THE NIH CATALYST

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Crowdsourcing

And Virtual Colonoscopies

BY LAURA STEPHENSON CARTER

When it comes to interpreting the results of virtual colonoscopies, radiologists "have a hard time taking the advice of computer aids," said senior investigator **Ronald Summers**, chief of the NIH Clinical Center's Clinical Image Processing Service. Computer-aided-detection (CAD) technology, which he helped develop for colorectal cancer screening, is supposed to make the radiologist's job easier. CAD is more effective than humans at finding tiny bumps on the scan that represent polyps, but it identifies mock polyps, too—residual fecal matter clinging to the colon wall, thick folds in the colon, or even artifacts such as surgical clips or hip prostheses. Even though radiologists should be able to tell the difference between true and false readings, they often ignore CAD's true findings.

Summers wanted to reduce what he suspected were perceptual errors involving the CAD system, but he needed to be able to observe its users in action. Radiologists, however, are too busy to participate in such observer-performance experiments. Then he stumbled on a way to get participants: crowdsourcing, also known as distributed human intelligence. It's a method for recruiting large numbers of anonymous laypeople, or knowledge workers (KWs), to perform simple tasks distributed over the Internet. He reported his findings in a recent issue of *Radiology* (*Radiology* **262:**824–833, 2012).

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Piecing Together the Autism Puzzle

NIH Researchers Tackling the Problem on All Fronts

BY SARAH RHODES, NIMH

Dan Hall's son was two years and nine months old when he was diagnosed with an autism spectrum disorder (ASD). "He was very verbal, then all of a sudden he stopped talking. We thought he was deaf," said Hall. "Back then people didn't really know what autism was, so it wasn't our first thought." That was 12 years ago. Hall has learned plenty about autism since then. Today he's the manager of NIH's National Database for Autism Research (NDAR), which consolidates autism biomedical data on 25,000 participants and makes it available to qualified researchers. "Data sharing really provides the opportunity to uncover and accelerate scientific research," said Hall. "Data aggregation is needed to help scientists uncover the patterns of what may be many autisms." He expects the NDAR database to grow to contain data on 100,000 participants within the next four years.

Dan Hall (right), who's the manager of NIH's National Database for Autism Research and has a teenage son with ASD, enjoys rafting on the Big Pigeon River (Hartford, Tenn.) with his family.

And so goes one of many NIH projects on autism, first described by psychiatrist Leo Kanner in 1943 as "the innate inability of certain children to relate to other people." ASDs—which include autistic disorder, Asperger syndrome (autism-like problems in social interaction and communication but normal intelligence and verbal skills), and "pervasive developmental disorder–not otherwise specified" (PDD-NOS), the disorder Hall's son has—are neurodevelopmental disabilities characterized by impairments in social interaction and communication and restricted, repetitive, and stereotyped patterns of behavior. Symptoms typically become apparent before the age of three. Although there is not yet a cure for ASD, there are ways to minimize symptoms and maximize learning.

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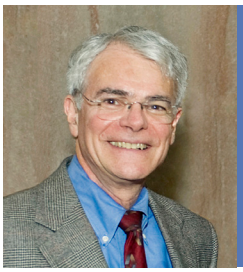


For Our Fellows At the NIH

BY MICHAEL GOTTESMAN, DDIR

Over the past 30 years, NIH intramural science has become increasingly dependent on talented postdoctoral fellows to conduct most of the innovative research done in our laboratories and to help with the training of our growing cadre of predoctoral students. In turn, NIH principal investigators (PIs) and NIH leadership have sought ways to ensure that the training experience here for fellows is among the best in the world. We are also working on new initiatives to improve that experience.

I want to take this opportunity to thank our nearly 4,000 fellows, including IRTAs (Intramural Research Training Awards recipients) and CRTAs (Cancer Research Training Awards recipients), visting fellows, and research and clinical fellows for their contributions to NIH research, and summarize why I think we provide one of the best environments anywhere for training and career development.

The primary goal of fellows is to work in laboratories that are doing cutting-edge research in which they can make contributions that will advance their careers.

By any quantitative standard, including publication rates, citations, technology transfer into marketed products, and recognition with prestigious awards and memberships in honorific societies, NIH intramural research and researchers are among the best of any institution in the country. Working as a fellow in an NIH lab is surely a world-class opportunity.

Our PIs are also aware of the importance of mentoring and advocating for their fellows. Consequently, the success rate for finding jobs after an NIH fellowship is very high. Fellows find jobs in industry, government, and academic centers as well as in many science-related fields that may not involve bench research.

Here at NIH, former NIH fellows and students occupy approximately 30 percent of our PI positions, a statistic that is consistent with the quality of both the fellows and their training here in a very competitive environment.

> NIH provides one of the best environments for training and career development.

The NIH Intramural Program has very active training directors and training programs within each institute and center. In addition, the Office of Intramural Training and Education, led by Sharon Milgram in the Office of Intramural Research, provides world-class coursework, counseling, and outreach activities to ensure a talented and diverse postdoctoral population at the NIH.

NIH provides many benefits to fellows including a premier health-insurance program managed by the Foundation for Advanced Education in the Sciences, availability of childcare services, Transhare Program benefits to encourage use of public transportation and reduce its cost, and stipends that are competitive with those offered at other premier academic institutions.

More recently, we have been working on two new initiatives for improving the quality of life for fellows at the NIH that parallel improvements for our NIH employee workforce: increased flexibility in work hours and backup daycare.

When I speak to fellows, it is clear that increased flexibility to allow them to manage home life and work life is extremely important. One of the new initiatives is a program that we are calling "Keep the Thread" that would allow IRTA and CRTA fellows, with agreement of their PIs and scientific directors, to take some time off to attend to personal responsibilities during their fellowship or take advantage of flexible hours to conduct their research. Please contact your PI and scientific director to discuss whether you would be eligible for this program.

The other new initiative is a backup daycare program for fellows (and NIH employees) whose regular daycare is not available and they have a short-term need for licensed caregivers either in the home or at another daycare center. For more information on backup care, visit http://www.ors.od.nih.gov/pes/dats/childcare/Pages/NIHBack-upCare-Program.aspx.

I am grateful to the scientific directors and the many individuals at NIH, including the Fellows Committee, who have been consistent, forcible, and convincing proponents for our NIH Fellows.

Any additional ideas you might have to improve the environment for our fellows are always welcome. ●

Got Genotype and Phenotype?

How to Submit and Access Data at dbGaP

BY KRISTOFOR LANGLAIS, OD; ERIN LUETKEMEIER, OD; AND KIMBERLY TRYKA, NLM-NCBI

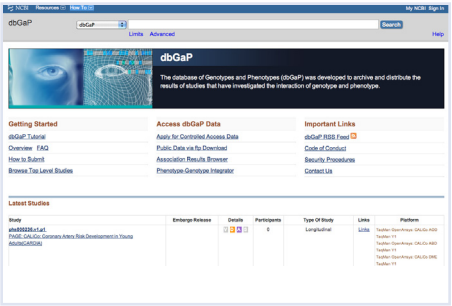
Genome-wide association studies (GWAS) can generate volumes of data about common genetic factors that influence health and disease. Sharing the data with other investigators enables many more insights to be gleaned and magnifies the value of the original research. In 2008, NIH implemented a policy for sharing data obtained in NIH-supported or NIH-conducted GWAS to make the data more readily available to a wide range of investigators, including NIH intramural scientists.

There are more than 1,400 published genome-wide associations for 237 common diseases and traits. NIH is updating its GWAS data-sharing policy to include a broader spectrum of sequence data such as whole-genome and whole-exome sequence and epigenomic data.

CENTRAL REPOSITORY

Under the NIH policy, both extramural and intramural investigators funded by NIH are expected to submit GWAS data to a central repository called the Database of Genotypes and Phenotypes (dbGaP), which was developed by the National Center for Biotechnology Information (NCBI).

The dbGaP archives and provides access to data from studies that have investigated the interaction of genotype and phenotype in a wide range of health conditions and diseases such as mental illnesses, cancer, autoimmune disorders, cardiovascular disease, diabetes, and age-related eye diseases. This rapidly growing and highly used database contains GWAS and other study data involving whole-genome, whole-exome, and other next-generation sequencing and array-based technologies.



Intramural and extramural investigators funded by NIH are expected to submit their GWAS data to dbGAP.

There are two ways to access dbGaP data: open (public) access, for basic study descriptions, variables, and protocols; and controlled access for individual and aggregate-level participant data, including exposure, genotype, pedigree information, and individual-level phenotypes. Researchers who wish to use controlled-access data must submit a data-access request.

NIH intramural researchers at nearly all the NIH institutes and centers (ICs) are conducting next-generation (or next-gen) –omics studies and are expected to deposit their results in dbGaP or other NCBI data repositories. Of the 267 studies available in dbGaP, 25 are by NIH intramural investigators. These intramural studies hold clues to the genetic underpinnings of lung cancer, amyotrophic lateral sclerosis, bipolar disorder, ischemic stroke, and other conditions.

Nearly 100 NIH intramural investigators have accessed dbGaP data for secondary studies on genetic risk factors associated with the major mood disorders, schizophrenia, asthma, and autism; insights into a key metabolic pathway and neurodegenerative diseases; and improved statistical methods to study X-linked diseases such as age-related macular degeneration.

HOW TO SUBMIT AND ACCESS DATA

In April 2012, to avoid some of the past confusion and facilitate wider intramural usage, NIH administrators developed clearer pathways for submitting data to and accessing data in dbGaP.

To submit data, investigators work closely with the GWAS program administrators from their institutes to prepare data-certification memoranda, which outline limitations in data use and ensure that data submission is consistent with the NIH GWAS policy and applicable laws and regulations. Certification memoranda are reviewed and verified by the appropriate institutional review board chairs and scientific directors and then approved by the NIH Deputy Director for Intramural Research.

To access dbGaP data, an investigator must first register with the dbGaP system, which requires approval from the investigator's supervisor, scientific director, and IC director or designated signing official. Once registered, an investigator can submit a request to access dbGaP data, which will be reviewed by the data-access committee(s) responsible for overseeing the particular dataset(s) requested.

For more information, visit http://gwas.nih.gov/06researchers1.html or contact the GWAS mailbox at GWAS@mail.nih.gov.

Other helpful Web sites:

- **dbGaP:** http://www.ncbi.nlm.nih.gov/gap
- **GWAS data repository policy:** http://gwas.nih.gov/
- **NIH GWAS data-sharing policy:** http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html

Langlais and Luetkemeier work in the Office of Biotechnology Activities, Office of Science Policy; Tryka is a dbGaP staff scientist at NLM-NCBI.

FROM THE FELLOWS COMMITTEE

Careers in Regulatory Affairs

BY MEGHAN MOTT, NIAAA

Regulatory professionals play critical roles in the health-care product lifecycle and protect public health by influencing the safety and efficacy of pharmaceuticals, medical devices, cosmetics, and complementary medicines. On February 14, 2012, experts spoke to NIH trainees about career opportunities in regulatory affairs.

Janice Chappell, a senior director of regulatory affairs at Aeras (Rockville, Md.), outlined the landscape of the field and the skills important for success. David Debany, a senior associate in regulatory affairs at Millennium Pharmaceuticals (Boston office), described the role of regulatory publishers and business analysts. Jason Urban, a scientist at FDA's Center for Drug Evaluation and Research (CDER) Office of Compliance (Silver Spring, Md.), shared insights into the process of transitioning from bench science to regulatory affairs. Nicole Gormley, a medical officer at the FDA's CDER Office of Oncology Drug Products, explained how her experience as an NIH clinical fellow prepared her as a clinical reviewer of investigational new drug applications. Elizabeth Glaze, a regulatory specialist in NIAID's Division of Microbiology and Infectious Diseases, discussed the roles toxicologists play in designing preclinical protocols and reviewing data in clinical trials.

There is no typical career path and no special degree needed. Regulatory affairs professionals come from the medical, research, pharmaceutical, project management, and manufacturing fields and can specialize in drugs, biologics, devices, or product development in clinical trials. They need to be excellent communicators, open-minded, active listeners with problem-solving abilities, and adaptable.

Attendees were urged to use the Regulatory Affairs Professionals Society, which offers courses, meetings, and resources; and LinkedIn to develop networks, conduct informational interviews, and determine the specialties and organizations to target.

To join the Subcommittee on Career Development, which sponsored the event, contact Cory Lago (lagocu@nhlbi.nih.gov) or Meghan Mott (mottmc@mail.nih.gov).

For information on past events, visit https://www.training.nih.gov/FelCom/CareerDevelopment. To see a videocast of the February 14 event, visit https://www.training.nih.gov/events/view/_2/776/Careers_in_Regulatory_Affairs. ●

FROM THE OFFICE OF INTRAMURAL TRAINING AND EDUCATION

The New NIH Academy, Apply Now

BY SHAUNA CLARK, OITE

Minorities get sick sooner, have more severe illnesses, and die sooner than whites, according to health-disparities expert David Williams at Harvard (Boston). This much has been known for years. NIH is dedicated to eliminating these health disparities—inequalities among populations in rates of disease incidence, prevalence, morbidity, and mortality—through research as well as training programs such as the NIH Academy.

The NIH Academy, which was launched in 2001, trains postbaccaulaureates (postbacs)—142 so far—to do research on health disparities. The hope is that this next generation of researchers and health-care providers will understand, and play a role in eliminating, health disparities. This year, the Office of Intramural Training and Education (OITE) is launching a bigger and better NIH Academy.

The "old" academy trained 12 to 16 postbacs a year; the new one will train as many as 100. Trainees can pursue either a certificate program that carries a time commitment of 30 to 40 hours over a 10-month period, or a more intensive fellows program with a time commitment of about 100 hours over 10 months. The certificate program is for those who may not have had previous exposure to the health-disparities field. The fellows program is an in-depth experience for those interested in careers that incorporate the elimination of health disparities.

Both programs will feature the theme of health disparities in vulnerable populations and will include journal clubs, seminars, expert-led discussions, community outreach, and career-development workshops. OITE's goal is to broaden trainees' understanding of the various determinants of health and to emphasize that eliminating health disparities is a critical component of improving the health of all Americans.

An added benefit of the new program is that for the first time all current NIH postbacs are eligible to participate, including trainees on satellite campuses. Letters of interest in the NIH Academy, emphasizing a strong desire to learn about health disparities, may be submitted to OITE between May 1 and August 1. Applicants will be notified of their acceptance in mid-August.

For more information about the NIH Academy visit http://www.training.nih.gov/new_nih_academy_home or contact Shauna Clark (clarkshauna@od.nih.gov). ●

Tenacious Tara

NIH Postdoctoral Fellow Combines International Interests with Neurology

BY MONIKA DESHPANDE, NCI

Don't let her ready smile and unassuming persona fool you. Postdoctoral fellow **Tara Kimbason** (née Kim) has a steely determination and an ambitious goal … to find a way to provide medical care to underserved people throughout the developing world.

As early as high school, this New York City–raised, only child of Korean-American parents dreamed of joining the Peace Corps so she could help people in other countries. But it would be several years before her dream came true. After graduating from the State University of New York at Binghamton (Vestal, N.Y.), she first went to Bethesda, Md., to do research at the Uniformed Services University of the Health Sciences and at NIH's National Institute of Neurological Disorders and Stroke (NINDS).

She managed to convince her worried parents that she was ready to join the Peace Corps and go off to a faraway country riddled with social and political strife: the Republic of Senegal, which lies on the west coast of Africa. As an urban primary health-care agent in Vélingara, her mission was to build awareness about sanitation, malaria prevention, and medical care. But the people of Senegal shunned her at first. They weren't used to American Peace Corps volunteers with Asian features and refused to talk to her. She was determined to win them over, however. She wore the local clothing, adopted local ways, and was helpful and respectful. Gradually they learned to trust her and invited her to join the local choir and welcomed her into their homes for meals. She even helped the community win a U.S. Agency for International Development grant to renovate a local hospital.

She wanted to play a bigger role in public health, though, and needed more training than what the Peace Corps could offer. So she returned to the United States to get an M.P.H. degree at Johns Hopkins Bloomberg School of Public Health (Baltimore). Then she spent a year in Afghanistan as a health-communications advisor and collaborated with the ministry of health to develop and lead a health-education training course for physicians and community health-care workers; conduct surveys and collect data; and produce and distribute health-related posters, pamphlets, and other materials. Again, the local people were suspicious of her. And again, through her determination, she gained their trust.

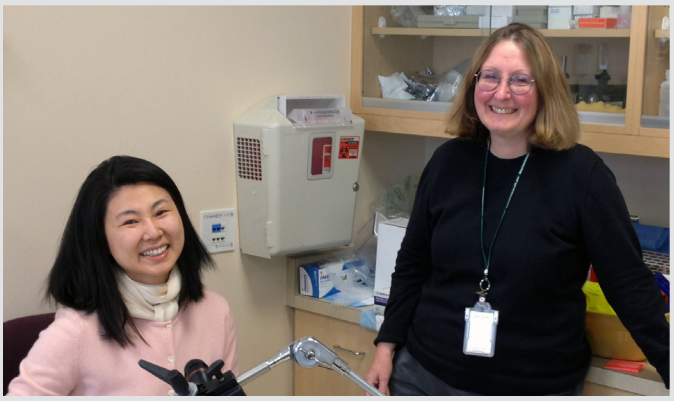
Kimbason enjoyed teaching people about health care, but she wanted to provide health-care services, too. That meant becoming a doctor. During her medical school clerkships, she discovered she particularly enjoyed working with patients who had neurological disorders. She liked doing research, too, and spent a summer doing neuroscience research at Columbia University College of Physicians and Surgeons (New York). She still had a hankering to practice international medicine, so she did an elective in which she traveled to remote villages at the Indo-Tibetan border to help set up mobile clinics, provide hands-on medical care, and treat patients with neurological disorders.

After getting her M.P.H. from Johns Hopkins, Tara Kimbason spent a year in Afghanistan as a health-communications advisor. Here she is wearing a traditional Afghani village dress.

"I saw people with stroke who did not know it could have been prevented," she said. "Some even thought it was 'destiny.'"

During her last year of medical school—she earned her M.D. from the University of Sint Eustatius School of Medicine (in the Netherlands Antilles)—she did a neurology rotation and an independent research project at the Emory Clinic Sleep Center (Atlanta). In 2010, she returned to NINDS, this time to do clinical research with **Mary Kay Floeter** as an associate investigator in a multicenter natural history protocol on oxidative stress in motor neuron disorders.

Kimbason is ready to solidify her clinical skills and will be leaving NIH in June to do a neurology residency at the Geisinger Medical Center (Danville, Pa.). She is determined to use all she's learned working at NIH and around the world, combine her clinical and research interests in neurology to help medically underserved people everywhere, and establish international collaborations in the prevention and treatment of neurological disorders. With her tenacity and spirit she is sure to succeed. ●



LAURA DANIELIAN, NINDS

NINDS postdoctoral fellow Tara Kimbason (left), who has been doing clinical research with NINDS senior clinician Mary Kay Floeter (right), will be leaving NIH soon to do a neurology residency at the Geisinger Medical Center (Danville, Pa.).

Hidden Treasures Discovered in Building 38

Proof That NLM is NIH's Own Treasure Island

BY HEATHER DOLAN

Imagine a book that features a life-sized human anatomy manikin; an overview of palm reading in Renaissance Europe; a post–World War I silent film of schizophrenic patients; the first systematic study of human motion; health and hygiene puzzle blocks from Communist China; and Adolf Hitler's medical records. Such a book exists, in the form of *Hidden Treasure*, which was published in honor of the NIH National Library of Medicine's (NLM) 175th anniversary (celebrated in 2011) and highlights 80 of the library's most mysterious and unusual items.

It was no easy task for the book's editor, NLM historian Michael Sappol, to choose which of library's 17 million treasures to include. He selected items for their visual appeal and ability to represent the breadth of NLM's rich collection—the charming and the disturbing; the beautiful and the repulsive; the intriguing and the informative—and included books, pamphlets, flyers, manuscripts, journals, lithographs, letters, postcards, posters, magazines, engravings, cartoons, objects, photographs, films, sound recordings, and slides. He also invited distinguished scholars, artists, collectors, journalists, and physicians to write commentary essays about each of the treasures.

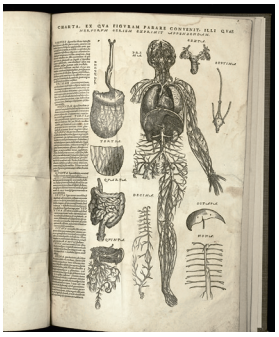
Capturing images of the final 80 was not easy either, said Arne Svenson, the New York photographer NLM hired for the project. More challenging than shooting in the library's cramped spaces and under "haunted house at high noon" lighting, said Svenson, was "finding creative ways to shoot books, books, and more books and make each resultant photo a compelling, individualized statement." To combat the limited space, he wedged himself between shelves. To counter the poor lighting, he used strobe lights, ordinary light bulbs, and even flashlights. And to keep the settings interesting, he and the book's designer, Laura Lindgren, scavenged the library's halls for unique locations. "A shelf of books, corners of rooms, file cabinets—anything and everything was a candidate for ambient background scenes," he said.

What follows is a sampling of the diamonds within the crown of *Hidden Treasure*'s jewels.

The Anatomical Paper Doll Epitomized

***THE EPITOME* (1543) BY ANDREAS VESALIUS; ESSAY BY ANDREA CARLINO, WHO TEACHES THE HISTORY OF MEDICINE AT THE UNIVERSITY OF GENEVA**

Composed by Flemish physician Andreas Vesalius, this book contains large woodcuts of human forms and illustrations of organs, vessels, and other bits of human anatomy, as well as instructions on how to cut them out "to build [a] multilayered anatomical paper doll and then glue it to one of the muscle figures [in] the book," Carlino wrote. Vesalius believed performing this exercise would enforce understanding of the composition and spatial arrangement of internal organs. NLM's copy of the book "is noteworthy because it is one of the few 1543 paper copies that have survived the spoiling effects of time—and the scissors of readers and owners."



Slide Show Follies As Therapy

***ST. ELIZABETHS MAGIC LANTERN SLIDE COLLECTION* (1855-1890S); ESSAY BY BENJAMIN REISS, A PROFESSOR OF ENGLISH AT EMORY UNIVERSITY (ATLANTA)**

Originally the Government Hospital for the Insane, St. Elizabeths is a Washington, D.C., psychiatric hospital that opened in 1855. Magic lantern displays (primitive slide shows) were developed in the early 1850s by Dr. Thomas Kirkbride of the Pennsylvania Hospital for the Insane and by two German émigré photographers for patient therapy and entertainment. Viewing images was intended to temporarily relieve patients' delusions. Magic lantern slides ranged from the instructive, such as illustrations of the hazards of alcohol and tobacco, to the bizarre, such as the image depicted here of "The Attack of the Monster [Flea]," in which a magnified flea is threatening an ax- and shears-wielding man.

"Given that many patients were delusional and/or medicated with dream-inducing opiates, one wonders about the wisdom of serving up these ready-made hallucinations, magnified to terrifying proportions," Reiss wrote. But some psychiatrists believed that "asylum amusements should feature techniques of 'revulsion'—that is, psychological interventions that would cause patients to recoil from their delusions by externalizing them."

The Lost Art of Dental Slapstick

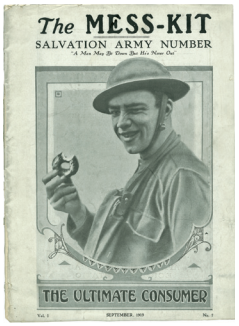
DENTAL CARTOONS* (1948) BY OTTO ELKAN; ESSAY BY ALYSSA PICARD, AUTHOR OF *MAKING THE AMERICAN MOUTH: DENTISTS AND PUBLIC HEALTH IN THE TWENTIETH CENTURY

These wry cartoons "not only document the international spread of American dental technology [in the 1940s] but also a transatlantic cultural preoccupation with access to good professional dental care, particularly in wartime," Picard wrote. "During World War II—when nearly all of Europe's professionally trained dentists had entered military service, been forced to flee, or been put in concentration camps—access to good dental care was severely restricted."

"Funny-isms" and "Ward Gossip"

***THE MESS KIT AND THE SILVER CHEV'* (1919); ESSAY BY JEFFREY S. REZNICK, NLM**

In the aftermath of World War I, at least 50 military hospitals produced in-house magazines between 1918 and 1919. "Endorsed by the Surgeon General's Office, magazines such as *The Mess Kit* of Camp Merritt Base Hospital, New Jersey, and *The Silver Chev'* of Camp Grant Base Hospital, Illinois, and *The Come-Back* of Walter Reed General Hospital, Washington, D.C., were brought to life by wounded soldiers and military staff who contributed articles, jokes, poems, illustrations, and other material," wrote Reznick.

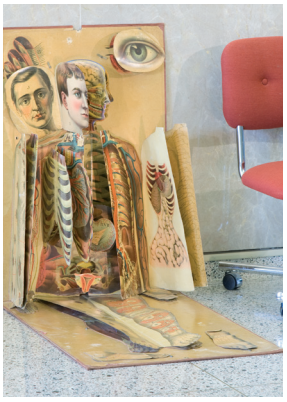


"Magazine work served to distract from bullet, shell, and bayonet wounds, influenza and other infectious diseases, gas exposure, gangrene, and shell shock [and provide] 'safety valves' to help relieve the stress experienced by frontline soldiers and their caregivers," he continued. "Editors playfully interwove a variety show of cartoons, embellishments, photographs, and texts."

The Phantom of the Anatomy Lecture

***WHITE'S PHYSIOLOGICAL MANIKIN* (1886); ESSAY BY MICHAEL SAPPOL, NLM**

Described by Sappol as "a gadget that does too much," this life-sized manikin has numerous flaps and openings revealing different layers of the human anatomy. In 1887, 25 states required the teaching of physiology in public schools. Three-dimensional, dissectible visual aids were needed, but the papier-mâché manikins imported from France ranged from $250 to $1,500. White's Manikin was a mere $35 and it remained for 20 years the visual anatomy tool of choice for many U.S. public schools. To photograph it artistically, Arne Svenson said he "added a totally incongruous contemporary red office chair as a way to create not only scale and a sense of place, but [also] a touch of humor to this somewhat grisly tableau."



Window Into History

Hidden Treasure "opens a window onto the diversity of the collection [and] onto the history of the library itself," said Jeffrey Reznick, chief of NLM's History of Medicine Division.

In 1836, the NLM was just a small collection of medical books on a shelf in the Office of the Surgeon General of the Army. Today it's housed at NIH and is the world's largest biomedical library, with a collection of over 17 million items in more than 150 languages. NLM also provides automated Internet services—including MedlinePlus, PubMed, and PubMed Central—that "deliver trillions of bytes of health data crucial to the lives of millions of people around the globe," said Reznick. "These collections belong to the public [and] people are welcome to look at any of this to learn more about it."

NLM is not a circulating library. Visitors, however, are welcome to apply for a free library card to access NLM matrials (including those featured in *Hidden Treasure*) in one of the reading rooms. For more information go to http://www.nlm.nih.gov/about/visitor.html. To learn about the collections and resources in NLM's History of Medicine Division, visit http://www.nlm.nih.gov/hmd/index.html In addition, *Hidden Treasure* is available through all major online booksellers. ●

Intramural Research Briefs

NICHD: CAREGIVING IMPULSE

Distinct patterns of activity, which may indicate a predisposition to care for infants, appear in the brains of adults who view an image of an infant face, according to a study done by NIH researchers and others. Images of infant faces appeared to activate circuits in the adults' brains that reflect preparation for movement and speech, and feelings of reward. Seven men and nine women were shown a series of images—puppy and kitten faces, full-grown dogs and cats, human infants, and adults—while their brain activity was recorded with a functional magnetic-resonance-imaging scanner. Infant images evoked more activity than any of the other images. However, additional studies are needed to understand whether what appears to be a parenting instinct in some adults is universal. (NICHD author: M.H. Bornstein; *Neuro Image* **60**:884–893, 2012)

CC, NIBIB: NEW CELL-LABELING METHOD ALLOWS FOR MRI TRACKING

NIH researchers and collaborators have developed a method for labeling transplanted cells so they can be tracked by magnetic-resonance imaging (MRI) to measure how many transplanted immune or stem cells reach their target. The researchers combined ferumoxytol, heparin, and protamine to form a complex that labeled nearly 100 percent of transplant cells for MRI in animal models. The technology, pending regulatory agency review, will be tested in humans in an ongoing trial in California. (NIH authors: M.S. Thu, L.H. Bryant, T. Coppola, E.K. Jordan, M.D. Budde, B.K. Lewis, A. Chaudhry, J. Ren, J.A. Frank; *Nature Med* **18**:463–468, 2012)

NIEHS: ARSENIC TURNS STEM CELLS CANCEROUS

Exposure to arsenic can turn normal stem cells into cancer stem cells and spur tumor growth. NIH researchers showed that when cancer cells are placed near—but not in contact with—normal stem cells, the normal stem cells rapidly acquire the characteristics of cancer stem cells. Malignant cells were able to send molecular signals through a semipermeable membrane and turn the normal stem cells into cancer stem cells. Further experiments are planned. [NIH authors: Y. Xu, E.J. Tokar, Y. Sun, M.P. Waalkes; *Environ Health Perspect* DOI:10.1289/ehp.1204987 (2012)]

NCI: TOBACCO CONTROL POLICIES PREVENT ALMOST 800,000 DEATHS

Twentieth-century tobacco-control programs and policies were responsible for preventing more than 795,000 lung cancer deaths in the United States from 1975 to 2000, according to an analysis done by NIH researchers and others. U.S. tobacco-control efforts have included restrictions on smoking in public places, increases in cigarette excise taxes, limits on underage access to cigarettes, and increasing awareness of the hazards of smoking. (NCI author: E.J. Feuer; *J Natl Cancer Inst* **104**:541–548, 2012)

NIAMS, NCI: ORIGINS OF TUMOR-INDUCING CHROMOSOMAL REARRANGEMENTS

A study by NIH scientists resolved longstanding questions about the origin of recurrent chromosomal rearrangements, or translocations, that drive human lymphomas and leukemias. Using B immune cells, the researchers discovered that the frequency of DNA damage was directly proportional to the frequency of translocations. They also found that an enzyme called activation-induced cytidine deaminase (AID) damages approximately 150 genes in the B-cell genome, thus making them susceptible to translocations. In AID's absence, gene proximity or interaction frequency was the driving force behind translocations. The researchers' results also suggest that inhibiting AID could prevent the development of many human cancers. (NIH authors: O. Hakim, T.C. Voss, G.L. Hager, A. Nussenzweig, W. Resch, A. Yamane, K.-R. Kieffer-Kwon, J. Cobell, H. Nakahashi, C. Ansarah-Sobrinhow, G. Liang, E. Mathe, R. Casellas; *Nature* **484**:69–74, 2012)

NHGRI: GENETIC BASIS OF TROPICAL FOOT AND LEG LYMPHEDEMA

A genetic variation may explain why four million people worldwide develop podoconiosis, a foot disfigurement resulting from barefoot exposure to volcanic soil. NIH researchers and their collaborators conducted a genome-wide association study analyzing DNA from volunteers—194 affected by podoconiosis and 203 unaffected—from the Ethiopian highlands. The researchers found that susceptibility to podoconiosis is increased—two to three times—by inheriting altered DNA in the HLA class II locus. (NIH authors: F.T. Ayele, A. Adeyemo, C.N. Rotimi; *N Engl J Med* **366**:1200–1208, 2012)

NIEHS: GULF OIL SPILL STUDY

On April 20, 2010, the Deepwater Horizon drilling rig exploded and, over the next 87 days, spilled nearly five billion barrels of crude oil into the Gulf of Mexico and contaminated 500 miles of coastline along Florida, Alabama, Mississippi, and Louisiana. NIEHS has been involved in this Gulf oil disaster since the very beginning, having offered safety training to more than 150,000 cleanup workers. Now a NIEHS team, led by epidemiology branch chief **Dale Sandler**, is seeking to determine possible physical or mental-health effects of the oil spill on the people who were involved in cleanup efforts. The Gulf Long-Term Follow-up (GuLF) Study, launched in February 2011, aims to include 55,000 of these workers, will last 10 years, and be the largest health study of its kind. It has acquired more than 10,000 participants so far. The researchers will use the results of a telephone survey and medical information to document potential mental, physical, and emotional health effects caused by exposure to crude oil and dispersants. Findings may help guide policy decisions on health care and services in the Gulf region and also guide responses to future oil spills. For more information, visit the GuLF Study Web site at http://www.niehs.nih.gov/GuLFSTUDY. ●

Eyes on the Goal

Anand Swaroop Seeks Therapies for Retinal Diseases

BY HEATHER DOLAN

"People over 40 are really scared of going blind," National Eye Institute (NEI) Senior Investigator **Anand Swaroop** told the scientific directors at their meeting on March 7, 2012. "After cancer and heart disease, blindness is probably the most feared of all."

He went on to describe his lab's work on promising stem cell advances that one day might be used to treat blinding neurodegenerative diseases. But Swaroop might not be doing eye research at all if his early career had gone the way he planned.

When he was doing postdoctoral work in genetics at Yale University (New Haven, Conn.), in the 1980s, he wanted to be the first to find the gene that causes Duchenne muscular dystrophy (DMD). When Louis Kunkel's group at Children's Hospital Boston beat him to it and identified the gene in 1986, Swaroop was disheartened.

But not for long. He found a different disease gene to work on: X-linked retinal pigmentosa 3 (RP3). Defects in *RP3* and several other genes cause retinitis pigmentosa, genetic eye conditions in which retinal degeneration leads to incurable blindness. And since *RP3* was near the DMD-inducing gene he was already working on, Swaroop figured it would be easy to transition to the field of eye research. While still at Yale, he wrote his first grant proposal to NIH: He proposed a novel strategy to identify genes for X-linked retinal diseases. NEI was impressed and funded him.

With a grant in hand, he went to the University of Michigan (Ann Arbor, Mich.) in 1990 to continue his eye research; he kept getting more and larger grants from NEI and other funding organizations. Finally in 2007, he came to NEI, where he established and now heads the Neurobiology-Neurodegeneration and Repair Laboratory.

In his quest to find the genetic defects behind and treatments for retinal diseases, he collaborates with other NEI and NIH scientists as well as with other researchers within the United States and several other countries.

CHRIS GUNN PHOTOGRAPHY

Senior Investigator Anand Swaroop (NEI) is battling retinal diseases that cause blindness.

Swaroop is interested in retinal photoreceptors and the retinal pigment epithelium (RPE), which is key to photoreceptors' survival. Abnormalities, dysfunction, and/or the death of retinal photoreceptors in retinal and macular degenerative diseases can cause irreversible vision loss.

The RPE is a barrier between the retina's neural network and the blood and maintains retinal cell homeostasis by providing nourishment and removing debris. "RPE is like the queen" in a game of chess, he said. She protects her "king"—the photoreceptors. In chess, "if the queen is gone, in many cases it results in checkmate. [In the eye], if RPE is dead, photoreceptors are gone, too."

Swaroop's new project is the development of stem cell–based therapies to replace defective or dying photoreceptor cells. He and his collaborators pioneered this approach by successfully transplanting photoreceptor precursor cells into degenerating mouse retinas. His team discovered that these precursor cells were more likely to grow and be successfully integrated into the degenerating retina than were mature brain- and retina-derived stem cells. (*Nature* **444**:203–207, 2006)

"We are particularly enthusiastic about Dr. Swaroop's project to combine his wide expertise in genetics and genomics with iPS cell technology to understand early-onset retinal degeneration," said NEI's scientific director, Sheldon Miller. Swaroop is obtaining iPSC (induced pluripotent stem cell) lines from people with Leber congenital amaurosis (LCA), a rare genetic disorder that appears at birth and causes blindness through the degeneration of photoreceptor cells. The iPSCs from these people have mutations in the *CEP290* gene.

One of Swaroop's recent discoveries was that, in the mouse, a mutated version of *Cep290* codes for a protein that interacts with the Mkks protein, which is important in the formation of the arms, legs, heart, and reproductive system. The combination of *Cep290* and *Mkks* mutants improved the function of the retinal photoreceptors in mice with LCA-like early-onset retinal degeneration. Targeting one or more interacting proteins might provide a therapeutic approach for treating human retinal diseases. (*J Clin Invest* **122:**1233–1245, 2012)

Swaroop ended his presentation to the scientific directors with a line from Helen Keller: "The only thing worse than being blind is having sight but no vision." He continues to work furiously towards his own vision—a world in which retinal diseases do not result in blindness. ●

More than one million teens and children in the United States are affected by an ASD. According to the March 30, 2012, issue of CDC's *Morbidity and Mortality Weekly Report*, an estimated one in 88 American children has been identified with an ASD, and it is almost five times as common among boys (1 in 54) as among girls (1 in 252). This estimate marks a 78 percent increase since 2007, when the CDC reported that about one in 150 children had an ASD. Some of the increase is due to the way children are identified, diagnosed, and served in their local communities, although exactly how much is due to these factors is unknown.

No one knows the exact cause of ASD, but scientists do think that both genes and environment play important roles. Although hundreds of genes are associated with ASDs, less than five percent of the autisms are single-gene disorders. Most ASDs are the result of rare genetic variants, and many are associated with genes for proteins that are involved in the formation or strengthening of synapses.

NIH has conducted and supported ASD research for more than 20 years. Although the National Institute of Mental Health (NIMH) is the lead institute for autism research—and the largest single source of funding for autism research in the United States—other institutes are doing autism research as well. Here we highlight a few of the NIH intramural scientists who are helping to assemble the autism puzzle.

ASD Clinical Research Team

One of NIH's distinguished autism researchers is senior investigator **Susan Swedo** (NIMH) who also studies childhood obsessive-compulsive disorder (OCD). In 1998, she led a NIMH team that discovered how a strep infection could trigger the abrupt onset of an OCD known as PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal infections). In 2006, she helped develop the NDAR and established NIMH's Pediatrics and Developmental Neuroscience Branch, one of only three U.S. multidisciplinary clinical-research teams dedicated to studies of ASDs. The team includes pediatricians, clinical psychologists, psychiatrists, neurologists, and speech pathologists. "One of the huge strengths of a fully integrated program such as this is our diverse training and experiences, which allow us to focus on different aspects of autism," said Swedo. "Each of us sees something the others don't."

LINDSAY WOOD, NIMH

LEFT NIMH has one of only three U.S. multidisciplinary clinical-research teams dedicated to the study of autism spectrum disorders. Here, Lisa Joseph is conducting a behavioral test with a child who is part of a clinical trial.

ASD is thought to consist of several similar overlapping disorders. The problem, said Swedo, is that "ASD is studied as a single disorder by most groups."

"Our goals are to get to meaningful subtypes of autism that link phenotype to genotype and etiology [and] lead toward new treatments that are efficacious and effective," said team member **Audrey Thurm**, a clinical psychologist who supervises the screening protocol for the branch.

Swedo's team is conducting a longitudinal study of at-risk toddlers (ones who already show signs of an ASD) to identify early predictors of the disorders. The researchers plan to identify connections between biological and behavioral markers and communication abnormalities.

Swedo and the team's pediatric neurologist, **Ashura Buckley**, are investigating how abnormal sleep patterns may contribute to ASD. They found that some children with autism have deficits in rapid-eye-movement (REM) sleep, which is the dreaming cycle, as well as differences in non-REM sleep, particularly in the deep or slow-wave cycle. "Since the absence of REM sleep has been associated with problems in memory consolidation, it is tempting to speculate that the REM deficits are associated with failure to learn the complexities of social interactions," said Swedo.

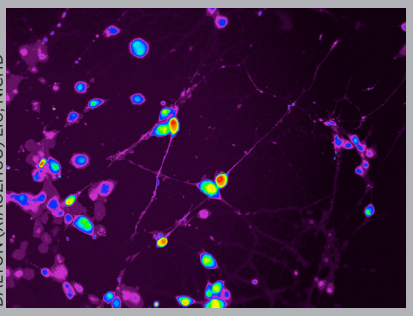
Buckley recently found that donepezil, which increases REM sleep in adults with Alzheimer disease, had the same effect in children with ASD who also have a REM deficit. The next step will be a full-scale clinical trial that Swedo will likely do in association with extramural collaborators. In addition, Thurm, Swedo, and Buckley will be looking at sleep and magnetic-resonance imaging (MRI) markers in toddlers who are at risk for autism.

Clinical Genomics

Among Swedo's collaborators is senior investigator **Owen Rennert** in the National Institute of Child Health and Human Development (NICHD).

"Swedo's group does the clinical phenotyping, and those diagnosed with ASD then come to us," he said.

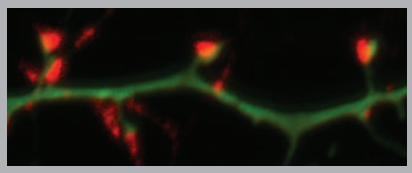
Rennert is investigating the molecular and cellular changes that occur in the autistic brain during development. To study ASD neuronal cells in culture, he reprograms skin cells from Swedo's ASD patients to form stem-like cells, which he coaxes to develop into neuronal cells. He then works with a cell-separation group at the National Institute of Neurological Disorders and Stroke to isolate the neurons from other neural cells and with outside researchers to analyze neuronal activity. Rennert predicts that they'll find abnormal signaling in the ASD neurons.



DALTON (XIAOZHUO) LIU, NICHD

LEFT Owen Rennert (NICHD) is investigating the molecular and cellular changes that occur in the developing autistic brain. He created these neuronal cells in culture by reprogramming skin cells from ASD patients.

RIGHT Serena Dudek (NIEHS) wants to know how environmental factors play a role in brain development and the normal synapse pruning process, which goes awry in ASD. Pictured: synapses on cortical neurons in culture.



MAILE HENSON, NIEHS

If the prediction holds, then Rennert plans to identify the genetic pathways affected in ASD. "There are over 300 genes identified as being involved so far," he said. "Therefore, it is likely that mutations in a host of rare alleles give rise to ASD and that they all contribute a very small percentage to the overall prevalence."

Scanning the Brain

While Rennert approaches altered neuronal connectivity in autistic patients at a cellular level, senior investigator **Alex Martin** (NIMH) uses MRI to look at connectivity in the brain as a whole. In collaboration with the Children's National Medical Center (Washington, D.C.), Martin and NIMH staff scientist **Stephen Gotts** use MRI scans to simultaneously view different regions in the brain and determine how different areas of the brain "talk" to one another. Martin is interested in a broad set of interconnected regions that make up the so-called social brain. "In the normal brain, this suite of areas is strongly interconnected and is composed of three minicircuits," he said. "What we don't know is what has gone wrong in the circuitry in ASD. Some circuits could be misfiring; others could be talking to each other too strongly or too weakly."

By comparing MRI data from high-functioning adolescent males with ASD to matched adolescent males developing normally, Martin showed that communication *between* these circuits, rather than *within* an individual circuit, is impaired. "In patients with autism, the degree of connectivity varies with the degree of social activity impairment," Martin said. He plans to do intervention studies in an attempt to "increase social communication abilities … to see if we can influence, using the intervention, the pattern of abnormal correlation," he said. "Basically, we are looking at biological markers of the intervention."

Martin is also using imaging techniques to view differences in the overall brain structure in autistic patients. Scientists have found that the prefrontal cortex of young children with ASDs is larger than that of children without an ASD. **Gregory Wallace** (NIMH), a research fellow in Martin's lab, collaborated with senior investigator **Jay Giedd** (NIMH) to confirm a hypothesis that, in ASD, early overgrowth of neurons in the cerebral cortex may be followed by prematurely arrested growth. They used MRI scans to compare cortical thickness in high-functioning male adolescents with ASD to that of typically developing males. The MRI data indicated that for the ASD group, significantly thinner cortex surrounded the left temporal and parietal cortical regions. A follow-up study in the same patients found age-related thinning of the cortex in the ASD group but not in the typically developing group.

Environmental Toxins?

Another researcher exploring the relationship between abnormal cortical architecture and ASD is senior investigator **Serena Dudek** at the National Institute of Environmental Health Sciences (NIEHS). She wants to know how environmental factors play a role in brain development and how synaptic plasticity (the process by which the brain adapts to changes in its internal and external environment) during postnatal development is different from plasticity in the adult. She focuses on the nerve-signaling phenomena underlying synaptic plasticity—long-term potentiation (LTP), which strengthens synapses, and long-term depression (LTD), which weakens synapses and results in synaptic pruning. "Any gene mutation or environmental toxin that influences synaptic transmission would [modulate] the likelihood of getting LTP or LTD during development," she explained. When such alterations occur during critical periods in development, there could be consequences for cognition with implications for ASD.

Dudek believes that the cortical overgrowth observed in ASD patients may be due to alterations in normal synapse pruning. As the brain develops through childhood it grows rapidly and the number of synapses per cerebral cortex neuron rises from about 2,500 in infancy to about 15,000—twice the number in the adult brain—by age three. As the brain matures, the synapses are pruned to get rid of the weaker connections and keep the strong ones. When the pruning process goes awry, then brain circuitry fails to develop properly.

Dudek proposes that in ASDs, there is a reduction in cortical pruning during early childhood, resulting in the early surge in brain volume. "We are trying to establish what exactly are the molecular processes behind synapse activity-dependent pruning." She believes that the pruning is regulated by the activity of different genes and could also be influenced by environmental toxins. But so far, no specific toxins have been identified as contributing to ASD.

CONTINUED ON PAGE 12

Autism

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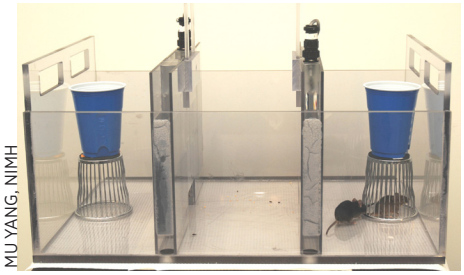
Dudek and senior investigator **Scott Young** (NIMH), with whom she is collaborating, may have uncovered another piece of the autism puzzle. They are trying to identify molecular mechanisms that regulate synaptic plasticity in the relatively unexplored CA2 region of the hippocampus, an area of the brain that plays a role in memory formation and spatial navigation.

Young has shown that the number of vasopressin 1b receptors, which are important for aggressive behaviors, is very high in the CA2 region. His group created knockout mice without those receptors; the mice showed impaired social-recognition memory and less aggression. Dudek found that both vasopressin and oxytocin can enhance synaptic responses in the CA2. "We think [CA2] is going to turn out to be a missing piece of the autism puzzle," she said. "There are a number of ASD-linked genes—and many neuromodulators and growth factors and their receptors—that are enriched in CA2."

Hundreds of Genes

Senior investigator **Jacqueline Crawley** (NIMH) began using mouse models in the 1990s to examine some of the hundreds of genes that are implicated in ASDs. Her lab developed now widely used methods to measure ASD-associated behaviors in a strain of mice that normally display autism-like behaviors such as low sociability, low number of vocalizations in social settings, and large amount of time spent in repetitive self-grooming.



MU YANG, NIMH

NIMH researchers recently found that in an autistic breed of mouse, an experimental compound increased social interactions and lessened repetitive grooming behaviors. After receiving the compound, an autistic mouse is trying to socialize with another (in the cage).

Recently, she and **Jill Silverman** (NIMH) published new data showing that an experimental compound, GRN-529, boosts social interactions and lessened repetitive self-grooming behavior in the mice. Crawley's team followed up on clues from earlier findings hinting that inhibitors of the receptor, mGluR5, might reduce ASD symptoms. [*Sci Transl Med* DOI: 10.1126/scitranslmed.3004017 (2012)]

GRN-529 is part of a class of agents that inhibit activity of a subtype of receptor protein on brain cells for the chemical messenger glutamate, which are being tested in patients with an autism-related syndrome. Although mouse brain findings often don't translate to humans, the fact that these agents are already in clinical trials for an overlapping condition strengthens the case for relevance, according to the researchers.

"Our findings suggest a strategy for developing a single treatment that could target multiple diagnostic symptoms," Crawley said.

Still, there is no overall cure for ASDs.

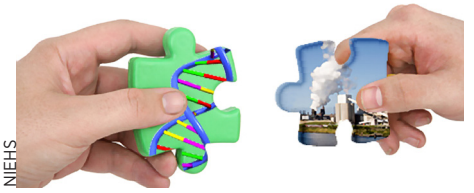
"Right now the interventions are behavioral," said Crawley. "They might get the child over the worst of the problems that may prevent . . . having meaningful social interactions, holding down a job, or living independently, but they don't cure the disorder." She hopes, however, that intervention at an early enough age could limit the impact of the symptoms and present "a real shot at a cure for autism."

And scientists might have another shot at developing a cure if they can learn more about the genetic mutations that affect synaptic proteins.

"Synapses are forming and weakening all of the time; it's a constant process," said Crawley. "There is tremendous interest right now in what each of those single gene mutations do, if they have common downstream mechanisms, and what drugs might act on them."

One researcher who knows a lot about the role of synaptic proteins in ASD is staff scientist **Andy Mitz** (NIMH), who, like Dan Hall, has a child with an autism-like disorder. Mitz is interested in the gene *SHANK3*, which encodes synaptic proteins. Errors in *SHANK3* result in the rare disorder his son has—Phelan-McDermid syndrome, characterized by severe physical and intellectual developmental delays, especially in speaking and communicating—and are associated with ASD.

"Fifty percent of those with Pheland-McDermid syndrome are on the autism spectrum," said Mitz, who founded the SHANK3 journal club. "It is connected to autism at every single level."



NIEHS

Incremental advances in brain research continue to fill in different parts of the autism puzzle, which is thought to include both genetic and environmental factors.

Insights

Gradual, incremental advances in brain research continue to provide insights into autism and other neurodevelopmental disorders. At NIH, autism research spans multiple institutes and disciplines, with each different approach filling in different parts of a complex neurological puzzle. As one NIH autism researcher put it, "the future of ASD will be one of personalized medicine—having a detailed multidimensional fingerprint of genetics and anatomy [that] overlaps with which interventions will be most effective." ●

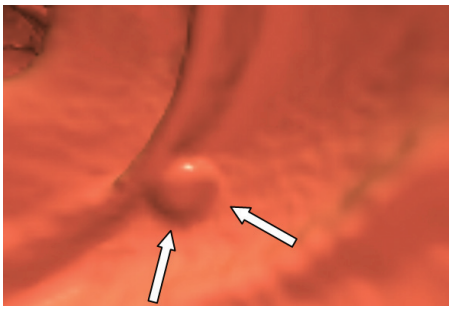
Virtual Colonoscopy

CONTINUED FROM PAGE 1

"This was one of the most fascinating submissions and papers that we've [ever] had," *Radiology* editor Herbert Kressel said in a podcast interview with Summers.

Colon cancer, the second leading cause of cancer death in the United States, can be prevented by removing colorectal polyps before they become malignant. Polyps can be detected by either a conventional colonoscopy, in which a colonoscope—a long, flexible, lighted tube with a tiny video camera attached—is inserted into the rectum and guided into the large intestine; or a virtual colonoscopy [computed tomography (CT) colonography], in which a CT scanner creates two- and three-dimensional images of the colon. Both methods require the patient to drink a bowel-clearing preparation the day before to be sure the colon is empty.

After obtaining approval from the Office of Human Subjects Research, Summers developed a project using crowdsourcing to assess how well KWs could correctly identify polyps on CT colonographies. He hired an Internet-based crowdsourcing service, which recruited 228 KWs. The KWs were given just one to two minutes of training to recognize features of polyp candidates in CT colonographic images. The CT data—from 24 randomly selected anonymized patients who had at least one polyp of six millimeters or larger—were analyzed by CAD software, and true polyps were confirmed by conventional colonoscopies.



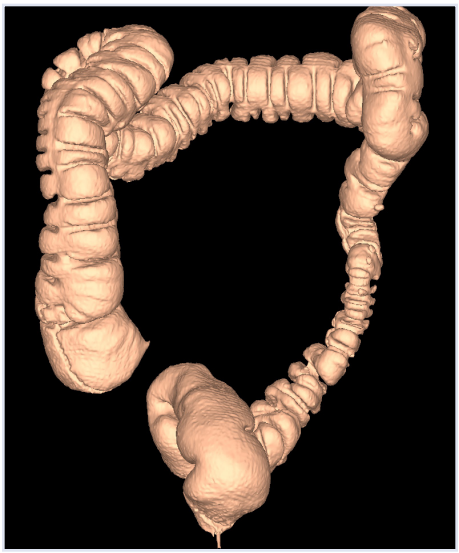
ZHUOSHI WEI, CC

The arrows point to a polyp detected in a CT colonography.

Summers was surprised that when the results were combined, the minimally trained KWs did about as well as a highly trained CAD system—about 85 percent. (The KWs were only shown 11 candidates for training, the CAD, more than 2,000.) He even did two trials, four weeks apart, and got the same results.

Summers will use the insights about how people perceive images to improve CAD systems and develop training programs to help medical personnel more accurately interpret CT colonographic images. He is already doing follow-up crowdsourcing studies to test how well people identify polyps when they can scroll through images as well as see polyp candidates from all angles.

Crowdsourcing studies have "the potential to change how these perception experiments in medical imaging are conducted," said Summers. "I think the outcomes will be better CAD systems." ●



ZHUOSHI WEI, CC

Reconstructed CT images create a 3D model of the colon.

To listen to the podcast of Summers's interview with Radiology editor Herbert Kressel, visit http://radiology.rsna.org/content/suppl/2012/02/23/radiol.11110938.DC2.

NIH ABBREVIATIONS

CBER: Center for Biologics Evaluation and Research, FDA
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CDC: Centers for Disease Control and Prevention
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
DOE: Department of Energy
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
FDA: Food and Drug Administration
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCCAM: National Center for Complementary and Alternative Medicine
NCBI: National Center for Biotechnology Information
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services

Collins: How Can We Do Better?

Collins Entertains and Educates the TEDMed Crowd

BY CAROLYN GRAYBEAL, NIAAA

GETTY AND TEDMED

At the TEDMed conference in April, NIH Director Francis Collins (right) took the stage with 15-year-old Sam Berns who has progeria and is a clinical trials volunteer.

"Get ready for this," said NIH Director Francis Collins, and with guitar in hand he hit off the first full day of TEDMed 2012, accompanied by singer-songwriter Jill Sobule, with a twangy number entitled "Disease Don't Care." A partner series of the popular TED (Technology, Entertainment and Design) conferences, TEDMed was established to focus on health and medicine. This April, the annual TEDMed conference was held in Washington, D.C., at the John F. Kennedy Center for the Performing Arts and was livestreamed to the NIH community in Wilson Hall (Building 1).

After his song, Collins took a more serious direction, addressing the need to shorten the timeline between the acquisition of fundamental knowledge about disease and its application. He presented some sobering statistics. Of the approximate 4,000 diseases for which the molecular mechanisms are understood, only about 250 have available treatments. The development of such therapeutics may take decades of basic research, drug development, and clinical trials, with a bill that can run upward of one billion dollars before the therapeutics are ready to treat patients. "We have to look at this pipeline and ask, how can we do better?" said Collins.

Indeed, the development of therapeutics need not always take so long. Such may be the case for Hutchinson-Gilford progeria syndrome, a rare genetic condition resulting in premature aging at approximately seven times the normal rate. In 2003, Collins and colleagues identified a molecular basis for progeria: the production of a toxic protein called progerin as the result of a gene mutation. Equipped with this knowledge, they screened FDA-approved drugs that seemed likely to have the best success in tackling progeria. Surprisingly, a rather unsuccessful cancer drug was observed to reverse the effects of progeria in cultured cells, and just four years after the mutated gene was identified, clinical trials were under way.

What made this story possible, and how can we have more successes like it? Collins highlighted the need for increased "partnerships between academia, government, and the private sector and patient organizations." Pharmaceutical agencies have drugs that, having failed to meet their intended purpose, languish unused. As biomedical research broadens our understanding of the molecular pathways involved in various diseases, such drugs could be cross-tested for their efficacy against other diseases.

Building cooperation among these sectors may facilitate the development of effective therapeutics, a process in which the NIH is already making inroads. Such efforts will need to be bolstered by continued public support, advancing biotechnical resources, and the recruitment of cross-disciplinary talent.

Collins sat down on stage with 15-year-old Sam Berns, who shared his experiences as a progeria patient and a clinical trials volunteer. "Progeria limits me in some ways, [and] being part of the clinical trials is rigorous, sometimes painful," Berns said. "But I remind myself that I am helping researchers develop treatments for myself and other kids and that really drives me along." That drug development for progeria has come so far in so short a time, Berns continued, "shows that if that drive exists, anybody can cure any disease, and hopefully we can eliminate those 4,000 diseases that Francis was talking about."

Collins was one of more than 50 speakers and presenters at TEDMed 2012 including CDC Director Thomas Frieden, Institute of Medicine Executive Officer Judith Salerno, and executive producer of the HBO documentary *The Weight of the Nation*, John Hoffman. You can also see Collins in *The Weight of the Nation*, which airs on May 14 and 15. ●

The HBO series on the obesity epidemic, *The Weight of the Nation*, which will air on May 14 and 15, will help launch one of the most far-reaching public health campaigns on the epidemic to date. To create the series, HBO partnered with NIH and other organizations, including the Centers for Disease Control and Prevention, and the Institute of Medicine.

Exercise Interest Group

BY MARK ROLTSCH, NHLBI

The **Exercise Interest Group** (EIG) provides a forum in which researchers, clinicians, and other interested persons from NIH and the extramural community can explore and promote epidemiological, clinical, and basic research on the effects of exercise in prevention and treatment of disease and disability. The EIG's goals include stimulating inter-institute collaborations to develop innovative research programs and initiatives investigating the effects of habitual exercise; stimulating interest in the outside scientific community to submit research applications to NIH to investigate the effects of exercise in prevention and treatment of disease and disability; maintaining an up-to-date list of experts in exercise science to serve as potential NIH study-section members and ad hoc grant reviewers; providing a forum for outside organizations with expertise in exercise science to provide input and feedback to NIH about important issues in this area; and providing a forum for developing educational programs and lectures in exercise science in the metropolitan Washington, D.C., area. The next meeting will be Wednesday, May 16, 1:00–2:00 p.m., Room 5185, Neuroscience Center, 6001 Executive Boulevard, Bethesda, Md. For more information about the SIG or the meeting, visit http://sigs.nih.gov/exercise or contact Mark Roltsch (roltschm@nhlbi.nih.gov or 301-435-0535).

Regulatory Affairs for Clinical Development

BY CARRIE LAURENCOT, NCI

The **Regulatory Affairs for Clinical Development** (RACD) interest group aims to expedite clinical development by providing accessible information on regulatory expectations during the development of clinical products. The group provides fellowship and education to those interested in navigating the complex regulatory requirements for the development of investigational agents and devices. The RACD interest group hopes to attract members of clinical–development teams including those involved in the chemistry and manufacturing processes, nonclinical in vitro and in vivo studies (including investigational-new-drug-directed pharmacology and toxicology studies), clinical studies, statistics, data management, regulatory affairs, and protection of human subjects in research. NIH intramural and extramural scientists, as well as staff at FDA and other federal agencies are welcome. The inaugural meeting will be held on Tuesday, May 22, 2012, 11:30 a.m.–12:30 p.m., in Building 10, Room 3-3750. Dinora Dominguez will give a presentation about ResearchMatch (http://www.researchmatch.org), a registry of volunteers who wish to participate in research studies. For more information and notices of meetings and events, join the LISTSERV (https://list.nih.gov/cgi-bin/wa.exe?SUBED1=RACD-L&A=1); visit the Web site (http://sigs.nih.gov/racd/Pages/default.aspx); or contact the group moderator Carrie Laurencot (laurencc@mail.nih.gov).

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

Bike Commuting

BY HEATHER DOLAN

With traffic around the NIH Bethesda campus getting worse by the day, biking to work could be a less stressful alternative to navigating rush hour. Only trouble is, there aren't enough conveniently located, sheltered bike-parking areas, and there's limited access to places where people can change, shower, and store their gear.

NIH's Office of Research Facilities (ORF) is coming to the rescue. Last summer, ORF launched the Facilities Support for Cycling Program, which aims to improve the bicycle commuting experience by providing more accessible bike parking as well as improved shower and locker facilities.

Existing bike racks, which can accommodate about 1,000 bikes, will be conveniently relocated by the end of spring 2012. Some have already been moved to outside Buildings 31C and 33, and another is slated for the west side of Building 10. Once the relocations are complete, an online map will be prepared.

As for the changing rooms, Project Officer Dave Derenick and Surveyor Bobby Klosowski assessed 84 locker and shower facilities campus-wide and submitted maintenance requests to address plumbing, lighting, and safety issues. By April 2012, 97 percent of these requests had been completed. Twenty-four showers—12 women's and 12 men's—are also being added in Building 10's F wing on floors 2 through 13.

To learn more, visit the NIH Bicycle Commuters Club Web site at http://www.recgov.org/r&w/nihbike/index.html. For more information on the ORF's program, contact Dave Derenick (derenickda@mail.nih.gov).
Happy bike trails.

TEAM MEMBERS HELPING TO CARRY OUT THE PROGRAM INCLUDE DERENICK, KLOSOWSKI, JEFF JONES, DIANE BOLTON, GLEN STONEBRAKER, COLLEEN BARROS, DAN WHEELAND, AND MEMBERS OF THE NIH BICYCLE COMMUTERS CLUB.

Recently Tenured

WILLIAM ANDERSON, NCI-DCEG

ROBERT NELSON, NIDDK

MAHENDRA RAO, NIAMS

PHILIP TOFILON, NCI-CCR

YI-KUO YU, NLM-NCBI

WILLIAM F. ANDERSON, M.D., M.P.H., NCI-DCEG
Senior Investigator, Epidemiology and Biostatistics Program, Biostatistics Branch

Education: University of Florida, Gainesville, Fla. (B.S. in chemistry); Tulane University School of Medicine, New Orleans (M.D.); Tulane University School of Public Health and Tropical Medicine (M.P.H. in epidemiology)

Training: Residency in internal medicine and fellowship in hematology and oncology at Tulane University School of Medicine; Cancer Prevention Fellowship Program at NCI

Before coming to NIH: Community-based hematologist and medical oncologist in West Monroe and Monroe, La.; founding board member of the Northeast Louisiana Cancer Institute (Monroe); staff physician and medical director of oncology unit at Glenwood Regional Medical Center (West Monroe); staff physician and medical director of oncology unit at Saint Francis Medical Center (Monroe); medical consultant for the Northeast Louisiana Tumor Registry (Monroe); clinical associate professor of medicine at Tulane University School of Medicine

Came to NIH: In January 1999 for training at NCI in cancer prevention and population-based science; in 2000 became a medical officer in NCI's Division of Cancer Prevention; in 2005 became a principal investigator in NCI's Division of Cancer Epidemiology and Genetics

Selected professional activities: Adjunct professor of pathology at the George Washington University School of Medicine (Washington, D.C.); adjunct professor of preventive medicine and biometrics at the Uniformed Services University of the Health Sciences (Bethesda, Md.)

Outside interests: Photographing birds and other wildlife

Research interests: After nearly 20 years as a private practitioner in hematology and medical oncology in rural northeast Louisiana, I developed an interest in cancer etiology, prevention, and descriptive epidemiology. In 1999, I came to NCI for training and stayed on to develop and lead a collaborative program in cancer-surveillance research. My experiences in private practice contributed to my broad interest in cancer—breast cancer in particular. I am trying to understand the effect of tumor heterogeneity on cancer etiology, pathology, gene expression, and survival, and how racial disparity and geographic variation affect cancer rates.

I supplement a hypothesis-driven approach to population-based science with biostatistical models such as mixture models, age-period-cohort models, and algorithms for replacing missing (or unknown) data and projecting future trends. My collaborators and I have made some intriguing discoveries that appear to characterize etiological heterogeneity.

We were the first to demonstrate that estrogen receptor (ER)–positive and –negative breast cancers have striking bimodal age distributions at diagnosis (that is, each of these cancers has two peak ages of onset instead of one). We found that ER-positive tumors are bimodal with a late-onset peak near age 70 years, whereas ER-negative breast cancers are bimodal with an early-onset peak close to age 50 years. Although bimodal age-incidence patterns are acknowledged for malignancies such as Hodgkin lymphoma (a cancer of the lymphatic system), bimodality is not as well established for solid tumors such as breast cancer. Bimodality is important because it suggests cancer heterogeneity in an otherwise homogenous cancer population.

My success would not have been possible without the expertise, support, collaboration, and close interaction with colleagues in the Biostatistics Branch. The combination of advanced epidemiological and biological knowledge, biostatistical expertise, rich history of descriptive epidemiology, and tradition of stellar contributions on robust epidemiological methods places the branch in a unique position to be a world leader in future descriptive epidemiological studies and cancer surveillance research.

ROBERT NELSON, M.D., PH.D., NIDDK

Senior Investigator, Diabetes Epidemiology and Clinical Research Section, Phoenix Epidemiology and Clinical Research Branch

Education: Loma Linda University School of Medicine, Loma Linda, Calif. (B.S. in human biology, M.D.); Harvard University School of Public Health, Boston (M.P.H.); University of California, Los Angeles (Ph.D. in epidemiology)

Training: Residencies in internal medicine and in public health and general preventive medicine, Loma Linda University; epidemiology fellowship, Diabetes and Arthritis Epidemiology Section at NIDDK (Phoenix)

Before coming to NIH: Medical officer at the U.S. Naval Hospital (Okinawa, Japan); staff member at the Cleveland Clinic Foundation (Phoenix and Cleveland)

Came to NIH: From 1985 to 1988 for training; returned in 1994

Selected professional activities: Editorial boards of the *American Journal of Kidney Diseases, Primary Care Diabetes*, and *Nephrology News and Issues*

Outside interests: Hiking; biking; jogging; scuba diving

Research interests: Diabetes mellitus is the leading cause of kidney failure in the United States. My research focuses on kidney disease associated with type 2 diabetes. We study diabetic kidney disease in a Pima American Indian population near Phoenix that has a high frequency of type 2 diabetes. We are identifying risk factors for diabetic kidney disease and characterizing the functional and structural changes within the kidneys that occur with the development and progression of the disease. We are also seeking to identify new biomarkers of diabetic kidney disease that will help us detect it at an earlier stage and identify people who will respond best to various treatments.

We are conducting a clinical trial to determine whether treatment with a particular blood-pressure medicine will protect the kidneys from the damaging effects of diabetes. We are also examining gene expression in tissue obtained from kidney biopsies to identify molecular pathways responsible for kidney injury caused by diabetes.

The ultimate goal of our work is to characterize the clinical course of kidney disease in type 2 diabetes, identify the factors that increase a patient's risk of developing this disease, and find better therapeutic approaches for its management and prevention.

MAHENDRA RAO, M.D., PH.D., NIAMS

Senior Investigator, Stem Cell Section, Laboratory of Stem Cell Biology; Director of NIH Center for Regenerative Medicine

Education: Bombay University, Mumbai, India (M.D.); California Institute of Technology, Pasadena, Calif. (Ph.D. in developmental neurobiology)

Training: Residency at Bombay University; postdoctoral training in neuroscience at Case Western University (Cleveland)

Before coming to NIH the first time: Associate professor at University of Utah School of Medicine (Salt Lake City)

First worked at NIH: May 2001 to October 2005 as senior investigator and chief of the Laboratory of Neuroscience in NIA

Before returning to NIH: Vice president, Regenerative Medicine, Life Technologies (Carlsbad, Calif.)

Returned to NIH: In August 2011 as director of the NIH Center for Regenerative Medicine

Selected professional activities: Working with international stem cell societies and regulatory agencies

Outside interests: Hiking; traveling

Research interests: My laboratory aims to use stem cells to improve our understanding of the biological processes controlling cell fate determination and tissue development. To accomplish this, we use stem cells to generate neurological disease models and to develop replacement therapies for neurodegenerative diseases. We hope versatile stem cells will become a source of replacement cells for damaged tissues.

One target for treatment with cellular therapies is Parkinson disease, which causes the death of nerve cells required for agile and controlled muscle movement. Symptoms of Parkinson disease include hand tremors and impaired walking. Alongside researchers at my previous position at Life Technologies, I developed methods to induce stem cell transformation into the type of nerve cells depleted in Parkinson disease. These nerve cells produce dopamine, a chemical signal that helps deliver the brain's orders to the muscles. We derived such nerve cells from embryonic stem cells and adult induced pluripotent stem cells.

Other targets for treatment are peripheral neuropathies, particularly those caused by Schwann cell defects. We have developed methods to obtain a pure population of Schwann cells and are working with collaborators to develop a model to investigate myelination—the production of the electrically insulating material myelin, which forms a layer around the axon of a neuron. We will use this model to screen for small molecules that modulate the process of myelination and so may aid functional recovery.

If you have been tenured in the past few months, *The NIH Catalyst* will be in touch with you soon to invite you to be included on these pages.

CONTINUED ON PAGE 18

Recently Tenured

CONTINUED FROM PAGE 17

PHILIP TOFILON, PH.D., NCI-CCR

Senior Investigator, Molecular Radiation Oncology Section, Radiation Oncology Branch

Education: University of Illinois, Urbana, Ill. (B.S. in physiology); University of Nebraska Medical Center, Omaha, Neb. (Ph.D. in pharmacology)

Training: Postdoctoral training in radiobiology in the Department of Neurological Surgery, University of California, San Francisco

Before coming to NIH: Professor of experimental radiation oncology and of neurosurgery at the University of Texas M.D. Anderson Cancer Center (Houston); faculty member at the Graduate School of Biomedical Science at the University of Texas Health Science Center (Houston); senior member of the Drug Discovery Department at the Moffitt Cancer Center (Tampa, Fla.); professor of oncologic sciences at the University of South Florida College of Medicine (Tampa, Fla.)

Came to NIH: From June 2001 until May 2006 as chief of NCI's Molecular Radiation Therapeutics Branch; returned in June 2011 as an investigator in NCI's Radiation Oncology Branch

Outside interests: Running; hiking

Research interests: In my lab, we are trying to understand the molecular determinants of cellular radiosensitivity—the susceptibility of cancer cells to the lethal effects of ionizing radiation. Our ultimate goal is to develop molecularly targeted agents that will make tumor cells more sensitive to radiation therapy. One project involves radiation-induced gene expression, which is thought to be the result of modifications in transcription [the copying of DNA into messenger RNA (mRNA)]. We recently found, however, that radiation induces changes in gene expression not by modulating transcription, but through regulating the translation of existing mRNAs into proteins. We are describing the mechanisms that mediate the radiation-induced translational control of gene expression and determining whether this process provides targets for tumor-specific radiosensitization.

We are also examining how the brain microenvironment affects the action of ionizing radiation on glioblastomas (GBMs), the most aggressive type of primary malignant brain tumors. This project involves irradiating human GBMs that have been transplanted into animal hosts: We implant human GBM stem-like cells—which have been isolated from surgical specimens and grown in vitro—into the brains of experimental mice. The goal of these studies is to use this model system to develop novel strategies for improving the treatment of GBMs.

YI-KUO YU, PH.D., NLM-NCBI

Senior Investigator, Quantitative Molecular Biological Physics Group, Computational Biology Branch

Education: National Taiwan University, Taipei, Taiwan (B.S. in physics); Columbia University, New York (M.A., M. Phil., and Ph.D. in physics)

Training: Postdoctoral training in the Department of Physics at Case Western Reserve University (Cleveland)

Before coming to NIH: Associate professor of physics at Florida Atlantic University (Boca Raton, Fla.)

Came to NIH: In May 2004

Outside interests: Playing classical guitar

Research interests: As a theoretical physicist working in biology, I have always been fascinated by the complexity in diverse organisms, all of which share a universal set of building blocks: water, ions, saccharides, fatty acids, amino acids, nucleotides, and other small molecules. However, our understanding of such complex systems is limited. My group is investigating on multiple levels—from the microscopic to macroscopic—how biomolecules function, interact with one another, and organize to form complex biological systems. Using theoretical physics and math, we are creating tools scientists can use to perform quantitative biological studies.

At the microscopic level, we have developed a method to accurately compute electrostatic forces and electrostatic energy between biomolecules. This method takes into account two major difficulties with biomolecules: their complex geometries and the presence of dielectrics (materials that do not conduct electricity well).

At the macroscopic level, we are exploring several areas in order to better understand how biomolecules organize to form complex systems. For example, we are looking at protein-protein interaction networks to clarify how proteins signal to each other and initiate DNA replication. My group has developed a mathematical framework that accounts for impaired communication between molecules, which, for example, can occur when proteases degrade proteins. We also use computational approaches to separate information from noise in massive biological data sets, thereby minimizing the misinterpretation of data.

In the realm of mass spectrometry (MS)–based proteomics, we have constructed computational tools for identifying peptides. MS can be used to determine a molecule's chemical structure by measuring the mass-to-charge ratio of charged particles. Unfortunately, charged particles from outside sources can be detected and appear in the data set as well. Our computational tools, however, limit the appearance of these false data.

We will ask for your CV and a recent photo, and then we will draft an article for your review.

STRIVING FOR EXCELLENCE IN LEADERSHIP, DIVERSITY, AND INCLUSION

Wednesday, May 16, 2012
10:00–11:00 a.m.
Lipsett Auditorium (Building 10)

Kenneth M. Yamada, chief of NIDCR's Laboratory of Cell and Developmental Biology, will give a presentation as part of NIH's 40th annual Asian American Pacific Islander Heritage Month observance. For questions or to request special accommodation, call Tyrone Banks (301-451-9692).

NIH CAREER SYMPOSIUM

Friday, May 18, 2012
8:30 a.m.–5:00 p.m.
Natcher Conference Center (Building 45); Lister Hill Auditorium (Building 38A)

The Office of Intramural Training and Education invites NIH graduate students and postdoctoral trainees to learn about scientific career options. Panel sessions cover academic, government, industry, and nonprofit career paths. More than 80 speakers will provide insights into the pluses and minuses of their current jobs and how they got there. To register, visit http://www.training.nih.gov.

REGULATING SYNAPTIC PLASTICITY

Friday, May 18, 2012
12:00–1:00 p.m.
Wilson Hall (Building 1)

As part of the Director's Seminar Series, Serena Dudek (NIEHS) will present "New Insights Into Regulating Synaptic Plasticity from an Unexpected Place." For questions or to request special accommodation, call 301-496-1921.

AUTHOR THOMAS L. FRIEDMAN AT NIH

Thursday, May 24, 2012
3:00–4:00 p.m.
Masur Auditorium (Building 10)

Journalist, columnist, author, and three-time Pulitzer Prize winner Thomas L. Friedman (author of *The World is Flat*) will present the annual J. Edward Rall Cultural Lecture in a talk entitled "That Used to Be Us: How America Lost Its Way and How We Find Our Way Back." The lecture will be broadcast live and later archived at http://videocast.nih.gov. For more information or to request reasonable accommodation, contact Jacqueline Roberts (robertsjm@mail.nih.gov or 301-594-6747).

INTERAGENCY ONCOLOGY TASK FORCE (IOTF) FELLOWSHIP OPPORTUNITIES

Applications Accepted Until May 31, 2012

The IOTF, an initiative between NCI and FDA, is offering joint fellowship training opportunities for Ph.D.s, M.D.s, and M.D.-Ph.D.s or their equivalents in cancer-related scientific research and research-related regulatory review. Fellowships begin in September 2012. For more information, visit http://iotftraining.nci.nih.gov/review.html and http://iotftraining.nci.nih.gov.

STETTEN SYMPOSIUM—NIH HISTORY

WEDNESDAY, JUNE 6, 2012
12:00–5:00 p.m.
Wilson Hall (Building 1)

The four Dewitt Stetten fellows in the NIH Office of History will present progress reports on their projects: biostatistics and biometry at the NIH, the problem of Leber's Hereditary Optic Neuropathy, Joseph Kinyoun (the founder of the forerunner of NIH/NIAID), and the origins of NIAAA and NIDA in the 1970s. For more information and to download a conference program, visit http://history.nih.gov/about/conferences.html or contact Sejal Patel (patelss2@mail.nih.gov or 301-451-9431).

NIH GRADUATE AND PROFESSIONAL SCHOOL FAIR

Friday, July 20, 2012
9:00 a.m.–3:00 p.m.
Natcher Conference Center (Building 45); Lister Hall Auditorium (Building 38A)

Summer interns and postbacs are invited. More than 100 colleges and universities will send representatives of their graduate schools, medical and dental schools, schools of public health, and other biomedical programs in hopes of recruiting NIH trainees. The event includes exhibits (10:00 a.m.–1:45 p.m.) and career and professional-development workshops. For more information, visit https://www.training.nih.gov/gp_fair.

PROFESSIONAL-DEVELOPMENT WORKSHOPS

Do you want to take your scientific career to the next level? It may be time to assess where you are professionally and consider options available via the NIH Training Center. Workshops include "Managing Up: Communicating with Your Boss" (1019); "Making Effective Presentations" (4006); "Time Management and Organizational Skills" (5110); and "Problem Solving for Results" (1022). For details about these and other courses, check out the "Professional Development" workshops in the course catalog at http://trainingcenter.nih.gov/default.aspx or call 301-496-6211.

VOLUNTEER TO READ FOR THE BLIND

Learning Ally, formerly Recording for the Blind and Dyslexic, provides digitally recorded textbooks and literature titles to more than 300,000 K-12, college, and graduate students who cannot read standard print due to blindness, visual impairments, or learning disabilities. If you can spare at least an hour a week, consider volunteering to come to the Building 31 studio to read and record science textbooks. To learn more, contact Kathryn Sparks (ksparks@learningally.org or 202-244-8990) or visit http://www.LearningAlly.org.

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For a limited time, Learning Ally is offering NIH employees a discount on an at-home one-year membership. If you have a child with a learning disability or visual impairment, he or she can receive unlimited access to audio and other textbooks for only $79 (a $20 discount off the regular price). You can also order free reading software (while supplies last). To apply for membership, visit http://www.LearningAlly.org and click on "Register Now" or e-mail Custservp@LearningAlly.org or call 800-635-1403. Use promo code NIHREG20.

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National Institutes of Health
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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.

LABORATORY CONFESSIONS

Flight Over NIH

RICHARD CHILDS, NHLBI

What was that strange object flying over the NIH on April 17? Rumor has it that this was the first approach of the great, mythical goose Swanhilda, who has long been prophesized to someday descend upon Bethesda to free her mortal geese from the tyranny of plastic coyotes and similar rogue attempts to chase the avian flocks away. So be it written that Swanhilda will "transformeth the world into anserine fields of tranquility. Beware, ye who loathe of geese." Well, it was either Swanhilda or the Space Shuttle *Discovery* riding atop a NASA plane. It's hard to tell from the photo.

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

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

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

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
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COPY EDITOR
SHAUNA ROBERTS

EDITORIAL INTERN
HEATHER DOLAN

CONTRIBUTING WRITERS
SHAUNA CLARK
MONIKA DESHPANDE
CAROLYN GRAYBEAL
KRISTOFOR LANGLAIS
CARRIE LAURENCOT
ERIN LUETKEMEIER
MEGHAN MOTT
SARAH RHODES
MARK ROLTSCH
KIMBERLY TRYKA

PHOTOGRAPHERS/ILLUSTRATORS
R. CHILDS, L. DANIELIAN, C. GUNN, M. HENSEN, D. LIU, A.SVENSON, Z. WEI, L. WOOD, M. YANG

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