THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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From Movie Star to Bioethics Fellow

Via Doctors Without Borders

BY LAURA STEPHENSON CARTER

"In my first mission I was just so scared," NIH postdoctoral bioethics fellow Chiara Lepora admits in the recently released documentary film *Living in Emergency: Stories of Doctors Without Borders*. "All of these patients are mine and I have to save their lives."

Lepora, a toxicologist from Italy, is one of four doctors featured in this gritty, realistic film about the international humanitarian group Doctors Without Borders/Médecins Sans Frontières (MSF). The film tells the story of providing emergency medical care in the war-torn Democratic Republic of Congo and post-conflict Liberia, where resources are scarce, conditions are harsh and often dangerous, and everyday life can be chaotic. By the time filming began in 2005, Lepora was no longer a scared beginner but a seasoned MSF veteran and head of mission in Liberia. Her fellow "cast members" included an Australian anesthesiologist, a nine-year MSF veteran; and two MSF first timers—a surgeon from Tennessee and a recent medical school graduate from Australia—who reported to her.

Lepora's other roles as an MSF volunteer included being a field physician in Angola, Democratic Republic of Congo; a women's health coordinator in Darfur, Sudan; and an emergency coordinator in Somalia, Chad, Cameroon, South Sudan, and the Philippines. She provided medical care to countless patients, led medical

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The NIH Undiagnosed Diseases Program: A Two-year Clinical Research Odyssey

Interview with William Gahl

BY RAYMOND MACDOUGALL, NHGRI

The sets of inches-thick medical records arrive in boxes and padded envelopes and accumulate around the desk of William Gahl, director of the NIH Undiagnosed Diseases Program (UDP). The two- and three-foot stacks represent cases that need to be reviewed and sorted, mostly by Gahl, who is also the clinical director at the National Human Genome Research Institute (NHGRI).

MADISON LOTIERZO

ABOVE
UDP Director William Gahl convenes the monthly medical review meeting of the NIH Undiagnosed Diseases Program.

They are among the hundreds of such records sent by doctors and their patients who are hoping to participate in the UDP. Gahl, who is known for his affable manner and wry sense of humor among his NIH intramural colleagues and patients, is filled with concern as he reads each desperate case. The influx has been unprecedented and Gahl knows that he can't accept all these people into this new clinical research program.

NIH has been bringing sick people to its Bethesda, Md., campus for decades. Usually, people are recruited to participate in clinical studies that have a defined focus such as the study of a particular cancer. When they volunteer to test new procedures or treatments, not only may they get help for themselves but they also contribute to

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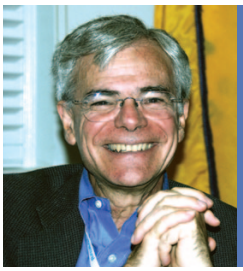

Volunteerism among Scientists: Passing the Torch

BY MICHAEL GOTTESMAN, DDIR

The following essay is as timely now as it was when it was published 10 years ago in The NIH Catalyst *(September–October 2000 issue). But in the interim our ethics regulations have made some kinds of service, especially serving as officers of professional societies, more difficult (but not impossible). Despite this, our scientists continue to serve, oftentimes at their own expense and on their own time.*

The early career training of researchers rarely touches on one important aspect of collegiality and community among scientists. Researchers in training are expected to learn how to form and nurture scientific collaborations as part of their scientific activities. However, they do not usually hear about the important role that scientists play as volunteers. In addition to the many services that scientists provide within their own institutions, such as membership on tenure and search committees, critical volunteer services to the scientific community as a whole include reviewing papers and serving on editorial boards and review panels (such as NIH study sections) and as officers and board members of scientific societies. In general, these are activities that are not directly compensated, but are absolutely essential if the scientific enterprise is to prosper.

These volunteer activities form the infrastructure that supports the culture of science. Because scientists offer these services for free (or nearly free), it helps reduce the appearance of conflict of interest in decisions about manuscripts and grants. It also allows scientific societies to function more effectively, allowing them to focus on the goals of their members. Most scientists give freely of their time for these activities, and researchers in training should be taught, by word and deed, that volunteer activities on behalf of research are desirable and laudable.

Of course, volunteering has significant benefits, even if they are less tangible than financial remuneration. Academic promotions are based to some extent on recognition by fellow scientists, and participating in the kind of review activities listed above is viewed as a sign of such recognition. Scientists who volunteer for review groups influence publications and grant distribution and thus may ultimately affect the direction of a field, extending the reach of their intellectual activities beyond what could be achieved within one laboratory, or even a group of collaborating laboratories. For early-career researchers, assignment to an editorial board or a study section is frequently a chance to meet more senior colleagues and join a community of scientists. Finally, the personal satisfaction that comes from volunteering time and energy in support of science can be substantial.

For fellows, there is at least one conspicuous avenue for volunteer participation—service on the NIH Fellows' Committee and its projects. Run by fellows for fellows, this group has substantially improved the quality of life for early-career scientists at NIH. Over the course of the year, this group has many opportunities for volunteer participation—serving on review committees for the FARE awards and other projects, hosting speakers for the Wednesday Afternoon Lectures, moderating their electronic bulletin board [and LISTSERV e-mailing list], as well as representing an institute on the committee itself.

Naturally, the amount of time one has to volunteer for such activities will depend on supervisors' approval and other pressing responsibilities. My intention here is to suggest that each of you strongly consider this use of at least some of whatever discretionary time you may find you have.

I may, of course, be preaching to the converted, for it seems to me that scientists volunteer more of their time for activities in support of their profession than any other discipline. Many professional societies thrive thanks to the many members who serve as officers or on their various committees or on the editorial boards of the society's journals. But to ensure the continued vitality of biomedical research, senior researchers need to make one more contribution: We need to encourage our colleagues who are just beginning their research careers to consider volunteering some of their time for activities such as this. The public, and science, will benefit if we do. ●

MICHAEL GOTTESMAN
DEPUTY DIRECTOR FOR INTRAMURAL RESEARCH

(ADAPTED FROM AN ARTICLE WRITTEN FOR A PROFESSIONAL SOCIETY FOR WHICH GOTTESMAN VOLUNTEER[ED])

Managing Editor's Note

BY LAURA STEPHENSON CARTER

When *The NIH Catalyst* debuted in February 1993, it was a bimonthly publication that promised to "showcase the excellent scientific research being conducted here at NIH and serve as an interactive communication mechanism where ideas are exchanged, opinions voiced, and issues examined." The goal was to "extend the spirit of the NIH Research Festival throughout the year."

For 17 years, the *Catalyst* has kept its promise and has been a lively vehicle for highlighting intramural activities at NIH. We began introducing some new elements over the past year, too, including Research Briefs (to be able to include as many institutes as possible in each issue), NIH History, Profiles, Laboratory Confessions, and a New Methods section that debuts with this issue.

But that wasn't enough. The *Catalyst* had begun to look dated, and its appearance was nowhere near as lively as the stories it contained. Typically publications are freshened, if not redesigned, every five to 10 years. We felt it was the *Catalyst's* turn to get a facelift.

So we turned to NIH's Medical Arts team for help. Working with Bonnie Hamalainen, Jessica Jackson, and Alan Hoofring, we began to explore ways to refresh and update the *Catalyst's* design. We've changed the masthead, typefaces and headlines, and even ink colors; have made the content easier to read and departments easier to find; and are using photography more effectively.

We're redesigning the Web site, too, and that should be unveiled in the coming months. There will be a real home page with a selection of individual articles (instead of just PDFs of whole issues), and links to multimedia content such as videos, audio interviews, slide shows, and other Web-only specials.

We hope you enjoy the *Catalyst's* new look. If you have any comments please let us know (e-mail catalyst@nih.gov, call 301-402-1449, or fax 301-402-4303) The *Catalyst* will continue to evolve to reflect your input, interests, and needs. Thank you for your continued support.

NIH Is Developing Social Media Guidelines

BY JOHN BURKLOW
DIRECTOR, OFFICE OF COMMUNICATIONS AND PUBLIC LIAISON

Over the past several years, the emergence of social media and new media (Web 2.0) has transformed the way we use the Internet. We recognize that many groups across NIH are looking for opportunities to use these new tools to engage others locally and globally. We also recognize that many of these new Internet-based platforms pose security risks and raise policy issues.

Some social media sites are blocked at the NIH firewall, and we have heard many at NIH express concern that the lack of access to social media sites denies NIH the opportunity to advance program goals by using these new communication media. The intent is to protect NIH staff and resources. Access to blocked sites is generally granted to personnel with demonstrable need. In cases in which we do have access to social media sites, we recognize that many employees are unfamiliar with existing policies, resources, and new efforts to provide guidance when using social media tools and services.

The NIH Office of Communications and Public Liaison, with the NIH Office of the Chief Information Officer (OCIO) and other NIH organizations, is working to create a new comprehensive policy for social media use across NIH. For now, however, you can refer to the current policies and guidance that have been developed over the past few years (see below).

You also should note that some institutes and centers (ICs) have already developed internal guidance and policies for social media. Please check with your IC communications director and chief information officer before beginning a project involving social media. If you need access to a blocked social media site, consult with your IC Information Systems Security Officer. ●

CURRENT POLICIES AND GUIDANCE

HHS General Guidance for Utilization of New and/or Social Media
http://www.hhs.gov/web/policies/webstandards/socialmedia.html
Standards and Policies
http://newmedia.hhs.gov/standards/
HHS YouTube Guidance
http://www.hhs.gov/web/policies/webstandards/youtube.html
HHS Blogging Standard
http://www.hhs.gov/web/policies/webstandards/blogging.html
HHS Center for New Media
http://newmedia.hhs.gov/
HHS OCIO Policy for Social Media Technologies
http://newmedia.hhs.gov/standards/ocio_03-31-2010_policy.html
Guidelines for Participating in Wikipedia from NIH
http://www.nih.gov/icd/od/ocpl/resources/wikipedia/index.htm
Federal Web Managers Overview of Web 2.0
http://www.usa.gov/webcontent/technology/other_tech.shtml
General NIH Guidance for Creating New Websites
http://www.nih.gov/icd/od/ocpl/resources/wag/documents/Developing_Issues.htm

FROM THE SISTER SCIENTISTS CLUB
Ladies Who Lunch: Sister Scientists at Work

BY SARAH RHODES, NIMH

"Are you a female postdoc?" asks the e-mail that you may have noticed at some point in your inbox. "Then the Sister Scientists Club may be for you!" Meeting at lunchtime almost every other Thursday, the Sister Scientists Club (SSC) is a social group for all female NIH postdoctoral, clinical, and visiting fellows.

The inspiration behind SSC is molecular biologist Ellen Daniell's book *Every Other Thursday: Stories and Strategies from Successful Women Scientists* (Yale University Press, 2006). This book charts the course of the author and six other scientists who met twice a month for 25 years to discuss their personal experiences of being women in the male-dominated world of science and how to navigate this sometimes-difficult environment.

A few years ago, female postdocs at NIMH began meeting every other week to start a similar support network, and soon they opened membership to postdocs and other trainees throughout NIH. SSC provides a supportive, nonjudgmental setting for networking and offers advice on various issues we face as women in science. We focus on personal and professional development and explore ways to deal with problems such as time management, the challenges inherent in academic and government structures, the hard road to tenure, the mentorship of students, and maintenance of a work-life balance. "Our goal is to develop a network of fellows from all NIH institutes to help make our journey in our scientific careers a little easier and a lot more fun!" says current SSC organizer Rebecca Dunfee.

Many SSC meetings are casual gatherings at which you can drop by to meet other members and bring up any issue for discussion. Most meetings are held every other Thursday at lunchtime in Building 10; approximately one in every three meetings is held after work at a Bethesda restaurant.

We've held other types of gatherings, too, including coffee hours and joint meetings with the local chapter of Graduate Women in Science. We even went to see a play about British biophysicist Rosalind Franklin (1920–1958), whose data Francis Crick and James Watson used to formulate their hypothesis on the molecular structure of DNA. (She might herself have benefited from a group such as SSC.)

We also frequently host guest speakers to talk to us about their lives and careers. In July, we hosted Donna Dean, past president of the Association for Women in Science and author of *Getting the Most out of Your Mentoring Relationships: A Handbook for Women in STEM* (science, technology, engineering, and mathematics) (Springer Science 2009). Dean, who worked at NIH for many years—she managed the NIH peer-review system, was senior scientific advisor to three NIH directors, and was the founding and acting director of the National Institute of Biomedical Imaging and Bioengineering—discussed ways to improve our mentoring experience both inside and outside NIH. She affirmed the importance of peer networks such as SSC for women scientists, particularly at the postdoctoral and early principal investigator levels, stating that "Peer mentoring relationships provide an excellent framework to explore work and life issues with colleagues who are at the same career stage as you." So stop eating your lunch at your desk and start putting your lunchtime to good use by joining SSC! For more information on the club including contact details visit http://womeninscience.nih.gov/resources/sisterclub.asp. ●

AWIS

LEFT Donna Dean, a past president of the Association for Women in Science and the founding director of the National Institute of Biomedical Imaging and Bioengineering, encouraged members of the Sister Scientists Club to improve their mentoring experience and affirmed the importance of peer networks, especially for women scientists.

NIH ABBREVIATIONS

CC: NIH Clinical Center
CIT: Center for Information Technology
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCCAM: National Center for Complementary and Alternative Medicine
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

From Movie Star to Bioethics Fellow

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field interventions for cholera and measles epidemics, implemented programs to help hundreds of severely malnourished children, defined and implemented emergency medical responses for victims of sexual violence, integrated human immunodeficiency virus (HIV) treatment into hospitals and health centers, supervised hundreds of medical and nonmedical staff, and was responsible for operations and quality improvements in a hospital, rural clinics, and a camp for displaced people. To avoid becoming burned out from the intense work, she returned to Italy between missions. But after six years with MSF she realized she needed more of a break to be able reflect on ethical questions that she could no longer ignore.

"I really accumulated so many questions while I was working," she said. "In an emergency you have little time to think about the questions. I was getting very uncertain and frustrated by having to act on things without necessarily being sure that I was doing the right thing."

So she applied, and was accepted, for a fellowship in bioethics at NIH. Her research has focused on the ethics of medicine in international conflicts and complex disasters, physician complicity with immoral regimes and practices such as torture, and the ethics of research on HIV and nutrition in resources-poor contexts. She is also on call for the Ethics Consultation Service, acts as observer on NIAID's Institutional Review Board, and participates in the meetings of the Clinical Center's Ethics Committee.

One of the questions that troubled Lepora while she was working with MSF was the dilemma of allocating limited resources. Physicians in the field often have to decide whether to provide resources to the worse off because they're more vulnerable or to those who are more likely to benefit from the help.

"There are cases where it's pretty clear that the only thing you can do is forget the worse off and focus on a group or population where you can actually have an impact," said Lepora. "It was a question that kept coming up again and again and again. There's a lot of good work that's been done on those questions from an academic point of view. But being in the field you don't necessarily have access to that or [if you do] you don't even have time to read it."

At NIH, Lepora not only has had time to read, do research, and reflect on such ethical dilemmas, but she has also taken advantage of other opportunities. Like the chance to get to know NIH, which she considers a "science empire," and to meet NIAID Director Tony Fauci, co-author of the textbook that MSF field physicians rely on: *Harrison's Principles of Internal Medicine* (McGraw-Hill). "In every field mission, even the most remote ones, we tend to have the *Harrison's* with us. Since I've been opening a lot of missions, I was the one bringing the first copy of it," Lepora said. "But you have to imagine that we travel with very limited baggage" and that included the hefty *Harrison's*. "Meeting [Fauci] was really impressive to me, because I just knew his name." She laughed. "I didn't even know he existed."

Lepora's two-year fellowship is ending and she's not sure what she'll do next. "On the one side [there's] all the opportunities that are here and on the other side the fact there is a lot that needs to be done and someone needs to do it." ●

To learn more about the film, visit http://www.livinginemergency.com.

ABOVE Chiara Lepora volunteered with MSF all over the world, including in (top) West Darfur, Sudan, in 2004, where she was working on women's health; (middle) in the Democratic Republic of Congo in 2003 during a measles epidemic; and (bottom) in Angola in 2002, during her first mission in which she was working in a nutritional emergency.

DOCTORS WITHOUT BORDERS/ MÉDECINS SANS FRONTIÈRES (MSF)

Doctors Without Borders/Médecins Sans Frontières (MSF) is an international medical humanitarian organization created by doctors and journalists in France in 1971. In 1999, MSF received the Nobel Peace Prize.

Every year, MSF provides emergency medical care to millions of people caught in crises in nearly 60 countries around the world. MSF provides assistance when catastrophic events—such as armed conflict, epidemics, malnutrition, and natural disasters—overwhelm local health systems. MSF provides independent, impartial assistance to those most in need and reserves the right to speak out to bring attention to neglected crises, to challenge inadequacies or abuse of the aid system, and to advocate for improved medical treatments and protocols.

On any given day, close to 27,000 doctors, nurses, logisticians, water-and-sanitation experts, administrators, and other qualified professionals can be found providing medical care in international teams made up of local MSF aid workers and their colleagues from around the world.

For more information on MSF, visit http://www.doctorswithoutborders.org.

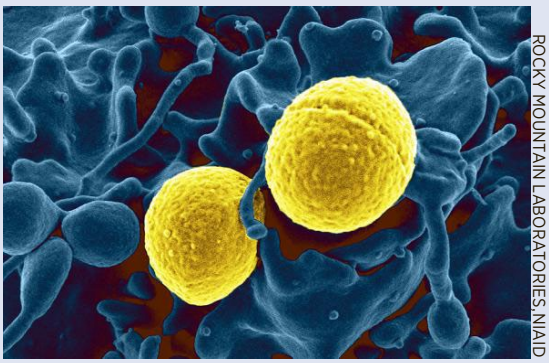
Research Briefs

NIAAA, NCI, NIMH: NEW COMPOUND IMPROVES OBESITY-RELATED HEALTH COMPLICATIONS

An experimental compound appears to improve metabolic abnormalities associated with obesity, according to a preliminary study led by NIAAA researchers. Previous studies showed that similar compounds block the activity of endocannabinoids, which are chemically similar to the active compound in marijuana and can help promote weight loss and diminish metabolic complications of obesity, such as diabetes and insulin resistance, changes in blood lipid composition, and fatty liver. However, there are unwanted behavioral side effects such as anxiety, depression, and suicidal thoughts. The NIH researchers collaborated with scientists outside NIH to develop a compound that selectively blocks the activity of endocannabinoid receptors in peripheral tissues and the group tested it in obese mice. The investigators found that the mice showed improvements in glucose regulation, fatty liver, and plasma lipid profiles without any of the behavioral side effects such as cannabinoid-induced immobility and hypothermia. The compound also reduced weight in mice with diet-induced obesity by about 12 percent, but did not affect weight in mice with a genetic predisposition for obesity. [*J Clin Invest* **120**:2953–2966, 2010]

NIAID: TREATMENT FOR *S. AUREUS* SKIN INFECTION WORKS IN MICE

Scientists from NIAID and the University of Chicago have found a promising treatment that in laboratory mice reduces the severity of skin and soft-tissue damage caused by USA300, the leading cause of community-associated *Staphylococcus aureus* infections in the United States. By neutralizing a key toxin associated with the bacteria, they found they could greatly reduce the damaging effects of the infection on skin and soft tissue. The researchers found that when the toxin alpha-hemolysin, or Hla, was either removed from *S. aureus* bacteria or neutralized through immunization, skin abscesses were significantly smaller, mice recovered faster, and there was little or no skin destruction occurred.



ROCKY MOUNTAIN LABORATORIES, NIAID

ABOVE NIAID scientists may have found a promising treatment that reduces the severity of skin and soft-tissue damage caused by community-associated *Staphylococcus aureus* infections. Shown here is the USA300 strain of *S. aureus* bacteria, colorized in gold, outside a white blood cell.

When *S. aureus* secretes Hla during infection in humans, the toxin pokes holes in a variety of different host cells, killing them. Scientists who have studied Hla for years have mainly focused on neutralizing the toxin, but until now no one had tested how its absence would affect the severity of USA300 skin infections and whether immunization against it could neutralize Hla.

The second portion of the study tested active and passive immunity; mice were either immunized with a nonlethal version of the toxin or injected with Hla-specific antibodies. Both types of immunization protected mice from skin lesions that typically destroy skin and surrounding tissue. The group noted that multiple *S. aureus* molecules must contribute to skin infection because simply removing or neutralizing Hla did not completely prevent the formation of skin abscesses, although the abscesses were smaller in size. [*J Infect Dis* **202**:1050–1058, 2010]

CC, NCI: THE WAY DOCTORS DISCLOSE A CANCER DIAGNOSIS MAKES A DIFFERENCE

CC and NCI researchers examined how cancer diagnoses were first given to patients and how satisfied patients were with the way they had received the information. A self-administered questionnaire was distributed to 460 oncology patients of the NCI being treated at the NIH Clinical Center. Of the 437 patients who completed the survey, 54 percent were told their diagnosis in person in the doctor's office, 18 percent by phone, and 28 percent in the hospital. Forty-four percent of patients reported discussions of 10 minutes or less, 53 percent reported discussions lasting longer than 10 minutes, and five percent could not remember. Treatment options were not discussed for 31 percent of those who could clearly remember. Higher mean satisfaction scores were associated with diagnoses revealed in person rather than over the phone and in a personal setting rather than an impersonal one, discussions lasting longer than 10 minutes, and inclusion of treatment options. The researchers concluded that physicians should disclose a cancer diagnosis in a personal setting and discuss the diagnosis and treatment options for a substantial period of time whenever possible. [*J Clin Oncol* **28**:3630–3635, 2010]

NIA: DENSE BONES MAY INCREASE RISK OF PROSTATE CANCER

A new study by NIA and John Hopkins University (Baltimore) researchers has found that men who developed prostate cancer had denser bones and a higher bone mineral content (BMC) than men who do not develop the disease. The men were enrolled in the Baltimore Longitudinal Study of Aging, a prospective cohort study initiated in 1958 by NIA. The BMC was serially measured in 519 participants (778 observations) from 1973 to 1984. Over the one to three decades after the last BMC measurement, the BMC was significantly higher in the 76 (14.6 percent) men who were

later diagnosed with prostate cancer. BMC appeared to decline to a greater extent with age among healthy controls. While the biology remains unclear, the findings suggest that host factors in the bony milieu might be associated with prostate cancer development and progression. [*BJU Int* **106**:28–31, 2010]

NIAAA: NEURAL CIRCUITS START AND STOP THE ACTION

An NIAAA scientist working with an investigator in Portugal identified the neural circuits in mice that signal the start and stop of an action sequence. The finding may advance the understanding of movement disorders—such as Parkinson and Huntington diseases—and open new avenues of research for their treatment and prevention. Previous studies have found changes in neural activity in the brain's dorsal striatum and substantia nigra during movement. In the current study, the researchers trained mice to press a lever exactly eight times to receive a sugar-water reward. As the mice learned the task, certain neurons in those brain regions exhibited a change in activity before the *first* lever press of a sequence, while other neurons showed a change in activity before the *last* press of a sequence.

The researchers next genetically altered mice to disrupt their NMDA receptors, which are involved in learning processes in the striatum. The modified mice could learn to press a lever to get their sugar water, but their sequence of learning was significantly impaired. The percentage of neurons generating start and stop signals were significantly lower than in control mice. The findings could have important implications for disorders in which these circuits degenerate, such as Parkinson and Huntington diseases. [*Nature* **466**:457–462, 2010] ●

Gene Tied to Kidney Disease, Sleeping Sickness in African-Americans

BY VICKI CONTIE, OD

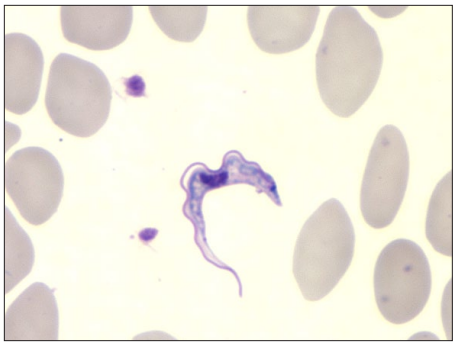
Variants of a single gene may help protect against a sometimes-deadly parasite infection, but at the same time raise the risk for kidney disease in African-Americans. The finding may eventually lead to better treatments for both conditions.

Long-term kidney disease affects about 23 million adults nationwide. The disease hits the African-American community especially hard, with rates as much as four times those in European-Americans. Two years ago, NIH-funded research teams reported that variations in or near a gene called *MYH9* were associated with an increased susceptibility to kidney disease among African-Americans. However, no specific *MYH9* variants were definitively shown to raise the risk.

In the new study, an international team of scientists that included three NIHers—Jeffrey Kopp (NIDDK), Cheryl Winkler (NCI-Frederick), and George W. Nelson (NIDDK)—and was led by Martin Pollak of Harvard Medical School (Boston) took a closer look at the genetic regions in and around *MYH9*.

As reported in the August 13, 2010, issue of *Science*, the researchers did an initial analysis of nearly 400 African-Americans. About half had a common type of kidney disease called focal segmental glomerulosclerosis, which can lead to kidney failure. The other half were healthy volunteers. A second analysis looked at a larger group of over 2,000 African-Americans. About half had end-stage kidney disease. (See *Science* **329**:841–845, 2010.)

The scientists found that two particular variants of a gene called *APOL1* were strongly linked to both types of kidney disease. The gene encodes the protein apolipoprotein L–1 (ApoL1), a major component of HDL, or "good," cholesterol. People who inherited two copies of the variants—one from each parent—had a significantly higher risk of kidney disease than people who had only one or no variant.



BLAINE MATHISON, CDC

ABOVE This Giemsa-stained light photomicrograph revealed the presence of a *Trypanosoma brucei* parasite, which was found in a blood smear. *Trypanosoma brucei* causes African sleeping sickness. Gene variants that help to protect against the parasite may also raise the risk for kidney disease in African-Americans.

Further analysis showed that the two *APOL1* variants were most common in West African populations and in African-Americans. The variants were not found in people with European, Chinese, or Japanese ancestry.

Suspecting that the two gene variants might offer an evolutionary advantage to people in Africa, the scientists focused on a little-known function of the ApoL1 protein. It's been shown to be involved in the body's defense against trypanosome parasites, including *Trypanosoma brucei*, which causes African sleeping sickness. This degenerative and sometimes fatal disease affects tens of thousands of people in Africa but isn't found elsewhere.

Laboratory tests showed that blood from patients who had variant forms of the ApoL1 protein destroyed the deadliest subtype of *T. brucei*. The researchers propose that *APOL1* variants may have helped to protect Africans against this lethal parasite, which may explain why these variants are so common in certain African populations today. ●

ADAPTED WITH PERMISSION FROM THE AUGUST 2, 2010, ISSUE OF *RESEARCH MATTERS WEEKLY* (HTTP://WWW.NIH.GOV/RESEARCHMATTERS).

the overall understanding of the natural history of disease.

But UDP is different. Since 2008, this trans-NIH initiative has embraced a broader view. Instead of focusing on a single disease, UDP tackles the hardest-to-diagnose disorders relying on a spectrum of NIH specialists—in endocrinology, immunology, oncology, dermatology, dentistry, cardiology, genetics, and other areas—to apply their expertise and come up with insights about each case. A unified diagnosis is the optimal but often elusive endpoint of their efforts.

In the roughly two years that the program has been operating, the UDP has responded to approximately 3,000 inquiries, received nearly 1,200 medical records, and accepted roughly 280 cases from all corners of the country. To be considered for the program, a patient must be referred by a physician and provide all medical records and diagnostic test results requested by NIH. Patients who meet the program's criteria are then asked to undergo an additional weeklong evaluation during a visit to the NIH Clinical Center.

"As doctors, we feel deep compassion for patients who have been without hope because they are sick and no one has been able to help them. For some, this program offers real hope and maybe even relief," said Gahl. "A principal mission of UDP, however, is the discovery of new diseases and variations of known diseases."

Gahl, NIH Clinical Center Director John Gallin, and NIH Office of Rare Diseases Research Director Stephen Groft are the principal architects of the program, which started with an initial investment of $280,000 and is now approved for $3.5 million per year.

"As doctors, we feel deep compassion for patients who have been without hope because they are sick and no one has been able to help them."


MAGGIE BARTLETT, NHGRI

FOLLOWING ARE EDITED EXCERPTS FROM A RECENT INTERVIEW WITH DR. GAHL.

Have your expectations for making diagnoses been met?

We expected to diagnose maybe 10 or 15 percent of the patients that we admitted, and we have achieved roughly that. We think we'll be able to diagnose more cases as more basic research is done on them.

Have your insights and research been able to help the patients?

For some patients, we not only make a diagnosis but also can provide treatment or refer them elsewhere. But even when there is no treatment, simply having our diagnosis can be helpful. You would be surprised at how patients appreciate having a diagnosis even though . . . it may mean certain morbidity or mortality. They find it comforting to have some certitude in their lives, some expectation, some prognosis that's associated with a diagnosis.

Could you describe one of your cases?

We diagnosed a woman whose muscles had grown so much in the previous 10 years that people wondered whether she was training as a bodybuilder or was on steroids. But most exercise was painful, and eventually her muscle mass grew so heavy that she felt exhausted all the time. The diagnosis was amyloid myopathy, a potentially fatal manifestation of amyloidosis in which amyloid fibrils build up in the skeletal muscles. Once that diagnosis was made—and it was made solely because of this program—she was able to get a stem-cell transplant at the Mayo Clinic in Rochester, Minn. Now she's recovering.

What does UDP offer that a patient may not find at another hospital?

First, UDP provides patients with coordinated access to many specialists. Second, different consultants can meet to discuss a given patient at the same time. We have what you might call a luxury of not being subject to financial considerations over physicians' time. Third, we offer state-of-the-art genetic analysis. Fourth, we plan to expand our basic research into the disorders we are seeing.

Who makes up the UDP staff?

Most are clinicians, including nurse practitioners, physicians, physician assistants, and schedulers. More than 50 senior attending physicians have carved out time for UDP cases. We have also called upon some people to do genetics testing and

LEFT
UDP Director William Gahl receives incoming mail containing medical records of NIH Undiagnosed Diseases Program applicants.

RIGHT
This three-year-old boy—who cannot talk, walk, crawl, or feed himself, and takes medication to control seizures—undergoes a neurological-development exam during his weeklong visit to the NIH Clinical Center as a participant in the Undiagnosed Diseases Program. There's no diagnosis yet, but the doctors think it's likely that he has a genetic condition affecting his nervous system. Senior staff clinician David Adams and genetic nurse practitioner Lynne Wolfe are conducting the exam.

MAGGIE BARTLETT, NHGRI

some basic research. We plan to expand the research arm of the UDP in the very near future.

Is there a unique part that genetics plays in the UDP?

There sure is. Before coming to NIH, our patients have been to centers throughout the country and have gotten the stardardized genetic tests that largely focus on a particular symptom. We consider those tests as a starting point.

At NIH, the NHGRI Genomics Core does million-SNP [single-nucleotide polymorphism] arrays on most of our patients; we can detect DNA deletions, duplications, copy-number variations, and runs of homozygosity [two identical forms of a particular gene, one inherited from each parent]. In some patients we are able to do whole-exome sequencing thanks to the NIH Intramural Sequencing Center.

Can you provide an example of how genetics has been applied?

We had a family of five adult siblings who all had the same problem affecting the large vessels in their legs and had problems walking. Their parents were fine. On a million-SNP array there was only one region in the entire human genome in which these five affected individuals were homozygous and their parents were not. This was a region that contained 92 genes, and one of them had a mutation in both alleles. We realized that this is, in fact, a new disease. We have submitted our findings for publication.

Can you describe a case in which whole-exome sequencing proved helpful?

We work with the NIH Intramural Sequencing Center to do whole-exome sequencing. All the protein-coding regions, or exons, are collectively known as the exome, which involves 1.7 percent of the entire genome or about 60 million of the 3.2 billion bases. We did whole-exome sequencing on seven families, including the parents and one or two children per family. We are looking for something in the affected family members that isn't present in the unaffected members. In one case in which the parents were first cousins, we found a region of homozygosity in the DNA of the affected individual and identified a mutation in both alleles in a gene that was known to be responsible for neurological disease. Previously it was thought that a mutation on only one allele was responsible for the disease. We had found a case of recessive inheritance. So whole-exome sequencing really bore fruit.

Can you imagine a time when either million-SNP array scans or whole-exome sequencing could become more commonplace in clinical diagnosis?

I think it won't be too long before whole-exome sequencing is part of the genetic portion of medical practice. In fact, we are trying to use the Undiagnosed Diseases Program as a testing ground to see under what conditions whole-exome sequencing, and perhaps at some point whole-genome sequencing, is beneficial. A lot of this depends upon the cost of sequencing. It is getting cheaper to perform whole-exome sequencing than to do directed molecular diagnostics for other genes. For example, checking all the genes associated with a neurological disorder such as spastic paraplegia costs more than whole-exome sequencing. But that's just the technical aspect. The other aspect is handling all the data that's generated. What software and algorithms are needed and how do you determine where there may be a pathogenic or causative abnormality? The individual cases that we see in the Undiagnosed Diseases Program provide a platform for answering these questions.

> "I think it won't be too long before whole-exome sequencing is part of the genetic portion of medical practice."

Will there be a constant flow of cases?

Roughly speaking, there is an unlimited supply. If we've seen 1,200 medical records, I'm sure there are five, 10, or 20 times as many out there that haven't come to us yet. We haven't really solicited these cases from the academic community, per se. Although many cases have been referred from academicians . . . we know that it is the American population who's responding

CONTINUED

NIH Undiagnosed Disease Program

CONTINUED FROM PAGE 9

to this program, because every time we have something on television, the press, or the radio, we get a blip in applications. Patients are going to their doctors and asking to apply. If we were to go to chairs of departments and ask whether they had any really tough cases, we could tap that, too.

MADISON LOTIERZO

ABOVE
NIH Undiagnosed Diseases Program staff members confer amid stacks of medical records submitted for review. From left, Cheryl Hipple, administrative staff member; Colleen Wahl, nurse practitioner; Michele Nehrebecky, nurse practitioner; Joan Rentsch, administrative staff member; and UDP Director William Gahl.

Have you ever dealt with so many varied cases?

I'm not sure that anybody deals with the diversity of medical cases that UDP does. We'll see anyone about anything as long as we have someone around here who knows a little bit about it. Even when we don't have the expertise, we do have the genetics. The good part is that we are helping people who wouldn't have been helped otherwise.

How will UDP create opportunities for greater interaction among clinical experts and basic researchers and resources at NIH?

There's an enormous wealth of expertise in all different areas of science here on campus. If we can simply identify who those people with particular expertise are and how it can be applied to our patients, we think we can engage them with a few simple demonstrations. That is one of our goals for the future.

Can you provide an example?

We have seen now three individuals who have vascular problems due to abnormalities in their VEGF—vascular endothelial growth factor. We have solicited the help and advice of several members of our intramural community, including Sylvio Gutkind at NIDCR and David Roberts at NCI. They have been extremely helpful.

How can interested NIH intramural researchers get involved?

We are making plans to present these cases to the intramural community and even the extramural community. We invite researchers to contact us—they can even e-mail or call me personally—and tell us about their area of interest so that we can be looking for cases that might be pertinent and that they might want to engage in. We'd be happy if somebody were to pick up this or that component of the clinical research. ●

For more information visit http://rarediseases.info.nih.gov/Resources.aspx?PageID=31#cat_70.

And you can learn more about the UDP at this year's Research Festival (October 5–8, 2010). Gahl will be one of the speakers at the Opening Plenary Session on Tuesday, October 5, 9:00–11:30 a.m., October 5, 2010, Building 10, Masur Auditorium. For more on the Research Festival, visit http://research-festival.nih.gov.

New NIDCD Device to Measure Inner-ear Membrane Could Have Broader Applications for the Study of Cell Motility

BY CHRISTOPHER WANJEK

Richard Chadwick and Núria Gavara of the National Institute on Deafness and Other Communication Disorders (NIDCD) have tinkered with off-the-shelf atomic-force microscopy (AFM) to probe cochlear tissue at the nanometer scale.

Their technique, published in the August 2010 issue of *Nature Methods*, has enabled for the first time the realistic measurement of elasticity and viscosity in the tectorial membrane of the inner ear. This new tool for microrheology, a method to characterize the material properties of living cells, can be applied to other tissues that detect or produce sound and may have broader implications for the field of cell motility. [*Nature Methods* **7**:650–651, 2010]

The tectorial membrane, with its jellylike consistency, covers the surface of the organ of Corti in the mammalian cochlea. Its role in hearing remains a bit of a mystery, largely because it has been difficult to study in detail. Planted in this membrane are projections from the outer hair cells, specialized cells that turn noise into signal, that is, convert mechanical sound waves into electrical impulses our brains interpret as sound. Sound waves induce hair-cell movement relative to the membrane, a mix of collagen and glycoand tectorin proteins.

Chadwick, chief of the Section on Auditory Mechanics in NIDCD's

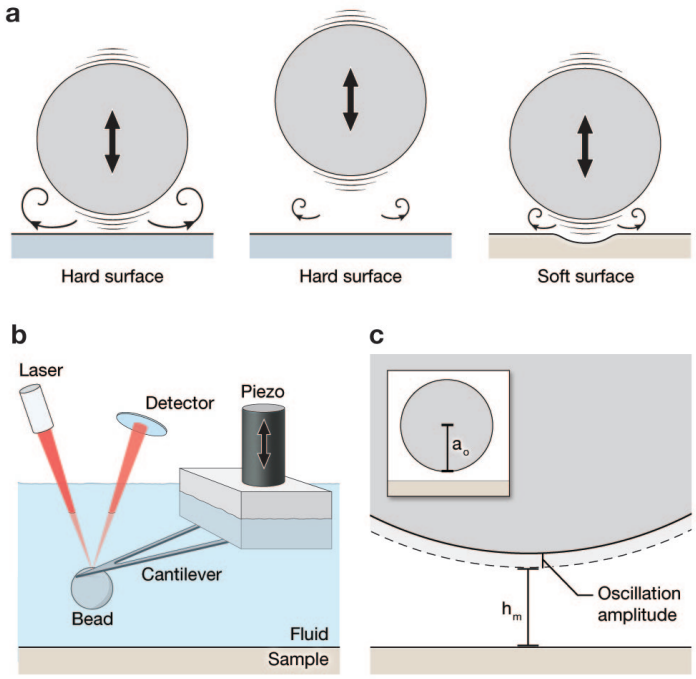
Laboratory of Cellular Biology, is among a growing body of scientists who think that the tectorial membrane is a slighted yet crucial component of the hearing process. Indeed, mutations in the alpha-tectorin protein have been linked to hearing impairment.

Chadwick's lab demonstrated in earlier work that the tectorial membrane is arranged as a gradient of collagen fibers and interstitial matrix, running from very stiff to very soft along the membrane—about a quarter-inch long in the human ear. Yet probing deeper has been difficult for lack of a proper technique for this elastic, anisotropic medium.

One technique, AFM, gets close but has a serious flaw: To measure the elasticity and viscosity of the material, the tip of AFM's cantilever needs to tap on the membrane, often damaging the tissue in the process. Also, standard AFM doesn't provide a realistic measurement of the tectorial membrane's everyday mechanical properties because the frequencies it uses to probe are outside the range of frequencies associated with normal hearing.

Chadwick carried in his head the concept of a hands-off measurement approach for years but was unsure how to best build an instrument. He met Gavara, who was experimenting with traction microscopy, at a meeting in Germany. Chadwick invited Gavara, a fellow physicist, to join his lab as a visiting fellow. Together with other lab members they set out to build a specialized device.

In the end, Gavara merely needed to tweak the lab's AFM. She replaced the standard needle at the tip of the cantilever with a spherical bead. Then she hovered the cantilever less than 100 nanometers above a sample of guinea pig tectorial membrane, oscillating the bead by 10 nanometers at a rate of 30,000 hertz, a frequency near the upper ranges of human hearing. Using the AFM's standard laser and detector, the researchers then analyzed the resulting hydrodynamic reaction force, in piconewtons, obtaining for the first time accurate measurements of elasticity and viscosity across the entire membrane.



Adapted from *Nature Methods* **7**:650–651, 2010:

FM-AFM can be used to measure mechanical properties of soft samples. (a) A hydrodynamic reaction force is strongest when a sphere is forced to oscillate close to a surface (left) and weakest when the sphere is far from the surface (middle) or when the surface is soft (right). (b) In a typical AFM setup, a cantilever with a bead attached to its end is used to probe the sample, a laser beam is focused onto the tip of the cantilever, and a photodetector measures the reflected light. Vertical oscillations of the cantilever and its height relative to the sample are controlled with a piezoelectric device. (c) The thin-gap assumption of the researchers' theory requires bead-sample gaps (h_m) much smaller than the bead size (a_0) and oscillation amplitudes much smaller than the bead-sample gap.

Their technique is sensitive enough to detect the graded viscoelastic properties of the tectorial membrane along the length of the cochlea in the 1–15 kilopascal range. (One pascal equals one newton per square meter; one kilopascal equals 1,000 pascals.)

Although the technique appears straightforward and uses off-the-shelf parts, the method was based on mathematical modeling that Chadwick had developed years earlier. "Having some expectation of what to see is crucial," Chadwick said.

This frequency-modulated AFM (FM-AFM) microrheology tool could be useful in the study of the larynx, where multiple cells and tissues are mechanically excited at acoustic frequencies. Beyond that, Chadwick speculates this could be a useful technique for any noncontact microrheology in which the introduction of a probe interferes with realistic measurements. He leaves the details up to the imagination of his NIH colleagues. ●

Recently Tenured


Mark Cookson, NIA


Miguel Holmgren, NINDS


Marisela Morales, NIDA


Katherine Roche, NINDS


Joel Schneider, NCI

MARK R. COOKSON, PH.D., NIA

Senior Investigator, Cell Biology and Gene Expression Unit, Laboratory of Neurogenetics

Education: University of Salford, Salford, England (B.Sc. in biological and biochemical sciences and Ph.D. in cell biology)

Training: Medical Research Council Neurochemical Pathology Unit (Newcastle, England); University of Newcastle (Newcastle)

Before coming to NIH: Assistant professor at the Mayo Clinic in Jacksonville, Fla.

Came to NIH: In February 2002

Outside interests: Playing guitar in a rock band—a real rock band, not the video game

Research Interests: As a cell biologist, I am trying to find the underlying pathways that lead to Parkinson disease and related disorders. I am interested in the effects of mutations in the genes associated with neurodegeneration at the cellular and molecular level.

We are investigating gene mutations that cause different forms of Parkinson disease, including mutations in *LRRK2* (which codes for the leucine-rich repeat kinase 2 protein) and *SNCA* (which codes for alpha-synuclein). The normal function of these genes may tell us something about the ways in which neurons protect themselves against damage.

We are also interested in two proteins: a mitochondrial kinase, PINK1, and an ubiquitin ligase, parkin, that together represent an alternative pathway for mitochondrial protection. Ongoing work in the laboratory suggests that the kinase activity of PINK1 is critical for preventing stress-induced mitochondrial fragmentation that would otherwise lead to cell death.

Our long-term goal is to understand the pathways involved in protecting neurons so that we may be able to harness them to prevent damage in Parkinson disease.

MIGUEL HOLMGREN, PH.D., NINDS

Senior Investigator, Molecular Neurophysiology Unit, Division of Intramural Research

Education: Universidad Autónoma Metropolitana, Unidad Xochimilco, Ciudad de México (B.A. in biology); Finch University of Health Sciences, Chicago Medical School (Ph.D. in physiology and biophysics)

Training: Postdoctoral training at Harvard Medical School (Boston); research on gating mechanisms of voltage-activated potassium channels

Came to NIH: In 2001 as an investigator in NINDS

Outside interests: Swimming, fishing, scuba diving

Research Interests: Our laboratory is exploring the structure and biophysics of ion channels and transporters in neurons. Neurons contain a variety of membrane proteins responsible for the continuous traffic of ions and molecules across the cell membrane. By combining molecular biology, chemical modification, and electrophysiological techniques, we are trying to determine how ions access their pathways; which regions of the proteins form permeation pathways that allow ions to move across the membrane; how the proteins regulate ion traffic; and how blockers, toxins, and other molecules interact with these proteins.

Recently, we began investigating how RNA editing alters the function of membrane proteins. RNA editing is a post-transcriptional modification believed to be a major mechanism in evolutionary adaptation. An enzyme converts adenosine into inosine, which is interpreted as guanosine by the cellular machinery. Although a growing number of messenger RNA substrates have been shown to be edited, very little is known about the functional consequences of these modifications. We are taking advantage of the apparent high levels of RNA editing in squid neurons to gain a better understanding of the structure and function of these important cellular machines.

MARISELA MORALES, M.S., PH.D., NIDA

Senior Investigator; Chief, Neuronal Networks Section

Education: Instituto Politécnico Nacional, Mexico City, Mexico (B.S. in biochemistry and microbiology); Universidad de Guanajuato, Guanajuato, Mexico (M.S. in cell biology; Ph.D. in cell biology)

Training: Neuroscience Division, University of Colorado, Boulder, Colo.; Salk Institute for Biological Studies, La Jolla, Calif.; Neuropharmacology Division, The Scripps Research Institute, La Jolla, Calif.

Came to NIH: In 1997 as senior research fellow in NIDA; became staff scientist in 2001

Outside interests: Hiking and camping with family

Research Interests: We are using anatomical, cell molecular, cell biological, and electrophysiological approaches to investigate the neurobiology of drug addiction. Our research focuses on 1) what is the brain circuitry through which addictive drugs have their habit-forming actions, and 2) what are the neuroadaptations that accompany the transition from recreational to compulsive drug taking.

We know that the ventral tegmental area (VTA) in the midbrain plays a role in goal-directed behavior and reward processing. We are studying the VTA's neuronal properties and synaptic connectivity to gain a better understanding of how it interacts with other brain structures to process information associated with addictive drugs. The dopaminergic neurons and GABAergic neurons in the VTA have been characterized, but we were surprised to find that glutamatergic neurons are present, too.

Evidence shows that stress affects behaviors associated with drug abuse. However, the neuronal pathways, neurons, and neurotransmitters that mediate interactions between stress and drugs of abuse are not well characterized. Our laboratory has provided evidence of synaptic connectivity between the reward and stress systems in the VTA.

KATHERINE W. ROCHE, PH.D., NINDS

Senior Investigator, Receptor Biology Section, Division of Intramural Research

Education: Duke University, Durham, N.C. (B.S. in psychology); Johns Hopkins University, Baltimore (Ph.D. in Neuroscience)

Training: Postdoctoral fellowship at NIDCD; investigated the cell biology of glutamate receptor transport and localization

Came to NIH: In 1995 as a trainee; in 2001 as an investigator

Other professional activities: Director of the NIH-Brown Graduate Partnership Program

Outside interests: Raising three children

Research Interests: In my laboratory we are studying neurotransmitter receptor expression and targeting to the synapse. Glutamate, the major excitatory neurotransmitter in the mammalian central nervous system, plays a central role in fast-excitatory signaling. It is also involved in synaptogenesis, synaptic plasticity, and the pathogenesis of certain neurologic diseases. Although glutamate acts as a neurotransmitter throughout the central nervous system, the response to glutamate is not uniform at all glutamatergic synapses and varies with the type of glutamate receptor expressed on the postsynaptic membrane. We are investigating synapse-specific expression of postsynaptic NMDA (*N*-methyl-D-aspartic acid) and metabotropic glutamate receptors.

We are using several cell-biology approaches to characterize the molecular mechanisms underlying neurotransmitter receptor transport and localization at the synapse, including 1) defining sorting motifs present in neurotransmitter receptor cytosolic domains, 2) isolating neurotransmitter receptor–associated proteins, and 3) determining the role of protein-protein interactions in trafficking and specific synapse localization. We hope to elucidate the mechanisms of neurotransmitter receptor trafficking in neurons and the role of accessory proteins at central synapses.

JOEL P. SCHNEIDER, PH.D., NCI-FREDERICK

Laboratory Chief, Chemical Biology Laboratory; Head, Peptide Design and Materials Section

Education: University of Akron, Akron, Ohio (B.S., in chemistry); Texas A&M University, College Station, Texas (Ph.D. in organic chemistry)

Training: Postdoctoral fellowship studying protein design, folding, and function at the University of Pennsylvania School of Medicine, Philadelphia.

Before coming to NIH: Professor of chemistry and biochemistry with a secondary appointment in materials science and engineering at the University of Delaware, Newark, Del.

Came to NIH: In 2010

Other professional activities: Editor-in-Chief of *Biopolymers-Peptide Science*; member of scientific council, American Peptide Society

Outside interests: Spending time with family

Research Interests: I came to NCI to head up the new multidisciplinary Chemical Biology Laboratory (CBL), which emphasizes chemical science at the interfaces of chemistry, biology, and materials science. The CBL conducts basic research central to the discovery of new small molecules, peptides, macromolecules, arrays, and materials that affect cancer and AIDS diagnostics and treatment.

We are a diverse group of synthetic organic chemists, chemical biologists, materials chemists, analytical chemists, and computational chemists who interact closely with each other and other labs to create a collaborative and stimulating research environment.

My own CBL section designs and characterizes novel biological materials for use in tissue regenerative therapy, parenteral delivery of therapeutics, delivery of cells, and antibacterial therapy. We are particularly interested in peptide and protein-based hydrogel materials formed by self-assembly mechanisms. Our basic research establishes how material composition and nanostructure influences material function, and lays the foundation for translating our discoveries to the clinic. ●

SYMPOSIUM: "A VISION FOR 2020 FOR WOMEN'S HEALTH RESEARCH"
Monday, September 27, 2010
8:30 a.m.—5:15 p.m.
(Registration opens at 8:00 a.m.)
Ruth Kirschstein Auditorium,
Natcher Conference Center (Building 45)

The NIH Office of Research on Women's Health, directed since 1991 by Vivian W. Pinn, will celebrate its 20th anniversary with a symposium that will highlight scientific advances that have increased the understanding of women's health, health differences between males and females, and implications for sex- and gender-appropriate clinical care and personalized medicine. Bernadine Healy, M.D., who as NIH director in 1991 launched the Women's Health Initiative, will give the keynote address. Award-winning actress Cicely Tyson is scheduled to make an in-person presentation during the afternoon session. She is an advocate for more research into the role of high blood pressure in stroke and heart disease, especially in minority patients. For details and to preregister, visit http://www.orwhmeetings.com/20thAnniversary or call 301-496-9472 or 301-402-1770.

FEAST ON EXCEPTIONAL SCIENCE AT PIONEER SYMPOSIUM
Thursday, September 30; Friday, October 1
Bethesda North Marriott Hotel
and Conference Center
5701 Marinelli Road, Bethesda, Md.

Join 120-plus recipients of NIH Director's Pioneer and New Innovator Awards for research presentations, poster sessions, and lots of opportunities for informal interaction during this annual gathering. Pioneer and New Innovator Awards support exceptionally creative scientists who propose highly innovative—and often unconventional—approaches to major research challenges. Presentations will be grouped thematically; for details, see the agenda at http://commonfund.nih.gov/pioneer/Symposium2010. The talks will also be videocast live and archived at http://videocast.nih.gov. The conference center is near the Metro Red Line White Flint station. On-site parking is available at hourly and daily rates. The symposium is free and open to the public, and no registration is required.

NIH RESEARCH FESTIVAL
Tuesday, October 5, through Friday,
October 8, 2010
Opening session: October 5, 9:00–11:30 a.m.
Masur Auditorium (Building 10)
Remaining sessions: Natcher Conference Center (Building 45), Building 10, and Parking Lot 10H

Don't miss the 2010 Research Festival, the annual showcase of NIH's intramural research. The festival begins on Tuesday, October 5, with opening remarks by NIH Director Francis Collins followed by a plenary session on "DNA Unwound: The Path from Characterization to Treatment of Rare and Common Genetic-based Disorders." Other activities including lectures, poster sessions, receptions, and the Technical Sales Association Research Festival Exhibit Tent Show will be held at various locations on campus. On Friday, October 8, there will be a symposium and a memorial service in honor of the late NIH neurobiologist Marshall Nirenberg. For details visit the Research Festival Web site at http://researchfestival.nih.gov. If you have additional questions or require reasonable accommodations, e-mail researchfest@mail.nih.gov.

NIH'S 2010 COMBINED FEDERAL CAMPAIGN KICKOFF
Thursday, October 7, 2010 (rain or shine)
10:00 a.m. to Noon
In the quad between Buildings 31C and 33

Great food, guest speakers, and charity expo. The Combined Federal Campaign (CFC) is the annual fundraising drive conducted by employees in the federal workplace. Come to the 2010 NIH CFC Kickoff and learn about some of the charitable organizations you can support through the CFC.

"INTRODUCTION TO THE PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH"
October 18, 2010, through March 9, 2011
Monday and Tuesday evenings,
5:00–6:30 p.m.
NIH Betheda campus
REGISTRATION DEADLINE:
October 8, 2010 (Registration is free)

The course is designed for physicians and other health professionals who plan a career in clinical research or who want a better understanding of the way clinical trials are designed and conducted. A certificate will be awarded upon successful completion of a final examination. Approximately 1,300 students registered for the 2009–2010 course, which was also broadcast to 21 domestic and international locations, viewed on the Web at four locations, and taught live in Ibadan, Nigeria. For additional information or to register, visit http://www.cc.nih.gov/training/training/ippcr/application.html or call (301) 496-9425. An e-mail confirmation will be sent to those accepted into the program.

ANNUAL WORKSHOP: INTRAMURAL AIDS TARGETED ANTIVIRAL PROGRAM
October 20–21, 2010; 8:30 a.m.–5:00 p.m.
Room 127, Building 5

Whether you have a submitted a proposal (deadline September 15, 2010) for IATAP funding or are considering submitting one in the future, you may be interested in attending a workshop at which Intramural AIDS Targeted Antiviral Program (IATAP) research projects for FY2009 and FY2010 will be presented. The projects focus on the development of targeted antiviral agents for human immunodeficiency virus (HIV), structural and functional studies of HIV proteins, or closely related areas in the molecular and cell biology of HIV. IATAP's funds are not meant to fund existing AIDS research activities normally carried out

by institutes, but are intended to encourage development of new projects by investigators who may not otherwise work in these areas. For more information about the workshop, contact William Eaton (eaton@helix.nih.gov or 301-496-6030) or Jackie Roberts (robertsjm@od.nih.gov or 301-496-1921).

NIH–HEALTH AND HUMAN SERVICES MENTORING PROGRAM

DEADLINE: October 15, 2010

NIH invites you to join the NIH–Health and Human Services (HHS) Mentoring Program. Permanent federal employees interested in serving as mentors and mentees across the NIH community are invited to join the NIH October 2010 cohort. The program's emphasis on developing leadership and management competencies at various levels will ensure a beneficial experience for both mentors and mentees. The HHS Mentoring Program does not supplant the NIH scientific mentoring and customized IC leadership mentoring programs that are available to employees in some institutes and centers. For more information, including links to online registration and upcoming information sessions, visit http://trainingcenter.nih.gov/hhs_mentoring.html.

"DEMYSTIFYING MEDICINE" COURSE CDS AVAILABLE

If you missed the 2009–2010 season of the popular "Demystifying Medicine" course—or are hankering for an encore—you can check online to download course materials and find out how to view archived videos of the sessions at http://demystifyingmedicine.od.nih.gov. Or you can order a copy of the course CD. The course, which is taught by clinicians, pathologists, and basic scientists and often features patients, helps bridge the gap between advances in biology and their application to major human diseases. To order a copy of the CD, e-mail your name and mailing information to Priyanka Basa at basap@faes.od.nih.gov.

THE SIG BEAT:

NEWS FROM AND ABOUT THE NIH SCIENTIFIC INTEREST GROUPS

New SIG: End of Life and Palliative Care

The NIH End of Life and Palliative Care (EOLPC) Special Interest Group (SIG) will provide a forum for networking and collaborative discussions among the end-of-life and palliative-care research community. NINR will host a kick-off lecture for the new SIG on Thursday, October 21, 2010, 3:30–5:00 p.m., in Room B, Natcher Conference Center (Building 45). Organized by a trans-NIH steering committee from NCI, NINR, NHLBI, NCCAM, NIA, and the CC, the EOLPC SIG will meet four times a year (October, January, April, and July) on the third Thursday of the month from 3:30 p.m. to 5:00 p.m., usually in Room J in the Natcher Conference Center. Lectures and discussions will reflect emerging scientific issues including challenging research methodologies, new technologies, interventions, treatments, resources, and training. For more information, contact Jeri Miller (jmiller@mail.nih.gov) or visit http://sigs.nih.gov/eolpc. You can also subscribe to the LISTSERV by visiting the Web site.

BIOMEDICAL COMPUTING INTEREST GROUP'S BOOK CLUB

Do Jokes Really Help You Think?

Find out on Thursday, October 28, 5:30–7:30 p.m., Building 10, Room 2C116 (Old Medical Board Room), when the Book Club will be discussing *You've Got to Be Kidding!: How Jokes Can Help You Think* (by John Capps and Donald Capps). If you are interested in being a reviewer or need more information, contact Jim DeLeo at 301-496-3948 or jdeleo@nih.gov. The book is available at the FAES Book Store (Building 10) and at the Politics and Prose Book Store in Washington D.C.

For more information on NIH Scientific Interest Groups, visit http://www.nih.sigs or check out the SIG pull-out section in the July-August 2010 issue of *The NIH Catalyst* (http://www.nih.gov/catalyst/2010/10.08.01/catalyst_v18i4.pdf). To find out how to create a new SIG, contact OIR Communications Director Christopher Wanjek (wanjekc@od.nih.gov).

FY2011 BENCH-TO-BEDSIDE AWARDS

DEADLINE for letter of intent: September 22, 2010

The Bench-to-Bedside program is soliciting proposals for the FY2011 award cycle. Up to $135,000 per year for two years is available to support clinical research intramural-extramural partnerships. All NIH intramural investigators are eligible to serve as project leaders on proposals that require partnership between a basic scientist and a clinical scientist. The proposals can involve only intramural investigators, but priority will be given to proposals with intramural and extramural partners. Extramural partners need to have an existing NIH grant, which will be supplemented for successful applicants. This year for the first time, extramural investigators are invited to initiate proposals and serve as project leaders with an intramural partner. The intramural partner will be responsible for coordination of all aspects of proposal submissions. Additional information, including submission instructions, is available on the Bench-to-Bedside Web site at http://www.cc.nih.gov/ccc/btb/awards.shtml or by e-mail to BenchtoBedside@mail.nih.gov. ●

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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.

IN FUTURE ISSUES:

- MALARIA RESEARCH
- RESEARCH FESTIVAL
- TOXICOGENOMICS

LABORATORY CONFESSIONS

Elevators Revisited

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

BY NAME WITHHELD

A recent confession that *The NIH Catalyst* featured (See "Going Down," July–August 2010 issue, page 20) left me perplexed. The author seemed to imply that elevator wait times are unproductive. This person went so far as to shut the elevator door on someone so as not to delay the journey back to the lab any further. On the contrary, waiting for the elevator is an ideal time to work. And I confess to deliberately using the elevator to my advantage—namely, as a means to ambush our fearless director, Francis Collins, to get face time with him.

Spend a few idle minutes in Building 10, and you'll know what I mean. It's a virtual Who's Who in clinical and basic research, not merely its residents but also the researchers who come and go. At the very elevators disparaged in the *Catalyst*, the notoriously slow set near Masur Auditorium, I have had detailed conversations with, for example, Dan Kastner on clinical research and Ron McKay on stem cells—all spontaneous and all very productive. Just try getting on their calendar otherwise.

That's when it dawned on me: Why not use the elevator setting to "meet" with Francis Collins? Here's a guy always willing to talk if he could only find the time. And I had a few ideas to pitch to him.

I knew he was to be at an informal meeting in Building 10 on the fifth floor. So I crashed it; it wasn't too far outside my field. When I saw Collins was about to leave, I headed out first to the elevator. The elevator came instantly but Collins wasn't there yet. I had to let it pass. Two more came, but Collins was stuck in the hallway in another conversation. When the fourth elevator came, empty, I decided to jump in and hold the door. I waited and waited and waited. I peaked out, and finally I saw Collins walking my way. Just him and me on an elevator; this would be sweet. But he never got on! He decided to take the stairs. Either he's into fitness, or he was corrupted by *The NIH Catalyst* about the impracticality of waiting for an elevator. Pity.

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