

## In the Name of Stadtman

BY SARAH FREEMAN, OIR

**TALENTED EARLY-CAREER SCIENTISTS** are finding their way to NIH thanks to a new recruiting program named for the late Earl Stadtman. During his lifetime, the legendary biochemist inspired and mentored many NIH researchers, including two who became Nobel Laureates—Michael Brown and Stanley Prusiner—and many others who were elected to the National Academy of Sciences. Stadtman died in 2008, but his ability to inspire lives on: In 2009 NIH launched a recruiting program for “Earl Stadtman Investigators.”

Typically searches for intramural scientists are conducted by individual institutes and centers. The search for tenure-track “Earl Stadtman Investigators,” however, is a trans-NIH effort that crosses all areas of biomedical research. It’s designed to attract a diverse group of highly talented early-career scientists who might not apply to a more narrowly defined position description at the NIH.

Of the more than 800 applicants in fall 2009, about 30 were invited to NIH to give seminars and be interviewed, and eight were hired into the 2009–2010 program. The 2010–2011 Earl Stadtman Investigator recruitment process is now under way.

“Each of these talented early-career scientists is taking a fresh look at an important biological or clinical problem,” said Michael Gottesman, Deputy Director for Intramural Research. “Using a combination of creativity

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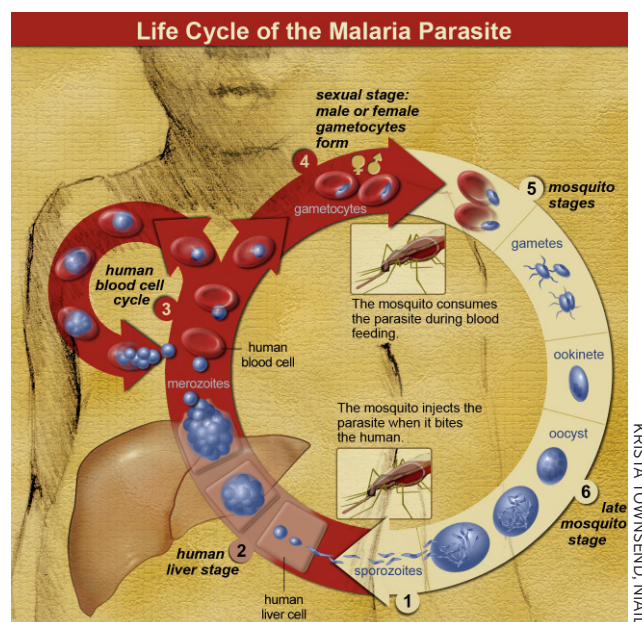
## Fighting Drug-Resistant Malaria

Rick Fairhurst and Others at NIAID Go Global

BY KRISTOFOR LANGLAIS, NICHD

**MALARIA RESEARCHER** Rick Fairhurst was only five years old when he first encountered smallpox, African river blindness, the Black Death, and other plagues—on the pages of his family’s encyclopedia, that is. The grisly photographs fascinated him—and, once he could read, so did the written descriptions of the diseases. But it was his stamp-collecting hobby that triggered his interest in malaria. When he was seven, he came across the World Health Organization’s 1962 stamps that depicted malaria-carrying mosquitoes. To date he has collected more than 100,000 stamps including about 2,000 commemorating the global effort to eradicate malaria.

Fairhurst has been studying malaria—and the parasites that cause it—at NIH since 2001. After earning M.D. and Ph.D. degrees at the University of California, Los Angeles (UCLA), he completed a residency in internal medicine and a clinical fellowship in infectious diseases at the UCLA Medical Center. Now a tenure-track investigator, he began his NIH career as a research fellow in NIAID’s Laboratory of Parasitic Diseases. In 2003, he became a staff clinician in Thomas Wellem’s Laboratory of Malaria and



An infected female *Anopheles* mosquito transmits *Plasmodium* parasites into humans. The early-stage parasites reproduce asexually in the liver; later stages invade red blood cells, triggering malaria. Some of the parasites develop into gametocytes, which mosquitoes ingest; the gametocytes develop in the insect gut and can infect humans and other hosts.

CONTINUED ON PAGE 12 ➔

### CONTENTS

**FEATURES** • [1] Fighting Drug-Resistant Malaria [1] In the Name of Stadtman [6] NIEHS Clinical Research Unit [9] Follow the Mitochondria

**DEPARTMENTS** • [2] From the DDIR: Systems Biology [3] NIH Abbreviations [3] News You Can Use: Measuring Web Site Performance [4] Training Page [5] Commentary: Women Scientist Advisors [7] The SIG Beat [8] Research Briefs [16] Colleagues: Recently Tenured [19] Announcements [20] Laboratory Confessions



## The Future of Systems Biology at the NIH

BY MICHAEL GOTTESMAN, DDIR

UNLESS YOU HAVE BEEN SEALED IN A locked room for the past few years, you have undoubtedly heard that purely reductionist approaches to biology are no longer enough to solve complex biological problems. Scientists realize that integrated, quantitative approaches are essential for assimilating large datasets and modeling complex systems. These quantitative approaches have also been called “integrative biology,” “systems biology and systems medicine,” “computational biology,” “bioinformatics” (for DNA sequence analysis), and even “physiology” by the old-timers. But for simplicity’s sake, let’s just call it “systems biology” and define it as a discipline at the intersection of biology, mathematics, engineering, and the physical sciences that integrates experimental and computational information.

Most of us have incorporated systems biology approaches into our research. Nearly all of the NIH scientific faculty have asked for colleagues with whom they can collaborate on such projects and for core facilities that can help support their own computational research. A few years ago, several of your colleagues approached me to encourage some longer-range planning in place of the usual more relaxed intramural approach. Chief among these were senior investigators who led a systems biology initiative: David Levens (NCI), Dan Camerini (NIDDK), Ronald Germain (NIAID), and Alan Michelson (NHLBI). Together with my senior advisors Paul Liu (NHGRI) and Charles Dearolf (OIR) they have formed a kind of kitchen cabinet to advise me.

The initiative issued a white paper that

recommended searching for a senior systems biologist who could help direct a center at NIH; encouraging recruitment of tenure-track investigators in this area; and finding resources (space, budget) for this purpose. Our scientific directors have also embraced these recommendations. Although there continues to be a strong commitment, we have been unable to hire anyone to develop and direct a systems biology center. We do, however, have alternative strategies.

An advertised search for a very senior systems biologist who had the skill and vision to develop a trans-NIH Center for Systems Biology at the NIH came up dry. At least two major candidates with whom we were beginning negotiations chose to remain elsewhere, despite what we thought were good opportunities at NIH. We will continue to seek leadership in this area, but may have to grow our own from internal candidates and new, more junior, recruits.

Our efforts to recruit tenure-track investigators in the area of systems biology were more successful. Over the past three years, NIAID’s Program in Systems Immunology and Infectious Disease Models (PSIIM) has recruited four tenure-track investigators—and has nearly completed the recruitment process for a fifth—who are extremely talented in diverse areas of systems biology (signaling network analysis using global RNAi methods, proteomics, computational modeling, and systems genomics and informatics). Last year, a trans-NIH search for systems biologists, combined with the Stadtman search for early-career investigators, led to the hiring of two additional outstanding early-career

scientists with systems biology expertise. And the majority of our new recruits use systems approaches in their work.

Our scientific staff has become more savvy about using bioinformatics and computational approaches to solve biological problems. In addition, several intramural centers have developed shared systems biology resources: NLM’s National Center for Biotechnology Information; CIT’s Division of Computational Bioscience; PSIIM in NIAID; the trans-NIH Center for Human Immunology, which is housed in NHLBI; and the NIH Chemical Genomics Center’s RNAi screening system. Other institutes are also developing systems biology programs.

NHLBI recently launched a Systems Biology Center and various institutes have created core facilities. We are also assembling a list of other systems biology resources so that any intramural scientist seeking help or a collaborator can know where to go.

The resource question, is, of course, not trivial. We are coming off a few years of flat budgets and facing the prospect of even more restrictions in spending in the intramural program. There is, however, general agreement that systems biology is one of the areas in which we must invest if we are to remain relevant. We have identified potential space for a new systems biology center; scientists who contribute to this effort will be given first priority to use it. But renovations and equipment may prove difficult to support. So, I urge patience while we continue to encourage hires in systems biology and support and share facilities that will enable the very best science to move forward. ●



## 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  
**NIHHD:** Eunice Kennedy Shriver National Institute of Child Health and Human Development  
**NIDA:** National Institute on Drug Abuse  
**NIDCD:** National Institute on Deafness and Other Communication Disorders  
**NIDCR:** National Institute of Dental and Craniofacial Research  
**NIDDK:** National Institute of Diabetes and Digestive and Kidney Diseases  
**NIHES:** National Institute of Environmental Health Sciences  
**NIGMS:** National Institute of General Medical Sciences  
**NIMH:** National Institute of Mental Health  
**NIMHD:** National Institute on Minority Health and Health Disparities  
**NINDS:** National Institute of Neurological Disorders and Stroke  
**NIHR:** 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

## Measuring Web Site Performance

BY ANN PORITZKY, OD

NIH HAS MORE THAN 1,700 PUBLIC-facing Web sites that are chock-full of information on health, biomedical research, clinical trials, jobs, training opportunities, research grants, and much more. But there has been no consistent way to measure the effectiveness of all these Web sites. Some institutes use Web analytics tools to determine how many times sites are visited, but may not know how well people are interacting with the sites or whether they are getting the information they seek.

So NIH awarded Evaluation Set-Aside funds to the Office of the Director's Online Information Branch (OD OLIB) to conduct a project entitled "Needs Assessment for Developing Web Analytics Best Practices for NIH." The project team will develop recommendations for improving the quality, consistency, and comparability of Web site measurement techniques among all of NIH's public-facing sites; suggest strategies for getting needed reports; and enable senior managers to make informed decisions about investing in their Web site content or functions.

Some NIH institutes and centers are already using Web measurement options to determine what's successful and identify problems that need to be addressed. Tools include WebTrends, Omniture, and Google Analytics; usability tests (testing Web sites on users); search analyses; online surveys; and free and fee-based business intelligence tools to compare sites with others inside and outside NIH.

Web analytics data can help institutes know what actions can drive visitors to Web sites. For example, WebTrends revealed that the number of visitors to NIA's SeniorHealth.gov Web site increased by almost 9,000 per month during a television public service

announcement (PSA) campaign about the site. After bookmarks promoting the site were distributed to libraries in areas where the PSAs aired, even more people visited the site.

Using Web analytics data can also expedite the process of redesigning or tweaking Web sites. NIDCR used online surveys, usability tests, card sorting (a method that finds patterns in how users would expect to find content), and search data to redesign its site and measure its effectiveness: 88 percent of usability testers rated the new NIDCR site "excellent" or "good" compared with 62 percent for the old site. And Web analytics data in 2010 alerted NIAID that two of its most popular pages provided no links to additional information about the H1N1 flu. NIAID quickly rectified the problem.

Still, there is much to be done to provide consistency across NIH for the way Web site performance is measured. The "Needs Assessment for Developing Web Analytics Best Practices for NIH" project team will be posting an online survey to collect information from institutes and centers about Web site measurement and information needs. The team will be sending survey links to several NIH groups including the Web Authors Group, Web Metrics Group, and NIH Communications Directors. Anyone else working on NIH public-facing Web sites is also invited to take the survey and can request the link from Ann Poritzky. Later, the team will present preliminary recommendations and request comments. A final report will be released later this year.

For more information or to request a recorded webinar of a presentation introducing the project, contact project team leader Ann Poritzky at [poritzkya@mail.nih.gov](mailto:poritzkya@mail.nih.gov). ●

## FROM THE OFFICE OF INTRAMURAL TRAINING AND EDUCATION

### Science Boot Camp

BY KEREN WITKIN, OITE

EACH SUMMER, MORE THAN 1,000 STUDENTS come to NIH to participate in the Summer Internship Program (SIP). Many are high school and college students who have had little or no research experience. The NIH can seem like a daunting place with its intense research environment. This summer, OITE will offer its first one-day Science Skills Boot Camp for interns who are new to research.

The program will focus not only on academic material—such as how to formulate a hypothesis and design experiments—but will also convey what it's like to work in the NIH research environment—how to behave in lab meetings, how to interact with scientists, and much more. The curriculum, a modification of the successful Community College Summer Enrichment Program (CCSEP), was shaped by suggestions from former SIP participants and mentors.

One workshop will showcase who's who in a research group, coach interns on how to interact effectively with their mentors, and encourage discussions on the nature of research. Another will address the scientific method and emphasize general frameworks for planning experiments, troubleshooting, and analyzing data. Students will also learn how to read scientific papers as well as how to present their own data in both informal and formal settings. Finally, students will be made aware of the myriad of resources available to them at the NIH.

The boot camp, which complements other OITE programs as well as the institutes' and centers' orientation sessions, is also a way for students to start developing their own social networks at NIH. Former interns have told us that students welcome opportunities to meet each other and discuss shared experiences. Networking is also key

to their development as scientists.

Many students consider their summer at NIH as a pivotal moment in their education in which they put book learning into action and begin clarifying their career goals. We hope that programs such as our summer journal clubs and the new boot camp help intramural scientists provide an outstanding summer research experience to their interns.

Boot camps will be held on the Bethesda campus on Wednesday, June 1, 2011, and Thursday, June 23, 2011. Participation is optional, but we hope that mentors will encourage inexperienced summer students to attend. Students can get a syllabus and register for either one of the camps from the OITE Web site at <http://www.training.nih.gov>. For details, contact Keren Witkin in the OITE office ([witkinkeren@od.nih.gov](mailto:witkinkeren@od.nih.gov)). ●

## FROM THE FELLOWS COMMITTEE

### WSA Scholars Award: Two Prizes for the Price of One

BY SARAH RHODES, NIMH

ALMOST EVERY POSTDOC AT NIH KNOWS about FARE (Fellows Award for Research Excellence), but many have never heard of the new annual Women Scientist Advisors (WSA) Scholars Award. It is one of many of the WSA Committee's initiatives aimed at highlighting the accomplishments and supporting the careers of women in the Intramural Program.

The two recipients of the award bestowed at the 2010 Research Festival in October were Elizabeth Grice (NHGRI) for her research entitled "Longitudinal shift in diabetic wound microbiota correlates with prolonged skin defense response" and Sita Laximi Thirunavukkarasu (NCI) for her

work on "Regulation of DNA replication by proteins involved in the splicing machinery."

Grice gave a presentation on March 4, 2011, during a Women's History Month seminar sponsored by WSA and the NIH Office of Research on Women's Health. Thirunavukkarasu had already left NIH and therefore was unable to participate.

This year's WSA Scholars will be selected from the pool of female FARE winners. So, get your FARE submissions in by the deadline (March 22, 2011) and you may be in the running for not one, but two, awards! For more information on the WSA, go to page 5 of this issue of the *Catalyst*, and for the full details of the 2011

WSA Scholars visit <http://sigs.nih.gov/wsa/Pages/NIHWSAScholarAward.aspx>. ●



Elizabeth Grice (left) is one of two recipients of a new award that highlights the accomplishments of female scientists in the Intramural Program. Also pictured: Michael Gottesman, Deputy Director for Intramural Research (center), and Rebecca Dunfee, WSA/FelCom representative (right).



## WOMEN SCIENTIST ADVISORS

### Quest for Equality

BY SARAH RHODES, NIMH

WHEN I HEARD THAT THE FELLOWS Committee was looking for a new liaison to the NIH Women Scientist Advisors (WSA) Committee I was intrigued, but a little confused. I am passionate about the promotion of women in science, yet I had no idea who or what the WSA was. Neither, it seems, did many of my fellow postdocs, staff scientists, and principal investigators (PIs). Shortly after I joined WSA as a liaison, however, I mentioned my new role to a female senior PI. Her positive reaction was quite at odds with the initially perplexed looks that I'd received from others. She told me that 18 years ago, the WSA had been responsible for identifying and fixing disparities in the salaries of tenured intramural scientists across the NIH. Women scientists—including the PI whom I was talking to—tended to have lower salaries than their male peers.

I learned that in 1991, then-NIH director, Bernadine Healy, established a task force to investigate the status of intramural women scientists at NIH. The task force's report highlighted areas of concern, including inequities in pay, resource allocation, recruitment, and retention as well as work-family balance issues such as flexibility and access to child care. In response to the task force's recommendations, the NIH-wide WSA committee was born. Its membership consisted of women scientists (generally senior ones) elected by each of NIH's institutes and centers.

Each WSA representative acts as a liaison between the women scientists in her institute and the NIH administration. Her responsibilities within each institute or center include meeting regularly with the scientific director to advise him or her about the current issues of importance to women

scientists; providing information about policies, programs, and issues of importance to the women scientists; organizing meetings for women scientists to discuss relevant issues or present programs of interest; serving or designating an alternate to serve on search committees; and attending monthly WSA committee meetings. As I already mentioned, one of the first issues addressed by that committee in the early 1990s was eliminating pay disparities at the NIH.

"The committee still makes real differences in the professional lives of women at the NIH," said Maria Morasso (NIAMS), who co-chairs WSA with Myra Derbyshire (NLM).

WSA also helps to develop strategies for increasing the number of tenured and tenure-track women scientists at NIH. Half of the postdocs at NIH are female, but women are still poorly represented at the higher levels. At a recent WSA meeting, Roland Owens, an assistant director in the Office of Intramural Research, spoke about current demographics and strategies for increasing the percentage of women on the NIH tenure track.

Other WSA activities include organizing the "Anita B. Roberts Lecture Series: Distinguished Women Scientists at NIH." To see archived videocasts of these lectures, go to <http://videocast.nih.gov/PastEvents.asp?c=151>. A new WSA initiative is the WSA Scholars Award, which honors the outstanding research of two intramural female postdocs annually (see page 4 of this issue for details). Some activities are pure fun, such as working with the NIH Health's Angels Runner Club to organize the upcoming second annual Halo Chase charity 5K run and one-mile walk around campus. The event will benefit NIH charities.

"We are very proud to be part of a committee composed of such hard-working, dedicated, and impassioned women," said Derbyshire.

For more information on the WSA, including contact details for your WSA representative, go to its Web site at <http://sigs.nih.gov/wsa/Pages/default.aspx>. ●

#### FOR FURTHER READING:

*Women in Science at the National Institutes of Health, 2007–2008*, describes a wide range of the roles, positions, and contributions of doctoral-level women across the NIH, including but not limited to clinicians, basic scientists, program directors, policy analysts, computer scientists, epidemiologists, geneticists, statisticians, and women in leadership positions. The women profiled shared not only their fascinating biographical information and research interests, but also thought-provoking descriptions of experiences that shaped their careers and insight on how they manage work-life balance, as well as their thoughts on the importance of mentoring—both being mentored and mentoring others.

This publication, which is not a directory of all doctoral-level women at the NIH, but rather a snapshot in time of just a few of the highly accomplished women at the NIH, was sponsored and prepared by the NIH Office of Research on Women's Health (ORWH) in collaboration with the NIH Coordinating Committee on Research on Women's Health (CCRWH), the NIH Institutes and Centers, and OD Offices. For more information or to download a copy, go to [http://womeninscience.nih.gov/women\\_science\\_book/index.asp](http://womeninscience.nih.gov/women_science_book/index.asp). To order hard copies of this publication, contact [womeninscience@nih.gov](mailto:womeninscience@nih.gov).

## NIEHS Clinical Research Unit Enhances Translational Research

BY ROBIN ARNETTE, NIEHS

ONCE UPON A TIME, CLINICAL research could not be performed on the NIEHS campus in Research Triangle Park, North Carolina. But that all changed with the July 2009 opening of a new 14,000 square-foot Clinical Research Unit (CRU) that will help NIEHS scientists in their efforts to determine how exposure to chemicals and other environmental agents influence a variety of diseases.

“Our ultimate goal for the CRU is to enable researchers to translate their basic laboratory findings to humans and to enhance the public health relevance of our research,” said NIEHS Director Linda Birnbaum when she approved the CRU’s opening in 2009. The unit supports simple medical tests and procedures such as the collection of easily accessible body fluids and tissues, pulmonary function studies, allergy skin testing, and ultrasound.

The CRU also fosters collaborative studies with clinical researchers at nearby Duke University (Durham, N.C.), the University of North Carolina at Chapel Hill, and the U.S. Environmental Protection Agency. During the first week of December 2010 the CRU enrolled its 500th study participant in its busiest week since its grand opening—42 new volunteers signed up to take part in clinical studies. During CRU’s first eight months, there were only two or three participants a week, said Darryl Zeldin, acting director of the Clinical Research Program. The number of volunteers has been steadily increasing because more NIEHS scientists have initiated clinical research projects.

“When the CRU was first envisioned years ago, everyone thought it was going to be a unit that primarily serviced the physicians on staff,” Zeldin said. “But, if you look at the people who are using the unit now, many of them are Ph.D.s. Their CRU work

allows them to translate what they’ve done for many years at the [research] bench.”

Thirteen tenured and seven tenure-track investigators are using the CRU. Ph.D. researchers outnumber the M.D. scientists two to one with more expected.

### CRU Scientists

Michael Resnick, head of the Chromosome Stability Group in the Laboratory of Molecular Genetics, and his colleagues are using CRU-supplied white blood cells and lung macrophages to understand factors that control Toll-like receptor (TLR) proteins. TLR proteins recognize bacteria and viruses and prevent infection. The researchers found that DNA damage affects the production of TLRs and that this cellular stress leads to inflammatory responses. They also discovered that humans exhibit a wide range of genetic variability in TLR response to environmentally induced stress. The results will appear soon in *PLoS Genetics*.

Resnick’s group started using human cell lines 10 years ago as a result of exciting findings in yeast model systems. The opening of the CRU came at the perfect time, he said. “Our research led us to consider using clinical samples, just as the CRU was taking shape.”

Ronald Mason, who leads the Free Radical Metabolism Group in the Laboratory of Toxicology and Pharmacology, works with human white blood cells provided by the CRU. He has determined that sulfur dioxide, a common urban air pollutant,

produces unstable molecules called sulfite radicals. His research suggests that sulfite radicals contribute to cell damage in persons with asthma and allergic inflammatory disorders and that exposure to sulfur dioxide exacerbates allergic reactions. He plans to publish his findings in spring 2011.

Michael Fessler, one of the M.D. researchers, is head of the Host Defense and Environmental Innate Immunity groups in the Laboratory of Respiratory Biology. In his work with the blood protein apolipoprotein A-I (apoA-I), he discovered a previously unknown signaling pathway that established a link between the immune system and the prevention of atherosclerosis. He tested human white blood cells provided by CRU healthy volunteers and determined that before apoA-I could perform its primary function of removing cholesterol from the body, it had to both activate and receive signals from the innate immune system. His findings, the first published report based on CRU data, appears in the journal *Cell Metabolism* (*Cell Metab* 11:493–502, 2010).

Even NIEHS Director Birnbaum, who also heads up the National Toxicology



STEVE MCCAW

(Left to right) Darryl Zeldin, acting director of the Clinical Research Program, CRU Medical Director Stavros Garantziotis, and physician-researcher Michael Fessler discuss patient charts, while nurses Brenda Yingling (standing) and Gina Musselwhite (seated) confer in the background.

Program, plans to take advantage of what the CRU has to offer. She and colleagues will examine the consequences of oral exposure to the endocrine disruptor bisphenol A (BPA). BPA is used to make polycarbonate plastics and epoxy resins and is found in water and baby bottles, compact discs, impact-resistant safety equipment, some thermal papers, and the lining of food cans. CDC's "2003–2004 National Health and Nutrition Examination Survey" found detectable levels of BPA in 93 percent of Americans who are six years old and older. Some laboratory animal studies report subtle developmental effects of low doses of BPA.

"We are interested in understanding how rapidly BPA is eliminated from the body and whether we can find any BPA present in the blood of subjects," said Birnbaum. The researchers are awaiting institutional review board approval for their study.

### The CRU Staff Makes It All Work

CRU-supported researchers interact with Medical Director Stavros Garantziotis; biologists Annette Rice and Jamie Marshburn, who process and distribute samples; nurse Brenda Yingling; study manager Neha Mehta; study coordinator Lisa Murphy; and receptionist Nicole Edwards. The CRU recently reached its maximum capacity of 40–45 study participants a week. So in January 2011, nurse Gina Musselwhite and study coordinator Jaime Bishop joined the team. Zeldin expects the new staff will help CRU increase its recruiting efforts and reach 50 to 100 study participants a week.

For more information, visit <http://www.niehs.nih.gov/research/clinical/join/durham/index.cfm> or read an article in NIEH's *Environmental Factor* at <http://www.niehs.nih.gov/news/newsletter/2009/june/cru.cfm>. To find out how to participate in a clinical research trial, visit <http://www.niehs.nih.gov/research/clinical/join/index.cfm> or contact the NIEHS CRU admissions desk at 919-541-9899. ●

## Flow Cytometry

BY SARAH FREEMAN

Like sands through an hourglass, so are the particles in a flow cytometer. Thousands of cells suspended in a stream of fluid flow steadily through a laser beam as the flow cytometer captures the light that emerges from them and analyzes their size, complexity, and phenotype to determine how healthy they are. Flow cytometry is routinely used to diagnose blood cancers and other diseases.

The Flow Cytometry Interest Group (FCIG) keeps its members and others apprised of the latest and greatest news in the field. On December 6, 2010, FCIG hosted the daylong "Cytometry for Clinical and Translational Medicine," which featured talks by several NIHers as well as a representative from a software company.

"Flow cytometry is objective," said Maryalice Stetler-Stevenson, one of the conference presenters and chief of the Flow Cytometry Unit in NCI's Laboratory of Pathology. "It's based on numbers and patterns." Stetler-Stevenson, who studies myelodysplastic syndromes and other diseases of the blood and bone marrow, said diagnosis can be difficult even after blood tests and bone marrow aspiration has been done. But flow cytometry has allowed her to look directly at the patterns of antigen expression in the cells. "The patterns are always exactly the same and predictable in normal cells but are usually different in abnormal cells," said Stetler-Stevenson. "Flow cytometry is very sensitive in detecting disease."

The FCIG serves as an information clearinghouse at NIH for basic and clinical investigators using flow and image cytometry. To learn more about this group, visit <http://sigs.nih.gov/fcig> or contact Bill Telford ([telfordw@mail.nih.gov](mailto:telfordw@mail.nih.gov)) or Jim Simone ([simonej@mail.nih.gov](mailto:simonej@mail.nih.gov)). ●

For a complete SIG list, go to <http://www.nih.gov/sigs> or see the July–August 2010 issue of *The NIH Catalyst*, pages 9–12, at [http://www.nih.gov/catalyst/2010/10.08.01/catalyst\\_v18i4.pdf](http://www.nih.gov/catalyst/2010/10.08.01/catalyst_v18i4.pdf).

### LOOK WHO'S VISITING NIH: ACTRESS ANNA DEAVERE SMITH

Actress and playwright Anna Deavere Smith performed excerpts from her one-woman play, *Let Me Down Easy*, in a packed Masur Auditorium last month. Smith bases her characters on real people she interviewed—including a rodeo bull rider, a physician in a New Orleans public hospital after Hurricane Katrina, and an orphanage founder who comforts children dying of AIDS—who were dealing with crises in health care. After the show NIH Director Francis Collins interviewed the actress "Actors Studio" style.



BILL BRANSON



## Research Briefs

### NIAAA: GENETIC VARIANT MAY LEAD TO SEVERE IMPULSIVITY

A multinational research team led by NIAAA scientists has found that a genetic variant of a brain receptor molecule may contribute to violently impulsive behavior when people who carry it are under the influence of alcohol. The researchers studied a sample of violent criminal offenders in Finland and sequenced DNA of the impulsive subjects and compared those sequences with DNA from an equal number of nonimpulsive Finnish control subjects. They found that a single DNA change that blocks a gene known as *HTR2B* was predictive of highly impulsive behavior. *HTR2B* encodes one type of serotonin receptor in the brain. The findings could lead to a better understanding of some aspects of impulsivity and may lead to strategies for diagnosing and treating some manifestations of impulsive behavior. The researchers caution, however, that impulsivity is a complex trait with multiple genetic and environmental causes. (NIH authors: L. Bevilacqua, David Goldman, et al; *Nature* 468: 1061-1066, 2010)

### CIT: USING GLOBAL UNIQUE IDENTIFIERS TO LINK AUTISM COLLECTIONS

Global unique identifiers (GUIDs) have the potential to link collections of research data, augment the amount and types of data available for individuals, support detection of overlap between collections, and facilitate replication of research findings. CIT and the Simons Foundation Autism Research Initiative worked together to show how disparate databases can be linked using GUIDs. The aggregation of the data will enable researchers to collaborate, efficiently share, and validate findings to speed research. The authors used their technique to run a test using one million simulated individuals and another using 8,000 real individuals to show that it works. (NIH authors: Glen Whitney, Matthew McAuliffe, Hailong Wang, Evan McCreedy; *J Am Med Inform Assoc* 17:689-695, 2010)

### NHGRI, NHLBI, CC, OFFICE OF RARE DISEASES RESEARCH: GENETIC CAUSE OF NEW VASCULAR DISEASE IDENTIFIED

Clinical researchers at NIH's Undiagnosed Diseases Program (UDP) have identified the genetic cause of a rare and debilitating vascular disorder. The adult-onset condition is associated with progressive and painful arterial calcification that affects the lower extremities yet spares the coronary arteries. The rare arterial condition, caused by calcium buildup in arteries below the waist and in the joints of the hands and feet, has been observed in nine individuals from three unrelated families, who are the only people known to have the disorder.



NIH researchers recently identified the genetic cause of a rare vascular disease that is associated with painful calcification in the arteries. Shown here: a knee X-ray reveals calcification in the main artery supplying blood to the lower leg.

The condition is called arterial calcification due to CD73 deficiency. Although symptoms include leg and joint discomfort, medical evaluations of the patients ruled out rheumatoid arthritis or other joint-related problems. Genetic analyses performed by the NIH researchers suggested a novel disorder and pinpointed the cause of the condition as mutations, or variants, in the *NTSE* gene. The NIH clinical researchers examined members of two families with the arterial calcification disorder as part of the UDP and identified a third case outside the country. Seven medical cases like those described in this study have been reported in medical journals over the past century, but these previous studies did not include any insights about the molecular basis of the disorder. (NIH authors: C. St. Hilaire, W. A. Gahl, M. Boehm, T. C. Markello, S. G. Ziegler, et al.; *N Engl J Med* 364:432-42, 2011)

### NIEHS, NCI: TWO PESTICIDES ASSOCIATED WITH PARKINSON DISEASE

New research shows a link between use of two pesticides, rotenone and paraquat, and Parkinson disease. People who used either pesticide developed the disease approximately 2.5 times as often as non-users. The study was a collaborative effort of NIEHS and the Parkinson's Institute and Clinical Center in Sunnyvale, Calif. The authors studied 110 people with Parkinson disease and 358 matched control subjects from the Farming and Movement Evaluation Study to investigate the relationship between Parkinson disease and exposure to pesticides or other agents that are toxic to nervous system tissue. Paraquat use has long been restricted to certified applicators, largely due to concerns based on studies of animal models of Parkinson disease. Rotenone is used as a pesticide to kill invasive fish species. (NIEHS authors: F. Kamel, J.A. Hoppin, M. Barber Richards, D. P. Sandler, D. M. Umbach; NCI author: A. Blair; *Environ Health Perspect* DOI:10.1289/ehp.1002839)

### NICHD: SURGERY ON FETUS REDUCES COMPLICATIONS OF SPINA BIFIDA

A surgical procedure to repair spina bifida (a condition in which the spinal column fails to close around the spinal cord), if undertaken while a baby is still in the uterus, reduces the need to divert, or shunt, fluid away from the brain, according to a study by NICHD and four other institutions. The surgical procedure to close the opening at the back of the spine is usually performed after the baby is born. The fetal procedure increases the chances that a child will be able to walk without crutches or other devices. However, infants who underwent this prenatal surgery were more likely to be born preterm than those who had the surgery after birth. Mothers who underwent the surgery during their pregnancies were at risk for uterine dehiscence, a thinning or tearing at the incision in the uterus. The study planned to enroll 200 expectant mothers carrying a child

# Follow the Mitochondria

BY MATT WENHAM, NIDDK

with the severe form of spina bifida—myelomeningocele—but it was stopped after 183 were enrolled, because of the benefits demonstrated in the children who underwent prenatal surgery. [NIH author: C.Y. Spong; *N Engl J Med* 2011 Feb 9 (Epub ahead of print)]

## NCI: GENE THERAPY TO TREAT A SOFT TISSUE TUMOR

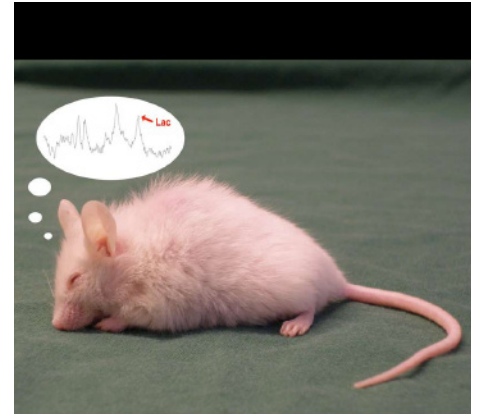
An intermediate-stage clinical trial of several dozen people provides evidence that a method that has worked for treating patients with metastatic melanoma can also work for patients with metastatic synovial cell sarcoma, one of the most common soft tissue tumors in adolescents and young adults. This study is the first to use genetically modified immune cells to cause cancer regression in patients with a solid cancer. Previous studies have shown that metastatic melanoma patients could be treated by infusion with their own genetically modified T cells. In this study, 17 patients with synovial cell sarcoma or metastatic melanoma whose tumors expressed NY-ESO-1 (a protein expressed in many cancers) received therapy with their own immune cells engineered to express a T-cell receptor capable of recognizing the NY-ESO-1 antigen. Tumors regressed in four of the six patients with synovial cell sarcoma and in five of the 11 melanoma patients. A partial response that lasted 18 months was observed in one of the synovial cell sarcoma patients, while two of the melanoma patients demonstrated complete ongoing regression responses that lasted 20 months or longer, which for patients with these diseases is significant. (NIH authors: P.F. Robbins, et al.; *J Clin Oncol* 29:917-24, 2011) ●

ANYBODY WHO HAS SPRINTED TO make a bus knows the effect of lactic acid on muscles—an aching, burning sensation that makes it hard to sprint for more than a short distance. Now, research by an NIH graduate student shows that lactate may play a very different role in the brain, providing one of the first biomarkers of aging in the central nervous system.

Jaime Ross is a Ph.D. student in the NIH–Karolinska Institute (KI) Graduate Partnerships Program (GPP) who is currently working at the KI in Stockholm. In work recently published in *Proceedings of the National Academy of Sciences* (November 16, 2010), Ross and her colleagues showed that high concentrations of lactate in the brain provided a marker of brain aging. The team used a transgenic mouse model that demonstrates signs of premature aging due to an accumulation of mutations in the DNA of mitochondria, the component of cells responsible for generating energy. The mice were studied with an imaging technique called proton magnetic resonance (MR) spectroscopy to examine the concentrations of various neurotransmitters and chemicals in the brains of anesthetized mice. (*Proc Natl Acad Sci USA* 107:20087-20092, 2010)

“We were looking for a change in levels of molecules [such as] GABA” (gamma-aminobutyric acid), a neurotransmitter, said Ross. “So it was surprising to find an increase in lactate.” Ross then confirmed the results by studying blood and other tissues via sensitive chromatographic techniques. Importantly, the team showed that the increased lactate concentrations were also seen in naturally aged mice, indicating that the results were due to the aging process itself.

The discovery marks the first link between abnormal metabolism and the aging process, and it provides a potentially useful marker of aging in the brain. Since



A prematurely aging mouse with “lactate on the brain.”

the MR imaging technique is noninvasive, it can be applied to live subjects, with the potential for use in humans. Ross is planning studies with collaborators at the KI to expand the work into human volunteers. The team has yet to determine whether the increased lactate concentrations are protective, destructive, or simply an indicator of other processes. In addition to doing human aging studies, the team plans to look at lactate concentrations after stroke.

Ross described the publication of her research as a rewarding outcome of four years of work in the GPP. She spent the first year of her Ph.D. at NIDA in Baltimore, taking classes at nearby Johns Hopkins University (Baltimore), before moving to Stockholm. Ross described her supervisors, Lars Olson at the KI and Barry Hoffer at NIDA, as “two great mentors.”

As for her next steps, Ross is focused on understanding the mechanism behind how mitochondrial dysfunction leads to aging—and finishing her Ph.D. Her husband, an Italian, is a postdoctoral fellow at the KI whom she met during an earlier stint at NIH, so future moves will have to work for both their careers. While a return to the United States is a possibility, Ross is led by a different motivation. “I’ll go wherever the mitochondria lead me,” she said. ●



and rigor, they are making inroads into important problems that have eluded understanding in the past.”

The investigators selected through the Earl Stadtman Investigators process are offered competitive salaries, research space, resources, supported positions, and an operating budget.

“It’s the equivalent of starting with an RO1 grant,” said Roland Owens, an assistant director in OIR and a member of the search committee. Tenure-track investigators at NIH have a good chance at becoming tenured. “The [success] rate, which is around 70 percent, is equal to or greater than comparable universities.”

The first eight people hired through the inaugural 2009–2010 Stadtman search process are Eric Batchelor, Haiming Cao, Zayd Khaliq, Jill Koshiol, Daniel Larson, Nasser Rusan, Douglas Stewart, and Jayne M. Stommel.

They “are all outstanding investigators,” said L. Michelle Bennett (NHLBI), a co-chair of the search committee. “This process identifies the best and brightest.”

“Earl Stadtman would have been pleased to have these terrific scientists associated with his name,” said Gottesman.

*The NIH Catalyst* interviewed the first crop of new investigators hired through the Earl Stadtman Investigators process. Following is a synopsis of who they are and why they are excited to be at NIH.

**Eric Batchelor**, who will join NCI’s Center for Cancer Research in May 2011, is completing a postdoctoral fellowship in systems biology at Harvard Medical School (Boston, Mass.). Trained as a physicist, Batchelor tackles science questions with a fresh approach. “My background in quantitative analysis offers a new perspective on some of the challenges in biology,” he said.

At Harvard, he is examining how the tumor suppressor protein 53 (p53) network detects cellular stresses, processes this information, and then makes appropriate cellular responses to maintain healthy cells. P53, which is mutated in half of all cancers, regulates the transcription of more than 100 genes within the cell and is activated in response to cellular stress. Batchelor hopes that his work will lead to a greater understanding of some of the most important signaling pathways in human cells.

Biochemist **Haiming Cao** came to NHLBI in January 2011 after completing a postdoctoral fellowship at the Harvard School of Public Health (Boston, Mass.). He uses mouse models to study the molecular and pathological basis of obesity with the hopes of developing effective therapies against obesity-related disorders such as diabetes and heart disease. He has found that palmitoleate, a hormone naturally produced by fat, enhances insulin action and reduces lipid accumulation in the liver and may protect against diabetes and weight gain. Palmitoleate has also shown promise in suppressing atherosclerosis and asthma. At NHLBI, he intends to search for other hormones that may fight human disease. He looks forward to “free thinking and unguarded scientific discussions” with colleagues and being able to “completely focus on scientific thinking and innovative experimentation.”

**Jill Koshiol** has been at NIH for awhile already. She has been an NCI Cancer Prevention Fellow since 2005. In August 2010 she became an investigator in NCI’s Division of Cancer Epidemiology and Genetics.

“By pursuing excellence both individually and as the first group of Earl Stadtman Investigators, I hope that we will set a precedent for future investigators that will empower them to reach and exceed all scientific bounds, just as

Dr. Stadtman did,” she said.

As an epidemiologist, she studies how infectious agents, such as the human papillomavirus, can cause cancer and affect outcomes. Measuring the responses to these agents in tumor tissue can help researchers understand how cancer begins. Koshiol will focus on tissue-based immune markers.

**Douglas Stewart**, who first came to NIH in 2004 as part of NHGRI’s Physician Scientist Development Program, became an investigator in NCI’s Division of Cancer Epidemiology and Genetics in August 2010. He is investigating neurofibromatosis type 1 (NF1), a disease characterized by the growth of tumors along nerves in the skin, brain, and other parts of the body. NF1 is caused by a single gene and about one in every 3,000 people worldwide suffer from this disease. Stewart sees patients every other week. When he’s not in the clinic he sequences the genomes of tumors associated with NF1. He hopes to start a rare-tumor clinic for NF1 with a specific focus on diagnosing glomus tumors. “Finding these rare disorders and figuring out new ways to treat them is what NIH does best,” he said.

**Zayd M. Khaliq** is finishing a postdoctoral fellowship in the Department of Neurobiology at Harvard Medical School and plans to have his NINDS lab up and running in spring 2011. Khaliq focuses on the brain’s dopamine neurons, which play an essential role in movement and reward-based behavior. Dysfunction of these neurons has been linked to a variety of brain disorders, including addiction, schizophrenia, depression, and Parkinson disease.

He is interested in the neuron firing mechanisms as well as in the development of pharmacological treatments. “The ability to work with clinical and translational researchers may help guide this research in the future to an area of potential drug development,” he said.

After completing a postdoctoral fellowship in the Department of Anatomy and Structural Biology at the Albert Einstein College of Medicine (Bronx, N.Y.), systems biologist **Daniel Larson** joined NCI's Laboratory of Receptor Biology and Gene Expression in February 2011. "I was really impressed with the science and collegiality at NIH," he said. "I was excited about being at a place where I would always be exposed to the latest and greatest in biomedical research." Larson intends to better understand gene expression in eukaryotic cells.

One of his first projects at NCI is developing and building custom microscopes that can look at RNA and gene expression in single cells. His laboratory uses biophysical and molecular approaches, including single-molecule microscopy, multiphoton microscopy, fluorescence fluctuation analysis, RNA visualization in fixed and living cells, and computational modeling.

Cell biologist **Nasser M. Rusan** came to NHLBI in February 2011 after finishing his postdoctoral fellowship in the Biology Department at the University of North Carolina (Chapel Hill, N.C.). Rusan is exploring the molecular interactions in mitosis. His work combines *Drosophila* genetics, high-resolution live-cell imaging, and functional genomic screening approaches to answer questions that have direct human health implications. "My immediate environment in Building 50 brings together biochemists, biophysicists, and cell biologists who think at the nanometer and micrometer level," he said. "My interactions with them will undoubtedly shed light on my research that is focused on how changes at the biochemical and cellular levels can result in changes at the tissue level in an animal."

**Jayne Stommel** came to NCI in September 2010 after spending six years at the Dana Farber Cancer Institute (Boston) as a postdoctoral research fellow and instructor. "I'm a Ph.D.," she said, "but I'm interested in clinical and translational questions . . . and high-risk projects."

Stommel is examining the therapeutic and biological roles of receptor tyrosine kinases (RTK) signaling networks in the common, deadly brain tumor glioblastoma multiforme (GBM). The average survival rate after GBM diagnosis is just 15 months. The RTK signaling networks are considered an attractive target for cancer therapy, but they are poorly understood; manipulating them has led to only some clinical success to date. Understanding these physiological factors that affect therapeutically relevant signaling pathways in cancer could lead to new therapies. ●



Eric Batchelor, Ph.D., NCI



NIH Office of History



Zayd Khaliq, Ph.D., NINDS



Daniel Larson, Ph.D., NCI

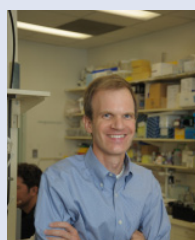
The new NIH-wide recruiting program for intramural scientists was named for legendary NIH investigator Earl Stadtman (above in 1952) who died in 2008.



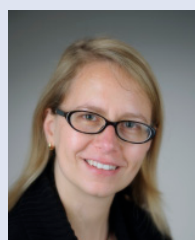
Haiming Cao, Ph.D., NHLBI



Jill Koshiol, Ph.D., NCI



Douglas Stewart, M.D., NCI



Jayne Stommel, Ph.D., NCI



Nasser Rusan, Ph.D., NHLBI

Vector Research (LMVR). There Fairhurst led a study that showed how people with a specific type of hemoglobin were less prone to developing severe malaria.

Malaria is caused by a parasite from the genus *Plasmodium*, a single-celled eukaryote with a complex, multistage life cycle. Several species of *Anopheles* mosquitoes transmit the parasites to people. As the infected mosquito bites into human flesh to obtain a blood meal, she injects spindle-shaped *Plasmodium* sporozoites into the victim's bloodstream. The sporozoites travel to the liver, invade liver cells, and during the next five to 16 days, reproduce asexually to form tens of thousands of merozoites per liver cell.

Over the next one to three days, the merozoites exit the liver and re-enter the bloodstream, where they begin invading erythrocytes (red blood cells) to avoid the host immune system, feed on cellular proteins, and reproduce asexually in safety. The infected erythrocytes rupture, releasing the merozoites to start repeated rounds of erythrocyte invasion. Thousands of parasite-infected cells in the host bloodstream trigger the illness and complications of malaria that can last for months if not treated.

The cycle continues as some merozoites develop into gametocytes, which mosquitoes ingest when they feed on infected hosts. The gametocytes enter a sexual reproduction phase in the insect gut and produce human-ready sporozoites that can infect anyone the mosquito bites. And the cycle goes on. Nearly one million people die of malaria each year, 85 percent of them children; most of the malaria-related deaths occur in Sub-Saharan Africa.

## Discovery

Fairhurst's 2005 discovery, published in *Nature*, was that hemoglobin type C impairs the ability of malaria parasites to cause severe disease. Hemoglobin comes in several varieties, with type A being the most common. But in parts of West Africa, one-fourth of the population has at least one

gene for hemoglobin C. Children with at least one hemoglobin C gene are less likely to develop the fatal cerebral form of malaria.

Fairhurst's team figured out how. The parasites produce proteins that make the surface of parasitized red blood cells sticky so the cells cling to blood vessel walls and avoid being cleared from the bloodstream. But C hemoglobin causes an abnormal distribution of the protein and thus makes the parasitized red blood cells less sticky (*Nature* 435:1117–1121, 2005).

By 2008, Fairhurst had become a tenure-track clinical investigator and chief of LMVR's Malaria Pathogenesis and Human Immunity Unit. Today he travels around the world as he continues to pry into the sinister pathogenic mechanisms of the several species of *Plasmodium*, especially the deadly *Plasmodium falciparum*, which is prominent in Sub-Saharan Africa, and *Plasmodium vivax*, which is common in Asia and South America.

*P. falciparum* has an exceptional talent for developing resistance to whatever drug it encounters. The first effective malaria treatment, known since the 17th century, was quinine, a compound derived from the bark of the cinchona tree. In the 1940s quinine was replaced by a more effective medication—the synthetic drug chloroquine. But by 1957, chloroquine-resistant *Plasmodium* had appeared along the Thailand-Cambodia border and spread to Africa, causing the deaths of millions of children. In 1972 Chinese scientists discovered artemisinin, which is derived from an herb that had been used in traditional Chinese medicine to treat malaria as early as 200 BC. But even artemisinin may be no match for the wily *Plasmodium*.

To prevent, or at least delay, the development of artemisinin-resistant *Plasmodium*, physicians administer artemisinin combination therapy (ACT), which combines the fast-acting drug with a slower-acting and longer-lasting one such as piperaquine. The piperaquine mops up



Rick Fairhurst has collected 100,000 stamps, 2,000 of them, similar to these, commemorating the global effort to eradicate malaria.

any remaining parasites and perhaps artemisinin-resistant ones. Today ACT has become the standard weapon against malaria. But history appears to be repeating itself. Fairhurst and his colleagues have observed hints of *P. falciparum* artemisinin resistance in Cambodia's Pursat province, again near the Cambodia-Thailand border.

"The appearance of artemisinin resistance is profoundly worrisome," said Fairhurst. "If our suspicion is correct—that parasites in Western Cambodia are becoming less susceptible to artemisinin—this finding could be a harbinger of worse things to come."

## Resistance Is Spreading

Resistance to chloroquine and other anti-malarial drugs spread from Cambodia to India and Africa. Fairhurst fears that artemisinin-resistant parasites may follow the same path.

"It is a time bomb; it is ticking," veteran malaria researcher Nicholas White told Reuters recently. "It has the potential of killing millions of African children." White, a professor of tropical medicine at Mahidol University (Bangkok) was one of the first to identify the artemisinin-resistant strain.

Fairhurst is collaborating with physicians and scientists around the world to assess whether artemisinin-resistant parasites are spreading beyond Cambodia. They have established testing and treatment sites in that country, other parts of Southeast Asia, and Mali, in West Africa, where they treat malaria patients with ACT and test their blood regularly for the quantity of the malaria parasites in order to gauge the rate of parasite clearance. The study results, which are expected in about a year, may



◀ **LEFT** In Cambodia, Rick Fairhurst tends to a young girl who is recovering from an episode of severe malaria.

▶ **RIGHT** In rural areas of Cambodia, NIAID researchers and their Cambodian colleagues collect blood samples to diagnose whether people have malaria. Anyone diagnosed with the disease will be taken to a hospital and treated.



provide clues to how resistance has arisen and how it might spread.

Mapping the “extent of artemisinin resistance is important if we are to eliminate the drug-resistant parasites and prevent their spread,” said Fairhurst. “The effort is likely to improve our chances of developing an in vitro [assay] . . . to test new drugs.”

NIAID has had a 20-year partnership with the University of Bamako in Mali and in 2002 designated the Malaria Research and Training Center (MRTC) in Bamako as an International Center of Excellence in Research (ICER). The ICER program helps to build sustainable research capacity in regions with high levels of infectious disease. The Mali ICER provides in-country support for state-of-the-art laboratories at the university and clinics in several rural villages. In addition, the ICER program has trained dozens of young Malian scientists at academic institutions and laboratories in Mali and the United States.

Fairhurst’s team is currently working with the MRTC on a large multiyear clinical study that will monitor the emergence of artemisinin resistance in Mali. Even though mosquito-proof bed nets and other measures are being used to protect people from infected mosquitoes, the number of malaria cases is on the rise. Researchers are not certain when artemisinin-resistant parasites will emerge in such settings.

Fairhurst and other NIAID researchers are also battling malaria in Cambodia. They have been collaborating with the National Center for Parasitology, Entomology, and Malaria Control (CNM), in Phnom Penh, since 2005. In 2008, NIAID and CNM opened a newly renovated malaria research

laboratory, which can rapidly analyze samples. NIAID also supports training exchanges involving NIH Fellows and Cambodian staff and is helping the lab to become a self-sustaining, locally run research center.

### NIH Trainees in Cambodia

Fairhurst and his trainees regularly travel to the Cambodia lab and field sites to treat patients, conduct clinical studies, and train students and clinicians in laboratory techniques. He is also carrying out a five-year study that involves 1,100 people at risk of acquiring malaria.

Typically, Fairhurst’s trainees work in a malaria-endemic country for three to four months before returning to NIH to analyze their field data. Chanaki Amaratunga, a visiting postdoctoral fellow and native Sri Lankan, came to the United States in 2007 to work with Fairhurst. “I realized after a two-year postdoc in India that I liked to work with people and do field work,” she said. “Working with Fairhurst promised everything I wanted.” Amaratunga enjoys working with Cambodian colleagues and is helping to facilitate a Cambodian-Chinese research collaboration.

Another trainee, Erika Phelps, assists with Amaratunga’s work and is pursuing her own research project on parasite drug resistance. “An important part of my training has been in the ethical aspects of working with patients with different social and cultural norms,” she said. “The only way to truly learn this is by working on site.”

In Mali, patients get themselves to the clinics, but in Cambodia, Fairhurst’s team must travel several hours into the

countryside to reach people with malaria. Patients are transported to field sites for treatment and participation in clinical studies that entail blood testing for parasites. The team uses a truck that can handle the worst of road conditions in rough mountain terrain. Getting from one field site to another can take seven hours on a good day to more than 10 hours on days when heavy rains have damaged the winding roads. Laboratory work is also challenging. Equipment, reagents, and office supplies are frequently flown in with the team, so careful pretrip planning and packing is essential. There are no local repair services, so a malfunctioning centrifuge or even a blown fuse can delay work for weeks or months.

Establishing and maintaining overseas facilities can be difficult, but they are crucial to NIH’s mission and a key part of the U.S. government’s global health agenda.

“If the U.S. is committed to successfully battling drug-resistant malaria, it should invest significantly in clinicians and scientists who are willing and able to meet malaria in person,” said Fairhurst. That means “establishing and staffing field sites in collaboration with local officials.”

Of the “Big Three” infectious diseases—malaria, human immunodeficiency virus infection and AIDS, and tuberculosis—“malaria is the number one killer, preying mostly on innocent children who are simply trying to reach their fifth birthday in the village where they were born,” said Fairhurst. “The disease continues to devastate the lives of countless people each year, sometimes affecting the same people over and over again for decades.” ●

**MORE MALARIA ON PAGE 14** ▶

# MALARIA RESEARCH AT NIAID

## LABORATORY OF MALARIA IMMUNOLOGY AND VACCINOLOGY (LMIV)

Patrick Duffy, M.D., Chief

The LMIV, which operates more like a small biotech firm than a typical research laboratory, develops and produces prototype malaria vaccines and conducts early-phase clinical trials of promising vaccine candidates. Its goal is to develop malaria vaccines that will reduce severe disease and death among African children and eliminate malaria from low-transmission areas of the world.

## LABORATORY OF MALARIA AND VECTOR RESEARCH (LMVR)

Thomas E. Wellems, M.D., Ph.D., Chief

LMVR is dedicated to studies of malaria and insect vectors of infectious diseases. Research groups maintain an array of on-campus and overseas activities investigating disease-transmitting insects and broad areas of malaria biology and pathogenesis. Basic discoveries support searches for new drug treatments, diagnostic tools, and vaccines.

## Apicomplexan Molecular Physiology Section

Sanjay A. Desai, M.D., Ph.D., Chief

This group focuses on how malaria parasites acquire nutrients and other essential solutes from the human bloodstream. The group identified two unusual ion channels that appear to play a central role in trafficking solutes between serum and parasite compartments. One of these channels, the plasmodial surface anion channel, is exposed on the infected erythrocyte surface and is generally recognized as an important drug target.

## International Studies of Malaria and Entomology Section

Robert W. Gwadz, Ph.D., Chief

Richard K. Sakai, Ph.D., Resident Scientist in Mali

Tovi Lehmann, Ph.D., Facility Chief

The scientists use ecological, behavioral, genetic, and molecular approaches to explore questions relevant to patterns of malaria transmission and vector control. Studies are conducted at NIAID facilities in Rockville, Md., and at the Malaria Research and Training Center (MRTC) in Bamako, Mali. Through NIAID's long-term collaboration with Malian scientists and physicians, the MRTC has become a well-equipped, highly productive program where research—on malaria and other vector-borne diseases—is led and conducted by Malian staff.

## Malaria Cell Biology Section

Louis H. Miller, M.D., Chief

Miller's group investigates the mechanisms by which malaria parasites first bind to and then invade erythrocytes (red blood cells). The scientists study parasite ligands and their erythrocyte receptors and how they interact on the surface of merozoites. (Merozoites are the form of the parasite that invades red blood cells). The group has identified the molecular mechanism that facilitates the invasion of malaria parasites and determined how to block the invasion with a ligand-blocking vaccine.

## Malaria Functional Genomics Section

Xin-zhuan Su, Ph.D., Chief

This lab develops genome-wide approaches to studying mechanisms of drug resistance, genome diversity, population genetics, and evolution of malaria parasites. The researchers use microarrays to genotype *Plasmodium falciparum* parasite isolates collected from



Thomas Wellems, NIAID

As she takes a blood meal, the female *Anopheles gambiae* mosquito can transmit malaria parasites.

the field; search for genes potentially associated with drug responses; and also screen *P. falciparum* parasites against thousands of chemical compounds for differences in their responses to the chemicals.

## Malaria Genetics Section

Thomas E. Wellems, M.D., Ph.D., Chief

Investigations in this section focus on the determinants of drug resistance, immune evasion, and disease virulence in malaria. Areas of study include antimalarial drug resistance and factors that affect clinical outcome after treatment; malaria protection conferred by human hemoglobinopathies and other red cell polymorphisms; antigenic variation in *Plasmodium falciparum* parasites; and molecular mechanisms of malaria parasite infectivity. In the 1980s, Wellems and NIAID scientist Russell Howard identified and characterized a unique protein called Pf HRP-2, which is found in abundance in the malaria parasite *P. falciparum*. Their work led to the development of the first rapid diagnostic test for malaria.

## Malaria Immunology Section

Carole A. Long, Ph.D., Chief

This group is interested in the interface between the erythrocytic stage of parasite infection and the immune system of the vertebrate host. By studying these host-parasite interactions in rodent models of malaria and in children and adults living in endemic areas, the researchers explore both innate and adaptive immune responses to malaria infection as well as responses to immunization with specific malaria vaccine candidates.



← This is a scanning electron micrograph of *Plasmodium gallinaceum*, which causes malaria in poultry, invading the midgut of the *Aedes aegypti* mosquito.

→ In NIAID's insectary, mosquito larvae are incubated in trays, and mature mosquitoes are transferred to round containers that can be accessed through a cloth sleeve. Here technician Andre Laughinghouse uses a filtered rubber tube to extract mosquitoes.



## Malaria Pathogenesis and Human Immunity Unit

*Rick M. Fairhurst, M.D., Ph.D., Chief*

Fairhurst's group integrates laboratory research activities with clinical field studies in Africa and Southeast Asia. It aims to improve our understanding of malaria pathogenesis and host genetic resistance and acquired immunity to malaria and to develop therapeutics and vaccines to reduce the mortality of malaria. The lab is investigating mechanisms of malaria protection conferred by hemoglobin and red blood cell polymorphisms; mechanisms of host inflammation associated with the sequestration of parasitized red blood cells; and parasite virulence factors.

## Mosquito Immunity and Vector Competence Section

*Carolina V. Barillas-Mury, M.D., Ph.D., Chief*

This section investigates how the interactions between the mosquito immune system and *Plasmodium* parasites affect malaria transmission. It studies interactions between parasites, gut microbiota, and mosquito midgut cells; characterizes immune pathways that mediate antiplasmodial responses; explores innate immune memory in mosquitoes; and investigates how *Plasmodium* evades some of these mosquito immune responses. (See page 16 for more about Carolina Barillas-Mury.)

## Vector Biology Section

*José M.C. Ribeiro, M.D., Ph.D., Chief*

Vector Biology Section researchers use molecular, biochemical, and pharmacological approaches to explore the biochemical

and pharmacological diversity found in the salivary glands of blood-feeding insects and ticks. Recently they have used vector salivary gland transcriptome analysis to discover new and interesting compounds, and they have developed tools for bioinformatic analysis.

## Vector Molecular Biology Section

*Jesus G. Valenzuela, Ph.D., Chief*

This section focuses on vector-host and vector-parasite interactions in leishmaniasis, a disease characterized by skin sores and spread by sand flies. The investigators combine basic, veterinary, and clinical research approaches to broaden their understanding of the relationship between immune responses to vector proteins in animals and humans and disease outcomes. They are trying to understand the molecular aspects of the sand fly's salivary and midgut proteins and hope to develop a vector-based vaccine against leishmaniasis.

## LABORATORY OF IMMUNOGENETICS

*Susan K. Pierce, Ph.D., Chief*

The research in the Laboratory of Immunogenetics focuses on the cellular and molecular mechanisms that underlie the signaling functions of immune cell receptors in autoimmunity and in infectious disease.

## Lymphocyte Activation Section (LAS)

*Susan K. Pierce, Ph.D., Chief*

LAS researchers are exploring the cellular and molecular mechanisms underlying immunological memory and B-cell activation during

immune responses. B cells are white blood cells, produced in the bone marrow, that proliferate and differentiate into short-lived antibody-secreting plasma cells as well as long-lived plasma cells and memory B cells. LAS scientists are conducting studies in collaboration with scientists in Mali, Africa (at the Malaria Research and Training Center at the University of Bamako in Mali), to get a detailed understanding of the generation and maintenance of immunological memory in response to natural malaria infection.

## OTHER MALARIA LABS AT NIH

Several other NIH institutes and centers are conducting malaria research including the John E. Fogarty International Center for Advanced Study in the Health Sciences, NICHD, and NIDDK. In addition, NIAID researchers are collaborating with scientists at the NIH Chemical Genomics Center in NHGRI, the Infrared Imaging and Thermometry Unit in NIBIB, and extramural scientists around the world. The NLM has a host of malaria resources at [http://www.nlm.nih.gov/mimcom/NLM\\_malaria\\_resources.html](http://www.nlm.nih.gov/mimcom/NLM_malaria_resources.html).

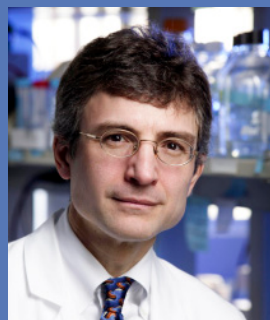
For more information on malaria, visit <http://www.niaid.nih.gov/topics/malaria/Pages/default.aspx>.

For more information on NIAID labs doing malaria research, visit <http://www.niaid.nih.gov/topics/Malaria/research/Pages/labs.aspx> <http://nidb.nih.gov/search/searchreport.taf?ipid=64627>.

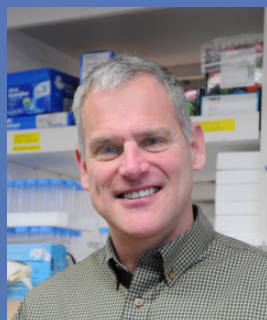
## Recently Tenured



Carolina Barillas-Mury, NIAID



Gregory Germino, NIDDK



Robert Heinzen, NIAID



James Melvin, NIDCR



Dennis Taub, NIA

**CAROLINA BARILLAS-MURY, M.D., PH.D., NIAID**  
*Senior Investigator; Chief, Mosquito Immunity and Vector Competence Section*

**Education:** Universidad del Valle de Guatemala, Guatemala City, Guatemala (B.S. in biology); Universidad Francisco Marroquín de Guatemala, Guatemala City (M.D.); University of Arizona, Tucson, Ariz. (Ph.D. in biochemistry)  
**Training:** Postdoctoral at Harvard University (Cambridge, Mass.); European Molecular Biology Laboratory (Heidelberg, Germany)

**Before coming to NIH:** Assistant Professor in the Department of Microbiology, Immunology and Pathology at Colorado State University (Fort Collins, Colo.)

**Came to NIH:** In October 2003

**Outside interests:** Spending time with husband and six-year-old daughter; traveling and visiting friends and family; painting and drawing

**Research interests:** We are interested in the interactions between the mosquito immune system and Plasmodium parasites that cause malaria. To infect mosquitoes, Plasmodium parasites must invade midgut epithelial cells. We investigate how the cells' defense responses affect parasite survival.

We recently identified a novel physiological barrier in the mosquito midgut that allows the gut microbiota to proliferate without activating an immune response.

This barrier, formed by a network of cross-linked proteins, also enhances malaria transmission by allowing Plasmodium parasites to go undetected as they develop.

Recent studies revealed that the mosquito immune system is more flexible than once thought and can learn to respond more effectively to pathogens that it has been previously exposed to. The number of circulating granulocytes increases in mosquitoes that have been pre-exposed to Plasmodium infection and mediates an innate immune memory response. We are trying to identify the factor in the mosquito hemolymph (circulatory fluid) that triggers hemocyte (mosquito equivalent of a white blood cell) differentiation and immune enhancement. We are also mapping *Plasmodium falciparum* genes that allow some African strains to evade the mosquito immune system.

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**GREGORY G. GERMINO, M.D., NIDDK**

*Deputy Director, NIDDK; Senior Investigator, Kidney Disease Branch*

**Education:** Loyola University, Chicago (B.S. in biology); Pritzker School of Medicine, Chicago (M.D.)

**Training:** Residency in internal medicine and clinical fellowship in nephrology at Yale-New Haven Hospital (Conn.); research fellowship at University of Oxford (Oxford, England).

**Before coming to NIH:** Professor in the Division of Nephrology and in the Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine (Baltimore); member, Board of Directors, Federation of American Societies for Experimental Biology  
**Came to NIH:** In 2009

**Other professional activities:** Adjunct professor of medicine, Johns Hopkins University School of Medicine

**Outside interests:** Running; co-managing family with physician-scientist spouse; watching daughter play soccer and son play piano

**Research interests:** I am particularly interested in polycystic kidney disease (PKD), which represents a heterogeneous collection of genetic disorders that involve abnormal tubular morphology. Tubules are fundamental structural units of many organs in the body, yet the processes that govern and maintain them are poorly understood. The kidney is one of the best examples of an organ in which tubular structure and function are integrally linked. Determining how renal tubules are formed and how their structure is maintained will provide important insights into kidney function and the organ's response to injury. Studying PKD provides a unique opportunity both to define the molecular processes that deter-



Jack Yanovski, NIDDK

mine tubular morphology and to develop novel therapies for a set of diseases with important clinical impact. While I was at Johns Hopkins I helped to identify *PKD1* and *PKHD1*, genes responsible for causing the autosomal dominant and recessive forms of the disease. I also developed novel cell-culture systems and preclinical mouse models to characterize the proteins and their role in cell signaling pathways. I am continuing my research in the Kidney Disease Branch of NIDDK.

#### ROBERT HEINZEN, PH.D., NIAID

*Senior Investigator and Chief, Coxiella Pathogenesis Section, Laboratory of Intracellular Parasites (Hamilton, Mont.)*

**Education:** St. Cloud State University, St. Cloud, Minn. (B.A. in biology); Washington State University, Pullman, Wash. (Ph.D. in microbiology)

**Training:** Postdoctoral fellowship in NIAID

**Before coming to NIH:** Assistant and associate professor of molecular biology, University of Wyoming (Laramie)

**Came to NIH:** In January 2003 as head of NIAID'S new Coxiella Pathogenesis Section

**Outside interests:** Enjoying outdoor recreational activities afforded by living next to one of the country's largest wilderness areas

**Research Interests:** We have a comprehensive research program that addresses the wide gaps in knowledge of *Coxiella burnetii* genetics, pathogenesis, and cellular microbiology. The bacterium *Coxiella* is a recognized category B biothreat agent that causes Q fever, a disabling flu-like illness. The organism invades mononuclear phagocytes, where it directs biogenesis of a lysosome-like parasitophorous vacuole (PV) in which it replicates. We have defined novel aspects of *Coxiella* PV formation and biochemistry, revealed pathogen-directed host cell survival responses, and identified a battery of secreted *Coxiella* proteins that are implicated in successful parasitism and virulence. We have also identified replicative and antigenic properties of *Coxiella* developmental forms and discovered a unique function of *Coxiella* lipopolysaccharide in shielding the organism from the host's innate immune system.

Our efforts have yielded important insights into *Coxiella* genome structure, genetic diversity, and pathogenetic potential. We also discovered a medium that supports host-cell-free growth of *Coxiella*, which was historically considered an obligate intracellular parasite. Finally, we have developed new tools for *Coxiella* genetic manipulation. These advances will help achieve the objectives of NIAID's biodefense initiative and enable the development of new countermeasures—such as vaccines and diagnostic reagents—against Q fever.

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

#### JAMES MELVIN, D.D.S., PH.D., NIDCR

*Senior Investigator; Clinical Director; Chief, Secretary Mechanisms and Dysfunction Section*

**Education:** Kent State University, Kent, Ohio (B.A. in biology); Case Western Reserve (DDS); School of Medicine and Dentistry, University of Rochester, N.Y. (M.S. in anatomy and Ph.D. in neurobiology and anatomy)

**Training:** Postdoctoral training at the National Institute of Dental Research and at the University of Cincinnati College of Medicine

**Before coming to NIH:** Director, Center for Oral Biology and professor of pharmacology and physiology at the School Medicine and Dentistry, University of Rochester

**First came to NIH:** In December 1985 for training; returned in June 2010

**Outside interests:** Biking; reading

**Research interests:** The quality of life for millions of Americans is adversely affected by salivary gland hypofunction, clinically referred to as xerostomia or dry mouth. Dry mouth is caused by a variety of etiologies ranging from xerogenic medications—such as certain antidepressants, antipsychotics, and antihistamines—and radiation therapy for head and neck cancers, to defects in the genes that encode for water and ion transport proteins, to autoimmune diseases such as Sjögren's syndrome (which damages tear- and saliva-producing glands and other organs). Saliva protects the upper gastrointestinal tract from microbial invasion as well as mechanical and chemical stresses. The research focus of my laboratory is to determine the molecular identity, structure, and physiological roles of the ion and water transport and channel proteins that regulate fluid secretion. Insight gained from these studies will provide critical information for developing rationales for preventing and/or treating exocrine gland dysfunction.

CONTINUED ON PAGE 18

**DENNIS D. TAUB, PH.D., MT (ASCP), NIA**

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

**Education:** Pennsylvania State University, University Park, Pa. (B.S. in microbiology and medical technology); Temple University School of Medicine, Philadelphia (Ph.D. in microbiology and immunology)

**Training:** Went directly from graduate school to NCI as a staff fellow, a tenure-track position

**Came to NIH:** In 1991 as NCI staff fellow; joined NIA in 1997 as Acting Chief, Laboratory of Immunology, and Director, Clinical Core Laboratory

**Other professional activities:** Editor-in-Chief, *International Journal of Medical Sciences* and *Journal of Inflammation*; editorial boards of several journals; member, Faculty 1000; member, National Scientific Advisory Council, American Federation for Aging Research

**Outside interests:** Participating in Autism Society activities; writing fiction and poetry; spending time with his son and family

**Research Interests:** We are characterizing the biological and molecular signaling events and functions associated with chemokine ligand-receptor interactions in the context of aging and disease. We have demonstrated the existence of a cooperative signaling network between chemokine and Wnt receptors and ligands that may control cell polarization and directional migration. We are also trying to understand the role of metabolic hormones on immune cell signaling and function, specifically orexigenic (hunger) and anorexigenic (satiety) hormones. Recent data have demonstrated that when ghrelin (a gastrointestinal hormone that stimulates appetite) is administered to mice, there is a dramatic reduction of disease- and age-associated inflammation, muscle wasting, and shrinking of the thymus. In contrast, leptin (a fat-

cell-produced hormone that suppresses appetite) promotes inflammation but also reverses thymic involution. We are currently examining the signaling pathways triggered by these hormones and their role in regulating T-helper and macrophage activation and differentiation.

Our data support the existence of a functional immunoregulatory network involving both circulating and immune-derived metabolic hormones within the immune system and their regulatory role in cytokine expression, cellular activation, differentiation, and cell survival.

.....  
**JACK YANOVSKI, M.D., PH.D., NICHD**

*Senior Investigator and Section Chief, Section on Growth and Obesity, Program in Developmental Endocrinology and Genetics*

**Education:** University of Pennsylvania, Philadelphia (B.A. in biology and psychology; M.D.; Ph.D. in physiological psychology)

**Training:** Residency in pediatrics, Children's Hospital of Philadelphia; fellowship in pediatric endocrinology at NICHD

**First came to NIH:** In June 1989 for training

**Other positions at NIH:** Chief of the Clinical Center's Pediatric Inpatient Unit, 1994–1998; in 1997 founded NICHD's Unit of Growth and Obesity

**Outside interests:** Listening to classical music (he met his wife—Susan Yanovski, M.D., program director in NIDDK—while singing in a choir she conducted); gardening; and spending time with his family

**Research interests:** We are elucidating the genetic underpinnings of the metabolic and behavioral endophenotypes that contribute to the development of obesity in children. In a cohort of children at risk for adult obesity that we have followed since 1996, we examine factors that can predict the progression to adult obesity. We have found that children with blood leptin levels that are high in proportion to body fat experience accelerated weight gain. Although the hormone normally suppresses hunger, most obese people

have high levels of it in their bloodstream and seem resistant to its appetite-suppressant properties. Leptin resistance also appears to be associated with obesity in some rare genetic disorders such as Bardet-Biedl syndrome—which is characterized by vision loss, obesity, mental retardation, and other problems—that are believed to alter leptin-receptor signal transduction.

Our lab has also investigated the importance of some ligands and receptors that help propagate leptin's signal within the brain. We also conduct clinical trials to examine approaches for the prevention and treatment of excessive body weight. For example, we found that when given in conjunction with a behavioral program, the oral diabetes drug metformin significantly improved weight loss and reduced insulin resistance in severely overweight, insulin-resistant children. We seek to improve our ability to predict which children are at greatest risk for obesity and its comorbid conditions and to develop more targeted, etiology-based prevention and treatment strategies for pediatric obesity. ●

## NIH Sourcebook

The *NIH Sourcebook*, at <http://sourcebook.od.nih.gov>, contains everything you need to know about your intramural position (but were afraid to ask). The searchable, no-nonsense format includes links to: About the Office of Intramural Research, Scientific Reviews of the Intramural Research Program, Intramural Research Scientific Programs, Committees Advisory to the DDIR, Board of Scientific Directors, Scientific Directors' Orientation Guide, Conflict Resolution and Staff Assistance,, Training Courses, Personnel Appointments and Procedures, Ethical Conduct and Mentoring, Intramural Research Program Personnel Policies, Research Conduct and Ethics Instruction Materials, and more.

## NIH-LASKER CLINICAL RESEARCH SCHOLARS SYMPOSIUM

Thursday, March 31, 2011

9:00 a.m.–12:30 p.m.

Masur Auditorium (Building 10)

The symposium celebrates a new partnership between the NIH and the Lasker Foundation: the Lasker Clinical Research Scholars program, an intramural-extramural partnership to nurture the next generation of clinical researchers (<http://www.nih.gov/science/laskerscholar>).

The presenters at the March 31 symposium include several physician-scientists who will discuss their own clinical research successes: Daniel Kastner (NHGRI), W. Marston Linehan (NCI), Charles Sawyer (Memorial Sloan Kettering Cancer Center, New York), and Christine Seidman (Harvard Medical School, Boston, Mass.)

## NIGMS AIDS-RELATED STRUCTURAL BIOLOGY MEETING

March 28–30, 2011

Monday and Tuesday: 8:00 a.m.–6:00 p.m.

Wednesday: 8:00 a.m.–1:00 p.m.

Natcher Building (Building 45)

Ruth Kirschstein Auditorium

Registration deadline: March 18, 2011

At this “25th Annual Meeting of the Groups Studying the Structures of AIDS-Related Systems and Their Application to Targeted Drug Design,” plenary sessions will cover the HIV life cycle, host-pathogen interactions, imaging, latency, viral-host recognition and structure-based drug design and resistance. The meeting is free and open to the public, but advance registration is required. To submit a poster presentation, check the speaker box on the meeting registration page and e-mail Joe Gindhart at [gindhartjg@nigms.nih.gov](mailto:gindhartjg@nigms.nih.gov). To register and for more information visit <http://meetings.nigms.nih.gov/index.cfm?event=home&ID=10905>.

## WEDNESDAY AFTERNOON LECTURES

Wednesdays, 3:00–4:00 p.m.

Masur Auditorium (Building 10)

Plus Special Lectures in March and April:

Monday, March 14, 10:00 a.m.: Rebecca Skloot,

author of *The Immortal Life of Henrietta Lacks*

Thurs., March 17, 3:00 p.m.: Fred Gage (Salk Inst.)

Monday, April 11, 3:00 p.m.: Jane Goodall

For a full schedule, visit <http://wals.od.nih.gov>.

## NCI'S BIOSPECIMEN RESEARCH NETWORK SYMPOSIUM: “ADVANCING CANCER RESEARCH THROUGH BIOSPECIMEN SCIENCE”

March 28–29, 2011

Bethesda North Marriot Hotel & Conference Center

Registration is now open

Hosted by NCI's Office of Biorepositories and Biospecimen Research, the symposium will address the impact of pre-analytical biospecimen variations on cancer research and molecular medicine, and the advancements in biospecimen science aimed at minimizing the impact of these variations. This two-day event will feature expert presentations, interactive discussions, and poster presentations from a broad range of stakeholders whose work involves biospecimens, including researchers, clinicians, industry representatives, and patient advocates. To get the latest information about registration, speakers, topics, and participation, visit <http://brnsymposium.com>.

## NHLBI MITOCHONDRIAL BIOLOGY SYMPOSIUM: “ADVANCES IN MITOCHONDRIAL DYNAMICS AND MITOCHONDRIAL-CYTOSOLIC COMMUNICATIONS”

May 16: 8:00 a.m.–7:00 p.m.

May 17: 8:00 a.m.–12:30 p.m.

Natcher Conference Center (Building 45)

Registration (free) deadline: April 29, 2011

Second in a series of Mitochondrial Biology Symposia hosted by the NHLBI, scientific session topics for this conference are to include:

“Mitochondrial Dynamics and Autophagy—From Basic Concepts to Disease Pathophysiology,” and “Mitochondrial Communication with the Cytosol—Fundamental Concepts and Role in Pathophysiology.” The keynote speaker will be Douglas C. Wallace, Chair in Pediatric Mitochondrial Medicine and Metabolic Disease, and director of the Center for Mitochondrial and Epigenomic Medicine at The Children's Hospital of Philadelphia. Poster session is on May 16, 5:00–7:00 p.m. To register and for more information go to <http://www.NHLBIMitochondrialSymposia.org>. For other questions, contact Elizabeth Meyer, [elizabethmeyer@strategicresults.com](mailto:elizabethmeyer@strategicresults.com).

## NCI'S CENTER FOR CANCER RESEARCH (CCR) AND DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS (DCEG) RETREAT

April 11, 2011

8:00 a.m.–5:00 p.m.

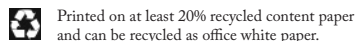
Natcher Conference Center (Building 45)

Abstract deadline: March 14

Registration deadline: April 1

The CCR and DCEG Staff Scientist and Staff Clinician Organization would like to invite all CCR and DCEG staff scientists, staff clinicians, and principal investigators to the annual retreat. Keynote presentations will be given by Ron Evans (Howard Hughes Medical Institute, San Diego) and Christopher Loffredo (Georgetown University, Washington, D.C.), career development sessions, workshops, topic lunches, and poster sessions. Evans is an authority on hormones, both their normal activities and their role in disease; Loffredo is an internationally known researcher on environmental and genetic causes of cancer and birth defects. This is a great opportunity to network with your peers and enhance your career. To register and for more information, go to <http://web.ncicrf.gov/events/clinician-retreat/2011/default.asp>.

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## CATALYTIC REACTIONS?

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

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

### IN FUTURE ISSUES:

- OBESITY RESEARCH
- HISTORY OF HEART VALVES
- SHARED RESOURCES

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

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## LABORATORY CONFESSIONS

### Back Gate Rendezvous

BY NAME WITHHELD

I slipped out the pedestrian exit on Cedar Drive doubled up with another employee. There's a two-gate system back there that requires an ID card to get in or out. It's supposed to be single file. We both had our IDs, and we were both going out, not in. So it's not that illegal, really. What I'm confessing is that I found the incident to be akin to an illicit affair. I didn't plan this back-gate rendezvous. It just happened.

If you're not familiar with the pedestrian gateway behind Building 31, it's where smokers go to escape the smoke-free campus. There's a first gate; you need to swipe your ID to get that to open. Then you enter a little box between gates. Once the gate firmly shuts and locks behind you, with the eerie metallic clink of a lockdown, you use your card again to unlock the second gate.

Try to visualize the opening of “Get Smart,” in which Agent 86 goes through a series of steel doors to enter headquarters (see <http://bit.ly/O4OuV>). That's what it's like sometimes getting in or out of the Cedar Drive exit.

I allowed this fellow, a smoker, to enter with me. I figured why not save him 60 seconds in his considerably shortened life. But on this fateful day, the second gate wouldn't open. We were trapped. With fumbling, nervous hands we tried his card, my card, his card again. Nothing worked. For a moment I felt as if I were snowbound with little chance of survival, and a strange feeling overtook me. I blushed, fell back, and then realized I was able to go back through the first gate.

Whew. As my heart rate settled down, I realized that unless one is prepared to face the consequences, it's better to do these things alone.

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

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