

## Clinical Center News

### Extramural Investigators Welcome

BY MAGGIE MCGUIRE, CC

NIH INTRAMURAL INVESTIGATORS MAY soon have company at the NIH Clinical Center (CC) when a new grant program offers access to extramural researchers who want to partner with them.

The move will help maintain the CC's status as a "national treasure," said NIH Director Francis Collins. "Opening its doors to a greater pool of researchers will welcome fresh perspectives and cultivate new opportunities for discovery that will translate to greater human health."

The CC launched a new Web site (<http://clinicalcenter.nih.gov/translational-research-resources/index.html>) that offers a "Collaborator's Toolkit" that includes a listing of the hospital's research resources—such as its metabolic unit, pharmaceutical-development capabilities, and advanced research-related radiology imaging services—and instructions for how extramural researchers can initiate partnerships with intramural scientists.

"The Clinical Center should be available for collaborations that will further enhance the translation of scientific observations and laboratory discoveries into new approaches for diagnosing, treating, and preventing disease," said CC Director and NIH Associate Director for Clinical Research John Gallin.

In addition to the new grant program called Opportunities for Collaborative Research at the NIH Clinical Center (<http://grants.nih.gov/grants/guide/notice-files/NOT-HD-12-025.html>), extramural

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## An NIH Research Dynasty in Building 3

### A Who's Who of Biomedical Researchers

BY HEATHER DOLAN

NIH'S BUILDING 3 WAS ONCE A researcher's paradise. For more than half a century, it was chock-full of remarkable scientists and bustling with activity. Before it closed in 2001, it had housed some of NIH's best biomedical investigators—pioneering malaria researchers, the first female board-certified heart surgeon, a fledgling leader of the pharmaceutical industry, three future NIH directors, 15 scientists who were inducted into the National Academy of Sciences, and five eventual Nobel laureates.

The historic building sat vacant for almost 10 years before extensive renovations began to transform it into the office building it is today. The outside, down to the landscaping, looks almost the same as it did in 1938. Even the trees are the same:

Workers were careful to preserve the root systems. But inside, the interior walls, elevators, stairs, restrooms, and mechanical, electrical, and telecommunication distribution systems were torn down and replaced. In March 2012, dozens of administrative staff members from six institutes (NIAID, NHLBI, NIDDK, NCI, NINR, and NIMHD) began moving in.

But listen carefully and you can almost hear the ghosts of the amazing people who once worked there.



COURTESY: NIH OFFICE OF HISTORY

NIH's Building 3, a hotbed of research until it was closed in 2001, was home to pioneering malaria researchers, the first female heart surgeon, three future NIH directors, five eventual Nobel laureates, and cars that could plow through a brick wall. (Photo circa 1950)

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## Then and Now

BY MICHAEL GOTTESMAN, DDIR

**THIS ISSUE OF THE *CATALYST* INCLUDES** an article about the renovation of Building 3 and reminiscences about the glory that was ours in the early 1950s when giants roamed the halls of NIH, especially Building 3. (Not to be outdone, Building 2 was no slouch either, but that is for another essay.)

You can read about the amazing concentration of future National Academy of Science members and Nobel laureates who rubbed shoulders there, and you might rightly ask, where are those shoulders to rub now? Even though things have changed, I would argue that the NIH intramural research program has retained its disproportionate impact on biomedical research.

The era of NIH support of research in universities and other extramural sites was just beginning in the 1950s—about 50 percent of the NIH budget was spent on intramural research then. So the top scientists in the world were attracted to NIH, where there were stable support for research, outstanding modern facilities and equipment, and colleagues who were interactive and interested in each other's work. Furthermore, NIH was a place where spouses could find jobs, and so couples—such as the Stadtmans (Thressa and Earl), the Tabors (Herbert Tabor and Celia White Tabor), and Jack Orloff and Martha Vaughan—were recruited together, adding substantially to the quality and gender diversity of the science here.

Today, the intramural budget is approximately 10 percent of the overall

NIH budget. Yet intramural NIH remains at the forefront of biomedical research: 50 investigators are members of the National Academy of Sciences; 50 are members of the Institute of Medicine; and the intramural program is consistently recognized for its cutting-edge research through awards, its more than 6,000 publications per year, and its high citation rates.

The same formula that brought luminaries to the NIH 60 years ago works to sustain this high productivity and impact today: long-term stable support, talented colleagues, and state-of-the-art resources. The National Human Genome Research Institute and the new NIH Center for Acceleration of Translational Science exemplify how NIH has kept ahead of the curve in developing technology that moves research, not incrementally, but in quantum jumps.

But we don't rest on our laurels. Three years ago the scientific directors initiated a program to recruit the most outstanding and diverse tenure-track investigators to NIH. We are using a global search process named after Earl Stadtman, one of Building 3's biochemical superstars and a mentor to many of the stars who came to the NIH to work with him. This search has so far identified nearly two-dozen highly creative and interactive scientists who will surely be future members of the National Academies and award winners.

In addition, in 2011 intramural scientists garnered three of the 20 Presidential Early Career Awards in Science and Engineering (PECASE); a fourth PECASE awardee has been recruited to NIH.

Finally, let me mention the critical role that the NIH Clinical Center (CC) has played in the pre-eminence of the NIH intramural research program. Since the CC's construction was completed in 1954, it has been an essential site for long-term natural history studies as well as early-phase and first-in-human clinical trials.

Recognized in 2011 by a distinguished Lasker-Bloomberg Public Service Award, the CC's medical milestones include the development of chemotherapy for cancer; the first use of an immunotoxin to treat a malignancy; identification of genes that cause kidney cancer, leading to the development of six new treatments; the demonstration that lithium helps depression; the first gene therapy; the first treatment of AIDS (with zidovudine); and the development of tests to detect AIDS and HIV and hepatitis viruses in blood, which led to a safer blood supply.

The recent request for applications for joint intramural-extramural collaborative clinical research (see article on page 1) will bring a new dimension and new talent to the CC, as will our partnership with the Lasker Foundation, the NIH-Lasker Clinical Research Scholars program (<http://www.nih.gov/science/laskerscholar>). The Lasker program seeks to recruit the best and brightest new clinical researchers to tenure-track positions at the NIH with the promise of long-term support either at the NIH or via an extramural grant mechanism after completion of the tenure track. ●



## Letters

### Early Graduate Programs at NIH

As I was reading the articles about NIH graduate education in the July–August 2012 issue of the *NIH Catalyst* (Michael Gottesman’s essay and Meghan Mott’s feature, “Grad Students Unite”), I was reminded of the early activities of the Foundation for Advanced Education in the Sciences (FAES). Its educational program was initiated in the 1950s by Daniel Steinberg, then chief of the Laboratory of Metabolism in NHLBI and the first FAES president. He is now a distinguished professor emeritus at the University of California, San Diego School of Medicine, and the sole survivor of the 12 FAES founders. The program, which aimed to enhance the education of postdoctoral fellows, began under the auspices of the U.S. Department of Agriculture, which had a similar program. No degree was offered, and the then–NIH Director James Shannon did not support the possibility of NIH offering a Ph.D. degree.

In the 1960s, the FAES initiated a joint Ph.D. program with the Biology Department of Johns Hopkins University (Baltimore). Students had two years of course study at Hopkins, did their thesis research at NIH, and received a Ph.D. from the university. In return for the Hopkins faculty teaching “our” Ph.D. students for two years, Steinberg, Earl Stadtman, and I gave lectures in the advanced biochemistry course at Hopkins. FAES had a similar, but less extensive program, with (I think) the Biophysics Department at the University of Maryland’s College Park campus.

I ceased participating in the Hopkins program when I went on sabbatical to Cambridge, England, in 1969. Alan Schechter [NIDDK] reminds me that the FAES programs continued under the sequential direction of him, Elizabeth Neufeld [former NINDS researcher], and David Davies [NIDDK], each for about a decade. DeWitt “Hans” Stetten was very active in

the FAES. When he was deputy director for intramural research, he proposed that the NIH have its own graduate program with authority to offer its own Ph.D. This idea did not receive widespread support from the NIH staff.

The FAES initiative, which involved major financial contributions from the FAES, was a pilot program for two or three new students a year. Ultimately, about 50 students received Ph.D. degrees, mostly from Johns Hopkins, for research done at NIH. Many of these students have gone on to have distinguished careers at NIH, the Food and Drug Administration, and elsewhere.

The FAES graduate program lasted until the mid-1990s, when it was folded into the NIH Graduate Partnerships Program. Graduate education at the NIH is one of the many FAES activities that have contributed to NIH being a wonderfully atypical federal institution.

—Edward Korn, Ph.D.

*Korn, chief of the Laboratory of Cell Biology and former scientific director (1989–1999) in NHLBI, is a past-president of FAES.*

### Resveratrol Revealed

It takes nothing away from the outstanding contribution of Jay Chung (“Resveratrol Revealed,” July–August 2012 *Catalyst*) to note that co-authors of the *Cell* paper include two other NHLBI senior scientists: Michael Beaven, now emeritus but still working at the bench, and Vincent Manganiello, for many years one of the world’s leading investigators of phosphodiesterases. I would have liked to have seen them, as well as the other co-authors, mentioned in the article.

—Edward D. Korn, Ph.D.

**Editor’s note:** *We updated our online edition of the Catalyst to note all the authors on the paper (Cell 148:421–433, 2012): Sung-Jun Park, Faiyaz Ahmad, Alexandra L. Brown, Myung K. Kim, Michael A. Beaven, Vincent Manganiello, and Jay H. Chung.*

### 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
- NHGR:** 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
- NIAD:** 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
- NIHES:** 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
- NIHRS:** National Institute of Nursing Research
- NLM:** National Library of Medicine
- OD:** Office of the Director
- OITE:** Office of Intramural Training and Education
- OIR:** Office of Intramural Research
- ORS:** Office of Research Services
- ORWH:** Office of Research on Women’s Health
- OTT:** Office of Technology Transfer



## FROM THE FELLOWS COMMITTEE

### Effective Poster: Planning, Preparing, Presenting

BY ROZA SELIMYAN, NIA

**AWARD-WINNING POSTERS HAVE** something in common, and it's not just the science presented. Presenting effective scientific posters can lead to interesting scientific discussions, opportunities for networking and collaborating, and even job offers. When you are planning, preparing, and presenting a poster, it is important to remember that it is a visual tool for science communication.

#### PLANNING

**Determine the poster's main message:** The first step is to define your message and keep the focus on it throughout the poster.

**Find out how much space is available:** Use the provided space effectively. It is not wise to have your poster occupy only one-third of the space provided or to have parts of it hanging from the sides of the display board. Most scientific events provide guidelines for preparing posters including the space available for each. If not, request this information from the organizers.

**Allow yourself plenty of time to prepare:** Even if you have all figures and tables ready, you should still give yourself enough time to prepare the poster. Laying out the figures in a logical and aesthetically appealing manner requires a considerable amount of time. In addition, you need time for editing. Asking your peers to look at the poster is a great idea, but this too requires time.

**Decide whether to have your poster printed:** Consider whether you have the time and money to have your poster printed. If not, one option is to print each section on separate pieces of letter-sized paper and assemble them on the poster board.

#### PREPARING

**Content:** Ask yourself what information is absolutely essential for conveying your main message, and avoid all other details. If necessary, you can mention other details during your presentation. Avoid the common mistake of repeating the same information in the "Summary" and "Conclusions" sections. The "Summary" section should present results; the "Conclusions" section should interpret them.

**Title:** Choose an interesting title.

**Layout:** Be sure the poster is organized, has a logical flow, and can be understood by the viewer. A typical format is Introduction, Goals/Objectives, Methods, Results, Summary, and Conclusions. Don't count on being able to explain everything during your presentation. You might not be standing by your poster the entire time, especially if you had to hang it up well before the session.

**Text:** The biggest difference between a scientific paper and a poster is that a paper *tells* and a poster *shows*. For a poster, have attractive graphics and figures. Use text sparingly; sentences and text blocks should be short and to the point. Keep in mind that everything—including figure legends and labels—on your poster should be readable from a six-foot distance.

**Colors:** Colors can make your poster more attractive, but too many colors or too-bright colors quickly become distracting and even tiring on the eyes. Choose contrasting colors: dark letters on a light background. (Avoid using light letters on a dark background.)

**Editing:** It is impossible to overemphasize the importance of editing. You should perform scrupulous editing, avoid typos, and ask your peers to check your poster as well.

#### PRESENTING

**Presentation is everything:** Careful planning and preparing are important for a successful poster presentation, but they will not matter much if you don't prepare well for your presentation.

**Practice:** Practice your presentation before a test audience.

**Adapt your presentation to your audience:** For people in your immediate field, a lengthy introduction may be boring. For others, be ready to provide more background information. Often your audience will include scientists from a wide range of disciplines, so be ready for their questions.

**Provide the context for your project:** Show your audience the big picture and then narrow their attention to your project. Interpret and relate results to the big picture.

**Show enthusiasm:** Avoid jargon, and explain your work simply and clearly.

**Engage your audience:** All your efforts in planning, preparing, and presenting a poster should be made by keeping in mind that the measure of success for a poster presentation ultimately comes to how well you engage your listeners.

For more information on preparing posters, go to <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1955747/> and <https://www.training.nih.gov/assets/GSC-PosterTips.pdf>.

ROZA SELIMYAN IS A MOLECULAR BIOLOGIST WORKING ON THE REGULATION OF GENE EXPRESSION. SHE HAS LED MANY JUDGING COMMITTEES AT VARIOUS SCIENTIFIC EVENTS COVERING A WIDE RANGE OF BIOMEDICAL TOPICS.

## Freeze...But First Move Quickly

### Replacing Energy-Guzzling Freezers Saves Research Dollars

BY CHRISTOPHER WANJEK

SCIENCE AT NIH IS ENERGY-INTENSIVE work in more ways than one. There's around-the-clock labor. And then there's the friendly neighborhood power plant providing the electricity to run all those instruments and machines...jokes about post-storm reliability aside.

Science is also expensive. The typical monthly PEPCO energy bill is in the \$5 million range. A not-so-insignificant portion of this amount is due to freezer use. There are at least 2,400 freezers on the Bethesda campus alone. Nearly every lab has one and many have two.

Freezers usually are the greatest single-source users of electricity in the labs. An old and inefficient freezer could use as much electricity as a 2,500-square-foot house.

This past summer, however, the NIH replaced 98 old freezers with 70 new ones, a scheme that will save approximately \$65,000 annually on energy costs. The purchases were part of an innovative program dreamt up by the NIH Office of Research Facilities (ORF), one of the offices that help keep this place running.

Because the winter of 2011–2012 was so warm, the NIH's utility bill was lower than expected. Better yet, the ORF found a way to funnel the savings into research. The ORF allocated \$685,000 to subsidize new freezer purchases by 50 percent. Labs accepted into the program contributed the matching funds.

That program—a huge success—is over. But if you want a new freezer at a discounted price, you aren't completely out in the cold. The Office of Research Services (ORS) Division of Scientific Equipment and Instrumentation Services has negotiated a discounted, bulk-purchase price through the end of December 2012. The

plan is to replace and even shed a few dozen additional freezers across the NIH.

What's the incentive? For starters, lab space. Newer freezers are sleeker and better insulated than models built just a decade ago. A new 19.4-cubic-foot freezer can hold as much as an older 23-cubic-foot freezer, about a 20 percent space savings. With careful consolidation two old freezers can be replaced with one new one. Also, energy savings can translate directly into more money for research, in this case, the subsidized purchase of freezers that normally go for about \$10,000 a pop.

If more freezers are replaced and more energy is saved—a combination of reduced electricity cost and reduced building cooling costs, because freezers generate so much external heat—NIH could save hundreds of thousands of dollars annually. In fact, Leo Gumapas of ORF's Division of Environmental Protection, who helped initiate the freezer program, has taken the initial steps in monitoring the precise energy demands of these freezers.

Contact Annalie Burke from the ORS Scientific Equipment Rental and Sales Branch ([burkea@ors.od.nih.gov](mailto:burkea@ors.od.nih.gov) or 301-496-9748) if you are interested in purchasing a new freezer. Dozens of labs that weren't able to participate in the subsidized program signed up in recent months for "phase two," the purchase of discounted freezers negotiated for FY2012. Now, these same prices will apply for "phase three" through calendar year 2012 if there is sufficient demand, Gumapas said.

The discounted prices include inside delivery, extended warranty, and preventative maintenance for the NIH main campus and Montgomery County lease facilities—options that otherwise would be costly. ●

## NEWS FROM AND ABOUT THE NIH SCIENTIFIC INTEREST GROUPS

### Breastfeeding

The Breastfeeding and Human Lactation Scientific Interest Group (BHL-SIG) was created, in part, to address issues raised in the January 2011 U.S. Surgeon General "Call to Action to Support Breastfeeding" report, the product of two years of work by a federal steering committee representing many HHS entities including NICHD. The document called for increased research support for topics related to breastfeeding. A diverse group of NIH scientists will gather to learn about and discuss research gaps and needed studies related to breastfeeding. For more information, contact the moderator, NICHD medical officer Tonse N.K. Raju ([rajut@mail.nih.gov](mailto:rajut@mail.nih.gov) or 301-402-1872) or visit the Web site at <http://sigs.nih.gov/breastfeeding>.

### Global Health

The mission of the Global Health Interest Group (GHIG) is to unite and strengthen the NIH community members interested in and conducting research projects related to the interdisciplinary field of global health. Activities include a seminar series, networking events, a LISTSERV, and an annual global-health retreat. For general questions or comments, contact Jessica Taaffe ([jessica.taaffe@nih.gov](mailto:jessica.taaffe@nih.gov)). For questions about the seminar series and suggestions for speakers, contact Priscilla Kelly ([priscilla.kelly@nih.gov](mailto:priscilla.kelly@nih.gov)). Visit the GHIG Web site at <http://sigs.nih.gov/globalhealth>.

### Stem Cell Seminar Series

**September 18:** Marc Ferrer (NHGRI); Building 50, Room 1227, 2:00–3:00 p.m.

**October 2:** Mark Krasnow (HHMI); Lipsett Amphitheater (Building 10), 2:00–3:00 p.m.

For more information and future seminar dates, go to <http://sigs.nih.gov/scig/Pages/default.aspx>.



## Of Monkeys, Mice, and Men

### The Promise of Hematopoietic Stem Cells

BY HEATHER DOLAN

**CYNTHIA DUNBAR MEANS BUSINESS.** Monkey business, that is. Dunbar, who heads the Laboratory of Molecular Hematopoiesis in the National Heart, Lung, and Blood Institute (NHLBI), is investigating human hematopoietic stem cells (HSCs), the precursors to all blood cell types. As it turns out, rhesus monkey (*Macaca mulatta*) and human HSCs are very similar.

Every year, between 45,000 and 50,000 people worldwide receive HSC transplants to treat life-threatening hematologic diseases, disorders that affect blood cells. “Most of the major advances in biomedicine have been based on hematologic diseases,” said Dunbar. “The first genetic disorder that was described and understood was sickle cell anemia,” a disease in which deformed red blood cells deliver less oxygen to the body’s tissues. Likewise, blood-related cancers as well as immune, metabolic, and red blood cell disorders caused by defective HSCs can be treated by transplantation of normal HSCs.

Dunbar first came to NIH in 1987 as a postdoctoral fellow in Art Nienhuis’s laboratory in NHLBI and worked on developing

gene therapies to correct mouse models of hematologic diseases. In the gene therapy she employed, viral vectors deliver a functional gene into disease-stricken target stem and progenitor cells. The therapeutic gene becomes integrated into the host cells’ DNA and produces the missing or defective protein in all daughter cells. Nienhuis’s group successfully developed gene therapy vectors and methods to modify mouse HSCs and developed models for HSC disorders such as leukemia and other diseases.

By 1992, Dunbar and Nienhuis moved the gene therapies into human clinical trials, but the human patients did not respond in the same way as the mice. Less than 0.1 percent of corrected HSCs were found in the patient’s bloodstream long-term. “At that point we realized that mice were not people and it was time to find a more relevant model,” said Dunbar during her Clinical Center Grand Rounds Lecture on June 13, 2012.

And that’s why Nienhuis and Dunbar, quite literally, began monkeyin’ around in earnest. In the late 1980s, they had begun to develop a model to transplant HSCs into rhesus monkeys. “Antibodies, cytokines, and other critical reagents cross-react between human and rhesus [monkey] cells,” said Dunbar. “So you can directly use what you work out in the lab with rhesus [monkeys] and translate it into human clinical trials.”

But Nienhuis was initially hesitant to let Dunbar work in the rhesus macaque facility when she was a postdoc. “He didn’t think I should work on the primates because he didn’t think women should go into the building alone at night,” Dunbar recalled. “It was a different time.” However in 1993, when Nienhuis left NIH to become the chief executive officer of St. Jude Children’s Research Hospital (Memphis, Tenn.),

Dunbar inherited the rhesus macaque facility. She relied on the critical knowledge and expertise of **Robert Donahue**, the veterinarian Nienhuis had recruited in 1990 to develop the primate model.

At first, just keeping the monkeys alive was a challenge. “Only half the animals would survive the [HSC] transplant,” said Dunbar. “But by the mid-1990s, it was rare to lose an animal from transplant complications.” Today, her laboratory uses genetic marking techniques as well as new imaging modalities to track, in monkeys, the output from individual HSCs, how long they last, and what blood cell lineages they contribute to. Dunbar’s laboratory used the primate model to develop HSC gene therapy approaches that have been successfully transferred to humans in several clinical trials. In 2000, 11 pediatric patients at Necker Hospital (Paris) received gene therapy for X-linked severe combined immunodeficiency (X-SCID), a disorder that affects T cells. Two years later, nine of the patients were seemingly cured and had restored their T cell counts. (*NEJM* 346:1185–1193, 2002) But by 2003, five of the cured patients had developed leukemia. Somehow, the therapies were curing X-SCID while simultaneously turning on oncogenes.

Dunbar’s group is still battling the gene therapy toxicity problem. “We must work out a way to get the benefits of an integrating vector without the risk of it turning on cancer-causing genes,” she said.

While the toxicity issues are being worked out, gene therapy remains a promising treatment for patients who would otherwise have no hope of surviving. “If you’re treating leukemia or X-SCID, taking those risks is probably worth it,” said Dunbar. It provides “some chance that these patients are surviving beyond age two.” ●



SUSAN WONG, NHLBI

Cynthia Dunbar, head of NHLBI’s Laboratory of Molecular Hematopoiesis, uses primate models to develop hematopoietic stem cell gene therapy approaches that have been successfully transferred to humans in clinical trials.



## NIBIB 10th Anniversary:

A Decade of Innovation for Health

BY SILVIYA ZUSTIAK, NICHD

FOR THE PAST 10 YEARS, THE NATIONAL Institute of Biomedical Imaging and Bioengineering (NIBIB) has harnessed the talents of engineers, biomedical researchers, and clinicians to tackle challenging medical problems. In June, NIBIB celebrated its 10th anniversary with a daylong scientific symposium that showcased the latest biomedical advances.

The program included two Nobel laureates; a patient with paraplegia who can now stand and walk for short periods of time thanks to a small device, developed by NIBIB-supported researchers, implanted in his back; and **Hari Shroff**, head of NIBIB's High Resolution Optical Imaging Lab, who described how new imaging tools provide clearer, faster, and less invasive movies of neurodevelopmental processes in living nematode embryos. A technology showcase featured live demonstrations and exhibits.

In his welcome address, NIBIB Director **Roderic Pettigrew** applauded the many advances made or supported by NIBIB: magnetic-resonance elastography, a non-invasive diagnostic tool that combines magnetic-resonance imaging (MRI) with sound waves; an MRI-guided focused ultrasound that can heat and destroy diseased or damaged tissue; a lung-on-a-chip device that mimics the mechanical and biochemical behaviors of the human lung and can be used for drug screening; and a micro-nuclear magnetic resonance (NMR) imager that can be used at the bedside to detect cancer cells.

NIH Director Francis Collins praised NIBIB's achievements in translational medicine and its contributions to the Human Connectome Project to map connections within the brain. NIBIB is developing high-speed MRI technology to shed light on how the brain integrates neural information. ●

## The NIBIB Intramural Labs

### LABORATORY OF CELLULAR IMAGING AND MACROMOLECULAR BIOPHYSICS (LCIMB)

<http://www.nibib.nih.gov/Research/Intramural/LCIMB>

*Richard Leapman, Ph.D., Chief and Senior Investigator; NIBIB Scientific Director*

The LCIMB develops new cutting-edge biomedical technologies based on engineering, mathematics, and the physical sciences for determining the organization, structure and interactions of macromolecular assemblies. Methods are applied within the cellular and tissue context, as well as to isolated cellular components. Ongoing techniques include electron microscopy, electron tomography, atomic force microscopy, and biophysical methods such as analytical ultracentrifugation and optical biosensing.

### LABORATORY OF MOLECULAR IMAGING AND NANOMEDICINE (LOMIN)

<http://www.nibib.nih.gov/Research/Intramural/XChen>

*Xiaoyuan (Shawn) Chen, Ph.D., Chief and Senior Investigator*

The LOMIN specializes in synthesizing molecular-imaging probes for positron-emission tomography, single-photon-emission computed tomography, magnetic-resonance imaging, optical imaging (bioluminescence, fluorescence, and Raman), contrast-enhanced ultrasound, photoacoustic imaging, and multimodality imaging. LOMIN puts special emphasis on high-sensitivity nanosensors for biomarker detection and theranostic nanomedicine for imaging, gene and drug delivery, and monitoring of treatment.

### MOLECULAR BIOMEDICAL IMAGING LABORATORY (MBIL)

<http://www.nibib.nih.gov/Research/Intramural/MBIL>

*David Bluemke, M.D., Ph.D., Lab Chief and Senior Investigator*

The MBIL is adjacent—and has access—to the Department of Radiology and Imaging

Sciences clinical imaging facilities. MBIL resources include workstations with advanced image-processing software for the analysis of biomedical images in cancer and cardiovascular disease. Ongoing research includes the evaluation of myocardial fibrosis in heart failure, the epidemiology of diabetes intervention and complications, and reduction of atherosclerosis using image-guided therapy.

### SECTION ON BIOPHOTONICS

<http://www.nibib.nih.gov/Research/Intramural/Biophotonics>

*George Patterson, Ph.D., Chief and Investigator*

The Section on Biophotonics develops probes and techniques for use in diffraction-limited and sub-diffraction-limited fluorescence imaging of cells and tissues. Methods and technologies include confocal, total internal reflection fluorescence, and wide-field microscopies; single-molecule imaging; fluorescence spectroscopy; and protein engineering.

### SECTION ON HIGH RESOLUTION OPTICAL IMAGING (HROI)

<http://www.nibib.nih.gov/Research/Intramural/HighResolutionOpticalImaging>

*Hari Shroff, Ph.D., Chief and Investigator*

The HROI develops novel technologies for studying biological processes at unprecedented speed and resolution. Research includes furthering the development of super-resolution optical-imaging techniques, particularly three-dimensional photoactivated localization microscopy (PALM); identification and screening of new photoactivable proteins and dyes for use in PALM or conventional imaging; and improving plane illumination microscopy in order to enable high-speed, noninvasive imaging of cells and embryos.

To learn more about NIBIB's programs and scientific advances, visit <http://www.nibib.nih.gov/Research/Intramural>.



## Intramural Research Briefs

### NHGRI: DEFINING THE NORMAL BACTERIAL MAKEUP OF THE BODY

A consortium of researchers—the Human Microbiome Project (HMP)—organized by NIH, has mapped the normal microbial makeup of healthy humans, producing numerous insights. Researchers found that nearly everyone routinely carries pathogens that cause no disease in healthy people. HMP researchers estimate that the human microbiome contributes some eight million unique protein-coding genes; the human genome contains only about 22,000. In a series of coordinated scientific reports published on June 14, 2012, in *Nature* and several journals in the *Public Library of Science (PLoS)*, the HMP reports on five years of research. (NHGRI author: J. A. Segre; *Nature* 486:207–221, 2012). To read the series of *PLoS* articles, go to <http://www.ploscollections.org/article/browse/issue.action?issue=info:doi/10.1371/issue.pcol.v01.i13>.

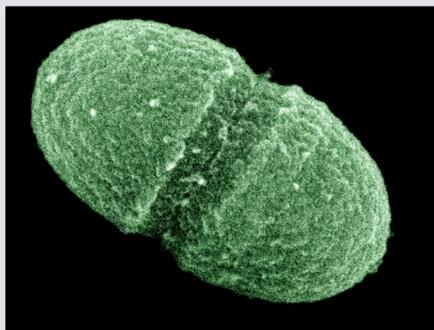
### NCI: HIGH-DENSITY MAMMOGRAMS DO NOT INDICATE INCREASED RISK OF DEATH

High mammographic breast density, which is a marker of increased risk of developing breast cancer, does not seem to increase the risk of death among breast cancer patients, according to a study led by NCI researchers (NCI authors: G. Gierach, L. Brinton, C. Schairer, S. Taplin, M. Sherman; *J Natl Cancer Inst* 104:1218–1227, 2012)

### NIAAA, NIMH, NIDA: A NEW DRUG REDUCES WEIGHT AND APPETITE IN OBESE MICE

A new drug studied by NIH researchers may aid those suffering from obesity by harnessing the body's own appetite-reducing mechanisms. (NIH authors: J. Tam, R. Cinar, J. Liu, G. Godlewski, D. Wesley, T. Jourdan, G. Szanda, B. Mukhopadhyay, L. Chedester, J.S. Liow, R.B. Innis, K. Cheng, K.C. Rice, G. Kunos; *Cell Metab* 16:167–179, 2012) [contributed by S. Flynn]

Expanded briefs at <http://irp.nih.gov/catalyst/v20i5/research-briefs>



U.S. DEPARTMENT OF AGRICULTURE

The bacterium, *Enterococcus faecalis*, which lives in the human gut, is just one type of microbe that will be studied as part of NIH's Human Microbiome Project.

### NHLBI, NIA: MRIs SHOW THAT SILENT HEART ATTACKS ARE COMMON

Magnetic-resonance imaging is more effective than electrocardiography at identifying “silent” heart attacks, also known as unrecognized myocardial infarctions, according to NIH researchers and international colleagues. They found that silent heart attacks are more frequent than previous studies have reported, particularly in certain populations such as older adults with diabetes. (NIH authors: E. Schelbert, J. Cao, P. Kellman, A. Aletras, C. Dyke, A. Arai; L. Launer, T. Harris; *JAMA* 308:890–897, 2012)

### NIA, NIAID: CALORIE RESTRICTION DOES NOT AFFECT SURVIVAL

Scientists have found that calorie restriction—a diet with the same nutrients as a standard diet but with approximately 30 percent fewer calories—does not extend years of life or reduce age-related deaths in a 23-year study of rhesus monkeys. Calorie restriction did, however, extend certain aspects of health. (NIH authors: J. Mattison, D. Barnard, A. Handy, R. Herbert, D. Longo, E. Tilmont, J. Young, R. de Cabo; *Nature* DOI:10.1038/nature11432)

### NIAID: SCIENTISTS MAP FIRST STEPS IN FLU ANTIBODY DEVELOPMENT

NIAID scientists have identified how one kind of immature immune cell responds to a part of influenza virus and have traced the path those cells take to generate antibodies that can neu-

tralize a wide range of influenza virus strains. The new understanding could speed progress toward a universal flu vaccine. (NIAID authors: D. Lingwood, P. McTamney, H. Yassine, J. Whittle, X. Guo, J. Boyington, C.-J. Wei, G. Nabel; *Nature* DOI 10.1038/nature11371)

### NINDS, CC: UNIQUE CELL TYPE IMPLICATED IN MULTIPLE SCLEROSIS (MS)

NIH scientists have found evidence that a unique type of immune cell contributes to MS. Their discovery helps define the effects of one of the newest drugs under investigation for treating MS: daclizumab. (NIH authors: J. Perry, S. Han, Q. Xu, M. Herman, L. Kennedy, G. Csako, B. Bielekova; *Sci Transl Med* 4:145ra106, 2012)

### OFFICE OF TECHNOLOGY TRANSFER (OTT) DENTAL PULP STEM CELLS

NIDCR senior investigator Pamela Robey and colleagues developed a technology to engineer living teeth by isolating and transplanting a patient's own dental pulp stem cells from post-natal dental pulp tissue (in wisdom teeth). OTT has executed its first license for stem cell therapy to develop and commercialize products that will regenerate human periodontal, dental pulp, and neural tissue to its pre-disease state.

### GLYBERA

A European advisory panel recently recommended the approval of the first gene therapy to be sold in a Western country—a drug to treat lipoprotein lipase deficiency (LPLD), a rare genetic disease that disrupts fat production in the body, causes pancreatitis, and puts patients at risk for cardiovascular disease. A Dutch company—UniQure—created a recombinant adeno-associated virus (rAAV) called Glybera, which expresses lipoprotein lipase in the patient's own tissue, restoring the body's ability to break down fat particles in the blood. UniQure entered into a licensing agreement with NIH to adopt a method developed by NHLBI senior investigator Robert Kotin and colleagues to manufacture large quantities of rAAV.

## A Pain-staking Intramural Research Program

NCCAM Has a New Scientific Director and a New Focus

BY HEATHER DOLAN

WITH THE ARRIVAL OF NEW SCIENTIFIC director **Catherine Bushnell**, the National Center for Complementary and Alternative Medicine (NCCAM) is redefining its intramural program. Bushnell, an internationally recognized pain and neuroscience researcher, has launched a program on pain research.

Every year, the U.S. health-care system spends over \$600 billion to treat the more than 100 million Americans who suffer from chronic pain, according to a recent Institute of Medicine report. “Clearly, there is a big gap between what patients and clinicians need and what we are achieving in pain management,” said NCCAM Director **Josephine Briggs**.

Bushnell hopes to bridge this gap using a combination of preclinical and clinical approaches. Her research will focus on the role of the brain in pain processing and control; how emotion, attention, environment, and genetics affect pain perception; and how chronic pain alters the brain response to analgesic drugs such as opioids.

Bushnell is no stranger to NIH and is looking forward to being back. She did her postdoctoral work in neurophysiology at the National Eye Institute (1978–1979) and was a staff fellow at the National Institute of Dental Research (1980–1984). She is returning from Montreal, where she was a professor of anesthesia and held other faculty positions at McGill University.

“I started my career at NIH, and so I was aware of the richness of the environment here,” said Bushnell. “It has a wonderful brain-imaging center [and] a rich neuroscience community.”

NCCAM’s intramural program, which began in 2001, previously did research on the effectiveness and safety of complementary and alternative (CAM) modalities used to

treat endocrinology-, diabetes-, and oncology-associated diseases. Under Bushnell’s leadership, the program will center on pain research and will touch on many other diseases as well. “Chronic pain itself leads to things like depression, anxiety disorders, cognitive deficits, and physical deficits,” she noted.

At first, Bushnell’s laboratory will make up NCCAM’s entire intramural program. She plans to transfer two postdocs and a staff scientist from McGill and will be hiring technical staff in the near future. Her laboratory will include two groups—one for rodent behavioral testing and brain imaging (in the Porter Neuroscience Research Center, Buildings 35 and 36) and one for human brain imaging and psychophysical testing (in Building 10). In the next four or five years, Bushnell hopes to expand the program and hire more principal investigators.

Bushnell’s group has recently demonstrated that chronic pain is more than just a symptom and may even be a disease in itself. Analyzing magnetic-resonance brain images of patients with fibromyalgia, a widespread pain disorder, she found evidence of a more rapid decrease in brain gray matter with age than in healthy individuals (*J Neurosci* **27**:4004–4007, 2007). In a related study, using positron-emission tomography to examine deep muscle pain, her group observed abnormal dopamine release in response to pain in fibromyalgia patients versus healthy participants (*Euro J Neurosci* **25**:3576–3582, 2007).

Under the umbrella of NCCAM, Bushnell hopes her program will also satisfy the public’s interest in alternative medicine. According to a 2008 NCCAM and National Center for Health Statistics study, an estimated 38 percent of adults and 12 percent of children in the United States



NCCAM’s new scientific director Catherine Bushnell, an internationally recognized pain and neuroscience researcher, is kick starting a program on pain research.

are using some form of CAM. “There are things that people use to try and treat their own pain, such as meditation, yoga practice, exercise, acupuncture, and various types of complementary treatments,” said Bushnell. “We’re interested in looking [at] these and how they work in the brain.”

The NCCAM intramural pain program will be a collaborative effort with other institutes studying pain, including NINDS, NIDA, and NIMH. Bushnell also foresees collaborations with NIDDK to understand neuropathic pain associated with diabetes; with NCI to investigate the debilitating pain experienced by cancer survivors; and with NIAMS to study arthritis-related pain.

With Bushnell as director, NCCAM’s intramural program faces an ambitious redirection. “It is an exciting and promising time in the field of pain research,” said Bushnell. “I look forward to strengthening our understanding of the mechanisms and modulation of pain.” ●

For more on Bushnell’s research, see the write-up in the **Recently Tenured** section, page 16.

Building 3 was built by the George Fuller Company of Bethesda in 1938 and is part of NIH's historic core of Georgian Revival Buildings along with Buildings 1, 2, 4, 5, and 6. First designated the Public Health Methods and Animal Unit Building, each floor featured a central corridor with laboratories, offices, and shared laboratory support space on either side; facilities for animal breeding were in the attic. The building's early occupants included researchers from the National Microbiological Institute (NMI), which became the National Institute of Allergy and Infectious Diseases (NIAID) in 1955; the Experimental Biology and Medicine Institute, which in 1950 became the National Institute of Arthritis and Metabolic Diseases (NIAMD), the forebear of the current National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the National Institute of Arthritis and Musculoskeletal and Skin Disease (NIAMS); and the National Heart Institute (NHI), now the National Heart, Lung, and Blood Institute (NHLBI).

During World War II, NIH research focused almost entirely on war-related problems including developing treatments for malaria and other tropical diseases. **G. Robert Coatney**, who in 1937 identified the malaria parasite in birds, set up a program at NIH's Washington, D.C., campus in 1938 to test potential antimalarial compounds in animals. He moved his lab to Building 3 in 1943. His research team tested the effectiveness of more than 2,000 compounds against infections caused by the avian parasite *Plasmodium gallinaceum* in young chicks. In 1960, he became chief of NIAID's Laboratory of Parasite Chemotherapy.

Another Building 3 inhabitant in the 1940s was **Nathan B. Eddy**, a trailblazer in the field of drug dependence. He worked with NIH chemist **Lyndon F. Small** (who sought to create nonaddicting painkillers) to evaluate compounds for their painkilling effectiveness and potential to be addictive.



ALL: COURTESY OF NIH OFFICE OF HISTORY

Later work with another NIH chemist, **Everette May**, led to the development of synthetic opioids, such as the 1960s drug pentazocine, that relieved pain without the potential for abuse.

In 1947, future Nobel Laureate **Arthur Kornberg** launched NIAMD's newly formed Enzyme and Metabolism section in Building 3. Noteworthy members of his laboratory included **Bernard Horecker** and **Leon Heppel**. Horecker is best known for his contributions to the pentose phosphate pathway, the end products of which are needed for amino and fatty acid synthesis. Heppel was a leader in the study of enzymes that modify RNA.

**Herbert Tabor**, who worked in another building, would join Kornberg, Horecker, and Heppel in Building 3 for weekly lunch seminars on enzymology. "We did, in a rather intensive way, every week including most holidays, have a three-quarters of one hour presentation on all the important topics in biochemistry," said Tabor, now a senior investigator in the Pharmacology Section in NIDDK. "It was particularly helpful to me—Kornberg and I only had M.D.s. Essentially, we learned biochemistry."

Kornberg left NIH to head the Microbiology Department at Washington University School of Medicine (St. Louis) in 1953 and then moved to Stanford University (Stanford, Calif.). In 1959, he shared the Nobel Prize in Physiology or Medicine for

the discovery of the mechanisms in the biological synthesis of RNA and DNA.

NHLBI was born in 1948 in Building 3, although at the time it was simply the National Heart Institute. In 1949, **James A. Shannon**—who had been a leader of New York University's Research Service at Goldwater Memorial Hospital on Welfare Island in New York and directed its antimalarial research group—was appointed NHI's first director of intramural research. Shannon, from his office on Building 3's second floor, recruited members to fill research positions in areas such as cell biology, chemical pharmacology, cardiovascular physiology, kidney and electrolyte metabolism, natural products chemistry, technical development, and cardiovascular surgery. He moved to Building 1 in 1952, where he served first as the director of intramural research for all of NIH and then as NIH director (1955–1968). He oversaw a period of increased construction, additional funding for research personnel and laboratories, and the creation of new research centers. He brought money from Capitol Hill and new optimism to NIH. To honor him for his many contributions, the central administration building (Building 1) was named for him in 1983.

Notable recruits from Shannon's former group at Goldwater Hospital were **Bernard B. Brodie**, **Robert Berliner**, **Robert Bowman**, and **Sidney Udenfriend**. Brodie was brought in as head of NHI's Laboratory

**LEFT**

The NIH campus in the 1940s included the historic core of six Georgian-style buildings, built in the late 1930s, and Buildings 7, 8, and 9, constructed in the 1940s. In keeping with the tradition of the random location of buildings, Building 1 (with the columns) is in the center; to the left, from front to back, are buildings 3, 8 (partially hidden), 5, 9 (partially hidden), and 7; to the right, from front to back, are buildings 6 (in the foreground), 2, and 4.

**RIGHT**

**Near right:** Thressa (shown) and Earl Stadtman worked in Building 3 and were outstanding biochemists and mentors who dedicated their careers to research at NIH. **Far right:** Building 3 featured what was then state-of-the-art equipment including this chemical fume hood.



for Clinical Pharmacology and later received a 1967 Lasker Award for his contributions to biochemical pharmacology. Berliner, an eminent renal physiologist, was appointed chief of the Laboratory of Kidney and Electrolyte Metabolism, served as director of intramural research of the National Heart Institute (1954–1968), and was appointed NIH deputy director for science 1969–1973. He left in 1973 to become dean of the Yale School of Medicine (New Haven, Conn.).

Bowman became chief of the Laboratory of Technical Development and invented the practical spectrophotofluorometer (SPF), an instrument originally designed to measure the concentration of antimalarial drugs. Udenfriend and Brodie helped Bowman develop the SPF. Udenfriend left NIH in 1967 to become the founding director of the Roche Institute of Molecular Biology (Nutley, N.J.).

Brodie recruited former Goldwater colleague **Julius Axelrod** as a technician who later went to graduate school at George Washington University School of Medicine (Washington, D.C.). Axelrod shared the 1970 Nobel Prize in Physiology or Medicine for work on the release and reuptake of catecholamine neurotransmitters.

Axelrod was taken with the research environment in Building 3. “It was a remarkable place,” he said in a 1991 *NIH Alumni Association Update* article. “We were all young, and working in a very charged atmosphere.”

In 1953, Shannon also hired 10 young physicians as clinical research associates to split their time between working in NIH’s new Clinical Center, taking care of patients, and in the laboratory. Two physicians to go

through this program, and who spent their first several months at NIH in Building 3 labs, later became NIH directors: **James Wyngaarden** and **Donald S. Fredrickson**.

Another Shannon recruit to later receive the Nobel Prize was **Christian Anfinsen**, who was appointed chief of NHI’s Laboratory of Cellular Physiology in 1950. Anfinsen shared the 1972 Nobel Prize in Chemistry for groundbreaking work in protein chemistry. Two of Anfinsen’s postdoctoral fellows who worked in his Building 3 laboratory are still at NIH—**Edward Korn** and **Martha Vaughan**—and they remember some of the building’s quirks.

Researchers often shared the Building 3 elevator with animals being transported to the top floor. “I once got in the elevator with a cow going up, who was urinating at the time,” chuckled Korn, now chief of NHLBI’s Laboratory of Cell Biology. “I was sort of ankle deep.”

Vaughan, now chief of NHLBI’s Laboratory of Metabolic Regulation, recalls the cumbersome ventilation system. Her lab’s air conditioner was a window unit positioned over a vent for a chemical fume hood in a basement laboratory. “When anybody used the chemical hood downstairs to carry away the noxious fumes, they would let us know,” said Vaughan. The warning alerted Vaughn to turn off the air conditioner, which would have sucked the fumes into her lab.

In 1950, Anfinsen recruited biochemists: **Thressa Stadtman**—who had been his research assistant at Harvard Medical School (Boston)—and her husband **Earl**. The Stadtman family became outstanding researchers and beloved mentors to later generations of NIH scientists. They

remained in Building 3 until its 2001 closing, except for several years in the mid-1950s when they worked at the Clinical Center. Initially, Earl Stadtman was disappointed that his labs weren’t ready when he arrived at NIH. “The laboratories in the basement of this building at that time were just a gaping hole,” he said in a 2001 interview with NIH’s Office of History. Fortunately, Arthur Kornberg offered the group the temporary use of a vacant laboratory on the first floor.

Thressa Stadtman studied the bacterial degradation of cholesterol, while Earl Stadtman researched fatty acid metabolism. Earl was appointed chief of NHLBI’s Laboratory of Biochemistry in 1962, and Thressa became one of its section heads in 1974.

The Stadtman family made several landmark contributions to the field of biochemistry, switching their research focus as they saw fit. In the late 1950s, Thressa’s studies of anaerobic metabolism systems led to the discovery of five of the 12 known vitamin B12-dependent enzymes. She also pioneered the field of selenium biochemistry, identifying many selenium-containing proteins. Selenium has been shown to have health benefits in animal studies and may be a necessary nutrient for humans.

Earl’s initial work in Building 3 helped to establish the role of coenzyme A in the synthesis of fatty acids. In the 1960s and 1970s, he and co-workers identified mechanisms for controlling the production of amino acids. In the 1980s, his team began investigating protein damage in relation to aging and found that the accumulation of

CONTINUED ON PAGE 12

**Building 3**

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damaged proteins may play a role in age-related disorders such as Parkinson disease.

Between them, the Stadtmans trained more than 100 postdoctoral fellows, including **Roy Vagelos**, **Michael Brown**, and **Stanley Prusiner**. Vagelos started as a clinical fellow in Earl's laboratory (1956–1958) and eventually rose to the level of section chief and ran his own suite of laboratories in Building 3. He left NIH in 1966 to become chairman of the Department of Biological Chemistry at Washington University School of Medicine in St. Louis, and in 1975 joined the pharmaceutical company Merck, became its president in 1976, and later served as chief executive officer and chairman of the board (1986–1994).

Vagelos's lab was on the second floor and "it was kind of a wild place," recalled **Michael Poston**, who joined Earl Stadtman's laboratory in 1961 and was a staff scientist at NIH until 1999. "They were full of themselves, and they had a lot fun."

Michael Brown was Earl's postdoctoral fellow from 1969 to 1971, before joining the faculty at the University of Texas Southwestern Medical School (Dallas). Brown and another NIH alumnus, Joseph Goldstein, were honored with the 1985 Nobel Prize in Physiology or Medicine for their discovery of mechanisms regulating cholesterol metabolism.

Stanley Prusiner, a postdoctoral fellow from 1969 to 1972, also in Earl's lab, went on to receive the 1997 Nobel Prize in Physiology or Medicine for his discovery of prions, which are proteins that have become infectious.

The first woman to be board-certified as a cardiac surgeon, **Nina Braunwald**, also did research in Building 3 during the 1960s and developed artificial heart valves, which she tested in dogs housed in Building 3's attic.

Other animals in Building 3, in the attic's animal breeding facility or in some of the labs on other floors, included cats, sheep, and even chickens. In fact, one group of physiologists kept chickens in their second-floor laboratory, next to the library where Stadtman's group held its journal club seminars. "Right in the middle of this impressive seminar, you'd get a bird next door [cackling when] it laid an egg!" said Poston. The physiologists kept a couple of pigs, too. "One day, we came out of [our lab meeting] and discovered they did a Caesarian section on a sow. She [had] delivered about eight piglets, right there in the middle of the lab."

There were even tales of an enormous mummified frog that workmen discovered lodged in a pipe in one of the labs.

By 2001 when Building 3 was closing, only the NHLBI labs remained. The physical, mechanical, and electrical systems were obsolete and unable to support the sophisticated instrumentation needed for state-of-the-art biomedical research. "It was decrepit as a laboratory building," said Poston. "I think the only thing that was holding the building together at the end was the paint."

But the research certainly never mirrored Building 3's physical deterioration. In 2001, the remaining scientists transferred to Building 50, where they continue to thrive today and remember Building 3 fondly.

"It was our building," reminisced Korn. "It was like a home." ●

More Building 3 photos at: <http://irp.nih.gov/catalyst/v20i5/an-nih-research-dynasty-in-building-3>

## An "Instrument" Worth Mentioning: The Anaerobic Laboratory



This oxygen-free, steel-framed box was the first of its kind to be used for biomedical research. Built in 1967 for \$250,000, NIH's anaerobic laboratory was primarily used by Earl and Thressa Stadtman's groups to work with certain enzymes and other biological compounds that are inactivated when exposed to oxygen. The room was filled with a mixture of nitrogen and hydrogen and contained a variety of instruments. Anyone working in the room had to wear a

special mask fitted with an air-delivery tube and be continually monitored—both visually and via a two-way communication system—by someone who sat outside the room.

Despite all the precautions, there were times when the mask failed or didn't fit properly. "The first time we used [the oxygen mask], we had a long, skinny-faced fellow who put it on," recalled former NHLBI scientist Michael Poston. "He was getting a little woozy." The Stadtmans eventually installed an oxygen monitor to guard against this sort of problem, but not before at least one man nearly passed out.



## Building 3 Luminaries

### MENTIONED IN THE ARTICLE:

**Christian Anfinsen** received the 1972 Nobel Prize in Chemistry for “for his work on ribonuclease, especially concerning the connection between the amino acid sequence and the biologically active conformation.”

**Julius Axelrod** was awarded the 1970 Nobel Prize in Physiology or Medicine for his work on catecholamine neurotransmitters.

**Robert Berliner** was an eminent renal physiologist.

**Robert Bowman** invented the practical spectrophotofluorometer, used to measure tiny amounts of substances in the body.

**Nina Braunwald** was the first woman to be board certified as a cardiac surgeon.

**Bernard B. Brodie** was an internationally renowned pharmacologist who was involved in the development of acetaminophen (with Julius Axelrod before coming to NIH) and won a Lasker Award in 1967 for his contributions to biochemical pharmacology.

**Michael Brown** shared the 1985 Nobel Prize in Physiology or Medicine for discovery of mechanisms regulating cholesterol metabolism.

**G. Robert Coatney** was a malaria researcher who identified the malaria parasite in birds.

**Nathan B. Eddy** helped to spearhead the field of drug dependence.

**Donald S. Fredrickson** served as NIH director (1966 to 1974) and was elected to the National Academy of Sciences for his accomplishments in lipid research.

**Leon Heppel** was one of first to investigate enzymes that modify RNA.

**Bernard Horecker** discovered key enzymes and phosphates in the pentose phosphate pathway, which is important for the synthesis of amino and fatty acids.

**Edward Korn** made landmark discoveries about two of the proteins responsible for cell movement, actin and myosin.

**Arthur Kornberg** was the 1959 Nobel laureate in Physiology or Medicine for being the first (along with Severa Ochoa) to synthesize DNA.

**Stanley Prusiner** received the 1997 Nobel Prize in Physiology or Medicine for the discovery of prions, a new biological principle of infection.

**James A. Shannon** was the National Heart Institute’s first scientific director, NIH’s first director of intramural research, and later served as NIH director (1955 to 1968).

**Thressa and Earl Stadtman** were outstanding biochemists and mentors who dedicated their careers to research at NIH. Thressa’s studies of anaerobic metabolism systems led to the discovery of five vitamin B12-dependent enzymes. She also pioneered the field of selenium biochemistry. Earl helped to establish the role of coenzyme A in the synthesis of fatty acids, identified mechanisms for controlling the production of amino acids, and investigated protein damage in relation to aging.

**Sidney Udenfriend** became the founding director of the Roche Institute of Molecular Biology in Nutley, N.J. (1967 to 1983).

**Roy Vagelos** became chief executive officer Merck Pharmaceuticals (1985 to 1986).

**Martha Vaughan** performed groundbreaking work on the role of cyclic nucleotides and G-proteins in regulating lipolysis in fat cells (married to Jack Orloff).

**James Wyngaarden** served as NIH Director (1982 to 1989).

### OTHER BUILDING 3 LUMINARIES

**Eugene Braunwald**, who had a lab in Building 3 during the 1960s, was a renowned cardiologist whose work has expanded the knowledge of heart diseases in the areas of congestive heart failure, coronary heart disease, and valvular heart disease.

**James Ferretti**, a leader in the application of pulsed Fourier-transform nuclear magnetic resonance techniques to the study of medically important chemical and biological systems, did this work in Building 3 during the 1990s.

**Evan Horning**, a pioneer of modern biochemical analysis techniques, was chief of NIAMD’s Laboratory of the Chemistry of Natural Products in Building 3 during the early 1950s.

**Herman Kalckar** was a pioneer in the study of cellular respiration; he worked in Building 3 in the early 1950s.

**Edward S. Josephson** was a pioneer in developing radiation sterilization of food; he worked on treatments against malaria and other tropical diseases in Building 3 during the 1940s and 1950s.

**Jack Orloff** worked in Building 3 in the early 1950s and served as NHLBI’s scientific director from 1974 to 1988 (married to Martha Vaughan).

**Sue Goo Rhee**, a former Stadtman postdoc, was head of the Laboratory of Cell Signaling when it was moved to Building 50 in 2001. While working in Building 3, he made major contributions to the understanding of cell signaling by enzymes, the phospholipases, and discovered a new class of signaling enzymes, now called peroxiredoxins.

**Nathan Shock**, a noted gerontologist and first scientific director of NIA, had an office in Building 3 in the 1950s.

**Luther Terry**, who had an office in Building 3 as NHLBI’s chief of General Medicine and Experimental Therapeutics in the early 1950s, served as U.S. Surgeon General (1961 to 1965).

**Bernhard Witkop** discovered the “NIH shift,” a phenomenon in organic chemistry, and helped form the NIH Visiting Fellows Program; he was in Building 3 in the early 1950s.

Many thanks to all who helped with the article on the history of Building 3: Edward Korn, Alan Schechter, NIH Office of History (Barbara Harkins, Hank Grasso, Victoria Harden, Michele Lyons), Eugene Braunwald, Dexroy Chism, Rodney Levine, Buhm Soon Park, Michael Poston, Herbert Tabor, Martha Vaughan, the *NIH Record* and others.

**Clinical Center News**

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investigators may access Clinical Center resources through previously existing funding relationships such as contracts, grants, and cooperative agreements. Administrative supplements to grants are also available for short-term Bedside-to-Bench Awards Program projects that involve partnerships between intramural and extramural investigators for translational research projects.

The CC, which received the 2011 Lasker-Bloomberg Public Service Award (<http://clinicalcenter.nih.gov/ccaward.html>) from the Albert and Mary Lasker Foundation, is a 240-bed hospital and research facility with more than 1,500 clinical research protocols underway. The recommendation that the NIH allow external investigators to use CC resources to stimulate a broader range of research came from the Congressionally mandated Scientific Management Review Board (SMRB). The SMRB was authorized by the NIH Reform Act of 2006 and charged with examining the NIH's organizational structure and providing recommendations for enhancing the agency's mission.

For more information, contact the Clinical Center Partnerships at [ClinicalCtrPartner@mail.nih.gov](mailto:ClinicalCtrPartner@mail.nih.gov) or 301-496-4121 or visit these Web sites:

- “Collaborating with NIH Intramural Investigators at the Clinical Center” Web site: <http://clinicalcenter.nih.gov/translational-research-resources/index.html>
- Opportunities for Collaborative Research at the NIH Clinical Center: <http://grants.nih.gov/grants/guide/notice-files/NOT-HD-12-025.html>
- SMRB's 2010 Report on the NIH Clinical Center: [http://smrb.od.nih.gov/documents/reports/CC\\_122010.pdf](http://smrb.od.nih.gov/documents/reports/CC_122010.pdf)
- Intramural Research Program: <http://irp.nih.gov>

## PI Profile Pages Go Live

The IRP Web Site To Offer Central Listing of NIH PIs

BY BEN CHAMBERS, SPECIAL TO THE *NIH CATALYST*

**FINDING INFORMATION ON THE** approximately 1,200 intramural principal investigators (PIs) spread across 23 NIH Institutes and Centers (ICs) has often depended on networking with other scientists or browsing multiple Web sites.

Until now.

In September 2012, the Intramural Research Program (IRP) Web site (<http://irp.nih.gov>) launched the first wave of PI profiles, which included nearly 400 researchers in six intramural programs: National Cancer Institute–Center for Cancer Research (NCI-CCR), National Human Genome Research Institute (NHGRI), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Dental and Craniofacial Research (NIDCR), National Institute of Neurological Disorders and Stroke (NINDS), and Center for Information Technology (CIT).

The IRP profiles provide uniform “snapshots” of intramural investigators’ research as well as links to more information on IC Web sites. Each profile includes “Research Topics” for an overview of an investigator’s work, “Biography” for educational training and other information, up to five “Selected Publications,” and a list of one or more of the 21 “Scientific Focus Areas” (SFAs) into which a PI’s research can be broadly categorized.

Visitors to the IRP site can look up PIs by name or by SFAs. For example, if someone is looking for research on chromosome biology, choosing that SFA on the search page will result in links to all IRP investigators with a major focus on chromosome biology. The PIs

themselves, with the help of others at their ICs, are determining the appropriate SFAs.

“There is a wealth of talent at the NIH, but sometimes it is hard to find just the person you want to work with or someone who can help you solve a thorny problem in the laboratory or clinic,” said Deputy Director for Intramural Research Michael Gottesman. “The new, uniform PI profiles will make all of our talented principal investigators easily and immediately accessible.”

The IRP PI profiles won’t replace current PI Web pages on IC Web sites; instead they will complement what may already exist and use information from PIs’ home profiles. To avoid the confusion caused when multiple profiles exist for each PI, the IRP Web site populates its profiles with data pulled from IC Web sites, so the information remains in sync. The IRP profiles will also provide visibility for PIs who don’t already have profiles on their IC Web sites.

The technical team tackling the challenge of compiling and formatting profile data from 23 intramural programs operating within unique information environments includes architect Jeff Shilling (NCI-CCR), Yang Fann (NINDS), Mark Fredriksen (NHGRI), and Rohit Paul (NCI-CCR).

PI profiles will be continually added to the IRP Web site throughout the year and into 2013. When completed, the IRP Web site will include profiles of all of the approximately 1,200 PIs at the NIH.

For more information on the profile integration process, contact Mark Fredriksen at [fredriksenm@mail.nih.gov](mailto:fredriksenm@mail.nih.gov) or 301-721-6345. ●



## Jeter's Leaders Visit NIAAA

BY MEGHAN MOTT, NIAAA

SUMMER IS BASEBALL SEASON, AND ON JULY 24 INTRAMURAL SCIENTISTS at the National Institute on Alcohol Abuse and Alcoholism (NIAAA) hosted the all-star team “Jeter’s Leaders” to teach them about the latest research in alcohol abuse and alcoholism. Approximately 100 high school students from Michigan and New York traveled to NIH to catch a glimpse of the big leagues in scientific research.

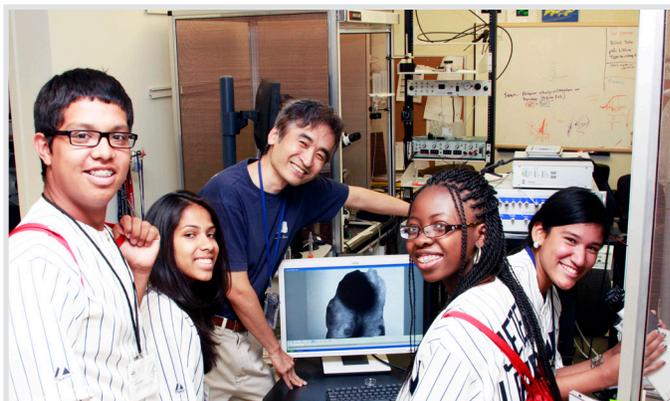
The Jeter’s Leaders Program is a youth leadership-development and social-change program started by Derek Jeter, captain of the New York Yankees. Funded by his Turn 2 Foundation, Jeter’s Leaders promote academic achievement and healthy lifestyles free of alcohol and substance use.

“By interacting with our Ph.D.s and health professionals, the students can gain a new perspective as they think about college majors and their future,” said NIAAA public liaison officer Fred Donodeo, who first invited Jeter’s Leaders to visit NIH in 2002. This year, their visit included a full line up of science presentations, interactive exhibits, and hands-on laboratory activities. The students spent the morning in Bethesda, at the Clinical Center, discussing alcohol abuse in adolescence, learning about the importance of minority involvement in health research, and taking a tour of the building.

For the second part of their double-header program, the students headed to Rockville. At the Fishers Lane facility, the rookies broke into smaller groups for site visits. They viewed the “Drunken Brain,” an interactive exhibit that shows how the brain functions normally and under the influence of alcohol. They also experienced the disorienting properties of alcohol intoxication by donning “Fatal Vision” goggles that simulate being under the influence. They even got to hold a human brain specimen from one of the world’s largest brain collections.

In a series of hands-on demonstrations, NIAAA principal investigator **Fumihito Ono** explained how studying zebrafish advances our understanding of alcohol exposure during development. “It is very rewarding to watch these students get involved in the lab because they are so excited and full of energy,” he said.

The event was a home run. “Exploring the labs and seeing where huge developments and discoveries are made was really cool,” said a student from Portage Northern High School in Kalamazoo, Mich.



PABAK SARKAR, NIAAA

NIAAA principal investigator Fumihito Ono showed Jeter’s Leaders zebrafish larvae exposed to alcohol in his Laboratory of Molecular Physiology.



JONATHAN STREET, NIDDK

NIDDK staff scientist Peter Yuen, who has owned a Nissan Leaf since December 2011, was pleasantly surprised to discover the charging stations in the Building 10 garage.

## Commuters Plug In

BY BRADLEY MOSS, OD

The memorable psychologist, writer, and counterculture icon Timothy Leary was famous for the line, “Turn on, tune in, drop out.” Although we don’t want employees to “drop out,” a new pilot program is encouraging owners of electric vehicles to “turn on” a charging station while they work.

With the help of the NIH Federal Credit Union (NIHFCU), eight parking spaces have been reserved on the Bethesda campus as electric-vehicle charging stations: four in the Clinical Center garage (P-2 and P-3 levels) and two each in the MLP-6 and MLP-7 garages. Spaces are painted eco green and marked “EV” for “electric vehicle.” Outlets have a kilowatt meter that records total power usage as the vehicles charge up.

Even without much fanfare, a few Chevy Volts and Nissan Leafs have been seen, dashboards blinking, powering up in the designated spaces. The pilot project will run until the NIHFCU’s \$2,000 donation of energy use is exhausted. However, if interest remains steady and a method to allow employees to pay for their own energy consumption is resolved, the parking staff envisions opening up additional charging stations at other locations on campus.

With an aim at reducing fossil-fuel consumption and pollution, even Leary himself might have found this program progressive... or at least “far out.”



## Recently Tenured



M. CATHERINE BUSHNELL,  
NCCAM



JEAN CELLI, NIAID



MARK LITTLE, NCI-DCEG



DORIAN MCGAVERN, NINDS



PAL PACHER, NIAAA

### **M. CATHERINE BUSHNELL, PH.D., NCCAM**

*Scientific Director; Senior Investigator*

**Education:** University of Maryland, College Park (B.S. in psychology); American University, Washington, D.C. (M.A. and Ph.D. in experimental psychology)

**Training:** Postdoctoral training at NEI

**Before coming to NIH:** Professor of anesthesiology and of dentistry and neurology; Canada Research Chair in Clinical Pain Research, McGill University (Montreal)

**Came to NIH:** In 1980 as staff fellow, National Institute of Dental Research (1980-1984); in July 2012 as scientific director of NCCAM

**Selected professional activities:** President (2011-2012) of the Canadian Pain Society; editor-in-chief of the International Association for the Study of Pain Press

**Outside interests:** Rock climbing; cross-country skiing; biking; kayaking

**Research interests:** My research is on the mechanisms of pain, the inability to feel it, and the underlying neurobiology. I study the consequences of acute pain becoming chronic, including the premature aging of the brain and cognitive dysfunction.

My team at McGill found that chronic pain causes brain changes. In chronic pain patients—including those with fibromyalgia, irritable bowel syndrome, and back pain—gray matter decreases more rapidly with age. Using positron-emission tomogra-

phy (PET), we demonstrated that dopamine release is altered.

We used behavioral assays of pain, anxiety, and cognition, and magnetic-resonance imaging and PET to show that rats have increased pain sensitivity after a nerve injury but develop changes in anxiety and cognitive function and a decrease in frontal cortical gray matter several months later. When rodents with nerve injuries were placed in enriched environments, their chronic pain behavior was reduced or eliminated. An impoverished environment exacerbated the behavior. I hope that a better understanding of chronic pain will help people manage it. (See story on page 9 for more on Bushnell.)

### **JEAN CELLI, PH.D., NIAID**

*Senior Investigator, Tularemia Pathogenesis Section, Laboratory of Intracellular Parasites*

**Education:** University Paris XI Orsay (B.S. in biochemistry and molecular genetics); University Pierre et Marie Curie, Paris (Ph.D. in microbiology)

**Training:** Postdoctoral training in the Biotechnology Laboratory at University of British Columbia (Vancouver, Canada)

**Before coming to NIH:** Institut National de la Santé et de la Recherche Médicale (France)

**Came to NIH:** In May 2004

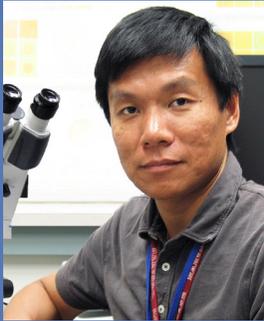
**Outside interests:** Mountain biking; hiking; doing photography

**Research interests:** I am interested in understanding how infectious agents survive within host cells to generate disease. My group studies the bacterial disease-causing pathogens *Brucella abortus* and *Francisella tularensis*, which cause zoonoses, diseases that can be transmitted between animals and humans. We combine microbiology, cell biology, and genomics to identify the molecular mechanisms by which such pathogens circumvent host defense mechanisms in order to survive and replicate within mammalian cells.

*Brucella abortus*, the most common zoonosis, causes brucellosis, a disease that infects cattle, goats, camels, dogs, and pigs. There are an estimated 500,000 new human cases of the disease worldwide each year. We are currently characterizing the mechanisms by which *Brucella* survives, proliferates, persists in, and exits the host cell.

*Francisella tularensis* is a highly infectious bacterium that causes tularemia, a disease that affects wild rabbits and other rodents. We have identified novel virulence genes required for this pathogen's intracellular proliferation. We are characterizing the genes' functions to better understand the *Francisella* molecular virulence mechanisms.

If you have been recently tenured, the *NIH Catalyst* will be contacting you soon about including you on these pages.



YIHONG YE, NIDDK

**MARK LITTLE, D.PHIL., NCI-DCEG**

*Senior Investigator, Radiation Epidemiology Branch*

**Education:** Trinity College, Cambridge, England (B.A. and M.A. in mathematics); New College, Oxford, England (D.Phil. in mathematics)

**Before coming to NIH:** Operational research executive at British Coal (London); research officer at Berkeley Nuclear Laboratories (Berkeley, England); principal scientific officer for the National Radiological Protection Board (Didcot, England); associate professor in statistics in the Department of Epidemiology and Biostatistics at Imperial College (London)

**Came to NIH:** In May 2010

**Selected professional activities:** Member of a National Council on Radiation Protection scientific subcommittee that advises on low-dose radiation; member of UK Health Protection Agency Advisory Group on Ionizing Radiation; editorial board member of *Radiation and Environmental Biophysics*

**Outside interests:** Playing viola and violin in the NIH Philharmonia orchestra and other music groups

**Research interests:** For 20 years, I have been developing mathematical models to analyze the relationship between radiation dose and cancer and cardiovascular disease after exposure to radiation and cigarette smoke.

I have quantified radiation-induced cancer at both low and high doses. I am exploring how low-dose exposure pre-conception, in utero, or postnatally is linked to the risk of pediatric leukemia. My findings suggest that 15 to 20 percent of childhood leukemias could be caused by postnatal exposure to natural background radiation.

Since joining NCI, I have been the lead statistician in the UK-NCI study of cancer risk after pediatric computed-tomography exposure and in the UK-NCI study assessing thyroid cancer risk in persons exposed during childhood to radiation fallout from the 1986 catastrophic accident at the Chernobyl Nuclear Power Plant (Ukraine).

In my high-dose radiation studies, I developed mechanistic models that explain why the relative risks of cancer in patients treated with radiation therapy are lower than in comparable subsets of the Japanese atomic bomb survivors.

I have also analyzed cardiovascular risk in moderate- and low-dose radiation-exposed groups, including the Japanese atomic bomb survivors. High-dose radiation is known to contribute to cardiovascular disease risk; the evidence for low-dose radiation, however, is inconsistent. I recently proposed a mechanism that shed light on moderate- and low-dose associations.

**DORIAN MCGAVERN, PH.D., NINDS**

*Senior Investigator; Chief, Viral Immunology and Intravital Imaging Section*

**Education:** Pennsylvania State University, University Park, Pa. (B.S. in microbiology); Mayo Clinic, Rochester, Minn. (Ph.D. in molecular neuroscience)

**Training:** Postdoctoral training in the Department of Immunology and Microbial Science, Scripps Research Institute (La Jolla, Calif.)

**Before coming to NIH:** Associate professor, Scripps Research Institute

**Came to NIH:** In March 2009

**Selected professional activities:** Adjunct professor at the University of Pennsylvania (Philadelphia) and at Scripps Research Institute; editorial board of *IntraVital*

**Outside interests:** Reading; seeing movies; diving

**Research interests:** My laboratory investigates pathogens that infect the central nervous system (CNS). Many pathogens induce serious CNS diseases, including encephalitis and meningitis, which can be caused in part by the immune system. The immune system is responsible for warding off microbes that invade all parts of the body and is therefore equipped with mechanisms to neutralize them. However, these mechanisms can sometimes cause tissue injury and disease. Many microbes can enter the CNS, and it is the unique dialogue between immune cells and the infected CNS that guides much of our research. We focus specifically on immune-cell surveillance of the infected CNS, pathogenesis of viral meningitis, mechanisms that give rise to viral persistence in the CNS and periphery, the effect of chronic innate immune stimulation during viral persistence, CNS immune regulation, and therapeutic approaches to purge persistent infections.

We use many contemporary approaches to gain novel insights into these phenomena, including intravital two-photon microscopy, a deep-tissue imaging technique that can watch immune cells respond to infections or cause disease in real time. Using this approach we have recently uncovered how the immune system damages blood vessels and induces fatal convulsive seizures during viral meningitis. We are developing new therapeutic approaches to modulate neuroinflammatory processes. The efficacy of these approaches is being evaluated using both infectious and noninfectious models of CNS inflammation.

CONTINUED ON PAGE 18

**Recently Tenured**

CONTINUED FROM PAGE 17

**PAL PACHER, M.D., PH.D., NIAAA**

*Senior Investigator; Chief, Oxidative Stress and Tissue Injury Section, Laboratory of Physiologic Studies*

**Education:** Semmelweis University of Medicine, Budapest, Hungary (M.D.); Hungary Academy of Sciences, Budapest (Ph.D. in cardiovascular pharmacology and cardiology)

**Training:** Postdoctoral training in cell biology in the Department of Pathology, Anatomy, and Cell Biology, Thomas Jefferson University (Philadelphia)

**Before coming to NIH:** Assistant professor of pharmacology at Semmelweis University of Medicine; visiting research scientist at Thomas Jefferson Medical University; senior cardiovascular pharmacologist at Inotek Pharmaceuticals (Beverly, Mass.)

**Came to NIH:** In November 2002

**Selected professional activities:** Associate editor, *Journal of Gerontology Series A*; regional editor, *Current Vascular Pharmacology*; on the editorial boards of *Free Radical Biology and Medicine* and *American Journal of Physiology: Heart and Circulatory Physiology*

**Outside interests:** Traveling; doing photography; building computers

**Research interests:** My main research interest is the lipid endocannabinoid signaling system (ES), a promising therapeutic target against inflammatory and other diseases. The ES is involved in various physiological processes, mediates the psychoactive effects of marijuana, and may significantly influence inflammation and subsequent tissue injury. We have explored the ES's roles in inflammation and tissue injury associated with ischemia and reperfusion (I/R), heart failure, cardiovascular inflammation, and other pathologies. Our studies have revealed that oxidative stress, which can disrupt cellular signaling, is involved in the activation of the ES, which in turn modulates

important redox (oxidation-reduction) and/or inflammatory signaling pathways.

We also showed that modulating peripheral cannabinoid type 2 receptors protects against I/R-induced tissue injury and vascular inflammation by decreasing the activation of endothelial cells and the inflammatory response and generating chemically reactive molecules containing oxygen or nitrogen.

We have also been exploring the therapeutic and translational potential of *Cannabis sativa*-derived cannabinoids or their synthetic, more stable analogs, which previously were considered to be inactive, in I/R and diabetic complications. We have found that some of the natural constituents of marijuana that do not act on conventional cannabinoid receptors and therefore lack psychoactive effects, are potent anti-inflammatory agents and may have tremendous therapeutic potential in inflammatory diseases and diabetic complications.

**YIHONG YE, PH.D., NIDDK**

*Senior Investigator, Physical Chemistry Section, Laboratory of Molecular Biology*

**Education:** Peking University School of Medicine, Beijing (B.S. in medicine); University of Pennsylvania, Philadelphia (Ph.D. in cell and molecular biology)

**Training:** Postdoctoral training in the department of cell biology at Harvard Medical School (Boston)

**Came to NIH:** In April 2005

**Selected professional activities:** Organizer of NIH's Protein Trafficking Interest Group; member of the American Society of Cell Biology and the Society of Chinese Bioscientists in America

**Outside interests:** Drawing; practicing Chinese calligraphy; learning to play piano with his daughter

**Research interests:** My research centers on the ubiquitin proteasome system (UPS), which controls the protein-degradation process, and its roles in the protein quality-control process at the endoplasmic reticulum (ER). A cell's protein homeostasis is maintained by eliminating aberrantly folded proteins. Defects in this process result in ER stress, which has been implicated in the pathogenesis of type 2 diabetes, cancer, and other diseases. We are trying to gain a better understanding of the molecular mechanisms that shuttle misfolded proteins from the ER into the cytosol, the liquid part of the cell, where they are degraded.

We have identified a cytosolic ATPase called p97 that drives the substrates into the cytosol for degradation. We also discovered a membrane protein complex that interacts with p97 to mediate the transport of substrates into the cytosol. Recently, we found a chaperone holdase that is essential for maintaining the solubility of misfolded ER proteins, a condition required for their turnover. We are investigating how these different machineries cooperate to act in ER quality control. We are also interested in determining additional functions of p97 by searching for novel interaction partners.

We are also exploring several other aspects of the UPS that are relevant to ER protein quality control. We are breaking apart the mechanism by which polyubiquitin chains are formed on a substrate, a process essential for the degradation of misfolded ER proteins as well as many short-lived proteins in eukaryotes. We are also examining how deubiquitinating enzymes disassemble ubiquitin conjugates to facilitate protein turnover. My long-term goal is to understand the various strategies used by cells to maintain protein homeostasis. We hope to use the knowledge to establish new therapeutics for type 2 diabetes and cancer. ●



**2012 NIH RESEARCH FESTIVAL: October 9–12**  
**Tuesday, October 9: Opening Plenary Session**  
 “The NIH at 125: Today’s Discoveries, Tomorrow’s Cures”

10:00 a.m.–12:15 p.m.

Masur Auditorium, Building 10

Remaining sessions: Natcher Conference Center (Building 45); Building 10, and Parking Lot 10H

Don’t miss this year’s festival featuring scientific symposia, poster sessions, workshops, a scientific equipment tent show, and more. The plenary session will be videocast (<http://videocast.nih.gov>). For more information, visit the Research Festival Web site at <http://research-festival.nih.gov>.

#### NIH SCIENCE EDUCATION CONVERSATIONS

Thursday, September 27, 2012

3:00–4:30 p.m.

Building 50, Room 1328/1334

The kickoff for this new monthly seminar series—to promote thinking and discussion about science education—will feature world-renowned science education expert Rodger Bybee, director emeritus of Biological Sciences Curriculum Study, who will present “Thinking Differently about How We Teach Science: Why Should NIH Care, and What Can NIH Do?” Future sessions in 2012 are on October 25, November 29, December 20. For more information, visit <http://science.education.nih.gov/sciedconversations> or contact Cynthia Allen ([allency@od.nih.gov](mailto:allency@od.nih.gov) or 301-496-1872).

#### INTERNATIONAL OPPORTUNITIES EXPO AND CAREER FAIR

Friday, September 28, 2012

12:00–4:30 p.m.

Natcher Conference Center (Building 45)

Postdocs and graduate students considering careers abroad won’t want to miss this event. For more information visit [https://www.training.nih.gov/international\\_expo\\_2012](https://www.training.nih.gov/international_expo_2012) or contact Shirley Forehand ([forehans@mail.nih.gov](mailto:forehans@mail.nih.gov) or 301-402-2174).

#### NATIONAL GRADUATE STUDENT RESEARCH CONFERENCE (NGSRC)

October 9–10, 2012

Natcher Conference Center (Building 45)

Lister Hill Auditorium (Building 38A)

The NGSRC will be held in conjunction with the NIH Research Festival (October 9–12). More than 100 advanced graduate students—who were chosen from an applicant pool of 500 and who are racially and ethnically diverse—from across the United States will come to the Bethesda campus for this NIH-sponsored scientific meeting. For more information, visit [https://www.training.nih.gov/events/recurring/nih\\_national\\_graduate\\_student\\_research\\_festival](https://www.training.nih.gov/events/recurring/nih_national_graduate_student_research_festival) or contact Shirley Forehand ([forehans@mail.nih.gov](mailto:forehans@mail.nih.gov) or 301-402-2174).

#### INTRODUCTION TO THE PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH

October 16, 2012, through March 26, 2013

Monday and Tuesday evenings

5:00–6:30 p.m.

NIH campus

Registration: free; deadline October 9, 2012

This course will be of interest to physicians and other health professionals planning a career in clinical research. The textbook, John I. Gallin’s *Principles and Practice of Clinical Research, Third Edition*, is optional but it may be helpful. For more information or to register, visit the course Web site at <http://www.cc.nih.gov/training/training/ippcr/application.html> or call 301-496-9425.

#### 2012 NIH COMMUNITY COLLEGE DAY

Friday, October 19, 2012

8:00 a.m.–4:00 p.m.

Natcher Conference Center (Building 45)

Lister Hill Auditorium (Building 38A)

Community college students and faculty will visit the NIH campus and learn about careers and training opportunities in the biomedical and health-care fields. To register and for more information, visit <http://www.training.nih.gov> or contact Shirley Forehand ([forehans@mail.nih.gov](mailto:forehans@mail.nih.gov) or 301-402-2174).

#### TRANSLATIONAL RESEARCH INTEREST GROUP (TRIG)

Lecture Series 2012–2013

Thursdays, 1:00–2:00 p.m.

Lipsett Amphitheater (Building 10)

Dates in 2012: September 13 (1:00–3:00 p.m.), October 25, November 8. For more information, visit <http://sigs.nih.gov/trig>.

#### SOPS FOR COLLECTION OF NORMAL HUMAN BIOSPECIMENS

NCI released a compendium of standard operating procedures (SOPs) to guide the successful collection, processing, storage, and distribution of normal human biospecimens for the NIH Genotype-Tissue Expression (GTEx) project. For more information, visit <http://biospecimens.cancer.gov/resources/sops> or contact [nciobbr@mail.nih.gov](mailto:nciobbr@mail.nih.gov).

#### NEW PROCESS TO ACCESS COMPILATION OF AGGREGATE-LEVEL GENOMIC DATA

NIH has implemented a new controlled-access process to enable intramural and extramural investigators to make a single request to access multiple aggregate data sets from the database of Genotypes and Phenotypes (dbGaP). For more information, go to [http://gwas.nih.gov/pdf/Compilation\\_of\\_Aggregate\\_Genomic\\_Data.pdf](http://gwas.nih.gov/pdf/Compilation_of_Aggregate_Genomic_Data.pdf) or contact Erin Luetkemeier ([gwas@mail.nih.gov](mailto:gwas@mail.nih.gov)).

#### TRANSFER AGREEMENTS MADE EASY!

The NIH Transfer Agreement Dashboard (TAD) takes the stress out of the Material Transfer Agreement (MTA) experience by helping users track and manage all their MTAs in one easy-to-use application. To obtain a TAD account, contact the TAD support team at [NIHTADSupport@mail.nih.gov](mailto:NIHTADSupport@mail.nih.gov) or visit the TAD Web site at <http://techtransferagreements.nih.gov>.

More online at <http://irp.nih.gov/catalyst/v20i5/announcements>

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## CATALYTIC REACTIONS?

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

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

**Online only:** Carolyn Graybeal’s article on NSF Director Sabra Suresh’s recent visit to NIH. Go to: <http://irp.nih.gov/catalyst/v20i5/features/subra-suresh-at-the-interface-of-engineering-and-biology>.

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<http://irp.nih.gov/catalyst>

## PHOTOGRAPHIC MOMENT

### Bucks Aplenty



DOUGLAS SAXTY, OD

Amateur photographer Doug Saxty caught these deer on camera as they roamed the NIH campus recently. Saxty—who is on campus nearly every day, either delivering histology slides during the week or driving the shuttle buses on weekends—loves the outdoors and photographing nature in the National Parks. He uses a Nikon D70 camera with a 70-300 zoom lens.

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