

From Earthquake To NIH Lab

BY CHRISTOPHER WANJEK

WATARU SAKAMOTO WAS INSERTING A long needle into the gut of one of his cancer patients to drain some fluid at the moment the 9.0 magnitude earthquake hit in Japan on March 11, 2011.

The quake lasted for a six-minute eternity, moved the entire island eight feet to the east, and culminated in a devastating tsunami that wiped out whole towns and took more than 15,000 lives. Then came the radiation horror as the Fukushima Daiichi nuclear facility began to fail a few days later, spewing radioactivity across the region.

The tsunami displaced hundreds of thousands of Japanese living in Fukushima, the stricken prefecture. Sakamoto—a surgeon at Fukushima Medical University and at a hospital in the small city of Koriyama—was one of them. Fearing the radioactive fallout from the unstable reactors, he moved his wife and three children (including a newborn) to Hokkaido in the north while he continued his work at the Koriyama hospital about 12 miles beyond the forced evacuation zone.

Sakamoto spoke of the confusion in the days after the quake, as most in the region were without power and phone connections. The hospital he was working in needed to take in patients from another hospital, just a few blocks away, that was heavily damaged.

Now Sakamoto and his family are in the relative calm of Rockville, Md.,

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2011 Research Festival

Packed with the Best NIH Has to Offer

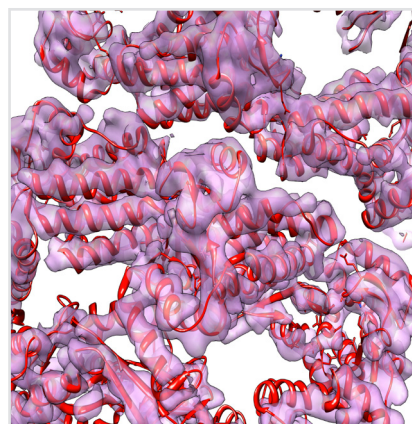
BY LESLEY EARL, NIDCR

ONCE UPON A TIME—IN SEPTEMBER 1986—the NIH Intramural Research Day was an all-day affair featuring eight talks, 20 workshops, 95 posters, and an evening picnic with jazz musical entertainment on the lawn outside Building 35. Over the years, the event has morphed into a multiday festival. In 2011 the NIH Research Festival featured a plenary session, concurrent symposia sessions with 20 topics and 120 talks, more than 400 posters, special exhibits, a scientific equipment tent show, and more. The picnic, now held at lunchtime, has become a “Taste of Bethesda” event with offerings from area restaurants and entertainment by local musicians.

The idea behind the original NIH Research Day was to “solve the institute silo problem [and] bring people together from all the different institutes and to have them present their work,” said Research Day founder and former Scientific Director Abner Notkins (NIDCR). “There was so much overlapping work going on in different institutes, and often people were not aware of that.”

Notkins also realized that NIH scientists were unlikely to meet researchers outside their own institutes except at “national and international meetings,” he said. It seemed “a little ridiculous, to have to go to Europe to meet people here at the NIH.”

Over the quarter-century since the NIH intramural community began setting aside a day to share and celebrate research, the festival has grown in length, breadth, scope, and



A. BARTESAGHI, D. SCHAUDER, S. SUBRAMANIAM, NCI

The Research Festival sessions were chock-full of exciting science. In the symposium on dynamic protein assemblies, researchers talked about the challenges of determining how proteins are structured (see page 11). Sriram Subramaniam (NCI) and his colleagues used automated cryo-electron microscopy to obtain high-resolution images of large protein structures such as the GroEL chaperone complex shown above. This density map obtained from cryo-electron microscopy, is superimposed on a structure of the same complex obtained using X-ray crystallography (the thin red spirals).

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Cognitive Resonance: How Do We Come Up with New Ideas?

BY MICHAEL GOTTESMAN, DDIR

I DON'T PRETEND TO BE AN EXPERT IN cognitive psychology, but I do spend a lot of time thinking about how scientists come up with innovative new hypotheses and new approaches to difficult scientific problems. And, of course, I want to be sure that we create an environment in the Intramural Research Program that optimizes the likelihood that creative lightning will strike our intramural scientists.

This commentary was stimulated by an article in my college alumni bulletin about how the Internet affects the way people think about problems. Some claim that acquiring and remembering information is no longer an essential element of learning, because so much is at our fingertips through search engines and the World Wide Web. We merely download the information onto our computers or our handheld gadgets. But what are the consequences of filling our brains with ways to obtain information rather than with the information itself?

One way to create new hypotheses is to let lots of information scurry around in the brain until there is an epiphany that organizes the knowledge around a central theme or explanation. How the brain works its magic is still unclear, but most of us have had the experience of pulling disparate information into a coherent hypothesis.

What happens, however, if the brain is devoid of the information that we need as a substrate for creative thinking? Eventually, our computers will be able to assemble data into new ideas for us (at which point, scientists may be obsolete), but that is not yet the case. Is it possible that fewer and

fewer new hypotheses will result from this lack of empirical information in our heads?

The situation is complex. It can be argued that search engines allow us to amass far more information than ever before and therefore aid, rather than limit, the creative process. If so, we must make a conscious effort to remember some of the stream of facts and ideas coming from our computers so we can ponder that information and transform it into new ideas and hypotheses.

There are other important sources of cognitive input that inform scientists about the natural world. Our own observations and experiments are critically important, as are those of our colleagues. We learn about work in other domains from conversations, publications, and lectures. This brings me to the main practical point of this essay: To do the best science it is imperative to draw widely from many sources of information.

Here is what I recommend:

- Be alert to the most interesting science in your own and distant fields. This effort will ensure that you don't try to solve a problem that has already been solved in a different system; that you learn the most effective techniques for solving problems in your field; and that you draw together information from multiple sources to generate new ideas.
- Take every opportunity to teach. Teaching helps you formulate facts into concepts.
- Read widely in the scientific literature. If you read only papers in your field you may be limited in your ability to make connections to generate new ideas. Read

your favorite journals from cover to cover; look for articles that catch your attention. By reading broadly, you should assimilate as much information as possible to inform your own scientific work. All laboratories and scientific interest groups should have journal clubs to keep you informed and sharpen your critical thinking skills.

• Go to lectures and seminars at NIH and general sessions at the professional meetings that you attend. Some of the NIH lectures are videocast and archived, and many feature outstanding speakers and are designed to expose a general scientific audience to exciting new ideas and approaches. Here is just a sampling of the many lectures at NIH:

- WALS (<http://wals.od.nih.gov>)
- Director's Seminar Series featuring recently tenured senior investigators (<http://www.nih.gov/about/director/dirsem.htm>)
- CC Grand Rounds (<http://clinical-center.nih.gov/about/news/grcurrent.html>)
- Demystifying Medicine series (<http://demystifyingmedicine.od.nih.gov>)
- Scientific Interest Groups lectures (<http://www.nih.gov/sigs>)
- NCI's Grand Rounds (<http://ccr.cancer.gov/news/StaffResources.aspx>)
- Neuroscience lectures (<http://neuroseries.info.nih.gov>)
- Immunology lectures (<http://www.nhlbi.nih.gov/resources/chi/meetings/thursday.htm>)

I would like to hear more about our scientific staff's strategies to assimilate important information and your ideas for new approaches to achieve "cognitive resonance." ●

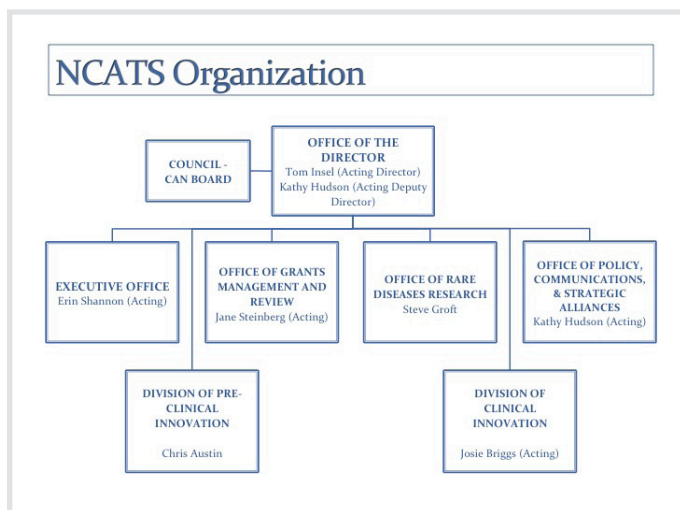
NIH Launches New Translational Science Center

BY ALAN SMITHEE

IN A MOVE TO RE-engineer the process of translating scientific discoveries into new drugs, diagnostics, and devices, NIH has established the National Center for Advancing Translational Sciences (NCATS). The action was made possible by Congress's approval of a fiscal year 2012 spending bill and President Obama's signing of the bill, which includes the establishment of NCATS with a budget of \$575 million.

NCATS will serve as the nation's hub for catalyzing innovations in translational science. Working closely with partners in the regulatory, academic, nonprofit, and private sectors, NCATS will strive to identify and overcome hurdles that slow the development of effective treatments and cures. Under the current system it can take almost 15 years for a discovery to be translated into an approved new drug. But the failure rate is more than 95 percent, and the cost per successful drug exceeds \$1 billion, after adjusting for all the failures.

"Millions of people are looking to science to deliver new and better ways to detect, treat, and prevent disease," said NIH Director Francis Collins. "Joining some of the best and brightest minds into NCATS is an important step in making the most of current scientific opportunities, examining the therapeutic development pipeline in a new way, and breaking down some of the barriers to translating discoveries into clinical advances for patients."



The National Center for Advancing Translational Sciences has no division between intramural and extramural science, but, instead, between pre-clinical research and clinical innovation.

The new center gathers existing NIH programs into an integrated scientific enterprise. The NCATS mission is to develop innovative methods and technologies designed to reduce, remove, or bypass bottlenecks in delivering new drugs, diagnostics, and medical devices to patients with a wide range of diseases and conditions.

A search is under way for a permanent NCATS director. In the meantime, the new center is being led by NIMH Director Thomas Insel as NCATS acting director and Kathy Hudson, NIH deputy director for science, outreach, and policy, as NCATS acting deputy director.

"Certainly all of us have been the patient or watched loved ones deal with illness, so we know that despite many incredible advances in medicine, there are still limitations," said Insel. "The goal of NCATS is to fix the parts of the pipeline that aren't working well to get safer and more effective medicines to patients faster. Who wouldn't embrace that?" ●

For more information visit <http://ncats.nih.gov>.

What Programs Became Part of NCATS?

Much of the planning for NCATS so far has involved coordinating the consolidation of several large, existing programs and offices, some with intramural components. These include the NIH Chemical Genomics Center and the Therapeutics for Rare and Neglected Diseases program, both part of the NIH Center for Translational Therapeutics (NCTT), which is directed by Christopher Austin. NCTT, previously part of NHGRI, is a major intramural component of NCATS. But NCATS is more about collaboration than a dichotomy between extramural and intramural domains. The real division is between preclinical research and clinical innovation; there will be more networking, blurring the line between intramural and extramural.

Programs integrated into NCATS:

- **Bridging Interventional Development Gaps**, which makes available critical resources needed for the development of new therapeutic agents
- **Clinical and Translational Science Awards** (previously part of the National Center of Research Resources—NCRR), which funds a national consortium of 60 medical research institutions working together to improve the way clinical and translational research is conducted nationwide
- **Cures Acceleration Network**, which enables NCATS to fund research in new and ways
- **FDA-NIH Regulatory Science**, which is an interagency partnership that aims to accelerate the development and use of better tools, standards, and approaches for developing and evaluating diagnostic and therapeutic products
- **Office of Rare Diseases Research**, which coordinates and supports research on rare diseases
- Components of the **Molecular Libraries**, which is an initiative that provides researchers with access to the large-scale screening capacity necessary to identify compounds that can be used as chemical probes to validate new therapeutic targets
- **Therapeutics for Rare and Neglected Diseases**, which is a program to encourage and speed the development of new drugs for rare and neglected diseases

The NCATS budget has been constructed from programs previously located in the NIH Office of the Director, NCRR, and NHGRI. NCRR's remaining programs will move to other ICs, including NIGMS, NIBIB, NIMHD, and the OD, to take advantage of existing synergies within their portfolios and missions.

**IN 2010 (additions to January-February 2011 listing in *NIH Catalyst*)**

Harry V. Gelboin (died on April 13, 2010, at 80) was chief of the molecular carcinogenesis laboratory at NCI from 1966 to 1999. His discovery of the genetic basis for the process by which normal cells are transformed into cancer cells is considered a major advance in the field.

IN 2011

Baruj Benacerraf (died on August 2, 2011, at 90), who was chief of NIAID's Laboratory of Immunology from 1968 to 1970, shared the Nobel Prize in Physiology or Medicine in 1980 for discoveries concerning genetically determined structures on the cell surface that regulate immunological reactions. A significant portion of his Nobel Prize-winning work was performed at NIH. After leaving NIH, he led the department of pathology at Harvard Medical School and was also president of the Harvard-affiliated Dana-Farber Cancer Institute.

Fred H. Bergmann (died on May 2, 2011, at 83) was a microbiologist who directed the NIGMS Genetics Program from its inception in 1972 until his retirement in 1988. He began working at NIH in 1961 as a biochemist in what is now NIDCR, where he studied the mechanisms of protein synthesis. In 1963, he transferred to what is now NHLBI to work in the laboratory of Dr. Marshall Nirenberg, who won the Nobel Prize in Physiology or Medicine in 1968 for deciphering the genetic code.

Baruch "Barry" Blumberg (died on April 5, 2011, at 85) shared the 1976 Nobel Prize in Medicine or Physiology (with D. Carleton Gajdusek of NINDS) for his work on infectious viral diseases. He discovered the hepatitis B virus and developed a preventive vaccine. He worked at NIH from 1957 until 1964 and then spent much of his career at the Institute for Cancer Research in Philadelphia, which merged into the Fox Chase Cancer Center in 1974.

Arnold Brossi (died on July 16, 2011, at 88) was an NIH scientist emeritus who headed NIDDK's Medicinal Chemistry Section from

1976 to 1991. He was widely recognized as one of the godfathers of alkaloid chemistry.

Morris E. Chafetz (died on October 14, 2011, at 87) was first director of the NIAAA (1970-1975) and a leading spokesman for the problems of alcoholism.

Wanda Chappell (died on July 18, 2011, at 93) was a chief nurse at the Clinical Center Department of Transfusion Medicine and NIH Blood Bank. In 1966, she developed a method for separating blood platelets from blood plasma.

Martin M. Cummings (died on September 1, 2011, at 90) was the director of the National Library of Medicine (1964-1983). During his tenure, the library emerged as a leader in the computer age and became one of the most advanced scientific libraries in the world.

Luise Fogarty (died on October 21, 2011, at 96), the widow of Congressman John E. Fogarty, for whom NIH's Fogarty International Center (FIC) is named. After the Congressman's death in 1967 she worked to realize her husband's goal of establishing FIC, which opened in 1968.

Lowell T. Harmison (died on March 30, 2011, at 74) came to NIH in 1967 as chief of the engineering section of the National Heart Institute's Artificial Heart-Myocardial Infarction Program. He held the first U.S. and foreign patents for the completely implantable artificial heart.

Shirley Carter Harris (died on October 17, 2011, at 73) worked as a physical science technician in NCI's Metabolism Branch for 33 years and retired in 1993.

Donald Harting (died on January 2, 2011, at 88) who served as NICHD director from 1965 to 1966 and assistant director and acting director before that, was responsible for implementing the plans for NICHD that were developed by its first director.

Rudiger "Roger" Haugwitz (died on July 18, 2011, at 79), a chemist at NCI, helped to develop anti-cancer drugs, including deriva-

tives of the chemotherapy drug Taxol, for more than two decades until his retirement in 2006.

Bernadine Healy (died on August 6, 2011, at 67) became the 13th NIH director in April 1991 and was the first woman to head the agency. After serving as director for two years, she was dean of Ohio State University Medical School (1995-1999) and president and chief executive officer of the American Red Cross (1999-2001). She was also a columnist for *U.S. News & World Report*. In 1994, she ran unsuccessfully for the U.S. Senate from Ohio.

Richard K.C. Hsieh (died on December 31, 2011, at 79), who traced his lineage to seventh-century China, retired from NLM in 1996 as director of international programs.

Donald M. Jerina (died on May 22, 2011, at 71), an organic chemist and biochemist in NIDDK, was chief of the Oxidation Mechanisms Section until 2006. An international leader in the field of chemical carcinogenesis, he pioneered research on cancer-causing polycyclic aromatic hydrocarbons (PAHs) that are widespread environmental contaminants, most notably in tobacco smoke, automobile exhaust, and the charred portions of grilled foods.

William B. Kannel (died on August 20, 2011, at 87), an epidemiologist, was the director of the Framingham Heart Study (1966-1979), which helped revolutionize the way heart disease is treated.

Harry R. Keiser (died on November 23, 2011, at 78) was the NHLBI clinical director from 1976 until his retirement in 1998. Keiser's research focus was on neurohormonal contributions to hypertension. He became a world authority on testing for pheochromocytoma, a rare but potentially curable cause of hypertension.

Carl Kupfer (died on April 7, 2011, at 83) was appointed the first director of NEI in 1970 and served for 30 years. He was also director of the Fogarty International Center in 1988.



Richard J. Levine (died on April 12, 2011, at 71), a senior investigator in NICHD's Division of Epidemiology, Statistics, and Prevention Research, made important contributions to our understanding of preeclampsia, a potentially fatal disorder of pregnancy.

Thomas E. Malone (died on March 7, 2011, at 84) served as the sixth NIH deputy director for nine years before retiring from NIH in 1986. He was the first African American to serve at such a senior level at NIH and was briefly the acting NIH director.

Richard Mercer (died on January 17, 2011, at 57) was an ophthalmic technician in NEI's Clinical Services Section since 1995.

Howard Nash (died on June 12, 2011, at 73), one of the lions of the NIH intramural program, was a senior investigator in the NIMH Laboratory of Molecular Biology. His career at NIMH spanned over four decades and was rich in scientific accomplishments and community service. His early investigations into the mechanisms of recombination in phage lambda laid the foundations for modern techniques of DNA manipulation.

Franklin A. Neva (died on October 15, 2011, at 89) was a renowned virologist, parasitologist, clinician, and former chief of NIAID's Laboratory of Parasitic Diseases. He shepherded parasitology research to become a program that involves some 400 NIAID scientific staff at laboratories in Bethesda and abroad.

Robert R. Omata (died on May 10, 2011, at 90), who served for nearly four decades at NIH, was instrumental in establishing bilateral cancer research partnerships to speed sharing of scientific information between the United States and other countries. During the 1960s, he helped bring young researchers to NIH from dozens of countries as chief of international postdoctoral fellowship programs at what is now the Fogarty International Center.

Morris B. Parloff (died on April 2, 2011, at 92), an authority of psychotherapy research, spent 30 years at the NIMH before retir-

ing as a branch chief in 1983. During World War II, he did counterintelligence work with the Army in Europe; he led a unit of German-Jewish refugee soldiers known as the "Ritchie Boys," named after the Maryland-based intelligence school where they were trained.

Marius Peacock (died on June 16, 2011, at 79) was a scientist from 1962 to 2008 at NIAID's Rocky Mountain Laboratories in Hamilton, Mont. He spent most of his career working with *Rickettsia*, the genus of bacteria that causes diseases such as Rocky Mountain spotted fever, and *Coxiella burnetii*, which causes Q fever. In 1997, a new species of bacterium that he had isolated from wood ticks was named after him, *Rickettsia peacockii*.

David Pearl (died on February 23, 2011, at 90), former chief of NIMH's behavioral sciences research branch, retired in 1984 after a 20-year career at NIMH. In 1982, he issued a government report about the links between violence on television and aggressive behavior in children.

Vincent E. Price (died on August 12, 2011 at 91) was a physician and biochemist, former deputy director of NIGMS, and a researcher in NCI. His research with amino acids led to an improved understanding of genetics at the cellular and molecular levels.

Brian Safer (died on February 6, 2011, at 68), a biochemist, worked at NIH from 1973 until retiring in 2003. He was chief of the molecular hematology branch of the NHLBI; his research focused on protein synthesis.

Harry Saroff (died on November 29, 2011, at 97) joined the Laboratory of Biophysical Chemistry of the National Institute of Arthritis and Metabolic Diseases, predecessor of the current NIDDK, in 1949, and became its Chief in 1977. He retired in 1979.

Philip E. Schambra (died on September 11, 2011, at 76) was the former director of NIH's Fogarty International Center and worked for closer ties between pure science and its clinical application.

Arthur Schatzkin (died on January 20, 2011, at 62), an NCI researcher, was internationally known for investigating the role of food and diet in causing cancer. He came to NCI in 1984 and since 1999 served as the chief of the Nutritional Epidemiology Branch in the Division of Cancer Epidemiology and Genetics. He was the first to describe an association between moderate alcohol intake and breast cancer risk, and led the landmark NCI Polyp Prevention Trial that showed that a low-fat, high-fiber diet, contrary to the prevailing hypothesis, had no effect on recurrence colon polyps.

Irene J. Underwood (died on February 11, 2011, at 98) was a retired librarian in NLM's History of Medicine Division.

Robert Weisberg (died on September 1, 2011, at 74), a geneticist and virologist, retired in 2008 after nearly 40 years at NICHD. He is best known for his elegant work in dissecting the genetics and molecular basis of site-specific recombination, packaging, and transcription anti-termination in bacteriophage lambda. After retirement, he moved to NCI's Laboratory of Molecular Biology as a scientist emeritus.

Storm Whaley (died on September 18, 2011, at 95) served as NIH's top communications official for 22 years before retiring in 1992.

T. Franklin Williams (died on November 25, 2011, at 90) served as the second director of NIA, a position he held from 1983 until 1991.

Sumner J. Yaffe (died on August 10, 2011, at 88), a former center director at NICHD, was considered the "Father of Pediatric Pharmacology." His research focused on the role of drug-metabolizing enzymes in nutrition and drug metabolism in the fetus, bilirubin metabolism, and the secretion of drugs in breast milk.

Elsie Yanchulis (died on August 28, 2011, at 86), a registered nurse who participated in research projects, spent 25 years at NIH and retired in the early 1980s as blood bank supervisor.

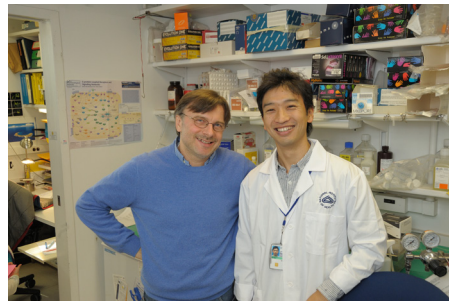
Earthquake-Displaced Scientist

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while he starts what he hopes will be a two-year stint at the NIH, presently in Jürgen Wess's NIDDK lab in Building 8 on the Bethesda campus. The NIH Japanese Scientists Association (NJSA) coordinated the visit; Fukushima Medical University is paying for Sakamoto's first year abroad.

NJSA, a volunteer organization of NIH and FDA Japanese researchers, was created in response to the Japanese earthquake disaster. Although lacking major funds, NJSA has sought to arrange for Japanese scientists to visit the NIH and also searched for surplus equipment to send to Japan.

Sakamoto is the first Japanese scientist to come to the NIH for an extended visit under an NJSA arrangement. (Researcher Misako Sato was working in Lalage Wakefield's NCI lab when the quake hit, and NCI allowed her to postpone her scheduled move to Sendai, Japan, for several months. In September, NJSA also helped Keiichi Itoi of Tohoku University, in Sendai, spend one month in Greti Aguilera's NICHD laboratory,



Jürgen Wess (left) invited Wataru Sakamoto to work in his lab at NIDDK after Sakamoto and his family were displaced by the earthquake in Japan in March.

while he stayed in the home of NIAID's Eric Long.)

Sakamoto, a gastrointestinal surgeon with both M.D. and Ph.D. degrees, wants to learn more about molecular biology to better understand tumor pathology as well as diabetes, which is on the rise in Japan.

Having arrived in October, Sakamoto already is elbow-deep in ongoing research in Wess's lab on G protein-coupled receptors, one of the largest protein families, which mediate the functions of myriad extracellular ligands such as neurotransmitters and hormones. Wess leads the Molecular Signaling Section in NIDDK's Laboratory of Bioorganic Chemistry.

Sakamoto has two goals for his stay—to publish in English and to present at a major international meeting in English. Although from highly industrialized Japan, Sakamoto so far has found his visit eye-opening in two ways: the NIH is huge, and the Bethesda area is expensive.

Grateful for the opportunity to come to NIH, Sakamoto looks forward to meeting new colleagues and collaborators. ●



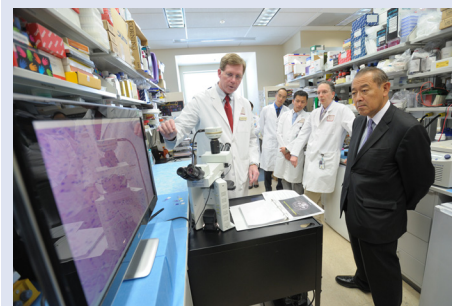
BOTH: BILL BRANSON

Scientist Wataru Sakamoto (top left) and his family left Japan after the 9.0 magnitude earthquake that devastated their country on March 11, 2011. He is now working at NIDDK with Jürgen Wess (top right) and hopes to be at NIH for two years.

NIH Hosts Japanese Ambassador and Vice Versa

NIH researchers wowed Japanese Ambassador to the United States, Ichiro Fujisaki, during his visit to NIH in June.

In November, he hosted a reception to celebrate the U.S.–Japan Biomedical Research Cooperation and mutual friendship among Japanese NIH researchers. He bestowed awards to NIH's Division of International Services—in recognition of its exceptional dedication in accepting Japanese researchers to NIH—and to Michael Gottesman (Deputy Director for Intramural Research) and senior investigators Keiko Ozato (NICHD) and Yoshi Yamada (NIDCR) for NIH's support of the Japanese research community after the March 2011 earthquake and tsunami disasters.



TOP Marston Linehan (NCI) and his team took turns explaining their research to Japanese ambassador Ichiro Fujisaki (right), who visited NIH in June. The ambassador was grateful for the help NIH provided to Japanese scientists after the March 2011 earthquake and tsunami disasters.

BOTTOM The Japanese Embassy honored NIH researchers with several awards. Pictured (left to right): Michael Gottesman, Keiko Ozato, Yoshi Yamada, and Ambassador Fujisaki



ERIN BRANSON



Bioethics Interest Group

BY CAROLYN GRAYBEAL

Each month the Bioethics Interest Group gathers to discuss complex bioethical issues that arise within biomedical research. The group was created in 1995 by Miriam Kely (then associate director of NIA extramural affairs and now an NIH volunteer and still the group's coordinator), who conceived of it as "an informal forum for individuals to discuss issues" arising from their research. Today, meeting formats include seminars, focused discussions, and debates.

Members' interests include issues concerning human subjects, genetic research, consent issues, end-of-life issues, and scientific integrity and misconduct. Speakers come from a variety of backgrounds, and discussions range from debates on informed consent to lectures on accommodating cultural differences when providing medical care abroad.

Barry Schwartz, a professor of social theory and social action at Swarthmore College (Swarthmore, Pa.), kicked off the season this fall with a talk entitled "Practical Wisdom: The Right Way to Do the Right Thing."

November's meeting featured NIMH scientist James Blair, who discussed his research on the neurobiology of psychopathy, and philosopher Walter Sinnott-Armstrong, a Duke University (Durham, N.C.) visiting scholar, who talked about the potential for using neural-imaging screening to detect people with a predisposition for violence.

In December Jason Karlawish, a professor of medicine at the University of Pennsylvania (Philadelphia), shared excerpts from his recent book *Open Wound: The Tragic Obsession of Dr. William Beaumont*, giving a historical perspective on the evolution of ethical conduct in medicine.

Meetings are held September through June on the first Monday of the month, 3:00 p.m.–5:00 p.m., in the lower level conference rooms of the Natcher Conference Center (Building 45). Anyone interested may attend. For a list of upcoming talks or to join the LISTSERV visit <http://sigs.nih.gov/bioethics/Pages/default.aspx> or contact Miriam Kely at kelytm@mail.nih.gov. ●

NIH Biomedical Computing Interest Group Book Club

Fourth Thursdays 5:30–7:30 p.m.; NIH Clinical Center Medical Board Room (10/2C116)

January 26: *301 Ways to Have Fun at Work* (by Dave Hemsath)

February 23: *Kant: A Very Short Introduction* (Roger Scruton);

Hegel: A Very Short Introduction (Peter Singer)

March 22: *Super Immunity: The Essential Nutrition Guide for Boosting Your Body's Defenses to Live Longer, Stronger, and Disease Free* (Joel Fuhrman)

April 26: *Social Intelligence: The New Science of Human Relationships*

(Daniel Goleman)

May 24: *Epigenetics: The Ultimate Mystery of Inheritance* (Richard C. Francis)

Also meetings on **June 28**, **September 27**, and **October 25**

All books are available at 20% off at the NIH Clinical Center FAES Bookstore.

For more information, please contact Jim DeLeo, 301-496-3848, jdeleo@nih.gov.

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

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA

CC: NIH Clinical Center

CCR: Center for Cancer Research, NCI

CIT: Center for Information Technology

DOE: Department of Energy

FAES: Foundation for Advanced Education in the Sciences

FelCom: Fellows Committee

FDA: Food and Drug Administration

IRP: Intramural Research Program

HHS: U.S. Department of Health and Human Services

NCATS: National Center for Advancing Translational Sciences

NCCAM: National Center for Complementary and Alternative Medicine

NCBI: National Center for Biotechnology Information

NCI: National Cancer Institute

NEI: National Eye Institute

NHGRI: National Human Genome Research Institute

NHLBI: National Heart, Lung, and Blood Institute

NIA: National Institute on Aging

NIAAA: National Institute on Alcohol Abuse and Alcoholism

NIAID: National Institute of Allergy and Infectious Diseases

NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases

NIBIB: National Institute of Biomedical Imaging and Bioengineering

NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development

NIDA: National Institute on Drug Abuse

NIDCD: National Institute on Deafness and Other Communication Disorders

NIDCR: National Institute of Dental and Craniofacial Research

NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases

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

NINR: National Institute of Nursing Research

NLM: National Library of Medicine

OD: Office of the Director

OITE: Office of Intramural Training and Education

OIR: Office of Intramural Research

ORS: Office of Research Services



Research Briefs



NCI

Melanoma on a patient's skin.

NHGRI, NIDCD, NCI: CERTAIN GENE MUTATIONS MAY CAUSE MELANOMA

Scientists have had little success in their search for an effective, long-lasting treatment for metastatic melanoma, a common form of skin cancer that is often fatal once it has spread. An NIH-led team of researchers has found that mutations in the gene for metabotropic glutamate receptor-3 (*GRM3*) cause some cases of the cancer. A biochemical analysis of *GRM3* alterations revealed that mutant *GRM3* selectively regulated the phosphorylation of a protein kinase called MEK. Melanoma cells expressing mutant *GRM3* had reduced cell growth and cellular migration after treatment with a selective MEK inhibitor, AZD-6244, which is currently being used in phase 2 clinical trials.

Further investigation into the mechanisms of *GRM3* activation of the MEK pathway is needed, but the study suggests that targeting MEK signaling in the presence of *GRM3* mutations may have a role in the treatment of melanoma. (NIH authors: T.D. Prickett, X. Wei, I. Cardenas-Navia, J.K. Teer, V. Walia, J. Gartner, J. Jiang, P.F. Cherukuri, A. Molinolo, S. A. Rosenberg, E.H. Margulies, Y. Samuels; *Nat Genet* 43:1119–1126, 2011)

NIDCD: DISCOVERY MAY ACCELERATE ADVANCES IN TREATING HEARING LOSS

A multi-institutional team, led by scientists at NIDCD and Harvard Medical School's Children's Hospital in Boston, has identified two proteins that may be the key components of the mechanotransduction channel in the inner ear. The

channel is where the mechanical stimulation of sound waves is transformed into electrical signals that the brain recognizes as sound. The study used mice in which two genes, *TMC1* and *TMC2*, had been deleted. The team observed that *TMC2* knockout mice had normal hearing, but mice with no functional copies of *TMC1* or *TMC2* had the classic behaviors of dizzy mice—head bobbing, neck arching, unstable gait, and circling movements—and they were deaf. The *TMC1* knockout mice were also deaf but they had no problem with balance. The team will continue to explore how *TMC1* and *TMC2* interact with each other and with other proteins. The genes may prove to be useful tools to screen for drugs or molecules that bind to the channel and could be used to prevent damage to hair cells. (NIDCD authors: Y. Kawashima, K. Kurima, V. Labay, T. Makishima, D.K. Wu, A.J. Griffith; *J Clin Invest* 121:4796–4809, 2011)

NIEHS: POTENTIAL NEW AVENUE FOUND FOR CANCER THERAPIES

Cancer can trick the body into producing new blood vessels to feed tumors. Vascular endothelial growth factor (VEGF) is known to play a role, but a team of researchers from NIEHS and several other institutions were the first to show that small molecules known as epoxyeicosatrienoic acids (EETs) are involved, too. VEGF and EETs work in concert to promote the spread of cancer by encouraging the growth of blood vessels that supply nutrients to the cancer cells. The findings suggest that blocking the production of EETs may eliminate the blood vessels that feed the tumors and this procedure could represent a novel strategy for treating cancer. To find out how EETs encourage the development of cancer, the team created two strains of mice, one with high levels of EETs and one with low levels. The mice with higher levels developed more metastatic tumors than did the mice with lower levels. The researchers determined that novel agonists such as 14,15-epoxyeicosa-5(*Z*)-enoic acid (EEZE), which is structurally similar to EET, block the effect of EETs and dramatically

slow tumorigenesis in mice. EEZE, however, has not been approved for human use and is only used for research. (NIEHS authors: M.L. Edin, C.R. Lee, F.B. Lih, K.B. Tomer, D.C. Zeldin; *J Clin Invest* 122:178–191, 2012)

NCI: NEW KIND OF LIGHT THERAPY DESTROYS JUST CANCER CELLS

Photodynamic therapy can kill cancer cells, but it can damage normal cells, too. NCI researchers have designed a new type of light-based therapy that allows the selective destruction of tumor cells in mice without harming surrounding normal tissue. The new method could theoretically work against tumors in humans, such as those of the breast, lung, and prostate as well as cancer cells in the blood such as leukemias. The researchers developed a photoimmunotherapy (PIT) that couples a monoclonal antibody (MAb), which recognizes specific proteins on the surface of cancer cells, with a photosensitizer molecule that, when exposed to light of the appropriate wavelength (near-infrared), rapidly damages cells. It turned out that a near-infrared fluorescent dye called IR700 had the most favorable chemical properties. Photoimmunotherapy using MAb-IR700, unlike conventional photosensitizers, which can cause damage to healthy tissue, does not appear to harm normal cells. The study also found that antibody doses required for diagnosis were significantly lower than those required for therapy. Nevertheless, after MAb-IR700 exposure, the targeted tumors decreased in size and eventually disappeared, suggesting a potential means of controlling cancers with far lower doses of MAb than are usually administered to cancer patients. Because the MAb-IR700 compound also emits a small amount of light, it can be used to monitor therapy as well. Although more testing will be needed, the scientists believe the PIT method has the potential to replace some surgical, radiation, and chemotherapy treatments. (NCI authors: M. Mitsunaga, M. Ogawa, N. Kosaka, L.T. Rosenblum, P.L. Choyke, H. Kobayashi; *Nat Med* 17:1685–1691, 2011) ●

Coffee May Boost Learning Potential

Caffeine Strengthens Neural Connections in Brain

BY ROBIN ARNETTE, NIEHS

AS AN AVID COFFEE DRINKER, SERENA Dudek looks forward to the bursts of energy that her three cups of java provide each day. It turns out that her regular caffeine consumption may bring an added benefit, strengthening the neural connections in one small area of her brain.

Dudek, a senior investigator at the NIEHS Neurobiology Laboratory in Research Triangle Park, N.C., is interested in the molecular mechanisms that regulate the strength of neural connections in the hippocampus. The hippocampus is buried deep within the brain and is important for learning and memory. She and her group found that caffeine dramatically increased the synaptic strength, or neuroelectrical signaling between neurons, in the cornu ammonis 2 (CA2) region of the rat hippocampus. The findings appeared recently in the journal *Nature Neuroscience* and suggest that caffeine worked specifically on CA2 neurons by blocking the inhibitory effects of the neurotransmitter adenosine on the neurons [*Nat Neurosci* DOI:10.1038/nn.2962 (2011)].

Dudek said that scientists have known for years that caffeine enhanced certain kinds of memory and cognition. Within the past decade, researchers discovered that caffeine blocked the activation of the adenosine A1 receptor by adenosine. Five years ago, Dudek's research group

discovered that synapses on CA2 neurons are much more resistant to strengthening than synapses in other areas of the hippocampus. Although the A1 receptors for adenosine are more highly concentrated in CA2 than in any other area, no one had documented caffeine's effect on this particular group of nerve cells. Therefore, she focused on the effects of caffeine on synaptic responses in CA2 after caffeine exposure in rodents.

"In general, the function of adenosine throughout the brain is to suppress neuronal synaptic transmission," Dudek explained. "But we expect the effects to be most acute in the CA2 because adenosine A1 receptors are so enriched there."

To get a sense of what was going on in the brain after caffeine exposure, Dudek's research team divided rats into three groups and orally administered one of three doses of caffeine: the equivalent of two large cups of coffee, a highly caffeinated energy drink, or a dose of caffeine that exceeded most people's daily consumption. Regardless of the dose, caffeine produced a sustained increase in synaptic responses in CA2, but not in the CA1 area of the hippocampus.

According to Dudek, levels of the inhibitor adenosine are thought to build up in the human brain during the day and drop during sleep. When a person ingests caffeine, the stimulant competes with adenosine at A1 receptors and strengthens the activity of CA2 synapses of the hippocampus. Dudek suggests that as a result of this increase in synaptic strength, the person could experience an increase in mental sharpness. Dudek was quick to point out, though, that her studies didn't address whether the animals were actually smarter after consuming caffeine, but her data add support to that hypothesis.



STEVE MCCAW, NIEHS

NIEHS senior investigator Serena Dudek and the team of scientists she led were the first to document that caffeine dramatically increases the synaptic strength in the CA2 region of the rat hippocampus, suggesting a possible increase in mental sharpness.

She also added that she didn't find a dose of caffeine that inhibited synaptic strength, so theoretically, more caffeine could lead to better memory. However, there is a downside to this approach.

"Caffeine obviously speeds up the heart rate, so we should keep its cardiac effects in mind before suggesting that anyone take caffeine as a cognitive enhancer," she said.

For future work, Dudek wants to look at other molecules that are enriched in CA2 neurons. One good example is work she collaborated on last year with John Hepler, a professor of pharmacology at Emory University School of Medicine in Atlanta, Ga. Hepler's group knocked out a CA2-enriched gene—*RGS14*—in mice and, in doing so, enhanced the capacity to increase synaptic strength in CA2. As a result of this gene knockout, the mice also learned faster.

Dudek said that no one really knows which brain functions CA2 neurons control, but finding that unknown is one of her top research priorities.

"We think CA2 neurons are involved in learning and memory, but our group will continue to look for the answer," she said. "We're super excited about this research because it's been like finding a new area of the brain to study." ●



popularity. But the driving force behind the Research Festival is much the same. “Many of us have little sense of the common ground we share,” said Deputy Director for Intramural Research Michael Gottesman in his introduction to the plenary session. “Bringing everyone together is an opportunity to share that common ground.”

The theme for the 2011 festival, which took place October 24–28, was “how the scientific understanding of human disease can advance our understanding and treatment of those diseases,” said **Gary Nabel (VRC)**, who co-chaired the event with **Robert Wiltrott (NCI)**. “Within that context,” Nabel continued, “we asked the scientists to come forth with the ideas they felt were the most compelling and of greatest interest.” This “grassroots effort” produced sessions on both basic and translational research, showcased work being done at multiple institutes, and highlighted the cutting-edge science being done in the intramural program.

The Research Festival is “packed with the best that NIH has to offer,” NIH Director Francis Collins said in a taped address for the plenary session. Entitled “Molecular Mechanisms of Human Diseases,” the session had a strong translational focus and included research presentations covering immune deficiency diseases, cancers, and neurological disorders.

Pamela Schwartzberg (NHGRI) described her research using model systems to understand the pathogenesis of primary immunodeficiencies. Her lab is studying a severe immune disorder called X-linked lymphoproliferative disease (XLP-1), which is characterized by “a really massive immune dysregulation, [which is] often triggered or exacerbated by infection with Epstein Barr virus,” she said. XLP-1 is caused by mutations in the *SH2D1A* gene, which encodes a small signaling molecule called SLAM-associated protein (SAP). Schwartzberg’s group has developed a SAP-deficient mouse



◀ **LEFT** Abner Notkins was a scientific director in 1986 in what is now NIDCR when he dreamed up the idea for the first NIH Intramural Research Day. He never would have guessed that in just a few years, the daylong celebration would become a popular week-long event.

line and has found many molecular and cellular pathways underlying the progression of XLP-1. Her research points the way to potential treatments for XLP-1 and other immune dysregulatory diseases.

Kevin Gardner (NCI) studies the molecular linkages between metabolic imbalance, genome stability, and breast cancer. He pointed out that there is a striking statistical correlation between obesity and breast cancer. His lab is studying the COOH-terminal binding protein (CtBP), a molecule that regulates genes such as *BRCA*, which is critical for protection against breast cancer. Gardner’s research shows that obesity-associated changes in metabolism may cause CtBP to decrease *BRCA* expression, leading to “a perfect storm” of decreased DNA repair and an increased chance of breast cancer.

Eric Hanson (NIAMS), one of the 2012 winners of the Fellows Award for Research Excellence (FARE), presented a genetics approach to studying NF-kappa-B essential modulator (NEMO) syndrome. NEMO syndrome is a rare immunodeficiency disorder caused by mutations in the *IKBKG* gene, an essential modulator of NF-kappa-B, an important transcription factor that plays a key role in regulating the immune response to infection. The syndrome can present as a range of disorders from immune deficiency and infectious susceptibility to autoimmunity and inflammatory disease.

Hanson determined that mutations in specific sections of *IKBKG* lead to changes in the activation state of NF-kappa-B. “We started with the phenotype of the individual and proceeded towards the genotype and

then function,” he explained. His work may lead to potential treatments for other inflammatory or immune system disorders.

Dennis Drayna (NIDCD) described how he uses genetics to understand the neuropathology of stuttering. “Stuttering is not a psychological or a social disorder,” said Drayna. “It is a biological disorder with neurologic origins.” Using genetic studies of several large consanguineous families, he found several genes in the lysosomal targeting pathway that when mutated correlate strongly with stuttering. “Mutations in the genes encoding [the] lysosomal targeting pathway appear to account for about 10 percent of familial stuttering” although the connection between the lysosomal targeting pathway and the neurological phenotype is not yet clear. Future studies involving the analysis of vocalizations in genetically altered mice may reveal a molecular and cellular link between these genetic mutations and familial stuttering.

To wrap up the plenary session, **Louis Staudt (NCI)** talked about locating the Achilles’ Heel of cancer through functional and structural genomics. He uses a genomics approach to study cell survival in diffuse large B-cell lymphoma (DLBCL), a heterogeneous mixture of B-cell cancers. Using a library of RNA interference vectors, he found several clusters of genes that are necessary for the proliferation and survival of cancer cells; one of these clusters lies in the B-cell receptor pathway. He presented clinical trials data that demonstrated a potential inhibitor of this pathway. “It’s early,” but the results are sometimes “dramatic.”

Nabel was pleased that the plenary session was a good start to the festival. “I was

➔ **RIGHT** Postdoctoral fellow Percy Pui Sai Tumbale (NIEHS) traveled from North Carolina to discuss her poster on “Structural basis of DNA ligase proof-reading by aprataxin with insights into AQA1 neurodegenerative disease” at the Research Festival. (Far right) Robert Wiltrot, one of the festival co-chairs and director of NCI’s Center for Cancer Research, helped organize the event.



BOTH: ERIN BRANSON

struck by the diversity of approaches that were being taken to address specific problems, and the use of animal model systems, the use of human clinical specimens, and the use of structural biology, biochemistry, and all of that, often within the same talk,” he said. The approach of using every available tool to address basic and translational research challenges continued through the remainder of the festival.

After the plenary session ended, attendees dashed from the Masur Auditorium (Building 10) across campus to the Natcher Conference Center (Building 45) to catch the first of four poster sessions and the beginning of four concurrent symposia that would take place over the next several days.

Later in the week, the two-day scientific equipment tent show opened in parking Lot 10H. “The technical sales association exhibits are really a good thing, because you sometimes see a lot of action and interaction and discussions there,” said festival co-chair Wiltrot. “That really suggests that our folks are looking for the best opportunities to apply new technologies that can accelerate their work. I think that’s a vibrant part of the festival.”

The true mark of the NIH Research Festival’s success is the collaborations it triggers. But there are no hard data on how many collaborations are sparked by the interactions that take place during festival week. “We should think about polling people after the festival in a formal way [and get] some feedback that we could then use to guide the next festival,” suggested Wiltrot.

Notkins suggested resurrecting an old tradition—having senior investigators, instead of only fellows, present some posters.

“It would give our postdocs an opportunity to meet and discuss scientific issues with some of our best-known scientists,” he said.

“I thought [the festival] was a great example of how the NIH takes basic science and capitalizes on it and moves it toward a practical benefit for people,” said Wiltrot.

It was a chance, as Gottesman put it, to “strut our feathers” and display, as we have done each year for the last quarter-century, the unique bench-to-bedside (and sometimes back again) research being done here at the NIH.

FESTIVAL HIGHLIGHTS

Dynamic Protein Assemblies

BY LESLEY EARL, NIDCR

WELCOME TO THE GAP . . . IN HOW WE visualize and understand biological structures, that is. Classical methods of determining biological structures have given us beautiful data about the very small (small, well-ordered protein and RNA molecules) and the very large (whole cells or organelle structures). But many biological mysteries surround the large, dynamic protein assemblies that are responsible for complex biological processes and yet cannot be seen by the classical methods of structure determination.

Historically, structural biology has come to mean X-ray crystallography or nuclear magnetic resonance (NMR) spectroscopy

or, more recently, cryo-electron microscopy (cryo-EM) technology, said **Sriram Subramaniam (NCI)**, a co-chair of the “Dynamic Protein Assemblies: Large and Small” session. However biological structures featured in this symposium were beyond the traditional applications of these methods.

Many of the session’s six presenters either combine multiple methods or use traditional methods in new and unique ways to examine the heterogeneous, dynamic molecular complexes that lie at the heart of many biological phenomena.

“This integration of different modalities allows us to look at biology at multiple scales, to go seamlessly from the atom-by-atom scale to the cellular scale and beyond,” said **James Hurley (NIDDK)**, the other session co-chair.

The opening presentation by FARE winner **Nicholas Noinaj (NIDDK)** was a perfect example of this idea of integrating different modalities. Noinaj used X-ray crystallography, small-angle X-ray scattering (SAXS), and EM to look at the structure of the transferrin receptor in *Neisseria* bacteria. *Neisseria* is associated with meningitis and gonorrhea. The transferrin receptor participates in stealing iron from host transferrin, a glycoprotein that binds iron. Deciphering this structure, Noinaj said, “represents a significant advancement in our knowledge of iron import by bacterial pathogens” and offers new data that will be useful for vaccine and drug development.

The next presentation, by **Adriaan Bax (NIDDK)**, addressed the well-studied influenza hemagglutinin envelope glycoprotein. Using a DNA-based liquid crystal

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NIH Research Festival Highlights

CONTINUED FROM PAGE 11

medium for NMR spectroscopy, Bax found that the two helices of the glycoprotein's membrane anchor form a tight hairpin structure within the membrane, stabilized by hydrogen bonds between the helices. Bax also found that the entire hairpin structure can rotate within the membrane. "The remarkable and highly unusual structure of [the envelope glycoprotein] fusion domain suggests a distinct function in the fusion process," said Bax. His findings are contrary to what's been reported in the literature—that the structure is a passive membrane anchor. "Don't take everything you read in the literature as a fact!"

Hurley also presented data from his own group and collaborators, including Gerhard Hummer (NIDDK), on the endosomal-sorting complex required for transport (ESCRT). The ESCRTs, Hurley explained, are too flexible to crystallize, too small for EM, and too big for NMR. Using SAXS, double-electron electron-resonance spectroscopy, electron-paramagnetic resonance spectroscopy, and single-molecule fluorescence resonance energy transfer, Hurley and colleagues determined both open and closed positions for the ESCRT protein complex. From this collection of structures, Hurley described a banana shape, whereby the ESCRTs force membrane curvature and induce membrane scission. The goal, Hurley said, is to "ultimately create a step-by-step molecular movie of how the budding scission and cargo-transport process works."

Although the structures of many proteins have been described, **Yun-Xing Wang (NCI)** pointed out that technical challenges have prevented scientists from determining many structures for messenger RNAs (mRNAs) despite their biological abundance and importance. Using SAXS, Wang presented a global topological structure of a regulatory protein—the Rev Response

Element (RRE)—from the mRNA of the human immunodeficiency virus (HIV). He found that in three dimensions, two protein-binding sites were brought into close proximity. Determining the RRE topology structure resolves the long-running mystery of how HIV virus selects its own mRNA, not the host RNA, for packaging.

The question addressed by **Wei Yang (NIDDK)** also involved protein–nucleic acid interactions, especially the recognition of DNA damage by the MutS protein complex. "There are unlimited varieties of DNA lesions and different pathways to repair damaged DNA," said Yang. She found that the increased flexibility of damaged DNA, rather than the mismatch itself, is recognized by the MutS protein, and "the energy derived from ATP [adenosine-5'-triphosphate] hydrolysis can be used to increase the accuracy of DNA lesion identification."

Subramaniam gave the session's final presentation on the use of cryo-EM to obtain high-resolution images of large protein structures including bacterial chemotaxis receptor clusters and the GroEL chaperone complex. "The work I presented is very much on our road map of looking at large, heterogeneous, complex assemblies," he said. He and his colleagues are "not satisfied with describing them as blobs."

The field of structural biology is changing. "A seamless integration across scales and fields is where it's going," said Hurley. "In the future, we may not really talk about structural biology. It may be viewed as the highest resolution and the most quantitative dimension of molecular and cell biology."

This session was co-chaired by Subramaniam and Hurley.

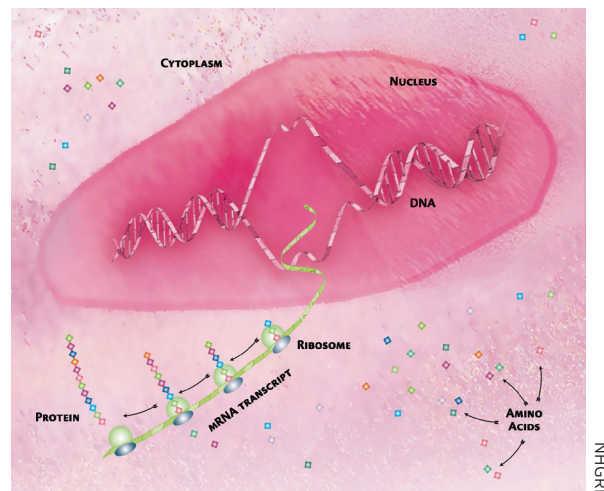
Capturing the Complexity of the Transcriptome

BY NATALIE GOLDBERGER, NCI

IF YOU THOUGHT THAT FIGURING OUT the genome—the entire DNA sequence of an organism—was complicated, try figuring out the transcriptome—the entire RNA sequence.

The transcriptome represents a very small percentage of the genome—less than five percent of the human genome—that is transcribed into RNA molecules. It includes messenger RNA (mRNA), which is translated into proteins as well as other types of molecules, which may influence cell structure and regulate genes. Because each gene may produce many types of RNA molecules, the transcriptome is more complex than the genome that encodes it.

Scientists compare transcriptomes of different types of cells to gain a deeper understanding of how each cell type functions and how changes in the normal level of gene activity may reflect or contribute to disease. By aligning the transcriptome of each cell type to the genome, it is possible to



To make a protein, a gene's DNA sequence is transcribed into messenger RNA (mRNA). This molecule, referred to as an mRNA transcript, leaves the nucleus and enters the cytoplasm. Ribosomes then read the transcript and use the information to assemble amino acids into proteins. The entire RNA sequence of an organism is called the transcriptome.

generate a comprehensive, genome-wide picture of which genes are active in which cells.

At the “Notes from the RNA-Seq Revolution: Deep Sequencing Transcribed RNA in Health and Disease” session, scientists from several institutes shared strategies for using a technique that is better than microarray profiling and other technologies at capturing the complexity of transcriptomes. RNA sequencing (RNA-Seq) uses high-throughput sequencing technologies to provide precise estimates of transcript abundance; catalogue all species of transcripts (mRNAs, noncoding RNAs, and small RNAs); detect novel, low-abundance transcripts; determine the transcriptional structure of genes; and measure allele-specific expression.

Senior investigator **Mark Cookson (NIA)** is researching genes involved in RNA editing—a process in which an RNA molecule is altered through a chemical change—within the brain. He is particularly interested in the action of adenosine deaminase on the RNA (ADAR) gene family. During brain development, the *ADAR-1* expression level increases. Using RNA-Seq, Cookson demonstrated that the expression change is due to RNA editing and not transcriptional regulation.

Andrew Oler (NIAID), a high-throughput sequencing bioinformatics specialist, is using RNA-Seq to analyze human and mouse platelet transcriptomes as well as identify platelet-specific genes and their major and minor isoforms. When a tear occurs in a blood vessel wall, the protease thrombin binds and cleaves the amino-terminus of protease-activated receptor 1 (PAR-1) to trigger the activation of platelets, which plug the tear. He showed that during platelet activation, PAR-1 expression is low in mice but high in humans and PAR-3 is increased in mice but low in humans.

RNA-Seq is even being used to help identify genes that contribute to the risk

for bipolar, or manic-depressive, disorder. Senior investigator **Francis McMahon (NIMH)** and colleagues at NIMH are using RNA-Seq to analyze the RNA within the prefrontal cortex of people with and without bipolar disorder. In a small study that involved 10 subjects, they identified 97 differentially expressed transcripts involved in various pathways including cell-cell signaling, ion transport, and synaptic and nerve impulses.

Postdoctoral researcher and FARE winner **Shurjo Sen (NHGRI)** is trying to improve the RNA-Seq protocol while studying atherosclerosis in cardiovascular disease. He recommended certain equipment to achieve clean, fast, and reproducible RNA-Seq results and better data yield. In his atherosclerosis research, Sen examined cardiac computed-tomography scans to detect calcium buildup in the coronary artery and then compared high- versus low-calcification groups. He observed an increase in categories for cell-surface receptor signaling pathways and regulation of cell adhesion in the high-calcification group.

A hurdle for using RNA-Seq technology is the enormous amount of raw data generated for each sample. Bioinformatics expert **Nirmala Akula (NIMH)** is dealing with the challenges of processing, analyzing, and storing RNA-Seq data. Akula maps the data to a reference genome, focuses on the quality of base-pair readings to improve the percentage of sequences that are mapped, and uses computer software to tally the number of mappable reads.

The researchers expect that once they overcome the barriers to widespread use of RNA-Seq—higher cost, high data-storage requirements, and the absence of a gold standard for analysis—this technique will become the predominant tool for transcriptome analysis.

This session was co-chaired by McMahon and Cookson.

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<http://irp.nih.gov/catalyst/v20i1>

Bringing Stem Cells to the Clinic

BY KATHERINE BRICCENO, NINDS

INDUCED PLURIPOTENT STEM CELLS (iPSCs) hold tremendous potential in many disciplines of biomedical research, both in the laboratory and in the clinic. Several of the NIH researchers who are exploring that potential described their work in a symposium entitled “iPSC Cells for Screening and Therapy.”

When Neural Circuits Go Awry

BY STEPHANIE COOPERSTEIN

NEURAL CIRCUITS IN THE BRAIN can go awry in many neurological disorders. At the Research Festival’s symposium entitled “Neural Systems Underlying Social Function in Normal and Pathological Conditions,” several NIH scientists talked about their attempts to gain insights into the neural systems underlying autism spectrum disorders, schizophrenia, and childhood psychopathy.

Immune-Targeted Therapies

BY LESLEY EARL, NIDCR

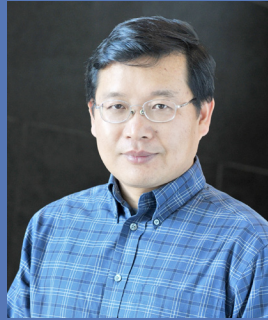
ONE OF THE MOST POWERFUL WEAPONS in a clinician’s disease-fighting arsenal is the patient’s own immune system. The focus of the “Advances in Immune-Targeted Therapies” symposium was on therapies that use the immune system to fight or prevent diseases, even those outside the traditional viral and bacterial vaccine targets. They focused on recent advances in creating effective immune-targeted therapies and the common challenges for clinicians using these treatments.



Recently Tenured



LEONARDO BELLUSCIO, NINDS



HUAIBIN CAI, NIA



WANJUN CHEN, NIDCR



JAMES GULLEY, NCI-CCR



MATTHEW HOFFMAN, NIDCR

LEONARDO BELLUSCIO, PH.D., NINDS

Senior Investigator, Developmental Neural Plasticity Section

Education: Manhattan College, Riverdale, N.Y. (B.S. in biology); Columbia University, New York (Ph.D. in neuroscience)

Training: Postdoctoral training in the molecular and functional basis of olfaction at Duke University Medical Center (Durham, N.C.)

Came to NIH: In 2002

Outside interests: Cooking; camping; taking photographs; spending time with family

Research interests: We are studying the mammalian olfactory system to understand neural plasticity and nerve regeneration in the brain. The olfactory system is always rewiring itself: Nasal epithelium cells, which are responsible for odor detection, are continuously regenerating from stem cells in the nose and forming new connections in the brain. This rewiring process provides a window into the development of the olfactory system and offers clues to the interdependence of an olfactory sensory neuron's molecular function and its effects on neural circuitry.

In particular, we are looking at olfactory neural circuits that show activity-dependent changes in connectivity. Each olfactory sensory neuron expresses one odorant receptor—out of more than 1,000 possibilities—that detects specific odor molecules. The receptor

type determines where the neuron projects its axons on the olfactory bulb (an area of the brain that processes odor information). But changing a neuron's olfactory receptor causes the neuron to project its axons to a different part of the bulb. We have shown that neural activity elicited by odor stimulation can alter the refinement of those axonal projections and also affect the organization of subsequent connections deeper in the olfactory bulb.

Through our work, we are trying to understand the relationship between neural plasticity and the nerve's capacity for repair. We use genetically engineered mice and rely on a multidisciplinary approach that involves biochemistry, molecular biology, and electrophysiological techniques, as well as in vivo imaging and optogenetic and behavioral techniques. Given the connection between olfactory dysfunction and neurological diseases such as Alzheimer disease and Parkinson disease, our work also maintains a strong translational focus.

If you have been tenured in the last year or so, *The NIH Catalyst* will be in touch soon to include you on these pages.

HUAIBIN CAI, PH.D., NIA

Senior Investigator; Head, Transgenics Section, Laboratory of Neurogenetics

Education: Peking University, Beijing, China (B.S. in biology); The Johns Hopkins University School of Medicine, Baltimore (Ph.D. in neuroscience)

Training: Postdoctoral training in the Division of Neuropathology, Department of Pathology, at The Johns Hopkins University School of Medicine

Before coming to NIH: Research associate in the Division of Neuropathology, Department of Pathology, The Johns Hopkins University School of Medicine

Came to NIH: In 2003

Selected professional activities: Editorial boards of *Molecular Brain* and *PLoS ONE*

Outside interests: Being a "soccer dad"; hiking and biking with family; running; playing golf

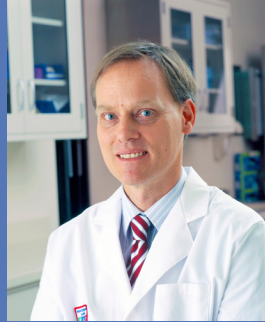
Research interests: I and my lab are interested in figuring out the cause of and developing a treatment for Parkinson disease (PD). PD, the most common degenerative movement disorder, affects millions of people worldwide and there is no cure. The symptoms—resting tremor, rigidity, slow movement, and postural instability—are caused by the degeneration of midbrain dopaminergic neurons. We are using a combination of in vivo mouse genetics and



ANDREW HOLMES, NIAAA



RICHARD KRAUZLIS, NEI



C. OLA LANDGREN, NCI-CCR



YIKANG RONG, NCI-CCR



ANNE SUMNER, NIDDK

in vitro molecular and cell biology approaches to investigate the molecular participants in the disease processes and explore the underlying pathogenic mechanisms.

We are studying the two most prominent genetic factors in PD—the gene for alpha-synuclein (*SNCA*) and the gene for leucine-rich repeat kinase 2 (*LRRK2*). Until now there has been no effective mouse model to help us study the pathology of dopaminergic neurodegeneration. Recently, however, we generated a new line of *SNCA* transgenic mice that developed profound motor disabilities and the progressive dopaminergic neurodegeneration found in PD.

We are collaborating with other laboratories at NIH and elsewhere to explore the pathogenic processes of synuclein and LRRK2 in the degeneration of dopaminergic neurons. We hope our findings will eventually reveal the cause of PD and lead to a cure for the disease.

WANJUN CHEN, M.D., NIDCR

Senior Investigator; Chief, Mucosal Immunology Section

Education: Shandong Medical University and Shandong Academy of Medical Sciences, Shandong, China (M.S. in microbiology and immunology); Qingdao University Medical School, Qingdao, China (M.D.)

Training: Internship in medicine at Qingdao Municipal Hospital (Qingdao, China); post-doctoral training in immunology at Harvard Medical School (Boston)

Came to NIH: In 1997

Selected professional activities: Co-organizer, 2011 Keystone Symposium, “TGF-beta in Immune Responses: From Bench to Bedside,”

Outside interests: Swimming; listening to music; gardening

Research interests: The mucosal immune system protects the mucous membrane—a protective lining of the respiratory, digestive, and urogenital tracts and other structures—against potentially harmful microbes and foreign antigens. Understanding that system is instrumental for developing strategies such as mucosal vaccination against infectious agents and therapies for allergy, inflammation, and autoimmune diseases.

Not all foreign antigens are pathogens, however; more than 100 kilograms of food antigens are processed each year by our gastrointestinal mucosa. The gut immune system has to differentiate between beneficial dietary antigens and noxious or infectious pathogens. Failure to tolerate dietary antigens may lead to intestinal hypersensitivity such as food-sensitive enteropathies (diseases of the intestinal tract); failure to expel infectious pathogens may contribute to disease.

During the complex and well-orchestrated immune responses in the mucosal system, T cells play a pivotal role in both immunity and tolerance. Many cytokines and factors influence mucosal T-cell immunity and tolerance with Transforming growth factor-beta (TGF-beta) perhaps the most important. I and my lab are elucidating the mechanisms by which TGF-beta regulates T-cell immunity and tolerance, and we are also manipulating T-cell immunity versus tolerance in animal models. We hope to understand the pathogenesis of autoimmunity and inflammation, cancer, and infectious diseases and to develop potential therapies for relevant human diseases.

JAMES GULLEY, M.D., PH.D., NCI-CCR

Senior Investigator; Head, Clinical Trials Group; Deputy Chief, Laboratory of Tumor Immunology and Biology; attending physician, Clinical Center

Education: Southern Adventist University, Collegedale, Tenn. (B.A. in chemistry); Loma Linda University, Loma Linda, Calif. (M.D. and Ph.D. in microbiology)

Training: Residency in internal medicine at Emory University (Atlanta); fellowship in medical oncology at NCI

Came to NIH: In 1998 for training; joined staff in 2001

CONTINUED ON PAGE 16 ►



Recently Tenured

CONTINUED FROM PAGE 15

Selected professional activities: Winner of the 2010 Presidential Early Career Award for Scientists and Engineers; staff physician, Walter Reed National Military Medical Center (Bethesda, Md.)

Outside interests: Kayaking; sailing; mountain biking; spending time with family

Research interests: The Laboratory of Tumor Immunology and Biology (LTIB) conducts translational research in tumor immunology, immunotherapy, mechanisms of tumor cell-immune cell interactions, and immune mechanisms. My clinical group takes promising findings in the lab and tests them in clinical trials both within the NIH Clinical Center and in other NCI-funded cancer centers and cooperating groups.

One vaccine developed within the LTIB is PSA-TRICOM for prostate cancer. Initial clinical studies led to two concurrent phase 2 studies in patients with metastatic prostate cancer. A trial at NCI demonstrated evidence of immune responses (better immune responses correlated with improved overall survival), and a multicenter randomized controlled trial showed a 44 percent reduction in the mortality rate for patients receiving the vaccine versus a placebo and an 8.5 month improvement in median overall survival. Based on these results, I am leading a global randomized controlled phase 3 study of PSA-TRICOM.

The LTIB is also studying brachyury, a transcription factor that is involved in epithelial to mesenchymal transition (a process important in embryogenesis and organ development in which epithelial cells change into less ordered, more varied, and more mobile mesenchymal cells). We have shown that brachyury is overexpressed in tumors compared with normal tissue and is associated with “stemness” and drug resistance. We have developed a vaccine that targets brachyury that is scheduled to enter a first-in-human trial.

MATTHEW HOFFMAN, B.D.S., PH.D., NIDCR
Senior Investigator; Chief, Matrix and Morphogenesis Section, Laboratory of Cell and Developmental Biology

Education: University of Otago School of Dentistry, Dunedin, New Zealand (B.D.S.); University of Rochester School of Medicine and Dentistry, Rochester, N.Y. (M.S. and Ph.D. in microbiology and immunology)
Training: Visiting fellow in NIDCR’s Cell Biology Section

Came to NIH: In 1994 for training; became staff scientist in 2000 and chief of Matrix and Morphogenesis Unit in 2004

Selected professional activities: Organized Gordon Research Conference on Salivary Glands and Exocrine Biology in 2009, was vice chair in 2009 and chair in 2011

Outside interests: Swimming with the DC Aquatics Club, a masters swim team; running and biking; hiking in the mountains; cooking; wine tasting

Research interests: My lab studies how salivary glands develop from the earliest stages of cell commitment, progenitor-cell maintenance, and differentiation; to growth and morphogenesis; to the formation of a functional gland. Elucidating how cells are directed along a series of cell-fate decisions is critical for understanding organogenesis and provides a template for future regenerative therapy. We are developing strategies to regenerate adult salivary tissue that has been damaged by radiation treatment for head and neck cancer, trauma, or diseases such as the autoimmune disorder Sjögren syndrome.

By understanding how salivary glands develop during embryogenesis, we can develop regenerative strategies for repairing damaged adult tissue. We focus on the roles of growth factors and the extracellular matrix, characterize stem cells in the gland and how they function, and investigate the genetic regulation of branching morphogenesis. We

also explore interactions among the various cell types in salivary glands—including epithelial and neuronal cells—as well as blood vessels and mesenchymal cells. We want to understand how these cells contribute to the local cellular microenvironment, or “niche,” of salivary progenitor cells. We are identifying changes that occur in the stem cell niche during damage to the glands. We hope our findings will help us use progenitor cells to repair or regenerate damaged adult tissue.

ANDREW HOLMES, PH.D., NIAAA

Principal Investigator; Chief, Laboratory of Behavioral and Genomic Neuroscience, Section on Behavioral Science and Genetics

Education: University of Newcastle upon Tyne (now Newcastle University), Newcastle upon Tyne, U.K. (B.A. in psychology); University of Leeds, Leeds, U.K. (Ph.D. in behavioral pharmacology)

Training: Postdoctoral training in behavioral neuroscience at NIMH

Came to NIH: In 1999 for training; became tenure-track investigator in 2003

Selected professional activities: Editor-in-chief of *Genes, Brain, and Behavior*

Outside interests: Bird watching

Research interests: My principal area of research interest is studying how stress affects the risk for developing neuropsychiatric disorders and addictions. My lab and I are using animal models to determine how exposure to stress and drugs of abuse affect an individual’s capacity for high-level cognitive and executive functions. Executive functions include the ability to inhibit inappropriate behaviors such as aggression and excessive fear and the capacity for controlling and avoiding potentially self-destructive activities as often occurs in drug and alcohol addiction.

One goal of this research is to uncover the genes that increase a person’s suscepti-



bility to these detrimental effects of stress in order to identify individuals who are particularly at risk. We are also trying to elucidate the neural systems and molecules that are compromised by stress as a first step in developing new medications for stress-related neuropsychiatric diseases ranging from post-traumatic stress disorder to alcoholism.

.....
RICHARD J. KRAUZLIS, PH.D., NEI

Senior Investigator; Chief, Eye Movements and Visual Selection Section, Laboratory of Sensorimotor Research

Education: Princeton University, Princeton, N.J. (A.B. in biology); University of California at San Francisco (Ph.D. in neuroscience)
Training: Postdoctoral training in NEI's Laboratory of Sensorimotor Research

Before coming to NIH: Professor, Systems Neurobiology Laboratory at the Salk Institute for Biological Studies (La Jolla, Calif.)

Came to NIH: In 1991–1997 for training; returned in 2011 as senior investigator

Selected professional activities: Serves on editorial boards for *Journal of Neuroscience* and *Journal of Vision*; senior editor for *Vision Research*

Outside interests: Exploring art and history; painting; running; spending time with wife and two sons

Research interests: My lab uses a variety of techniques to manipulate and monitor neural activity to understand the brain mechanisms that link motor control to sensory and cognitive processing. My previous work has covered pursuit (following a moving target) and saccadic (jerky) eye movements; physiological studies of the cerebellum and cerebral cortex; psychophysical studies of visual motion perception and visual attention; and computational modeling of eye movements.

While I was at the Salk Institute, my lab determined that the superior colliculus—a structure on the roof of the midbrain best known for its role in the motor control of orienting movements—contains a priority “map” that keeps track of behaviorally relevant objects in the visual field.

Activity in this map is important for deciding where and when to look, but we demonstrated that it also plays a crucial role in the control of spatial attention (the ability to select only the relevant bits of information for perception and action). Although this higher-order function is normally associated with areas in the cerebral cortex, our findings raise the possibility that it is built on top of older brain systems rather than developed de novo. Determining how these cortical and subcortical systems interact will be a focus of the work in my lab at NIH.

.....
C. OLA LANDGREN, M.D., PH.D., NCI-CCR

Senior Investigator; Chief, Multiple Myeloma Section, Metabolism Branch

Education: Lund University, Lund, Sweden (B.A. in medicine); Karolinska Institute, Stockholm, Sweden (M.D. and Ph.D. focusing on diagnostics and prognostics of Hodgkin lymphoma)

Training: Residency in hematology and internal medicine at Karolinska University Hospital (Stockholm, Sweden)

Before coming to NIH: Attending physician and clinical researcher (lymphoproliferative malignancies and related precursors) at Karolinska University Hospital

Came to NIH: In 2004 as a visiting fellow, later as a research fellow, in NCI-DCEG; in 2009 joined NCI-CCR as principal investigator

Selected professional activities: Editorial boards for *Haematologica* and *Leukemia and Lymphoma*

Outside interests: Traveling; listening to music; socializing

Research interests: My major research interests are in the treatment, causation, diagnostics and prognostics, and natural history of multiple myeloma and its precursor states—monoclonal gammopathy of undetermined significance and smoldering (slow-growing) myeloma. I also study related hematologic malignancies and their precursor states including chronic lymphocytic leukemia and monoclonal B-cell lymphocytosis. I focus on the treatment-, host-, disease-, and immune-related factors in the pathway from precursor to full-blown malignancy.

I am also examining novel therapies for multiple myeloma and its precursor states; identifying predictors for progression from precursor to malignancy and outcome; defining roles for infectious antigens, inflammation, chronic immune stimulation, and immune modulation in hematopoietic carcinogenesis; and assessing and defining host- and disease-related diagnostic and prognostic markers.

My lab recently generated data—using advanced imaging and molecular profiling—that suggest that a fraction of the patients diagnosed with smoldering myeloma actually have early myeloma. We are now developing treatment trials for early myeloma patients. Our ultimate goal is to eliminate evidence of minimal residual disease. By treating these patients with highly effective therapies and carefully monitoring them, we hope we are laying the groundwork for a cure for myeloma.

If you have been tenured in the last year or so, *The NIH Catalyst* will be in touch soon to include you on these pages.



Recently Tenured

CONTINUED FROM PAGE 17

YIKANG RONG, PH.D., NCI-CCR

Senior Investigator and Head, Eukaryotic Genome Maintenance Unit, Laboratory of Biochemistry and Molecular Biology

Education: University of Science and Technology of China, Hefei, Anhui, China (B.Sc. in biology); University of Utah, Salt Lake City (Ph.D. in genetics)

Training: Postdoctoral training at the University of Utah

Came to NIH: In January 2002

Outside interests: Playing video games

Research interests: Although the fruit fly *Drosophila melanogaster* is one of the best model organisms for genetic research, we have lacked the tools for targeting specific genes for mutation by homologous recombination. For more than 20 years, yeast and mouse researchers have been able to use gene targeting to introduce specific mutations into almost any gene. I helped develop gene-targeting methods in *D. melanogaster* to allow researchers worldwide to mutate many different loci that were not previously identified in traditional mutant screens. My group is interested in studying the mechanisms for DNA double-strand break (DSB) repair in *D. melanogaster*. I have introduced a site-specific DSB system in which one can control the position, number, and timing of DNA breaks as well as the surrounding genomic environment. We have found that the genomic structure around the DNA break dictates the repair mechanism and template.

My lab is also studying cellular response to DNA damage. For example, a eukaryotic cell responds by stopping the progression of various cell-cycle programs to ensure proper repair of the damage or by inducing cell death so that irreparably damaged cells can be eliminated. These responses are partly controlled by the p53 tumor suppressor, the ataxia telangiectasia mutated (ATM) checkpoint kinase, and the Mre11 protein complex. We have gen-

erated knockout mutants of p53, ATM, and members of the Mre11 complex and are characterizing the mutant phenotypes. Our work will contribute to a better understanding of how eukaryotic organisms maintain the physical integrity of their genomes and shed light on how genome instability could give rise to human cancers.

ANNE SUMNER, M.D., NIDDK

Senior Investigator; Chief, Ethnicity and Health Section, Diabetes, Obesity, and Endocrinology Branch

Education: Brown University, Providence, R.I. (B.A. in English literature); University of Pennsylvania School of Medicine, Philadelphia (M.D.)

Training: Residency in internal medicine at Reading Hospital and Medical Center (Reading, Pa.); fellowship in nutrition and metabolism at the Hospital of the University of Pennsylvania (Philadelphia); fellowship in endocrinology, diabetes, and metabolism at the Medical College of Pennsylvania (Philadelphia)

Before coming to NIH: Assistant professor of medicine, assistant professor of biochemistry, and attending physician at Allegheny University of the Health Sciences (Philadelphia); attending physician and chief of the Lipid Clinic and the Hypertension Clinic at the Philadelphia VA Medical Center (Philadelphia)

Came to NIH: In 1998

Selected professional activities: Serves on Board of Governors of the Association of Black Cardiologists; member of the American Heart Association Science Committee on Diabetes and Council on Nutrition, Physical Activity, and Metabolism; serves on the editorial boards of *Journal of Clinical Endocrinology and Metabolism*, *Obesity*, and *Ethnicity and Disease*; serves on Senior Advisory Council of *Global Heart*

Outside interests: 18th- and 19th-century American history, especially the Underground Railroad and the canal system

Research interests: I do epidemiologic and metabolic research on racial differences in cardiometabolic disorders—especially obesity, diabetes, and heart disease—that focuses on people of African descent. My work has shown certain cardiovascular risk factors do not translate across races. For example, I and my lab found that the current guidelines used to predict insulin resistance—such as central obesity and ratio of triglyceride level to high-density lipoprotein cholesterol level—are inaccurate for blacks.

By understanding the relationship between insulin resistance and glucose and lipid metabolism in blacks, we hope to identify the pathways that lead to cardiometabolic disease. Then improved screening tests and more effective interventions can be developed, and the medical and social costs that communities and individuals experience as a result of the high prevalence and chronicity of cardiometabolic diseases can be minimized.

Our studies are designed to examine the combined importance of metabolism, diet, exercise, living conditions, and education on disease development and outcomes. Although our research is focused on African-Americans and Africans living in the United States, we are collaborating with investigators in Africa and the Caribbean to expand our studies. We will also be considering the role of genetic background.

The public health implications of racial differences in disease risk factors are profound. African-Americans on average falsely appear to be at lower risk of cardiovascular disease and type 2 diabetes and thus may not be appropriately screened, diagnosed, and treated. ●

**PUBLIC HEALTH EDUCATION, CERTIFICATE AVAILABLE AT FAES**

WALK-IN REGISTRATION: JANUARY 9–18, 10:00 a.m.–4:00 p.m. (evening, January 17, 5:00–7:00 p.m.) Building 60, Suite 230

Looking for a way to enhance your public health horizons without leaving campus? The Foundation for Advanced Education in the Sciences (FAES) Graduate School at NIH is offering graduate-level evening courses in public health as well as a certificate of public health. To qualify for the certificate, students must complete 21 credit hours: one year of statistics (six credits); four three-credit courses (one in each of the disciplines of epidemiology, health policy and management, social and behavioral sciences, and environmental health sciences); and a three-credit independent project. The courses are available to anyone with a bachelor's degree and are open to all students whether or not they are pursuing formal certification. FAES also offers opportunities for intramural scientists to teach. Information about the Spring Semester classes, which begin the week of January 23, 2012, can be found at <http://www.faes.org>; public health courses are listed at http://faes.org/download_catalog ("Spring 2012 Supplement"). Information about these courses can also be found in the "2011–2012 Catalog" (pages 51–55 of the online PDF catalog and 41–45 of the printed catalog). For more assistance, contact Stephen E. Marcus at marcusst@mail.nih.gov.

NIH MANAGEMENT INTERN PROGRAM

RECRUITING: February 24–March 19, 2012

The NIH Training Center is pleased to announce the new recruitment season for Management Interns (MIs). The MI Program is a highly competitive, two-year administrative-management career-development program for current NIH employees. MIs come from a variety of job backgrounds including both scientific and administrative. Upon completion of the program, MIs transition into an

administrative-management career in one of many areas throughout the NIH enterprise. Current GS-7 through GS-12 NIH employees are invited to apply. For program FAQs and details about eligibility, visit <http://www.jobs.nih.gov/intern/mi.html>.

INTERFACING GLYSCIENCE WITH DISEASE AND CLINICAL PRACTICE

Tuesday, January 24, 2012

8:30 a.m.–5:00 p.m.

Natcher Conference Center (Building 45)

Advance registration not required

This symposium, hosted by the NCI-funded Alliance of Glycobiologists for Detection of Cancer and Cancer Risk (<http://glycomics.cancer.gov>), will highlight key developments in glycoscience and provide compelling examples of disease treatment and prevention. Presentations will emphasize the many ways glycans and their binding proteins influence fundamental biological processes and how these discoveries are advancing medicine. Speakers include: John Magnani, Ph.D., Glycomimetics, Inc.; Ira Pastan, M.D., NCI; Robert Sackstein, M.D., Ph.D., Harvard Medical School; Carole Bewley, Ph.D., NIDDK; Ronald Schnaar, Ph.D., Johns Hopkins University; Robert Haltiwanger, Ph.D., State University of New York at Stony Brook; Richard Cummings, Ph.D., Emory University; Michael Pierce, Ph.D., University of Georgia. The symposium will conclude with a session led by Dr. David Walt of Tufts University, who is the chair of a special panel at the National Research Council. He will answer questions from the audience on the importance and future directions of glycoscience. For more information and an agenda, visit <http://glycomics.cancer.gov/meetings-events/20120124>. For questions, contact Karl Krueger (301-594-1044 or NCIGlycomicsAlliance@mail.nih.gov). Sign language interpreters will be provided. Individuals with disabilities who need reasonable accommodation to participate in this meeting should contact Annalisa Gnoleba (301-594-7635 or gnolebaad@mail.nih.gov).

BREAST CANCER IS TOPIC AT GENOMICS IN MEDICINE LECTURE SERIES

February 3, 2012

8:00–9:00 a.m.

Lower Level Auditorium

Suburban Hospital, 8600 Old Georgetown Road, Bethesda, Md.

Stanley Lipkowitz, M.D., Ph.D., senior investigator in NCI's Laboratory of Cellular and Molecular Biology, will talk about breast cancer diagnosis and treatment. He will introduce the genomic characterization of breast cancer used in the clinic to define breast cancer subtypes as well as to stratify risk and determine treatment. Dr. Lipkowitz will also discuss how genomics is likely to affect the future management of breast cancer. All are welcome to attend. Parking is free, and refreshments will be served before the lectures. Advanced registration is not required; those requesting continuing medical education credits can sign in on site. For more information on this lecture and the ones scheduled for March 2, April 13, May 4, and June 1, visit <http://www.genome.gov/27546022>, or contact Susan Laine at Suburban Hospital (slaine@suburbanhospital.org) or Alice Bailey at NHGRI (baileyali@mail.nih.gov).

ADVANCING CANCER RESEARCH THROUGH BIOSPECIMEN SCIENCE

February 22–23, 2012

Bethesda North Marriott Hotel and Conference Center, Bethesda, Md.

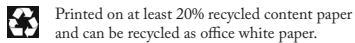
Registration closes on January 25

Hotel cutoff date is January 31

NCI's Biospecimen Research Network Symposium will highlight new developments in the field of biospecimen science to address the significant effect of pre-analytical biospecimen variables on cancer research and molecular medicine. For more information and to register, visit <http://brnsymposium.com>.

PLEASE SUBMIT ANNOUNCEMENTS FOR MARCH-APRIL ISSUE, BY FEBRUARY 1 TO: catalyst@nih.gov.

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CATALYTIC REACTIONS?

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

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

WE STILL HAVE NOT YET IDENTIFIED THE MASKED SURGEON. SEE [HTTP://IRP.NIH.GOV/CATALYST/V19I5/LABORATORY-CONFESSIONS](http://irp.nih.gov/catalyst/v19i5/laboratory-confessions).

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

Address correspondence to:
Building 1, Room 333, NIH
Bethesda, MD 20892
Ph: 301-402-1449
Fax: 301-402-4303
e-mail: catalyst@nih.gov

The NIH Catalyst online:
<http://irp.nih.gov/catalyst>

LABORATORY CONFESSIONS

There's Not an App for That

BY NAME WITHHELD

I was inspired by the NIH Research Festival committee's efforts to create smartphone-friendly Web sites, documents, and applications (a.k.a. “apps”). You know the saying: There's an app for that. But actually, many apps we could use at NIH haven't been created. Here are my top five ideas:

5. Boring warning: I need an app to give me personalized warnings about whether the lecture or meeting I'm about to attend will bore me to tears. An e-notification of whether my PI is in attendance would be key, too.
4. Partner alert: No one seems to wear rings anymore, and no one seems to share last names. An app alerting me to who's married to whom at the NIH would avoid embarrassing situations.
3. Reception food alert: I need a map, updated hourly, of free food around campus so I can plan my mooching accordingly. Otherwise, finding food is totally up to chance for now.
2. E-mail filter: I need a real e-mail filter, not something that merely filters spam but rather something that informs the sender to leave me alone because I have left the planet Earth. My attempt to create one by blocking any e-mail address with the “@” symbol unfortunately stopped the approximately 1.8 percent of e-mail I actually do need to read. So some tweaking is necessary.
1. Building 10 map: I write these words via an iPhone on the ninth floor of Building 10 in the north-facing south wing in the A corridor adjacent to the J wing, and I have just four words to say: Get me outta here.

EDITOR'S NOTE: HAVE A LATE-NIGHT LABORATORY CONFESSION? WE MIGHT PRINT IT IF IT IS INDECENT ENOUGH.

PUBLISHER

MICHAEL GOTTESMAN
Deputy Director for
Intramural Research, OD

EDITORS

JOHN I. GALLIN
Director, NIH Clinical Center
HENRY METZGER
Scientist Emeritus

MANAGING EDITOR

LAURA STEPHENSON CARTER

WRITER-EDITOR

CHRISTOPHER WANJEK
Director of Communications, OIR

COPY EDITOR

SHAUNA ROBERTS

EDITORIAL INTERN

HEATHER DOLAN

CONTRIBUTING WRITERS

ROBIN ARNETTE
KATHERINE BRICCENO
STEPHANIE COOPERSTEIN
LESLEY EARL
NATALIE GOLDBERGER
CAROLYN GRAYBEAL
ALAN SMITHEE

PHOTOGRAPHERS/ILLUSTRATORS

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