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Crowdsourcing

Accelerates Toxicity Testing

BY JENNIFER SARGENT, NIAMS

Scientists at the National Institute for Environmental Health Sciences (NIEHS) have turned to crowdsourcing to help analyze massive datasets and develop new models to predict the toxicity of pharmacological and environmental chemicals.

Crowdsourcing involves using collective intelligence to answer a problem. The idea is that many hands make light work—or, in this case, that many heads make for more efficient problem solving. And what better way to get a scientific crowd together to tackle a problem than to issue a challenge? It might even be right for *your* project.

Crowdsourcing initiatives "get the best and the brightest contributing their knowledge to get the best result," said NIEHS Deputy Director **Rick Woychik**, who helps steer NIH policy for big-data challenges.

In 2013, scientists at NIEHS, the National Center for Advancing Translational Sciences (NCATS), the University of North Carolina (UNC; Chapel Hill, N.C.), and two nonprofits—DREAM (Dialogue for Reverse Engineering Assessments and Methods) and Sage Bionetworks (Seattle, Wash.)—partnered to launch a Toxicogenetics Challenge that asked participants to use genetic and cytotoxic data to develop algorithms to predict the toxicity of different chemicals. Analyses such as these are aimed at understanding why different people exposed to the same chemical in the same environment display different reactions.

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The Festival That Amost Wasn't

Report From the 2013 Research Festival

BY LESLEY EARL, NCI

Neither snow, nor rain, nor the gloom of a government shutdown could keep NIH's Research Festival from happening. It was just postponed a little.

Led by co-chairs **Dan Kastner**, the scientific director of the National Human Genome Research Institute (NHGRI), and **Luigi Ferrucci**, the scientific director of the National Institute on Aging (NIA), the festival served up a feast of basic science and translational medicine.

Although the festival was originally scheduled for early October, the 16-day government shutdown forced the organizers to rapidly reschedule the events for November 6 to 8 instead. Most of the planned events took place—including the plenary session, many concurrent symposia, and a much-anticipated Scientific Directors Poster Session and Cook-off—but the Vendor Tent Show had to be rescheduled for the spring, and the National Graduate Student Research Conference had to be cancelled.

DARRYL LEJA, NHGRI

This design represents the two 60th anniversary celebrations that the 2013 Research Festival recognized: that of the NIH Clinical Center, which opened in July 1953; and of James Watson and Francis Crick's landmark paper that first described the DNA double-helix structure, published in *Nature* on April 25, 1953.

"The silver lining, perhaps, of the shutdown was that NIH emerged as one of a very short list of government activities that everybody agreed has incredible value," said NIH Director **Francis Collins** in his opening remarks at the plenary session.

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The NIH Intramural Clinical Research Program: Changing the Trajectory of Care

BY STEVEN HOLLAND

Deputy Director for Intramural Research **Michael Gottesman** recently reviewed the profound effects that the NIH intramural research program (IRP) has wrought over the years on the current conduct of general medicine, including the use of automated blood-cell counting, vaccine development, coronary imaging, protection of the blood supply, and genomic analysis.

Following up, I wanted to highlight some ongoing intramural approaches and trials at the Clinical Center that promise to change understanding and practice in the future.

The treatment of patients with severe illness is special. There is a lot of anguish, a lot of anxiety, and often a lot of death. It takes a special and invested commitment from all involved—patients, nurses, doctors, scientists, administrators, and directors—to sustain the conviction, momentum, and support necessary to carry us through the times that are inevitably trying and painful. But if this is where the battle lines are drawn, dare we walk away?

The successes of antiretroviral therapy for human immunodeficiency virus (HIV) started at NIH originally with zidovudine (AZT); was perfected over the years with infection prophylaxis, multidrug combinations, and simplified delivery; and has culminated in a widespread group of drug targets and the cognate drugs that have given us a new paradigm for how serious diseases can be turned. The unconquered frontiers of immune reconstitution and HIV-associated malignancies are slowly yielding through innovative IRP studies.

The eruption of excitement around the dramatic and successful treatments of cancer with chimeric antigen receptors has finally persuaded even the long-standing skeptics that immune control of cancer is real, harnessable, and effective. The deep intramural commitment to the immune control of cancer by **Steve Rosenberg**'s lab (NCI), exploring cell-mediated mechanisms, and **Ira Pastan**'s lab (NCI), using humoral ones, both anticipated and facilitated this development. This effort to focus, train, and release the latent powers of immunity on specific tumors has emerged as one of the most critical and important ways in which we will address cancer in the future.

Development of new tools is essential, of course. But just as critical is learning how to use the tools that already exist. **Lou Staudt**'s group (NCI) has dissected the molecular signature and definition of lymphomas, enabling their detection and tailoring of treatments. Staudt, **Kieron Dunleavy** (NCI), **Wyndham Wilson** (NCI), and colleagues have honed the chemotherapy of lymphoma to a fine edge, using the NIH-established principles of multiagent chemotherapy to achieve terrific cure rates while reducing the need for more toxic therapies.

In the infectious-disease realm: While working to create new drugs for tuberculosis, **Clif Barry**'s lab (NIAID) has shown how to use the old drug linezolid to successfully treat multidrug-resistant tuberculosis. **Cindy Dunbar**'s group (NHLBI) turned eltrombopag, a drug used for severe thrombocytopenia, into a drug that can rescue a significant number of people who have severe aplastic anemia.

Perhaps our greatest area of shining success is one that has been a jewel in our diadem for decades: our unique capacity as a community of like-minded investigators to identify specific patient phenotypes; recruit similar patients and their families; bring them in for study; genotype them; understand the underlying mechanisms; and—with hard work and good luck—develop new therapies. For example, the extraordinary work of **Marston Linehan**'s group (NCI) in dissecting and defining the metabolic basis of kidney cancers has changed diagnosis, screening, therapy, and survival.

The list of new diseases (and their genes) discovered at NIH stretches way back, but the pace of discovery in the past few years has been breathtaking: novel autoinflammatory diseases (DIRA, NOMID); novel immunodeficiencies (*DOCK8*, *PLCG2*, *VPS45*); novel endocrinopathies (*ARMC5*, *NT5E*, *EHHADH*); novel metabolic syndromes (Proteus); novel cancer syndromes (*HIF2A*, *GATA2*); and the remarkable yield of the Undiagnosed Diseases Program led by **Bill Gahl**. All these new diseases and genes provide even more targets for the massed investigative power of NCATS, promising even more new drugs for the future.

And then there's the **Julie Segre**'s team (NHGRI), which championed genome sequencing to track a microbe's spread.

This essay presents a very brief, necessarily inadequate, and incomplete sampler of some of the many things that are ongoing and outstanding in the Clinical Center's intramural clinical program. What we have changed about the practice of medicine so far is only the prologue. ●

Precision Medicine

Using Genomics to Get Patients the Right Treatment

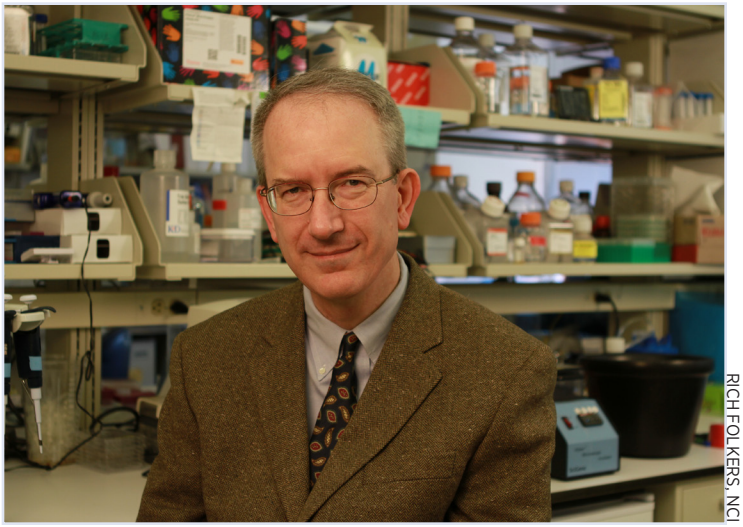
BY CHRIS PALMER, NCI

More than a decade and about three billion dollars were sunk into sequencing the first human genome. Now, that feat can be accomplished in as little as five days and runs about $4,000. The process is getting quicker and cheaper by the day. This reduction in the time and cost of genomic sequencing is the foundation of personalized medicine in which genetic analysis may point to the most effective treatments.

"This is a particularly exciting time for us because we have tools that are just jaw-dropping in their power to examine the human genome," **Louis Staudt** told the audience that had gathered at Suburban Hospital on November 1, 2013, for the first talk in the 2013–2014 Genomics in Medicine Lecture Series.

Staudt, director of the National Cancer Institute's (NCI) Center for Cancer Genomics and co-chief of NCI's Center for Cancer Research Lymphoid Malignancies Branch, studies the molecular basis of human lymphoid malignancies. In his talk, "Practicing Precision Medicine in Cancer Using Genomics," he described how molecular tools that probe DNA and RNA expression can be used to more accurately diagnose various cancer subtypes and identify genetic abnormalities that can make some patients' tumors respond better to cancer-fighting drugs.

One example cited by Staudt of the need for accurate diagnosis comes from a study of endometrial cancer by researchers in The Cancer Genome Atlas project at NCI (*Nature* **497:**67–73, 2013). The conventional tool for diagnosing the four major subtypes of endometrial cancer is histological analysis, in which biopsied tissue is stained and visually analyzed. Unfortunately, this method may result in the more aggressive serous-like subtype being misdiagnosed as a less aggressive subtype, resulting in inadequate treatment. Molecular tools, however, can easily distinguish these subtypes so patients can be treated appropriately. "The current ways that we're diagnosing cancer and treating cancer are changing before our eyes," said Staudt. "We're moving from histological diagnosis to genomic diagnosis as fast as we can."



RICH FOLKERS, NCI

Louis Staudt, the director of NCI's Center for Cancer Genomics, described how molecular tools can distinguish genetic differences in cancer subtypes and lead to better diagnoses and treatment.

In his own research, Staudt has used gene-expression profiles to differentiate two previously unknown subtypes of diffuse large B-cell lymphoma (DLBCL), which kills 10,000 people in the United States annually. The two subtypes, ABC and GCB, are characterized by elevated expression in distinct subsets of genes; the ABC subtype accumulates mutations that activate the B-cell receptor-signaling pathway.

Staudt worked with NCI colleague **Wyndham Wilson** (NCI) to evaluate the B-cell signaling inhibitor ibrutinib in patients with ABC DLBCL. In a pilot study conducted at the Clinical Center, they observed complete and partial responses in patients whose tumors were resistant to chemotherapy. Based on the findings, Staudt and Wilson led a multicenter phase 2 trial of 70 patients with refractory DLBCL: Patients with the ABC subtype had a 40-percent response rate compared to five percent in patients with the GCB subtype. Staudt noted that the beneficial effect of ibrutinib and other targeted therapies relies on "the distinction between molecular subtypes of cancer."

Staudt predicted that "Genetic profiling will become so inexpensive that patients will get it [in the] course of their standard care." He envisions that one day soon, he'll be performing more "non-clinical-trial clinical trials" by crunching the genetic data from patient tumors—potentially millions of them—to divine detailed molecular signatures of cancer subtypes that can each be treated with targeted therapies. "Until we study the great diversity of cancer," he said, "we can't fully appreciate its nature." ●

The Genomics in Medicine Lecture Series is a collaboration of NHGRI, Suburban Hospital (Bethesda, Md.), and Johns Hopkins University School of Medicine. The lectures are held on the first Friday of the month, 8:00–9:00 a.m., in the lower level auditorium of Suburban Hospital. All are welcome to attend. For more information, including how to watch archived videos of the presentations, go to http://www.genome.gov/27553517.

NIH CLINICAL FELLOWS DAY

Career Advice from the Pros

BY ERIC BOCK, CC

Persevere, learn from your mistakes, and work with collaborators, NIH Director **Francis Collins** told attendees at the first annual NIH Clinical Fellows Day, held on Friday, October 25, 2013. "Science doesn't work as a lonely enterprise," he said. "Make friends, seek out mentors, and look for the chance to team up with others."

Throughout the day, several other successful NIH physician-researchers offered career advice, too, including **Susan Leitman** (CC); **Marston Linehan** (NCI); **Elaine Jaffe** (NCI); **Electron Kebebew** (NCI); **Steven Holland** (NIAID); **Anthony Fauci** (NIAID); **H. Clifford Lane** (NIAID); and **Henry Masur** (CC). Below is an edited compilation of what they had to say:

What is rewarding about performing both research and patient care?

Leitman: A love of science motivates us. At NIH, we're pushing the envelope and are on the leading edge of discovery. The rewards of combining research and patient care are that we move the field forward and are always learning. The ability to collaborate is another benefit of academic medicine.

Linehan: There's nothing more honorable than taking care of patients. Having the opportunity to pursue ideas and take care of patients enabled us to make the progress we've made. If you are in an environment where you can collaborate, that's what medical science should be.

Jaffe: You have to do what you enjoy and what excites you. You have the opportunity to learn and grow from your patients. There's a unique opportunity with every patient to learn something to advance science.

Kebebew: What I enjoy about my work is I get to follow my nose. I wanted to make a significant impact on peoples' lives. At NIH, every patient you take care of is on a protocol that studies an important question. There's no better place than NIH to be exposed to the cutting edge of science.

Holland: People joke that "NIH" stands for "Not in a Hurry" or "Nerds in Heaven." Ask yourself if you are the right nerd for this heaven.

What were obstacles in transitioning from a trainee to an independent physician?

Leitman: I would have liked to have had training in statistics, time management, and leadership, but NIH didn't offer courses in those when I first came here (1980s). NIH offers such courses now and I recommend taking advantage of them. It's also important to learn to delegate with grace, to devise a scheme to distribute [tasks] among fellows and support staff.

Linehan: The biggest step was deciding whether I was going to tackle a question that was substantive. Another obstacle was deciding how to focus. People were skeptical of our decision to pursue the gene for kidney cancer, and it was initially difficult to find the right collaborators. But I persisted because my patients were dying and I didn't know of a better way to help them. It took me awhile to find my niche.

Jaffe: For women, balancing family with work was a challenge (in the 1970s), but today family demands are more equally shared. The biggest obstacle at NIH is that there's so much happening that it's tempting to go in 10 directions at once and not finish anything. Use your time wisely and don't get distracted. Don't start something new until you've finished what you've already begun.

Kebebew: Define your career goals and make sure they are in line with whichever institution you're transferring to. Take on challenges and start early to look for funding opportunities. Apply for eight to 10 grants to get a decent career-development award.

Holland: You're moving into an arena where the field is vast. You've got to define the problem you are going to explore and understand that you won't be able to master it in two years.

Fauci: Science is more complicated today. The resources are constrained, but the opportunities are unlimited. Since you cannot do it all, pick out a research question that is relevant and answerable.

Lane: The challenge is being able to identify the question that is relevant and [that] you can address. Maintain focus and don't get distracted by issues you can't control (such as furloughs or Continuing Resolutions).

Masur: Debt and attaining grants are big obstacles. Develop a passion, and stick with it as an investigator. Keep your clinical skills up-to-date so you can understand relevant questions.

How did you apportion research time?

Holland: The risk is in not getting your research finished. Choose what you're able to do and follow it. Set your eye on why, and you can't go far wrong. If you focus and keep working, it's hard to fail.

Linehan: The most important thing is to understand that what you learn about science during training is more important to you than what you work on. You're learning how to think about and do science. And read, read, read. Be the most critical person you can be. The most important person you don't want to fool is yourself. ●

The NIH Clinical Fellows Day was hosted by the Clinical Center's Office of Clinical Research Training and Medical Education and by the Foundation for the Advancement of Sciences. Read more career tips in the *NIH Catalyst* online at http://irp.nih.gov/catalyst/v22i1/the-training-page.

Crowdsourcing

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The Toxicogenetics Challenge was the brainchild of **Raymond Tice**, chief of the Biomolecular Screening Branch within the National Toxicology Program (an NIEHS-based interagency program for testing and evaluating substances in the environment), and **Allen Dearry**, director of NIEH's Office of Scientific Information Management.

"We're limited by our own experiences," said Tice. But "there are other groups...that will take a novel approach and potentially come up with something really exciting."

"This partnership and challenge [provide] powerful scientific insights and meaningful public-health impact by accelerating the pace of toxicity testing," Dearry added.

The three-month competition, which began on June 10, 2013, comprised two subchallenges that required the development of computer models to predict 1) how an individual's genetics affect responses to chemical exposures and 2) chemicals' toxicity to cells based on chemical-structure information.

The participants had access to data from one of the largest population-based toxicity studies ever conducted. They tested 884 human lymphoblastoid cell lines (from the NIH-led 1000 Genomes Project) that had been treated with 156 chemicals. The datasets were generated by NIEHS, NCATS, and UNC scientists. NCATS used its robotic equipment to conduct high-throughput assays that measured the effect of eight different concentrations of adenosine triphosphate (ATP). The lower the ATP concentration, the worse the cell population was growing.

The response was great: 34 teams submitted 99 entries to the first subchallenge; 24 teams submitted 85 entries to the second.

"The submission of so many models is a further testimony to the value of the data generated through our collaboration with NIEHS and UNC," said **Anton Simeonov**, NCATS's acting deputy scientific director. The challenge "capitalized on NCATS's [ability to] test thousands of chemicals, the NIEHS expertise in toxicology, and the UNC expertise in genomics."

The winning teams for both subchallenges were from the Quantitative Biomedical Research Center at the University of Texas Southwestern (Dallas). They will work with UNC and NIEHS researchers to publish their findings and algorithms in *Nature Biotechnology*.

Challenges such as the Toxicogenetics Challenge lead to a better understanding of the relationships between chemicals and genes, genes and pathways, and between genes and diseases, said Tice. ●

NCATS

The Toxicogenetics Challenge—hosted by NIEHS, NCATS, UNC, and two nonprofits—dared the computational informatics "crowd" to develop algorithms to predict the toxicity of 156 different chemicals. NCATS's Chemical Genomics Center used its Tox21 robot system to conduct high-throughput screens as part of the challenge.

NIH ABBREVIATIONS

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

Bill Gates Asks NIH Scientists for Help in Saving Lives

And Explains Why the Future Depends on Biomedical Innovation

BY REBECCA BAKER, NIAID

BILL BRANSON

Microsoft co-founder Bill Gates (left) visited NIH recently to tour labs, meet with institute directors, and deliver a lecture on "Why the Future Needs Biomedical Intervention," in which he thanked NIH for partnering with the Bill and Melinda Gates Foundation in projects that address poor health in developing countries. NIH and the Gates Foundation together provide more than half of all global-health research funding. After the talk, NIH Director Francis Collins (right) asked Gates questions that had been posed by NIHers.

"One of the makers of our modern world." A "visionary" in global health with "the energy and perseverance … to transform the world."

NIH Director **Francis Collins** was describing Superhero … err … global-health philanthropist Bill Gates, who co-founded Microsoft and the Bill and Melinda Gates Foundation. Gates visited NIH's Bethesda campus on December 2, 2013, to tour research labs, meet with institute directors, and deliver the David E. Barmes Global Health Lecture, "Why the Future Needs Biomedical Intervention."

The Gates Foundation, which was established in 2000 and has donated $28 billion for projects that include addressing extreme poverty and poor health in developing countries, "stands as a leader in the fight against many of the world's leading causes of death and disability," said Collins in introducing Gates. "In fact, [it has] transformed our approach to global health."

NIH and the Gates Foundation together represent 57 percent of all funding for global-health research and development on diseases that disproportionately affect populations in low-and middle-income countries: NIH supports 40 percent and the Foundation supports about 17 percent.

"I want to thank you for your partnership in many things that we do together," Gates told the crowd that had packed into Masur Auditorium. "It's a very broad partnership, touching a lot of your different institutes, [that] is growing over time."

NIH and the Gates Foundation are working together on many projects including determining enteric disease risk associated with malnutrition; developing HIV and malaria vaccines as well as innovative tuberculosis therapeutics; assessing the population effects of anti-retroviral therapy to reduce HIV transmission; developing nutritional biomarkers; understanding iron and malaria interactions; and more.

The Gates Foundation also focuses on providing vaccines to children in poor countries. Around the time Gates and his wife, Melinda, were establishing their foundation, they were astounded to learn that 250,000 children died each year of rotavirus, a diarrheal disease, even though a vaccine existed to prevent it. Only wealthy countries, however, could afford it. The foundation wanted to make that vaccine—and others—available and affordable to poor countries, too.

Vaccines for rotavirus as well as for measles, meningitis, and the pentavalent vaccine (which provides protection against diphtheria-tetanus-pertussis, hepatitis B, and *Haemophilus influenzae* type b) provide cost-effective and lasting protection against disease and are key tools for saving lives.

"A lot of [the] rotavirus constructs were created at NIH," Gates noted. He also cited the contributions of NIH intramural scientists **John Robbins** and **Rachel Schneerson**, who developed a vaccine to eradicate bacterial meningitis caused by *Haemophilus influenzae* type b. Robbins and Schneerson won the Lasker Award in 1996 for what the Lasker Foundation described as their "groundbreaking work and bold, visionary and imaginative leadership in the development and commercialization of the *Haemophilus influenzae* type b vaccine and bringing the vaccine to market, leading to the eradication of *Haemophilus influenzae* type b, typhoid, and pneumococcus."

"The effect of these vaccines is truly miraculous," said Gates. The Gates Foundation helps provide vaccines at tiered pricing so children in poor countries can receive them at marginal costs. "Over time, the cost of making most vaccines will get down to something like 20 or 25 cents per child treated and yet it can give you lifelong protection.

"To achieve the [foundation's] ambitious goals, we need your help," Gates continued. He acknowledged that developing vaccines is tough, especially for diseases such as human immunodeficiency virus (HIV) for which there is no natural immunity. Developing an HIV vaccine has been an important but elusive goal for both the foundation and NIH. "I'm certainly optimistic that we will get an HIV vaccine, although you couldn't give a timeframe for it." He lauded the "quite phenomenal" contributions by NIH intramural researchers in characterizing antibodies to HIV.

Another "very promising area" of intramural research is viral-based vaccine constructs that convert host cells into "a factory" of disease-fighting antibodies, enabling "protection more rapidly than natural immunity," Gates said. He was "thrilled" that NIH researchers "are pushing [vaccine research] forward."

Still, Gates expressed disappointment that U.S. funding for global health is dwindling even though funding from other countries is increasing. "Investing in research has huge paybacks in improving the human condition [and] in reducing health costs," he said. "I am an optimist. I think we'll be able to convince people that those investments should be restored and grow."

"It's really the kind of basic science work that you do that's made all of this [work] possible," Gates said. "We are just at the beginning of what we can do together." ●

The annual David E. Barmes Global Health Lecture was established in 2001 to honor the late David Edward Barmes, an ardent and lifelong supporter of global health, and is sponsored by NIDCR and the Fogarty International Center. A videocast of the Gates lecture is at http://videocast.nih.gov/launch.asp?18190.

NEWS FROM AND ABOUT THE NIH SCIENTIFIC INTEREST GROUPS

New SIG: Neuron-Glia Interactions

Research on brain function at a cellular level focuses on neurons, but non-neuronal cells, called glia, regulate neuronal communication and function in many ways. All types of glial cells can detect and influence functional activity in neurons. This rapidly emerging science cuts across all traditionally separate fields of brain-function research at NIH. The Neuron-Glia Interactions (NGI) SIG will bring together scientists investigating the relationships of neurons and glia, share the latest research on neuron-glia interactions, and serve as a platform for discussion and collaboration.

NGI will also serve those seeking information on and education about these relationships applying to their own research on processes of development, basic biological functions and mechanisms, and plasticity, in addition to diseases models and pathology. To encourage mentoring and career development, postdocs and students will have the opportunity to present their work to the group as part of the seminar series. The NGI SIG will also host speakers from outside NIH. NGI will meet the first Tuesday of every month and is open to members of the NIH community and researchers in the Baltimore-Washington metropolitan area. For more information, e-mail Amy Shafqat, amy.shafqat@nih.gov. To join the LISTSERV, send your request to neuron-glia@list.nih.gov.

New SIG: Dietary Supplements

The Dietary Supplement SIG was created to bring together NIH program officials and intramural investigators who are interested in dietary supplement research. As defined by Congress in the 1994 Dietary Supplement Health and Education Act, a dietary supplement is a product (other than tobacco) that is intended to supplement the diet; contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and other substances) or their constituents; and is intended to be taken by mouth as a pill, capsule, tablet, or liquid. The SIG will sponsor a monthly seminar series and quarterly meetings, and it will serve as a forum for discussion of current and future activities occurring in the field of dietary supplements. It is open to everyone at NIH and associated agencies (FDA, USDA, etc.) who share an interest in dietary supplements research.

To join the Dietary Supplements SIG and receive notifications of meetings and other events, contact Cindy Davis at davisci@mail.nih.gov.

About Scientific Interest Groups at NIH

NIH Scientific Interest Groups (SIGS) are assemblies of scientists with common research interests. These groups sponsor symposia, poster sessions, and lectures; offer mentoring and career guidance for junior scientists; help researchers share the latest techniques and information; act as informal advisors to the Deputy Director of Intramural Research (DDIR); provide advice for the annual NIH Research Festival; and serve as hosts for the Wednesday Afternoon Lecture Series. Many of the SIGs are co-sponsored by neighboring academic and government institutions and welcome interested non-NIH scientists. Information about group activities or new groups is published in the *NIH Catalyst* (http://irp.nih.gov/catalyst) and on the DDIR Web Board, which is for NIH staff only (http://www.nih.gov/ddir/DDIR.html). Some central coordination for the groups is provided by the Office of Intramural Research. The complete list of SIGs is at http://www.nih.gov/sigs. ●

Research Festival

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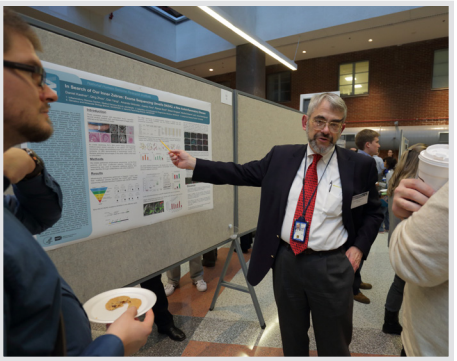
This year's festival celebrated two 60th anniversaries: James Watson and Francis Crick's landmark paper that first described the DNA double-helix structure, published in *Nature* on April 25, 1953 (*Nature* **171:**737–738, 1953); and the NIH Clinical Center, which was dedicated on July 2, 1953, and admitted its first patients four days later on July 6. In fact, the whole Research Festival took place in the Clinical Center—Masur Auditorium and in the newly opened Foundation for Advanced Education in the Sciences (FAES) Academic Center—instead of the Natcher Building (Building 45), where it's been held for years.

ERNIE BRANSON

Cutting the ribbon to celebrate the opening of FAES's new space in Building 10, where the Research Festival took place: (from left to right) FAES Executive Director Christina Farias; CC Director John Gallin; NIH Director Francis Collins; Deputy Director for Intramural Research Michael Gottesman; and Angela Gronenborn, president of FAES (former senior investigator in NIDDK and now at the University of Pittsburgh).

"We really wanted to make a translational connection," said Ferrucci. "We wanted to invite the people who are in the labs—our community—to celebrate instances where we can translate [basic science] into human health."

The plenary session featured three talks that highlighted how the focuses of the Festival—modern translational science at the Clinical Center and the study of DNA—have become intertwined in 21st century research. The first presentation, by Kastner, illustrated how new technologies have allowed researchers to discover the genetic basis of rare diseases using smaller and smaller cohorts of patients.



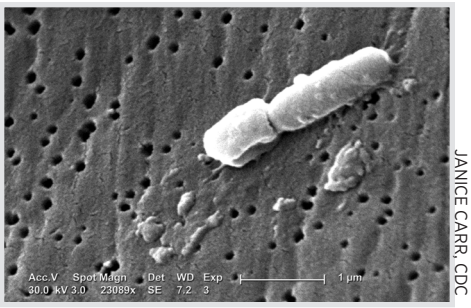
ERNIE BRANSON

In this year's Research Festival, even the Scientific Directors (SDs) presented posters. Dan Kastner, Research Festival co-chair and NHGRI SD (left), won first place for his poster and for his chocolate chip cookies. Luigi Ferrucci, fellow co-chair and NIA SD (right) explained his poster to Deputy Director for Intramural Research Michael Gottesman.

"With the advent of whole-exome sequencing and whole-genome sequencing, we have tools [that] allow us to take these cohorts of relatively rare patients, or even small families, and crack those cases in ways we weren't able to before," said Kastner. One of the cases he highlighted involved a young child who came to the NIH Clinical Center with early-onset stroke and fever. While the child was treated with steroids and began to get better, it wasn't until years later, when another child with the same symptoms came to the Clinical Center, that a sequencing analysis on just six individuals revealed that a single gene, with recessive inheritance, was responsible for the disorder. Mutations in the same gene, encoding the adenosine deaminase protein ADA2, were later found in several more patients with similar symptoms. "I think there's a very bright future in being able to solve some of those medical mysteries," said Kastner. "It allows us to . . . begin to parlay that [knowledge] into targeted therapies for those patients."

NHGRI senior investigator **Julie Segre** described another medical mystery that she and other NIH intramural investigators helped solve: What was causing the antibiotic-resistant *Klebsiella pneumoniae* infections that occurred at the NIH Clinical Center during 2011? In June of that year, a patient colonized with the bacterium was transferred to the Clinical Center; several weeks after her discharge, other patients at the Clinical Center were found carrying the same strain of antibiotic-resistant bacteria.

Traditional techniques for identifying bacteria can only broadly identify the strain. Segre, however, used new techniques for DNA sequencing to sequence the entire genome of each patient's infection, and she detected single base-pair changes. By tracing the path of infection through the hospital from patient to patient, she could help identify which additional methods were needed to eliminate the bacteria from the Clinical Center. "What has really driven me into this area of research is the extent



JANICE CARR, CDC

Julie Segre (NHGRI) described her team's efforts to determine the cause of antibiotic-resistant *Klebsiella pneumoniae* infections that were occurring among gravely ill, immune-compromised patients in the NIH Clinical Center in 2011. This scanning-electron micrograph reveals some of the ultrastructural morphologic features of the bacterium.

to which health-care-associated infections contribute to the public's concern about seeking health care," said Segre. "Hospital infection control, with mandatory testing, is going to be crucial." (To read more, see the November-December 2012 issue of the *NIH Catalyst* at http://irp.nih.gov/catalyst/v20i6/intramural-detectives.)

Next it was **Cynthia Dunbar's** turn to describe her own detective work. Dunbar, a senior investigator in the National Heart, Lung, and Blood Institute (NHLBI), studies how hematopoietic stem cells produce cells that repopulate the immune system. Her model is the rhesus macaque because its hematopoietic and immune systems closely match that of humans. After introducing genetically "barcoded" hematopoietic stem cells into the macaques, she applied high-throughput sequencing techniques to detect cells derived from the original stem cells. She found that myeloid cells and B cells are closely related in the hematopoietic hierarchy, but there is no evidence for a common lymphoid progenitor. Most interesting were her findings regarding natural killer cells, which showed an ontogeny distinct from T, B, and myeloid cells. "The molecular techniques [allow] us to approach the body like science fiction investigators in ways we never imagined would be possible," said Dunbar.

After the plenary session, the Research Festival continued with poster sessions and concurrent symposia and, of course, the Scientific Directors Poster Session and Cook-off, a competition for the best poster presentation and the best home cooking.

Ferrucci "suggested the cook-off," said Kastner. "He [said he] would prepare a batch of traditional Italian biscotti and he threw down the gauntlet to the other scientific directors, to see [whether] they could measure up to his standards of culinary excellence." In the end, the 2013 NIH Research Festival weathered the bumps of the government shutdown and subsequent rescheduling.

"It was [a] terrific...opportunity for people to get together again after the shutdown, to make scientific and other connections [at] the NIH," said Kastner.

"I thought [the festival] was re-energizing," said Ferrucci. "I felt that spirit come out . . . the enthusiasm, of just doing the science [and] finding and showing your results."

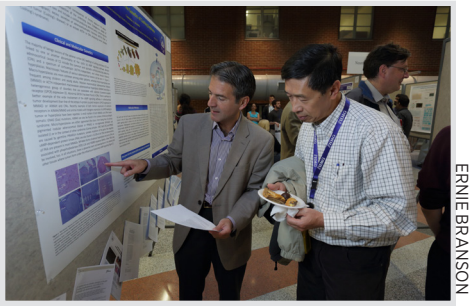
To see a video of the plenary session, go to http://videocast.nih.gov/launch.asp?18152 For a YouTube video of Festival highlights, go to http://youtu.be/TilycWcU_zk.

POSTERS AND COOKIES AND SCIENTIFIC DIRECTORS, OH MY

BY JENNIFER SARGENT, NIAMS

One of the strengths of the intramural research program is that those in leadership maintain productive labs. And so it was fitting that the scientific directors (SDs) presented scientific posters at the Research Festival (and competed in a cooking competition).

Constantine Stratakis (NICHD) presented an overview of recent advances in understanding Cushing syndrome, a disorder characterized by obesity and muscular weakness due to high concentrations of the hormone cortisol. His work represented the combined efforts of more than 100 trainees in his lab over the past 20 years.



ERNIE BRANSON

NICHD Scientific Director Constantine Stratakis (left) explained his poster to NHGRI Deputy Scientific Director Paul Liu. Stratakis's poster provided an overview of recent advances in understanding Cushing syndrome.

NCCAM's scientific director **Catherine Bushnell** highlighted changes in the brains of patients who suffer from chronic pain. Even Deputy Director for Intramural Research **Michael Gottesman** joined in the fun (his lab is in NCI) with a poster featuring the analysis of biomarkers that determine drug resistance in cancer cells.

It was a rare occasion for fellows to turn the tables on the SDs and quiz them on their scientific knowledge. Judges evaluated the posters and voted by secret ballot to determine the winner. To ensure fairness, each of the institutes nominated a fellow to serve on the panel of judges.

Festival goers were invited to savor a spectacular array of homemade treats. Much of the spread was inspired by the directors' cultural heritages, reflecting the vibrancy and international diversity found in labs throughout NIH. In addition to many variations of the traditional American chocolate-chip cookie, attendees were treated to a cornucopia that included rugelach, Greek baklava, Italian biscotti, Hungarian sausage, Louisiana pecan kisses, and chocolate-covered strawberries.

And the winners? Well, there was only one: **Daniel Kastner,** Research Festival co-chair and scientific director of NHGRI. He took the prize with his poster describing his group's recent identification of a new autoinflammatory disease, adenosine deaminase 2 deficiency, in which the deficiency of a protein leads to a spectrum of vascular disease and systemic inflammation. And he won over the crowd and the judges with his "Butterlicious Chocolate Chip Crepes with Funfetti Frosting."

Kastner thoroughly experimented and optimized his methods in the kitchen. Check out the video at http://youtu.be/hjuo4D_WDdw.

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SELECTED SYMPOSIA

SUGAR, SUGAR

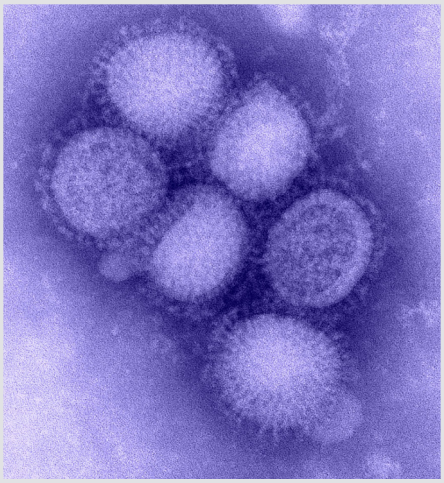
BY ERIC BOCK, CC

When Julie Andrews sang, "Just a spoonful of sugar makes the medicine go down" in the 1964 Disney film *Mary Poppins*, could she have inspired budding scientists to one day explore the therapeutic value of sugars? After all, the field of glycobiology, which is the study of complex sugar molecules, or glycans, was launched more than 20 years after the movie came out. Today, scientists at NIH and elsewhere hope that a better understanding of glycobiology can be leveraged for therapeutic and diagnostic purposes and may even lead to the development of more effective vaccines.

Malfunction of a nuclear-cytoplasmic signaling pathway involving the simple glycan *O*-linked *N*-acetylglucosamine (*O*-GlcNAc) is involved in immunity-linked human diseases ranging from diabetes to lupus, explained **John Hanover** (NIDDK), who has identified and characterized the genes encoding the enzymes of *O*-GlcNAc cycling.

The intracellular carbohydrate *O*-GlcNAc plays an important role in the innate immune response of the nematode *Caenorhabditis elegans* and may hold the key to understanding the immune response to pathogens, according to FARE Winner **Michelle Bond** (NIDDK). Loss of the enzymes governing the addition and removal of *O*-GlcNAc triggers stress- and immune-responsive genes.

In the vaccine arena, **Joanna Kubler-Kielb** (NICHD) described the development of vaccine candidates consisting of carbohydrate antigens bound protein carriers in order to protect against infections caused by Gram-negative bacteria genera such as Bordetella and Brucella. **Jeffrey Gildersleeve** (NCI), whose lab uses carbohydrate antigen microarrays to study immune responses to vaccines, has identified new biomarkers for predicting clinical responses to cancer vaccine therapy.



JANICE CARR, CDC

Flu vaccines may be improved once scientists have a better handle on glycobiology and glycans. Seema Lakdawala (NIAID) is researching the role of glycans in the 2009 pandemic H1N1 flu virus and found that the receptor specificity of H1N1 is more complex than previously thought. Shown: Transmission electron micrograph of the H1N1 influenza virus.

Even flu vaccines may be improved once scientists have a better handle on glycobiology and glycans. **Seema Lakdawala** (NIAID), who is researching the role of glycans in the 2009 pandemic H1N1 flu virus, found that the receptor specificity of H1N1 is more complex than previously thought. Evidence suggests that flu viruses infect host cells by binding to a wide range of acidic sugars.

From the 2013 Research Festival's session "The glycobiology of immunity and infection," chaired by Pamela Marino (NIGMS), and held on November 8, 2013.

To see a videocast of the 2013 Research Festival plenary session presented on November 6, 2013, go to http://videocast.nih.gov/launch.asp?18152

PAIN, PAIN, PAIN

BY ADAM J. KUSZAK, NIDDK

Increasingly, researchers across NIH are tackling chronic pain in an attempt to understand its mechanisms and how to treat or prevent it. That news should come as welcome relief to the 100 million Americans who suffer from debilitating, persistent pain, which may be triggered by physical trauma; may be linked to arthritis, cancer, or other conditions; or may have no apparent cause at all.

Take fibromyalgia, a disorder characterized by widespread musculoskeletal pain, abnormal pain processing, fatigue, sleep disturbances, memory problems, psychological distress, and mood issues. No one knows for sure what causes it, but it affects three million to six million Americans. NINR's **Brian Walitt** outlined the ailment's history and discussed current debates on whether fibromyalgia is a product of disordered neural pain processing or a result of psychological and cultural factors.

NCCAM's Scientific Director **M. Catherine Bushnell** has identified one effect of fibromyalgia-associated chronic pain on the brain: According to magnetic resonance imaging studies, fibromyalgia patients have reduced gray matter in brain regions related to pain processing. Bushnell has also investigated links between other chronic-pain conditions and the brain. She found that successful surgical treatment of chronic lower-back pain slowly reverses brain atrophy, and long-time yoga practitioners have higher gray-matter density in pain tolerance regions of the brain. Her work suggests that neuroprotective approaches may benefit chronic-pain patients.

Even diet may play a role in controlling chronic pain as many pain-signaling compounds are derived from dietary fats. **Christopher Ramsden** (NIAAA) and extramural colleagues conducted a clinical trial to assess how dietary modification could decrease

the incessant pain of chronic headaches. They hypothesized that pain signals could be decreased by altering dietary proportions of omega-6 and omega-3 fatty acids. Indeed, these dietary modifications did alter pain-signaling compounds and reduce headaches. The researchers are conducting a larger trial to expand upon these encouraging results.

New insights into the mechanisms of nociception (perception of pain) came from NIDCR's **Mark Hoon** and FARE Award Winner **Leah Pogorzala**, who works in his lab. They are studying sensory neural circuits involved in thermosensation and itch; those pathways overlap with pain signaling. Pogorzala has identified neuron populations that respond to hot and cold stimulation; Hoon explained the delineation of neuronal pathways for itch responses. Their findings are paving the way to a greater understanding of sensory and pain perception.

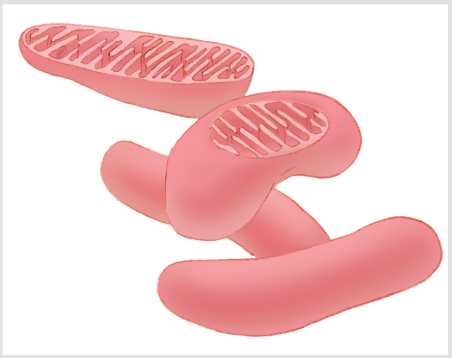
From the 2013 Research Festival's session "Pain and nociception: From patients to molecules," chaired by Mark Hoon (NIDCR), and held on November 6, 2013.

AGING MOLECULARLY

BY REBECCA BURGESS, NCI

The seemingly unstoppable process of aging is the major biological risk factor for many chronic diseases including cancer, heart disease, and type 2 diabetes. The discovery that aging not only is an accumulation of random damage, but also is governed by molecular mechanisms that are susceptible to manipulation and intervention, suggests that trans-NIH aging research could potentially address multiple chronic diseases all at once.

One important area in this field is cellular energy sensing and balance. Aging has been linked to increased obesity, declining mitochondrial function, and decreased thermogenesis, indicating a switch from "energy-using" to "energy-storing" mode. Reversing this energy mode through caloric restriction has been shown to extend life span. How the cell senses and responds to its energy state involves the sirtuin proteins, which alter chromatin organization and gene-expression programs.



JUDITH STOFFER

Aging has been linked to increased obesity, declining mitochondrial function, and decreased thermogenesis, indicating a switch from "energy-using" to "energy-storing" mode. Mitochondria (shown above) are the cells' power plants. Damaged mitochondria accumulate during aging and are marked for elimination by a self-eating process called mitophagy.

Jay Chung (NHLBI) presented data showing a new way the mammalian sirtuin 1 (SIRT1) senses the energy status of the cell: It has an adenosine triphosphate (ATP)–dependent peptide switch that is "on" during energy depletion, whereas excess ATP binds this switch region and blocks SIRT1 activity in the "off" state. Global chromatin organization by SIRT1 is also altered by DNA damage, causing global gene-expression changes similar to those found in aged cells. New work from **Philipp Oberdoerffer** (NCI) suggests that DNA damage signals chromatin structure to affect the way cells repair DNA damage.

To better understand the cellular changes that occur upon caloric restriction, **Jennifer Lippincott-Schwartz** (NICHD) examined cell components in nutrient-deprived yeast. She found that cells display an "self-eating" response, called lipophagy, which involves digesting intracellular lipids. Lipophagy requires fusion of individual mitochondria into a tubular network, suggesting that lipid recycling and mitochondrial function are amplified for an efficient response to starvation.

Damaged mitochondria, in contrast, accumulate during aging and are marked for elimination by a different self-eating process called mitophagy. This process requires the parkin protein, whose gene, *PARK2*, is mutated in some autosomal recessive forms of Parkinson disease. **Chiu-Hui Huang** (NINDS) discussed her team's new mouse model for Parkinson disease, which required more than simply eliminating endogenous parkin. To see Parkinson-like effects, they had to mimic age-dependent mitochondrial DNA damage accumulation with a second mutation in a mitochondrial DNA polymerase.

Age-related decreases in mitochondria-rich, heat-producing brown fat relative to lipid-storing white fat is linked to the onset of obesity, type 2 diabetes, and other disorders. FARE Award winner **Lingyan Xu** (NIDDK) identified a role for forkhead box (FOX) family transcription factors in brown versus white adipocyte balance. Xu found that mice deficient in the protein Foxa3 have increased energy expenditure and thermogenesis due to the "browning" of white adipose tissue. These mice were protected against age-related obesity and insulin resistance, suggesting that Foxa3 ablation could be a novel therapeutic target to treat aging-associated metabolic disorders.

As the links between metabolism and aging continue to emerge, the ancient Hippocratic notion of food as medicine may unlock a modern fountain of youth.

From the Research Festival session "Molecular Mechanisms of Aging," chaired by Felipe Sierra (NIA), sponsored by the GeroScience Interest Group, and held on November 8, 2013.

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Research Festival

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NEUROGENETIC ANALYSIS

BY MEGHAN MOTT, NIAAA

New technological advances are revolutionizing our understanding of the human brain and may provide clues to treating, preventing, and curing brain disorders and diseases. NIH researchers with expertise in genetics, physiology, and microscopy are collaborating to map brain function in hopes of discovering how neural circuits control behavior and of determining how disruptions in brain function occur in such diseases as schizophrenia and autism.

Chi-Hon Lee (NICHD) combines behavioral, imaging, and molecular genetic approaches to study visual circuit development and function in Drosophilia. By selectively inactivating and restoring the synaptic activity of different types of neurons, Lee's lab is dissecting color-vision circuits that drive color learning. Another Drosophila researcher, **Susan Harbison** (NHLBI), investigates the genetic networks underlying sleep and their interactions with the environment. She uses high-throughput genotyping to observe heritable differences in sleep patterns and has demonstrated how significant changes in sleep occur in just a few generations. She is also investigating how DNA polymorphisms and variation in transcript, protein, and metabolite concentrations lead to differences in sleep.

Jeffrey Smith (NINDS) uses optogenetics to unravel the brain networks responsible for breathing. Optogenetics involves taking a gene for light-activated membrane channels targeted to a single neuron type, inserting it into a mouse genome, and then shining a light into the brain to turn those neurons on or off. He is also using whole-cell patch-clamp recording techniques to study the biophysical and synaptic properties of respiratory circuits in the brainstem and to explain the neurogenesis of respiratory movements.

NIH

NIH researchers are mapping brain function to determine how neural circuits control behavior and how disruptions in brain function occur in diseases such as schizophrenia and autism.

To understand how neuronal circuits develop, **Tudor Badea** (NEI) combines molecular genetics tools—conditional gene ablation and reporter-gene replacement—to label individual neurons in the retina, visualize the morphology and connectivity of specific cell populations, and study their role in the visual system.

Fumihito Ono (NIAAA) wants to answer fundamental questions about neuromuscular development and function. In particular, he uses the genetic tools of locomotor mutants, cell-specific transgenics, and a chemically inducible gene-expression system to see how neuromuscular synapses form in zebrafish.

In other research exploring synapses, FARE Award Winner **Carmelo Sgobio** (NIA) studies presynaptic calcium modulation in midbrain neuron terminals. He uses tetracycline-controlled transcriptional activation to reveal how synaptic transmission at nerve terminals is mediated and regulated.

From the 2013 Research Festival session "Neurogenetic analysis of behavioral circuits," chaired by Harold Burgess (NICHD) and Kevin Briggman (NINDS), and held on November 7, 2013.

T CELLS THROUGH OLD AGE

BY CHRIS PALMER, NCI

T cells play an important role in the immune system's response to pathogens and tumor cells. However, to prevent autoimmunity, the body's T-cell population must be monitored to ensure proper development and homeostasis. Several labs at NIH investigate the molecular pathways that regulate normal T-cell development as well as the challenges to T-cell homeostasis brought on by cancer chemotherapies and the natural aging process.

To minimize autoimmunity, T cells expressing self-reactive T-cell antigen receptors (TCR) undergo programmed cell death (apoptosis). **Paul Love** (NICHD) created knock-in mice in which TCR signaling is significantly reduced, disrupting apoptosis. Surprisingly, the mice failed to develop autoimmune diseases, leading Love and his colleagues to suggest the existence of a compensatory pathway for immune tolerance that results in the increased development of regulatory T cells (Tregs). **Xuguang Tai** (NCI) has identified the pro-apoptotic and pro-survival signaling mechanisms by which a transcription factor called forkhead box P3 regulates the development of regulatory Tregs that help prevent autoimmune disease.

Nan-ping Weng (NIA) has developed a next-generation sequencing method to characterize the diversity of TCRs. His group discovered that CD4 T cells have twice as many unique TCRs as CD8 T cells do, and the group observed age-related alteration of TCR repertoire in people 45 to 65 years old, but not in people 75 to 94 years old.

Joy Williams (NCI) reported that the development of medullary thymic epithelial cells (mTEC), which depends on the presence of a type of thymocyte—called single positive (SP) thymocytes and eliminates autoreactive T cells—relies on the activation

of a particular pathway. When this pathway is activated, mTECs can develop even in the absence of SP thymocytes.

Frank Flomerfelt (NCI) discovered that the thymus, brain, and testes-associated gene (*Tbata*) regulates thymic epithelial cell proliferation and thymus size by blocking a pathway implicated in cell-cycle progression. His group observed that *Tbata* expression increases with age and that deletion of *Tbata* results in a larger thymus later in life.

Treating cancer often leads to immunosuppression. FARE Award Winner **Liat Izhak** (NCI) studies the cross-modulation among the various immunosuppressive mechanisms that are driven by Tregs and natural killer T cells.

From the 2013 Research Festival's session "T-cell development, aging, and thymus regeneration," co-chaired by Paul Love (NICHD) and Nan-ping Weng (NIA), and held on November 8, 2013.

USING RNAI TO DISCOVER GENES

BY SUMAN MUKHERJEE, NIDDK

Gene silencing through RNA interference (RNAi) has become a standard laboratory tool for assessing gene function, but to make the jump to discovery on a large scale most intramural scientists need help. This is where the NCATS's Trans-NIH RNAi Screening Facility comes in: Using genome-wide RNAi screening, intramural investigators can make exciting discoveries about the role of genes and pathways associated with human diseases. **Scott Martin**, the leader of the Trans-NIH RNAi Screening Facility, outlined how his team goes about helping intramural scientists to develop and perform genome-wide RNAi screens. RNAi studies on this scale also need careful data analysis. **Gene Buehler** (NCATS) uses computational analysis to eliminate false-positive results and to identify disease-associated genes. His work has been critical to the success of the many screening projects the NCATS team has helped develop.

Lesley Kane (NINDS) and colleagues are using genome-wide RNAi screening to better understand the parkin-mediated mitochondria quality-control mechanism. Mutations in the gene *PARK2*, which codes for parkin, are known to cause Parkinson disease. Using a cell-based, high-content assay of parkin translocation, Kane's group has identified several new genes involved in this process and recently published its findings in *Nature (Nature* **504:**291–295, 2013).

Another NINDS group, led by **Barrington Burnett**, uses genome-wide RNAi screening to identify genetic modifiers of spinal muscular atrophy (SMA). SMA is a debilitating neurological disease that leads to muscle weakness and wasting and is caused by a deficiency of the survival motor neuron (SMN) protein. The screen identified a number of genes—including some associated with splicing and protein stability—that affect SMN protein concentrations.

Matthew Hall (NCI) gave a presentation on a microRNA functional genomic screen that identifies novel regulators of proteins that mediate resistance to the chemotherapy drug cisplatin. Hall has identified several microRNAs and their targets that are responsible for tumors becoming resistant to cisplatin. His group is currently following up this work with a whole-genome RNAi screen of protein-encoding genes.

CARLEEN KLUMPP, NCATS

Gene silencing through RNA interference (RNAi) has become a standard laboratory tool for assessing gene function, but to make the jump to discovery on a large scale most intramural scientists need help. NCATS's Trans-NIH RNAi Screening Facility has automated systems, like the one shown here, that perform genome-wide RNAi screening.

The audience was also treated to a presentation by FARE Award Winner **Tuan Tran** (NIAID). Tran described a novel method for assessing malaria risk: Looking for naturally acquired antibodies specific for the *Plasmodium falciparum* parasite protein PfRH5, whose presence predicted protection from malaria in a cohort of children and adults in Mali.

From the 2013 Research Festival's session on "Genes and pathway discovery in the context of human diseases," chaired by Scott Martin (NCATS) and Natasha Caplen (NCI), and held on November 7, 2013.

READ MORE ONLINE AT:
http://irp.nih.gov/catalyst/v22i1/the-best-research-festival-ever

Tricking Viruses into Treating Disease
BY REBECCA G. BAKER, NIAID

Optogenetic Manipulation of Neural Circuits and Behavior
BY JOSEPH P. TIANO, NIDDK

Seriously Studying Stem Cells
BY ERIC BOCK, CC

Breast is Still Best: Infant Dietary Guidelines Get an Update for the 21st Century
BY REBECCA BURGESS, NCI

Natural Born (Cancer) Killers
BY CHRIS PALMER, NCI

IN 2012

Benjamin T. Burton (died on December 22, 2012, at age 93), an NIDDK associate director for disease prevention and technology transfer, was at NIH for more than 34 years. He helped develop protein supplements to fight malnutrition and build new technology for kidney dialysis.

IN 2013

R. Wayne Albers (died on September 28, 2013, at age 85), who came to NIH in 1954, was a world-recognized neuroscientist noted for his research in the field of membrane cation transport and neuronal excitability. He was a former chief of the Section on Enzyme Chemistry in the NINDS Laboratory of Neurochemistry.

Lynne Angerer (died on March 30, 2013, at age 68) was chief of the developmental mechanisms section in NIDCR and a world-renowned expert in developmental biology. Using sea urchins, she unraveled the core regulatory processes that direct the early development of animal embryos. Her husband and long-term scientific collaborator is NIDCR Scientific Director Bob Angerer.

Joanne Hebb Belk (died on March 4, 2013, at age 89) directed NIH's compliance with the Freedom of Information Act (1977–1998).

Costan W. Berard (died on January 5, 2013, at age 80) came to NCI in 1963. As chief of the hematopathology section (1970–1980), he and colleagues revolutionized the treatment of malignant lymphoma and Hodgkin disease. He was chairman of the department of pathology and laboratory medicine at St. Jude Children's Research Hospital in Memphis (1980–1997).

John "Jack" Bieri (died on July 30, 2013, at age 93) served as head of the nutritional biochemistry section in NIDDK's Laboratory of Nutrition and Endocrinology (1955–1983). His studied the metabolism of vitamins A and E and essential fatty acids and developed the NIH standard diet for laboratory rodents.

George F. Borge (died on August 7, 2013, at age 75) was a staff psychiatrist at NIMH, where he developed his interest in treating alcoholism and depression. He served as chief of the psychiatry service at Edward Hines Jr. V.A. Hospital outside Chicago (1976–1999).

Thomas P. Cameron (died on November 28, 2013, at age 87) was a veterinarian who later became a captain in the U.S. Public Health Service and an official at NIH. When he retired in 1993, he was an assistant coordinator of NCI's environmental carcinogenicity program.

Sheldon Cohen (died March 26, 2013, at age 94) joined NIH in 1972 as a training consultant to NIAID. The following year, he became chief of the Allergy and Immunology Branch, and later the director of the institute's Immunology, Allergic, and Immunologic Disease Program (1977–1988). He continued to work at NIH as a scientific advisor at NIAID and as a visiting scholar at the National Library of Medicine's History of Medicine Division.

Ricardo V. "Rick" Dreyfuss (died March 14, 2013, at age 58) was a photomicroscopist He worked for more than 25 years—until his death—in the Division of Medical Arts, Office of Research Services. His photomicrographs graced the covers of countless scientific journals.

Juliana D. Franz (died on May 24, 2013, at age 84), who practiced psychiatry in Maryland for more than 50 years, worked as a medical officer and psychiatrist at NIMH (1953–1970).

Emil Frei III (died on April 30, 2013, at age 89) was one of the first to use combination chemotherapy to treat cancer. He was at NCI for 10 years in the 1950s and 1960s, where he did his seminal work on chemotherapy for which he subsequently won a Lasker award in 1972. Frei also held senior leadership positions at the M.D. Anderson Cancer Center (Houston) and the Dana-Farber Cancer Institute (Boston).

Audrey Georges (died on March 6, 2013, at age 76) retired in 2009 as administrative lab manager at NEI after a 17-year career at NIH.

Ronald Herberman (died June 2, 2013, at age 72) was a senior investigator and held leadership positions in NCI (1966–1985). His lab discovered a new category of lymphocytes, now called natural killer cells. Later he studied their role in resistance to cancer growth. He left NIH to become the founding director of the University of Pittsburgh Cancer Institute.

Jean Hickman (died on August 26, 2013, at age 89), who retired in 2008 after 57 years at NIH, was a bench scientist in the Laboratory of Physical Biology in the National Institute of Arthritis and Metabolic Diseases (1951–1984). After the institute split into NIDDK and NIAMS, she became a scientific review officer in the NIAMS Extramural Program.

Daniel Hommer (died on January 2, 2013, at age 64) had been chief of NIAAA's section on brain electrophysiology and imaging since 1992. He was world-renowned for his discoveries on structural and functional differences in brains of alcoholic and nonalcoholic individuals. He co-directed the electrophysiology unit of NIMH's Clinical Neuroscience Branch (1982–1987).

Juan-Teh Jeang (died on January 27, 2013, at age 54), a researcher at NIAID's Laboratory of Molecular Microbiology, studied the factors that influenced the spread of retroviruses. In 2004 he co-founded *Retrovirology*, which became the highest ranked journal in the field. He did postdoctoral work in NCI.

Edward J. Leonard (died on December 28, 2013, at age 87), one of the early NIH clinical fellows (1950s), retired after a 49-year career at NIH as director of the Immunopathology Section in NCI's Laboratory of Immunobiology. Among his major accomplishments was the identification of macrophages, neutrophils, and their chemoattractant factors.

Carol H. Letendre (died on August 22, 2013, at age 75), a former deputy director of NHLBI's Division of Blood Diseases and Resources, spent 32 years at NIH, 20 of them at NHLBI. She helped guide research that led to such advances as an understanding of the role of blood clots in heart attacks. Early in her career, she was a research chemist in NICHD's Laboratory of Biomedical Sciences.

W. Chadwick "Chad" Leyshon (died on May 20, 2013, at age 87) began his career in 1954 as a medical technician in the Clinical Center. He later worked as a biologist at the National Institute of Dental Research (now NIDCR).

Lewis "Lew" E. Lipkin (died on September 24, 2013, at age 87) was head of the Imaging Processing Section in the National Institute of Neurological Disease and Blindness (now NINDS) and later head of NCI's Imaging Processing Section. In the 1970s, he conceived of and initiated the real-time picture processor, one of the first special-purpose hardware computers developed for gray-scale image processing and designed to aid in biological image analysis. He worked at NIH 1962–1994.

Walter Magruder (died on November 28, 2013, at age 98) retired from the federal government in 1974 after 40 years of service. His career spanned many agencies, including NIH—with the National Microbiological Institute (now NIAID), NCI, and NIAMS.

Robert L. Martensen (died on September 26, 2013, at age 66) directed the Office of NIH History until his retirement (2007–2012). Previously, he had been a physician in emergency rooms and intensive-care units and a professor in bioethics and medical history at Harvard and Tulane. At NIH, he expanded the Stetten fellow research program, which brings in postdocs in medical history, and built up the office.

Nancy K. Mello (died on November 25, 2013, at age 78), who became a leading researcher in the field of substance abuse, directed a research program at NIMH's National Center for Prevention and Control of Alcoholism. In 1974, she and her husband co-founded the Alcohol and Drug Abuse Research Center at McLean Hospital (Belmont, Mass.).

John Milner (died on December 31, 2013, at age 66), well known for his broad understanding of nutrition and its role in cancer prevention, was chief of the Nutritional Science Research Group in NCI's Division of Cancer Prevention (2000–2012). After leaving NIH, he became the director and senior scientist at the U.S. Department of Agriculture's Human Nutrition Center (Beltsville, Md.).

Peter T. Mora (died January 11, 2013, at age 88) conducted research for about 25 years at NCI and helped develop protease inhibitors to help prolong the lives of AIDS patients. Mora, who arrived at NCI in the late 1950s, retired in the mid-1980s as a supervisor in cancer research in NCI's macromolecular biology section.

Candace B. Pert (died on September 12, 2013, at age 67) was a neuroscientist and pharmacologist who, while in graduate school, helped to discover the opiate receptor. She held several research positions at NIMH (1975–1987), culminating as chief of the Section on Brain Biochemistry. In 1987, she left NIH to form a biotech company with her husband.

Robert Neil Philip (died on January 30, 2013, at age 89), a former NIAID epidemiologist, served for more than 30 years in the Public Health Service, including appointments at NIH in Bethesda (1949–1956) and at NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Mont. (1960–1982). Philip was recognized internationally for his contributions to the diagnosis and control of Rocky Mountain spotted fever. Philip's father, Cornelius B. Philip, had also worked at RML (1930–1970).

Michael Potter (died on June 18, 2013, at age 89), a scientist at NCI whose research led to greater understanding of tumors and the immune system, won the Lasker award in 1984 for his fundamental research into the genetics of immunoglobulin molecules. He joined NCI in 1954 and worked there for more than 50 years. He was a principal investigator in NCI's Laboratory of Cell Biology and was chief of the Laboratory of Genetics (1982–2003).

Milton Puziss (died on October 9, 2013, at age 93), a microbiologist who helped develop the first human vaccine against anthrax in the United States in the late 1950s, joined NIAID in 1968 and retired as chief of the bacteriology and virology branch in 1986.

Sonia I. Skarlatos (died on August 6, 2013, at age 59) was deputy director of the NHLBI Division of Cardiovascular Sciences. During her 20-year career with NHLBI, Skarlatos became a national and international leader in vascular science and was one of NIH's most respected leaders in advancing an agenda to support translational research. Skarlatos's husband is Howard Kruth, a senior investigator in NHLBI.

John L. Swanson (died on July 8, 2013, at age 76) helped revitalize NIAID's Rocky Mountain Laboratories (RML) by championing the latest tools and methods in microbiological investigation in the 1980s. He came to RML in 1979 and started internationally recognized research programs on the bacteria that cause gonorrhea, chlamydia, and Lyme disease. He was chief of RML's former Laboratory of Microbial Structure and Function (1979–1997) and retired in 2001.

Rodney Ulane (died on March 7, 2013, at age 69) was a NIH microbiologist and director of scientific programs at the Office of Extramural Research and spent a total of 24 years at NIH. He held various positions beginning in 1971 including in what is now NIAMS, NICHD, Center for Scientific Research, and NIGMS. He left NIH in 1991, to run M.D.-Ph.D. programs at two medical schools, and returned to NIH in 2009.

Charles L. Williams, Jr. (died on January 5, 2013, at age 96), represented the United States at international health conferences and was a director of international research at NIH. After 26 years in the U.S. Public Health Service, Williams became deputy director of the Pan American Health Organization, a branch of the World Health Organization, in 1967. He was later executive vice president of the American Association for World Health (1979–1980). ●

READ EXPANDED VERSIONS OF THESE OBITUARIES AND ADDITIONAL ONES ONLINE AT:
http://irp.nih/catalyst/v22i1/obituaries

Recently Tenured

SUSAN AMARA, NIMH

JULIA COOPER, NCI-CCR

MARIANA KAPLAN, NIAMS

SCOTT YUNG HO KIM, CC

SAM MBULAITEYE, NCI-DCEG

SUSAN AMARA, PH.D., NIMH

Scientific Director of NIMH; Principal Investigator, Laboratory of Molecular and Cellular Neurobiology, Section on Molecular and Cellular Signaling

Education: Stanford University, Stanford, Calif. (B.S. in biological sciences); University of California, San Diego (Ph.D. in physiology and pharmacology)

Training: Postdoctoral training at U. of California, San Diego, and Yale (New Haven, Conn.)

Before coming to NIH: Professor and chair of the Department of Neurobiology and co-director of the Center for Neuroscience at the University of Pittsburgh

Came to NIH: In 2013

Selected professional activities: Member, National Academy of Sciences (chair, Section 23); past president, Society for Neuroscience; Board of Scientific Counselors, NIAAA Scientific Advisory Board, Gladstone Institute of Neurological Disease; scientific advisory board, Brain and Behavior Research Foundation; scientific advisory board, and Gill Center for Biomolecular Medicine

Outside Interests: Traveling around the world with her husband; relaxing with a good cup of coffee

Research interests: My research examines the effect of psychostimulant and antidepressant drugs on the signaling properties, physiology, and acute regulation of neurotransmitters. My lab has demonstrated that transporter proteins can serve dual functions as transporters and as substrate-gated ion channels, revealing additional mechanisms by which carriers regulate neuronal excitability. Such transporter proteins are targets for addictive drugs and for medications that treat mental disorders such as depression and attention deficit hyperactivity disorder. These proteins play key roles in neuronal communication, memory, and learning.

As the scientific director for NIMH's intramural research program, I am promoting an environment that is conducive to productive research and the training of clinical and basic scientists. NIMH researchers study the behavioral, systems, cellular, and molecular mechanisms of normal brain function as well as conduct clinical investigations into the diagnosis, treatment, and prevention of mental illness (including mood disorders and anxiety, schizophrenia, obsessive-compulsive disorder, attention deficit hyperactivity disorder, and pediatric autoimmune neuropsychiatric disorders). The intramural research program has the opportunity to do many innovative things at different levels and that one can't do elsewhere. The ability to be nimble and occasionally take risks is a unique aspect of the intramural research program.

JULIA PROMISEL COOPER, PH.D., NCI-CCR

Senior Investigator and Head, Telomere Biology Section, Laboratory of Biochemistry and Molecular Biology

Education: Emory University, Atlanta (B.S. in biology); University of Colorado Health Sciences Center, Denver (Ph.D. in biochemistry/biophysics/genetics)

Training: Postdoctoral training at NIADDK (now NIDDK and NIAMS); University of Colorado at Boulder (Howard Hughes Medical Institute); and Imperial Cancer Research Fund (London; now Cancer Research UK)

Before coming to NIH: London Research Institute, Cancer Research UK

Came to NIH: In 1992 for training

Selected professional activities: Organized several international conferences

Outside interests: Traveling; hiking; eating; cooking; going to the theater; spending time with her adult children

Research interests: I and my lab focus on telomeres, the nucleoprotein complexes that form the ends of linear chromosomes. Telomeres protect our genomes and choreograph chromosome movements; they affect a range of biological processes from cancer avoidance to healthy gamete formation. They prevent the degradation and fusion of chromosome ends and ensure that natural chromosome ends do not elicit the cell-cycle arrest pathways that respond to

damage-induced DNA breaks. Telomeres are a particular focus of our research on tumorigenesis (which is associated with genomic instability and telomerase activation) and aging (which is accompanied by a progressive decline in telomere length). However, the complete repertoire and underlying mechanisms of telomere function are not yet understood.

The telomeres of fission yeast are remarkably similar to those of humans but provide precise genetic manipulability. Concepts we have developed by studying fission yeast telomeres have been shown to predict observations in mammals. We are exploring the cell-cycle regulation of telomere function, the fascinating roles taken on by telomeres in controlling spindle formation and centromere assembly during meiosis, and surprising ways in which some cells (such as telomerase-minus cancer cells) can survive in the absence of canonical telomeres.

MARIANA KAPLAN, M.D., NIAMS

Senior Investigator; Chief of the Systemic Autoimmunity Branch

Education: National Autonomous University of Mexico, Mexico City (M.D.)

Training: Internal medicine residency at the National Institute of Medical Sciences and Nutrition (Mexico City); rheumatology fellowship/postdoctoral training at University of Michigan (Ann Arbor, Mich.)

Before coming to NIH: Professor of medicine, Division of Rheumatology, U. of Michigan

Came to NIH: In 2013

Selected professional activities: Member, American Society of Clinical Investigation; Lupus Foundation of America Scientific Advisory Council; adjunct professor, University of Michigan; Section Editor, *Journal of Immunology* (2009–2013)

Outside interests: Spending time with her family; traveling; playing piano; reading literature; listening to music

Research interests: My research has focused on unraveling the fundamental mechanisms that lead to the development and perpetuation of systemic autoimmune disorders, particularly systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), and their associated organ damage. I and my lab are trying to determine how and why premature vascular damage and atherosclerosis occur in SLE and RA, with an interest in how innate immune responses contribute to endothelial perturbations. We are characterizing how abnormal neutrophil responses in autoimmune disorders contribute both to the loss of immunological tolerance and to end-organ damage, including the putative role of neutrophil extracellular traps (networks of extracellular fibers, primarily composed of DNA from neutrophils, which bind pathogens). I am also interested in doing preclinical and clinical studies and trials to identify novel biomarkers and therapeutic targets that may prevent premature vascular damage and chronic inflammation in systemic autoimmunity.

SCOTT YUNG HO KIM, M.D., PH.D, CC

Senior Investigator, Department of Bioethics

Education: Wheaton College, Wheaton, Ill. (B.A. in philosophy); University of Chicago, Chicago (Ph.D. in philosophy); Harvard Medical School, Boston (M.D.)

Training: Residency in psychiatry, Massachusetts General Hospital (Boston); National Research Service Award in Geriatric and Neuropsychiatric Psychopathology Research, University of Rochester (Rochester, N.Y.)

Before coming to NIH: Co-director, Center for Bioethics and Social Sciences in Medicine, University of Michigan (Ann Arbor)

Came to NIH: In 2013

Selected professional activities: Author of *Evaluation of Capacity to Consent to Treatment and Research* (Oxford, 2010); professor of psychiatry (adjunct), U. of Michigan

Outside interests: Trout fishing; music; sports (remains a loyal Michigan Wolverine)

Research interests: Most of my work has focused on the ethics of human subject research—the assessment of the decision-making capacity of people who are potential subjects of clinical research; surrogate consent for dementia research; ethics of sham neurosurgical trials; and informed consent and therapeutic misconception—as well as some work on the reform of institutional review boards.

Because bioethics is still an evolving field in terms of empirical research, I'm very interested in using a variety of methods to integrate theoretical and empirical approaches. For example, we've used a method called democratic deliberation in which our subjects spend a day learning and deliberating about a complex bioethical issue. We can then obtain from them more considered ethical views than just their impressionistic opinions. We've also used mixed methods (in-depth qualitative interviews along with experimental surveys that use a philosophical linguistics framework) to examine whether research subjects conflate research participation with treatment—a phenomenon called "therapeutic misconception" that is thought to be highly prevalent but which we are finding may be due to a measurement problem. And I've begun some new collaborative projects in the Department of Bioethics, which I'm finding to be a wonderfully collegial place.

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

CONTINUED ON PAGE 18

Recently Tenured

CONTINUED FROM PAGE 17

SAM MBULAITEYE, M.D., NCI-DCEG

Senior Investigator, Infections and Immunoepidemiology Branch, NCI Division of Cancer Epidemiology and Genetics (DCEG)

Education: Makerere University, Kampala, Uganda (MBChB and M.Med. in internal medicine); University of Cambridge, Cambridge, U.K. (M.Phil. in epidemiology and biostatistics)

Before coming to NIH: Senior medical officer, Uganda Virus Research Institute (Entebbe)

Came to NIH: In 2000 as a research fellow; became tenure-track investigator in 2005

Selected professional activities: Adjunct lecturer at George Washington University School of Public Health (Washington, D.C.); editorial board member, *International Journal of Cancer* and *Frontiers in Cancer Epidemiology and Prevention*; co-editor-in-chief, *Infectious Agents and Cancer*

Outside interests: Biking; hiking; jogging; running marathons; stargazing

Research interests: Burkitt lymphoma (BL) is the most common childhood cancer in Africa and the third most common lymphoid malignancy in developed countries. My work seeks to measure the association between malaria markers (parasite prevalence, load, and genotypes) and the immune response to malaria proteins in patients at risk for BL. I am interested in understanding how this relationship is modified by other infections—such as Epstein–Barr virus (EBV), human immunodeficiency virus (HIV), and stool parasites—that are common in children with BL. I am the principal investigator in the Epidemiology of Burkitt Lymphoma in the East African Children and Minors (EMBLEM) study, a multiyear, multisite study of childhood BL (http://dceg.cancer.gov/research/cancer-types/lymphoma-burkitt-hodgkin-non-hodgkin/burkitt-lymphoma-emblem). Using questionnaire data and genomic methods, I will evaluate the association between malaria-resistance gene polymorphisms, malaria parasite diversity, and EBV genetic variants with BL. Additionally, in collaboration with the NCI Office of Cancer Genomics, I am using fresh-frozen tumor tissues collected from a subset of BL cases to conduct BL tumor genome sequencing. My studies may lead to the discovery of molecular abnormalities that drive BL and that may be targeted for therapy or prevention.

My work on BL outside of Africa seeks to measure the risk of BL in immunosuppressed populations, such as those who are HIV-positive or receive immunosuppression medications to prevent rejection of transplanted organs. I am conducting studies to investigate whether BL in settings where malaria is absent differs from BL in Africa. ●

PECASE WINNERS

The Presidential Early Career Awards for Scientists and Engineers (PECASE) are the highest honor bestowed by the U.S. government on outstanding scientists and engineers beginning their independent careers. NIH intramural scientists have been on the list of PECASE recipients every year since 1997. Congratulations to the 2012 winners: **Jessica Gill** (NINR), who is seeking effective ways to identify trauma patients who are at high risk for psychological and neurological deficits and inform the interventions that will support their recovery; **Susan Harbison** (NHLBI), who is investigating the genetic networks underlying sleep and their interactions with the environment; and **Todd Macfarlan** (NICHD), who is exploring fundamental mechanisms of gene regulation and epigenetic inheritance during embryo development.

DEMYSTIFYING MEDICINE

Tuesdays, starting January 7, 2014

4:00–6:00 p.m.

Building 50, Conference Room

The "DeMystifying Medicine" course, in its 13th year, bridges the gap between advances in biology and their application to human disease. Each class features presentations by a clinician, a researcher, and often a patient. For more information visit http://demystifyingmedicine.od.nih.gov or contact Win Arias at ariasi@mail.nih.gov.

January 7: "Worldwide Emergence of Drug-resistant Infections and What's Being Done about It"; Anthony Fauci (NIAID), Jeffrey Taubenberger (NIAID)

January 14: "Itching (Pruritus): Mechanisms, Diseases, and Treatment"; Mark Hoon (NIDCR); Irwin Arias (NICHD/CC)

January 21: "Cancer Screening: Science vs. Intuition (Example Prostate Cancer)"; Barnett Kramer (NCI), Peter Pinto (NCI)

January 28: "Adaptor Diseases: Bridging Cell Biology and Medicine"; Juan Bonifacino (NICHD), Craig Blackstone (NINDS)

February 4: "Obesity: Etiology, Pathogenesis, and Why Weight Loss Is Difficult"; Jack Yanovski (NICHD), Kevin Hall (NIDDK)

February 11: "HIV: Changing Paradigms and the Washington-Baltimore Scene"; John Coffin (NCI), Henry Masur (CC)

February 18: "Pertussis (Whooping Cough): A Lesson in Vaccines"; John Robbins (NICHD), Alexandra Freeman (NIAID)

February 25: "Chromosomal Translocation: Cellular Mechanism and Clinical Consequence"; Tom Misteli (NCI), John Barrett (NHLBI)

March 4: "The Intestinal Microbiome: Role in Nutrition, Metabolism, and Inflammation"; Yasmine Belkaid (NIAID), Warren Strober (NIAID)

March 11: "Water, Water Everywhere and Not a Drop to Drink"; Karen Frank (CC), Gordon Hager (NCI)

March 18: "Drug-Induced Liver Injury: Who, What, When, and How"; Leonard Seefe, (formerly NIH/FDA), Chris Austin (NCATS)

March 25: "Human Papillomavirus: Preventing Cancer"; Douglas Lowy (NCI), Carter Van-Waes (NIDCD)
April 1: "Sleep: Perchance to Dream"; Carolyn Beebe Smith (NIMH), Susan Harbison (NHLBI)
April 8: "Drug Resistance in Cancer: Mechanisms and Management"; Michael Gottesman (NCI), Antonio Tito Fojo (NCI)
April 15: "HAV and HCV RNA Viruses: Clinical and Basic Advances and Challenges"; Marc Ghany (NIDDK), Nihal Altan-Bonner (NHLBI)
April 22: "Transplanting Hearts and Other Organs"; Jonah Odim (NIAID), Allison Sklarew (Washington Regional Transplant Community)
April 29: "Malaria: Origin and Advances in the World's Major Killer"; Beatrice Hahn (University of Pennsylvania), Carolina V. Barillas-Mury (NIAID)
May 6: Finale (to be announced)

"PLASTICITY BEYOND THE SYNAPSE—REGULATION OF MYELINATION BY ACTION POTENTIALS"

Neuron-Glia Interactions (SIG) Lecture
Tuesday, February 4, 2014
2:00–3:00 p.m.
Building 40, Room 1201/1203

Douglas Fields (NICHD senior investigator and section chief; editor-in-chief of *Neuron Glia Biology*) will be making a presentation at the Neuron-Glia Interactions SIG meeting. All meetings and the SIG are open to all members of the NIH community and extramural researchers in the Baltimore-Washington metro area. For more information contact Amy Shafqat at amy.shafqat@nih.gov. To join the LISTSERV, send your request to neuron-glia@list.nih.gov. (See page 7 for more on this SIG.)

THE OFFICE OF DIETARY SUPPLEMENTS (ODS) RESEARCH SCHOLARS PROGRAM

Letters of Intent due May 2

The ODS Research Scholars Program is a one-year competitive scholarship opportunity to study the role of dietary supplements in health promotion and disease prevention. This program is targeted to early-career scientists, including tenure-track investigators, early independent scientists, research fellows, staff fellows, and postdoctoral fellows who have at least one year of postdoctoral research experience. Projects are generally limited to one year of funding and cannot exceed $100,000. For more information, contact Cindy Davis at davisci@mail.nih.gov.

POSTDOCTORAL RESEARCH ASSOCIATE (PRAT) PROGRAM

Application deadline: March 7, 2014

The PRAT program, sponsored by NIGMS, is now accepting applications for the fall 2014 class. PRAT is a competitive fellowship program providing up to three years of support for fellows conducting research within the NIH or FDA Intramural Research Programs. Fellows participate in an ongoing scientific seminar series tailored to the PRAT program, as well as receive additional training in a variety of career skills and mentoring. Research proposed by PRAT fellows encompasses a wide variety of emerging areas of science, but a particular emphasis is placed on projects incorporating aspects of quantitative and systems pharmacology or computational biology. Additional information about eligibility, definition of research areas of emphasis, and the application process can be found at http://www.nigms.nih.gov/Training/pages/PRAT.aspx or contact the PRAT program director at prat@nigms.nih.gov or 301-594-3827.

TRANSFORMATIONAL MEDICINE IN THE MITOCHONDRIAL AGE

Wednesday, April 2, 2014
8:00 a.m.–4:00 p.m.
(WALS 3:00–4:00 p.m.)
Poster Abstracts due February 28, 2014
Event URL: https://2014migsymposium.eventbrite.com

All are welcome to attend this day-long symposium, which includes the Wednesday Afternoon Lecture in the late afternoon. The morning session on "Mitochondria and the Brain" and the afternoon session on "Mitochondria, Cancer, and Innovative Technology" will feature scientists from NIA, NICHD, NINDS, NHLBI, NCI, Johns Hopkins, and the University of Maryland School of Medicine. The WALS speaker, Doug Wallace (Perelman School of Medicine, University of Pennsylvania), will give a presentation entitled "A Mitochondrial Etiology of Metabolic and Degenerative Diseases, Cancer and Aging." Registration is not required unless you wish to submit a poster abstract. Two poster abstracts will be chosen by intramural NIH scientists for platform presentations. The WALS portion will be videocast and archived at http://videocast.nih.gov. To submit poster abstracts or for information about the speakers, go to https://2014migsymposium.eventbrite.com. To request reasonable accommodation, contact Steve Zullo at steven.zullo@nih.gov or 240-271-7097 or call the Federal Relay, 800-877-8339.

NIH MANAGEMENT INTERN PROGRAM

Unlock a New Career Path
Recruiting: April 7–11, 2014

The NIH Training Center is pleased to announce the new recruitment season for Management Interns (MIs). The MI program is a highly competitive, two-year career-development program for current NIH employees. MIs come from a variety of job backgrounds including scientific and administrative fields. On completion of the program, MIs transition into an administrative or management career in one of many areas throughout NIH. Eligible employees are invited to apply. For program FAQs, upcoming information sessions, and details about eligibility, visit http://trainingcenter.nih.gov/intern/mi/.

NLM SPECIAL EXHIBIT: FROM DNA TO BEER

http://www.nlm.nih.gov/exhibition/fromdnatobeer
On display through April 18, 2014
History of Med. Reading Room, NLM (Bldg. 38)

"From DNA to Beer: Harnessing Nature in Medicine and Industry" explores some of the processes, problems, and potential inherent in technologies that use microorganisms for health and commercial purposes. ●

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CATALYTIC REACTIONS?

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

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

Dale Lewis, a staff scientist in NCI's Laboratory of Molecular Biology, took the prize-winning photo (above, right).

PHOTOGRAPHIC MOMENT

Doing It Right

DALE LEWIS, NCI

Dale Lewis (NCI) won first place in the third annual "In-Focus Safe Workplaces for All" photography contest for this image that shows how postdocs **Sangmi Lee** (left) and **Zhong Qian** are safely handling radioactive materials in the lab. Both are wearing protective face shields, clothing, and gloves while they are disposing of the materials in approved containers. Lewis, who has been at NIH for more than 19 years and has been taking pictures for as long as he can remember, also won second place in this year's contest for a photo of window washers in action. Sponsored by the Division of Occupational Health and Safety in the Office of Research Services, the "In-Focus Safe Workplaces for All" contest challenged anyone with a passion for photography to use their imagination and creativity to capture an image of workplace safety and health and share it with the NIH community.

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

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