutritional, metabolic, and genetic determinants of this highly fatal disease.

I use prospective data from cohort studies in which a group of people who do not have pancreatic cancer are tracked over time. I was the first to demonstrate that higher serum insulin concentration and other markers related to insulin resistance increase pancreatic cancer risk. These findings support the hypothesis that diabetes may affect risk directly through insulin resistance.

Other modifiable factors that I have observed as contributors to pancreatic cancer are adiposity, high fat intake (particularly fat from animal foods), heavy alcohol use, poor teeth, and many other unhealthy lifestyle factors (including smoking, poor dietary quality, and physical inactivity). We estimated that at least 27 percent of pancreatic cancer is accounted for by an unhealthy lifestyle. I continue to research the mechanisms by which these factors contribute to pancreatic cancer.

Since 2006, I have been collaborating with a multidisciplinary team of investigators, at NCI-DCEG and extramurally, in a large-scale effort known as PanScan. We are conducting the first genome-wide association study (GWAS) for pancreatic cancer. The GWAS has already shown a link between certain alleles of the gene for ABO blood type and pancreatic cancer.

If you have been tenured in the past several 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.

The Relevance of Yeast Genetics to Cancer

Geneticist David Botstein Describes Evolution at Work

BY HEATHER DOLAN

BILL BRANSON

David Botstein talked about the connection between his yeast research and cancer during his presentation at the second annual Nirenberg Lecture on January 4.

Understanding the molecular genetics of yeast evolution provides plenty of insights into cancer biology. So says renowned geneticist David Botstein, who presented the second annual Marshall W. Nirenberg Lecture at NIH on January 4.

Botstein, the director of Princeton University's Lewis-Sigler Institute for Integrative Genomics (Princeton, N.J.), was an undergraduate at Harvard University (Cambridge, Mass.) when he heard Nirenberg give a talk in 1962. Nirenberg went on to win the Nobel prize in 1968 for helping to break the genetic code. Botstein described how listening to Nirenberg was a transformative experience, affirming his decision to become a geneticist. In 1980, Botstein and three colleagues published a landmark paper that proposed a method for mapping human genes and set the stage for the Human Genome Project.

In his lecture, entitled "Evolution and Cancer," Botstein discussed parallels between yeast biology and human cancer. His laboratory examines how constraints, such as limiting nutrients, affect the yeast *Saccharomyces cerevisiae*. He found that withholding certain nutrients leads to "fitter" variant strains that are better able to survive without those nutrients. He demonstrated that yeast adapt to limitations in glucose, nitrogen, sulfate, or phosphate in only a few ways, suggesting that yeast regulatory networks use a limited number of altered gene expression routes to improve fitness.

"There are striking similarities between genetic events and the fitness trajectories we see in experimental events in yeast and cancer," he said. For example, breast cancer cells that develop into malignant tumors have acquired mutations that make them lethal through only a limited number of gene expression pathways. This process is analogous to how yeast strains that survive under a constraint develop fitness via only a handful of gene expression pathways.

Botstein is also interested in distinguishing driver mutations from passenger mutations in cancer cells. Driver mutations are those that contribute to cancer development and allow cells to grow and divide more rapidly, whereas passenger mutations do not contribute to cell growth or cancer.

He watched evolution at work as he gathered data from 600 yeast cultures that were put through more than a thousand generations of growth. His lab produced sterile yeast cells that have driver mutations. The researchers then examined sterile versus non-sterile mutants by comparing the DNA nucleotide sequences of each mutant type.

This analysis, said Botstein, mirrored the comparison of driver and passenger mutations in human cancer. He found that sterile yeast cells with passenger mutations in the gene *ERG1*, which is involved in cholesterol biosynthesis, were fitter than non-sterile yeast cells with passenger mutations in the genes *ELO1* and *GAS1*, which are involved in fatty acid elongation and chromatin silencing, respectively.

Botstein also emphasized the importance of basic science. "Basic scientists do what we do in the pursuit of understanding," he said. "It's not that we don't care [about patients], it's we can't predict—nobody can—the solution to most problems until more is understood. And understanding is what we do."

He urged NIH to understand that "there has to be a balance between basic science, which gives you understanding, and something that will cure Mrs. Jones's cancer tomorrow," he said. "If we starve basic science, there will be nothing left."

NIH Director Francis Collins thanked Botstein for "presenting an eloquent basic science lecture [and] also pointing out its translational significance." He added that NIH "would embrace heartily your arguments about the critical nature of supporting basic science." ●

Marshall W. Nirenberg, Nobel prize–winning biochemist and geneticist, served the NIH community for 48 years as head of the Section of Biochemical Genetics at NHLBI. The Marshall Nirenberg Lecture Series honors this distinguished researcher and others who have made significant contributions to the study of genomics. To watch a video of this lecture and others in the Wednesday Afternoon Lecture Series, go to http://videocast.nih.gov/PastEvents.asp?c=3.

FARE IS BACK FOR FISCAL YEAR 2013

NIH intramural trainees are invited to submit applications for the annual Fellows Award for Research Excellence (FARE) competition. Each winners will receive a $1,000 travel award to attend a scientific meeting, present his or her work at the 2012 NIH Research Festival, and serve as a judge for the next FARE competition. (Note: NHLBI Fellows do not receive the monetary award but will be acknowledged as awardees if selected.) Applications and abstracts must be submitted online by March 22. Winners will be notified by August 15. For more information, visit https://www.training.nih.gov/felcom/fare.

FOOD DRIVE FOR SAFRA FAMILY LODGE

March 12–30, 2012

Sponsored by Service and Outreach Subcommittee, Fellows Committee

The Edmond J. Safra Family Lodge provides a place to stay for families and caregivers of adults who are at the NIH Clinical Center. This food drive will help provide services for lodge residents, who may not have the means or time to travel off campus for food. Please donate nonperishable foods to designated areas outside cafeterias, food courts, and coffee shops in buildings 38A, 35, 40, 10, 31, and 50 and in Frederick. For more information contact Shu Hui Chen (shuhui.chen@nih.gov).

NIH-DUKE TRAINING PROGRAM IN CLINICAL RESEARCH

Applications Accepted Until April 15, 2012

The NIH-Duke Training Program in Clinical Research is designed for physicians and dentists who desire formal training in the quantitative and methodological principles of clinical research. Courses are offered at the NIH Clinical Center via videoconference. Academic credit may be applied toward a Master of Health Sciences in Clinical Research from Duke University School of Medicine. For applications, contact Benita Bazemore (bbazemore@cc.nih.gov). For other information, go to http://tpcr.mc.duke.edu.

TARGETING AGING TO DELAY MULTIPLE CHRONIC DISEASES: A NEW FRONTIER

Thursday, March 8, 2012

11:30 a.m.–12:30 p.m.

Masur Auditorium (Building 10)

Sponsor: Geroscience Scientific Interest Group

Dr. James L. Kirkland, director of the Robert and Arlene Kogod Center on Aging at the Mayo Clinic in Rochester, Minn., will discuss cell senescence and other aging topics. For more information, contact Felipe Sierra at sierraf@nia.nih.gov.

THE BENEFITS AND PERILS OF DUAL USE

March 13, 2012

3:00–4:00 p.m.

Neuroscience Center, Conference Rooms C/D

6001 Executive Boulevard, Bethesda

Presenter: Henry T. Greely, J.D., director of the Center for Law and the Biosciences at Stanford University. Greely will lay out how the revolutions in neuroscience, though driven, and funded, by scientific and medical imperatives, have the potential to be "dual use," involving both biomedical applications and addressing societal challenges. The theories and technologies produced by neuroscience are likely to be used to predict behavior, read minds, ascribe responsibility, treat non-disease behaviors, and generally enhance the human experience. To learn more about this NIMH talk and others, visit http://innovation-speakers.nimh.nih.gov.

NCI SYMPOSIUM: TRANSLATIONAL GENOMICS

March 15–16, 2012

Kirschstein Auditorium (Building 45)

Register Now

This symposium will provide a forum for the advancement, implementation, and exchange of information on noncoding RNAs, next-generation sequencing, and epigenomics and genetic variation for translation into clinical practice with the ultimate goal of improving the health of patients with cancer. Topics include noncoding RNAs, the dark matter of the genome; next-generation sequencing for next-generation medicine; and epigenomics and genetic variation. View a list of speakers and register online at http://web.ncifcrf.gov/events/TranslationalGenomics. Registration is free but seating is limited. For additional information contact Laura Hooper at hooperl@mail.nih.gov.

INFORMED CONSENT FOR PEDIATRIC BIOBANKING

March 27, 2012

1:00–3:00 p.m.

Lipsett Amphitheater (Building 10)

Sponsor: Biospecimens Interest Group (BIG)

The presentation will explore the controversy about using stored pediatric biospecimens from grown donors and the ethics of seeking or waiving consent for studies when pediatric donors reach the age of majority. Confusion about ethical and legal obligations and the complicated logistics of re-contacting pediatric donors and/or their families have plagued pediatric investigators despite the potential for advancing scientific knowledge. Broadcast live at http://videocast.nih.gov. For information, contact Helen Moore (moorehe@mail.nih.gov, 301-496-0206) or Yaffa Rubinstein (rubinsty@mail.nih.gov or 301-402-4338).

2011–2012 DIRECTOR'S SEMINAR SERIES

12:00–1:00 p.m.

Wilson Hall (Building One)

For questions or special accommodations, call 301-496-1921.

March 16, 2012: Adrian Ferré-D'Amaré, Ph.D. (NHLBI), "Catalytic and Gene Regulatory RNAs: Structural Biology, Physiology, and Evolution"

April 20, 2012: Ola Landgren, M.D., Ph.D. (NCI-CCR), "Multiple Myeloma and Its Precursor Disease: The Future Is Already Here"

May 18, 2012: Serena Dudek, Ph.D. (NIEHS), "New Insights into Regulating Synaptic Plasticity from an Unexpected Place"

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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.

WE STILL HAVE NOT YET IDENTIFIED THE MASKED SURGEON. SEE HTTP://IRP.NIH.GOV/CATALYST/V19I5/LABORATORY-CONFESSIONS.

LABORATORY CONFESSIONS

Just a Thought

BY NAME WITHHELD

Something very strange happened on my 60-minute train commute home. I had prepared, as always, to browse a dozen or so scientific papers on my iPad. I had neatly downloaded these before I left work. I also had considerable e-mail to answer, so I had planned to bang these out, too.

Then an apparent tragedy struck. Nestled in my warm coach, with my shoulder to the window, I opened the iPad and found I had no battery life. I can only imagine that the outlet at my home that I thought was giving this machine juice the night before was in fact dead. And so I was left alone with absolutely nothing to do. I couldn't do a crossword puzzle because I had canceled my newspaper in favor of an online subscription; I couldn't read, for I do that, too, through this waffle-thin device; and I clearly couldn't tackle that looming mound of e-mail.

Lost, helpless, and a bit angry, I gazed out of the window. Then, in a few minutes, as the panic settled, that's when it happened. I had a thought. Never mind what that thought was. What surprised and thrilled me was the mere fact that I had an opportunity to think. I don't remember this happening in more than 10 years. During the whole 21st century, my life has been more about reaction than about spontaneous action. I react to papers; I react to e-mail; I react to phone calls and elevator conversations. I cram my entire day with input. Let's walk and talk, I'd say to a trainee.

I now am re-addressing my priorities and leaving ample wakeful time to let my mind wander. Now I say to myself, let's walk . . . period. Just a thought.

EDITOR'S NOTE: HAVE A LATE-NIGHT LABORATORY CONFESSION? WE JUST MIGHT PRINT IT.

The NIH Catalyst is published bimonthly for and by the intramural scientists at NIH.

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