THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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Resveratrol Revealed

Discovery by NHLBI Researchers

BY JUSTIN CHEN, NICHD

Many believe that resveratrol—a chemical found in red wine as well as in grapes, peanuts, and other plants—protects against aging-associated diseases such as type 2 diabetes. But no one has fully understood how it works. In February, senior investigator **Jay H. Chung** and colleagues at the National Heart, Lung, and Blood Institute published a paper explaining how resveratrol affects enzymes that increase the activity of the aging-associated protein Sirtuin 1 (Sirt1). (*Cell* **148**:421-433, 2012).

Over the years, resveratrol and Sirt1 have been the subjects of intense debates that have thrown reputations, grants, and the biology of aging into question. At the heart of the resveratrol story is the human desire for good health and longevity. Resveratrol mimics the effects of calorie restriction (CR), which since the 1930s has been known to stretch, and even double, the lifespans of mice. CR can also prevent cancer, heart disease, neurodegenerative diseases, age-related loss of muscle mass, and type 2 diabetes in mice. But most humans will not tolerate the kind of restricted diets that have been imposed on mice. Instead scientists are looking to resveratrol and other CR-mimicking compounds that show promise as anti-aging agents.

A major breakthrough occurred in 2000 when scientists at the Massachusetts Institute of Technology (Cambridge, Mass.),

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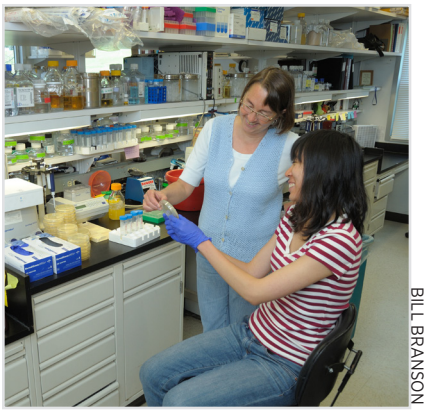
Grad Students Unite

The NIH Graduate Partnerships Program

BY MEGHAN MOTT, NIAAA

On the road to doing independent scientific research, graduate school is a rite of passage. And so is the NIH—at least for the students who choose to do their dissertation work there. Their Ph.D. still comes from an academic institution, but it's based on research done in an NIH intramural laboratory. This setup is all part of the Graduate Partnerships Program (GPP).



BILL BRANSON

Graduate student Xuefeng Yin (right), who is getting her Ph.D. in microbiology from Peking University in China, is doing her dissertation research in the lab of NICHD senior investigator Gisela Storz (left) .

"GPP offer[s] depth and breadth in research topics, world-class resources in and outside the lab, and leading scientists [who are] happy to collaborate and contribute to your training," said **Kimberly Decker**, who got her Ph.D. in molecular biology from Johns Hopkins University (Baltimore) in 2011 and did her research at the National Institute of Diabetes and Digestive and Kidney Diseases. She's now a postdoctoral fellow at the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

"The NIH is a unique place to get a Ph.D.," said **Augustin Luna**, who is getting a Ph.D. in bioinformatics from Boston University (Boston) and working in **Mirit Aladjem**'s lab at the National Cancer Institute (NCI). "Since there are primarily postdocs here, what is expected of a student . . . is higher than in other places. [And] there is always acknowledgement and credit for work done."

The GPP typically attracts students who are interested in translational or clinical research. They often provide an intellectual spark in the lab, bringing new ideas and questions that a principal investigator may not otherwise consider. They are "very independent, mature, highly motivated, and productive," said Deputy Director for Intramural

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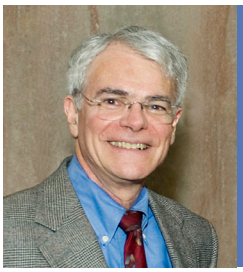


Once and Future Graduate Education

BY MICHAEL GOTTESMAN, DDIR

This issue of the *Catalyst* includes an article by Meghan Mott about the history and current status of the NIH Graduate Partnerships Program (see page 1). The article summarizes the birth of the program as a natural progression of NIH's long-term interest in supporting graduate students in our laboratories and clinics and describes the outstanding situation for our graduate students in formal partnerships as well as those in individual agreements with degree-granting universities. The article and my discussions with the author evoked some happy (and not so happy) memories that I thought I would share.

For almost as long as there has been an intramural program, there have been graduate students here. You cannot keep students away from one of the most exciting, vibrant, and creative environments anywhere for conducting biomedical research. Originally, they wandered in because there was someone here with whom they wanted to work; or they followed scientists, who were constantly being recruited from academia; or they were here in another capacity and wanted to earn a doctoral degree as a reflection of the scholarly work they were already doing. The most famous personification of the last situation was Julius Axelrod, winner of the 1970 Nobel Prize in Physiology or Medicine for his work on neurotransmitters. He earned his Ph.D. from George Washington University (Washington, D.C.) based on research he was already conducting at NIH.

In the 1970s, then–Deputy Director for Intramural Research (DDIR) DeWitt "Hans" Stetten was convinced that having a degree-granting graduate school at the NIH would enrich our research community. But a survey of intramural scientists at the time revealed only lukewarm enthusiasm for this idea. About half of the senior investigators who were contacted indicated that the mission of the NIH did not include training graduate students. Instead, the Foundation for Advanced Education in the Sciences (FAES), a nonprofit that has been fostering scientific education at NIH since 1959, continued to expand its graduate-level courses and other programs.

When Harold Varmus became the NIH director in 1993, one of his goals was to establish a formal graduate program here. He enlisted me as his DDIR to move this vision forward. We felt that the presence of graduate students would ensure a more critical intellectual environment at the NIH; allow us to undertake longer-term projects suitable for graduate theses; and enable us to share the riches of this place with students who would benefit enormously from an NIH experience. We had discussions with NIH senior faculty about developing a unique curriculum for our graduate scholars, requirements for admission, faculty responsibilities, and a mechanism for central oversight of the students. When the time came for me to present our detailed proposal to the Advisory Committee to the Director (ACD) on June 3, 1999, I was excited and confident that our proposal would earn the endorsement of the ACD.

The rest is history; many of the members of the ACD—particularly those who had been at the NIH and benefited (like me and Harold Varmus) from the training here—were enthusiastic. But other prominent academics on the ACD worried about whether NIH had the know-how to take on this new responsibility; whether establishing a new graduate program was a good idea when the United States was already beginning to produce more Ph.D.s than the country could employ as independent investigators; and whether (perhaps with tongue in cheek) we might be so successful that all of the top graduate students in the country would flock here, undermining NIH-supported academic centers.

So we put our heads together, and the idea for the Graduate Partnerships Program (GPP) was conceived. We decided not to seek independent status as a degree-granting institution, but agreed to work with many partners to provide training for students who could benefit from spending time at NIH.

As the article makes clear, the GPP has been a huge success. But where do we go from here? The GPP has grown haphazardly over the past 12 years. Programs have been added without consideration of the overall balance of students. We need to think about what we would like our graduate student body to look like. Then we should ask potential partners and GPP directors to make a case for how new partnerships would advance our overall goals. Our extramural colleagues who are experienced as graduate educators can help us evaluate our programs as well as suggest how best to move forward. While for the moment we won't initiate any new institutional agreements, new graduate students who are under individual agreements will continue to come to the NIH. As I previously noted, there is no way to keep them away—nor would we want to. ●

Linking Genes, Environmental Exposure, and Disease

Using the NIEHS Environmental Polymorphisms Registry

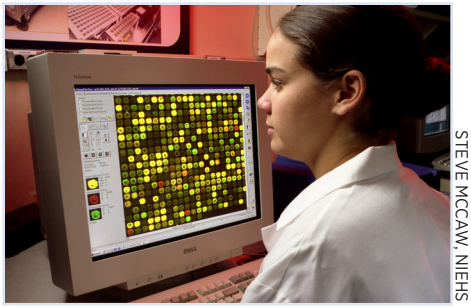
BY ROBIN ARNETTE, NIEHS

Large cohort studies usually begin with a group of individuals who were exposed to a common risk factor or who exhibit a particular set of health traits. Researchers then analyze the individuals' DNA for gene differences, also known as polymorphisms, that may be linked to disease.

But if scientists want to initiate cohorts the other way around, starting with polymorphisms to look for associated traits or disease risks, they might consider using the Environmental Polymorphisms Registry (EPR) (http://www.niehs.nih.gov/research/clinical/join/epr/), a project sponsored by the National Institute of Environmental Health Sciences (NIEHS) in Research Triangle Park, N.C. The EPR provides access to DNA from more than 17,000 individuals, who may be called back for more detailed studies. By looking at DNA variants in the genes first, investigators can validate previous results and do more stringent biological experiments.

When the EPR was launched in 2005, its goal was to help researchers understand how the interaction between genes and environmental exposures led to the development of disease. As the number of DNA deposits grew, EPR administrators were pleased to find that their repository offered several advantages, one of them being its strong representation of minorities.

"The EPR was set up to reflect the diverse populations of North Carolina," said **Stavros Garantziotis**, principal investigator in the NIEHS Laboratory of Respiratory Biology and medical director for the NIEHS Clinical Research Unit. "Now 25 to 30 percent of the active EPR population is African-American and approximately six percent is of Hispanic origin."



STEVE MCCAW, NIEHS

Researchers who receive samples from the NIEHS EPR may use several techniques—such as microarray technology, shown above—to determine the function and expression levels of new genes.

HOW TO ACCESS EPR SAMPLES

EPR offers an easy application process and is available to intramural researchers as well as other scientists interested in using its data. Detailed instructions appear on the EPR Web site (http://www.niehs.nih.gov/research/clinical/join/epr/researchers/index.cfm), but, essentially, scientists must:

- Complete a request form
- Submit a brief project proposal
- Sign a Material Transfer Agreement

All documents must be submitted to Garantziotis by e-mail at garantziotis@niehs.nih.gov. He coordinates the EPR steering committee review. If approved, investigators receive DNA for analysis. If researchers want to take the project one step further and conduct a study by contacting EPR volunteers, the steering committee needs to authorize the project a second time before scientists go through the usual process of working with their Institutional Review Board (IRB). This additional EPR approval protects volunteers by affirming that the study is beneficial and worthy of their time.

One researcher involved in an ongoing EPR study is **John Cidlowski**, head of the NIEHS Laboratory of Signal Transduction. He studies glucocorticoids, steroid hormones that suppress inflammation, and their receptors. Previous research suggests that single nucleotide polymorphisms (SNPs) in the glucocorticoid receptor gene increase the risk of cardiovascular events and metabolic syndrome in Caucasian populations.

But "the incidence of glucocorticoid receptor SNPs has not been well determined in non-Caucasian populations," Cidlowski said. "So our lab is comparing gene expression profiles of macrophages isolated from EPR participants, which are then exposed ex vivo to glucocorticoids."

POWERFUL GENETICS TOOL

The EPR will be even more useful after three upgrades: a detailed questionnaire, the ability to use geospatial information, and, in the future, linking EPR to electronic medical records.

The questionnaire contains more than 100 questions that cover 30 major health topics, such as lung and heart health, endocrine and reproductive issues, and occupational exposures.

Geospatial Information Systems technology connects the EPR population to home addresses, which yield a wealth of knowledge including general location, census data, socioeconomic stresses, pollution exposures, and water sources.

Linking EPR volunteers to electronic medical records will give scientists instant access to cross-sectional and longitudinal health information so that they can follow the development and progression of a disease. "We will be careful to ask for consent and have it vetted by the IRB," Garantziotis said.

With these added features, the EPR enhances its utility and reinforces its research significance by testing for complex diseases and uncommon traits that exist in the population. ●

Women's Education—Women's Empowerment

A Panel Discussion on Women's Leadership

BY SILVIYA ZUSTIAK, NICHD

"Educate a boy, and you educate an individual. Educate a woman, and you educate a community," said NCCAM Director **Josephine Briggs**, who delivered the opening remarks for a NIH Women's Leadership Panel Discussion entitled "Women's Education—Women's Empowerment," held in observance of the 2012 Women's History Month (March).

Four of NIH's accomplished women shared their stories about what it was like to be pioneers and fight for having it all–a career and a family: **Yvonne Maddox**, deputy director for NICHD; **Susan Shurin**, acting director for NHLBI; **Belinda Seto**, deputy director for NIBIB; and **Janine Clayton**, acting director for ORWH. Only 30 years ago, this panel might not have been possible: Women then were expected to be homemakers. It took many strong-willed women to rebel against tradition and carve a path for us all. Nowadays women are becoming increasingly involved in conventionally male-dominated fields such as science, engineering, and politics.

The panelists led us through their journeys of acquiring an education and the crucial people and events that shaped their career paths. A story shared by Maddox left a deep impression on me. She told us how she used to sleep in her office during graduate school and when her female mentor discovered that, she simply advised her to get used to it: Being a woman in science meant working harder than any man. Maddox followed the advice and worked hard to build a career that would give her a long-lasting satisfaction while also raising her family.

All panelists had accumulated their own pieces of wisdom to impart to the next generation of leaders, both men and women: Seek out many mentors and be a good mentee, be proactive, tackle the situation at hand, know what you want and go for it at your own pace, let the life you lead be of your creation, take calculated risks, adopt rigorous standards and always challenge yourself, and finally, be a generous mentor and teacher to others.

A true leader is one who learns from the difficulties to be overcome and turns them into victories, added Seto. Other advice also emerged from the panelists' incredible personal stories: Don't give up, don't accept that something is impossible, be true to yourself, be your own advocate, be a good role model—you are one even if you don't realize it. Shurin also reminded us that we must take responsibility if we really want to make a change.

I think that we, the women in the audience, all felt similarly that day—the times are changing. Some argue that women still need to work harder than men, but it is not as difficult as it once was, because we have a choice. It is up to us to take the challenge and in pursuit of a career, to become an integral part of a drive to shape a society that is tolerant of sex differences in any profession. ●

ERNIE BRANSON

(Left to right) Yvonne Maddox (deputy director for NICHD), Susan Shurin (acting director for NHLBI), Belinda Seto (deputy director for NIBIB), and Janine Clayton (acting director for ORWH) shared their stories of being pioneers in a male-dominated scientific world.

2012 NIH RESEARCH FESTIVAL

October 9–12, 2012

Don't miss this annual showcase of NIH intramural research. The opening session—"The NIH at 125: Today's Discoveries, Tomorrow's Cures"—celebrates NIH's humble beginnings as a one-room laboratory created within the Marine Hospital Service in 1887. Other features: concurrent symposia, posters, the scientific equipment tent show, and opportunities to enjoy lively entertainment and conversation with colleagues. For more information, contact Jacqueline Roberts (robertsjm@od.nih.gov or 301-594-6747).

The BTRIS Information Center

A Support Team Stands Ready to Help You

BY JIM DELEO, CC

The BTRIS Information Center (BIC) opened on April 19, 2012, in the NIH Library through a combined effort of the members of the NIH Clinical Center and the NIH Office of Research Services. BTRIS—the Biomedical Translational Research Information System—is a user-searchable repository of clinical research data from the Clinical Center and other NIH Institutes and Centers. BTRIS development began in 2008 in the NIH Clinical Center Laboratory of Informatics Development (LID), which is under the leadership of **Jim Cimino**.

BTRIS is available to all investigators working in human studies at NIH. It provides access to data associated with research subjects. In addition, BTRIS provides all NIH researchers access to all BTRIS data in subject de-identified form. BTRIS contains a vast amount of data, including laboratory results, vital signs, radiologic reports (with links to radiographic images), medication administration data, and clinical documents. It provides users with advanced search, filtering, and aggregation methods to create data sets to support ongoing studies and to stimulate ideas for new research.

Multiple reports are available through BTRIS—reports that can easily be produced with a user-friendly series of prompts. BTRIS also provides some analytic support tools such as the Lifelines2 visualization tool from the University of Maryland (College Park). LID's Computer Science Section led by **Jim DeLeo** is also available for consultations and support pertaining to more specialized data analyses, especially analyses that support the translational research and translational medicine objectives of the NIH Roadmap. As BTRIS continues to develop, data from new sources and new report features will be added monthly.

MICHAEL SPENCER

The support team at the BTRIS Information Center in the NIH Library will help investigators use a searchable repository of clinical research data (left to right, Rhonda Sanford, Shweta Bhangdia, Teferra Alemayehu, Mark Schermerhorn, and Jim DeLeo).

The BIC, which is located on the first floor of the NIH Library near the information desk, provides information and general support to those wanting to use BTRIS to view, analyze, and extract BTRIS data. A basic kiosk BTRIS tutorial and handouts will be available whenever the library is open. Personnel trained to use the BTRIS will staff the BIC Monday through Friday from 8:30 a.m. to 3:30 p.m. They will demonstrate BTRIS and provide consultation on data access and data processing. For more information, contact Jim Cimino (ciminoj@cc.nih.gov or 301-443-9696) or Jim DeLeo (james.deleo@nih.gov or 301-496-3848).

Additional support is available by calling the BTRIS Hotline (301-827-8270) and by e-mailing btrissupport@mail.nih.gov. Also, an NIH-wide BTRIS Interest Group has been established to bring together present and prospective BTRIS users so they can communicate, learn and share experiences related to using BTRIS, and develop a voice, vision, and communication channel to enhance BTRIS service. See adjacent column for details on this interest group.

For more information about BTRIS, visit http://btris.nih.gov. ●

BTRIS Interest Group

BY JIM DELEO, CC

This interest group brings together present and prospective users of the Biomedical Translational Research Information System (BTRIS) so they can communicate, learn and share experiences related to using it in their work, and develop a voice, vision, and communication channel to enhance its service. Initially, BTRIS membership will be open to NIH employees only, and meetings will take place monthly starting in Fall 2012. These meetings will consist of talks and brainstorming sessions. For more information, contact the chair, Jim DeLeo (jdeleo@nih.gov or 301-496-3848). To join the LISTSERV, go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=btris&A=1. A Web site is being planned.

Neuro-infectious Disease Interest Group (NIDIG)

BY AVINDRA NATH, NINDS

NIDIG is a forum for the exchange of ideas for developing research projects on the effects of the human immunodeficiency virus (HIV) and other infections on the brain and the development of new diagnostic and therapeutic approaches for these infections. Research seminar meetings will be held on the third Wednesday of each month, 10:00–11:30 a.m., in Building 10, Room 2-3750. The presentations are preceded by a 30-minute period in which researchers can interact in a more relaxed manner. The forum also invites selected extramural investigators from other institutions to present their findings and interact with members of the NIDIG. We maintain a LISTSERV (https://list.nih.gov/cgi-bin/wa.exe?SUBED1=NEURO-ID-RESEARCH&A=1) and a Web page (http://sigs.nih.gov/neuroID/Pages/default.aspx). In February each year, the group holds a retreat. For more information, contact Barbara Jaruga (Barbara.jaruga@nih.gov). ●

Resveratrol

CONTINUED FROM PAGE 1

who were working with yeast, proposed that CR worked through the Sir2 protein (the yeast version of mammalian Sirt1). Then, in 2003, Harvard (Cambridge, Mass.) researchers reported that resveratrol increased the activity of Sirt1, in a test tube, and extended the lifespan of yeast. Suddenly, it seemed possible that resveratrol might be a cure for aging. Unfortunately, laboratories in the United States and England have failed to replicate the original breakthrough results.

Chung—who earned an M.D.-Ph.D. from Harvard, trained in internal medicine at Brigham and Women's Hospital (Boston), and first came to the NIH as an endocrine fellow in the National Institute of Diabetes and Digestive and Kidney Diseases—was initially interested in resveratrol because of its antidiabetic effect in mice. "The problem with resveratrol is that it interacts with many proteins and by itself would probably not be a good drug," he explained. "To translate resveratrol research into the clinics, we need to find the target of resveratrol that produced its antidiabetic effect."

In the *Cell* study, Chung's lab used tissue culture and mouse models to demonstrate that resveratrol doesn't directly affect Sirt1 but instead inhibits a group of enzymes known as phosphodiesterases (PDEs), particularly PDE4. PDEs normally decrease the concentration of cyclic adenosine monophosphate (cAMP), a signaling molecule whose levels increase with CR and exercise and plays a key role in metabolic regulation. When PDEs are inhibited, however, cAMP concentrations rise, leading to a cascade of protein-protein interactions that activate Sirt1. Treating obese mice with a PDE4 inhibitor reproduced all the metabolic benefits of resveratrol, including its antidiabetic effects.

BILL BRANSON

Jay Chung (above) and colleagues recently described how resveratrol protects against aging-associated diseases such as type 2 diabetes.

NIH's unique environment of "allow[ing] one to take on risky projects even without having significant background or expertise in an area" made it possible to do the kind of work that has led to Chung's discovery. "Prior to this work, I had no background in animal research," he explained. Chung plans to continue his investigation of resveratrol through clinical trials that will use PDE inhibitors to treat people at risk for type 2 diabetes.

The *Cell* paper has "certainly raised the profile of PDEs as the target for a number of diseases," Chung said. Researchers working with mice have shown that PDE inhibitors can improve memory, prevent obesity, and protect against aging-related diseases such as Alzheimer disease and Parkinson disease. "The next chapter in resveratrol research is to identify the specific targets for whatever indication you're looking at—whether it's diabetes or neurodegeneration."

Although Chung is excited about the potential of PDEs, he is more reserved when discussing the anti-aging properties of the sirtuin family of proteins. Despite these uncertainties, Chung's finding suggests that PDEs may be the missing link in the resveratrol-Sirt1 story—but it may not be the end of the story. ●

NIH ABBREVIATIONS

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

Something Old, Something New

NICHD Neuroscientists Link Neuron Age to Memory Formation

BY HEATHER DOLAN

Deep in the center of the brain is the cashew-size hippocampus, an organ essential to the formation of new memories. Without it we'd only remember the old ones. Scientists thought they understood how certain cells within the hippocampus played a crucial role in episodic memory. But recently, two NICHD neuroscientists—**Christopher McBain** and **Kenneth Pelkey**—contributed to a discovery that has turned that thinking on its head. (*Cell* **149:**188–201, 2012)

Episodic memory requires both pattern separation and pattern completion. In forming distinct memories of similar events, pattern separation allows one to distinguish between similar-but-different cues, such as your father's face and his brother's face. Pattern completion involves recalling more complete memories based on partial cues: For example, seeing your father's face triggers your recall of where you last saw him. Scientists have long thought that the granule cells (GCs) in the hippocampus's dentate gyrus (DG)—one of only two brain areas in which neurogenesis occurs during adulthood—was responsible for pattern separation and were another hippocampal region, area 3 of the cornu ammonis (CA3), supported pattern completion.

Susumu Tonegawa at the Massachusetts Institute of Technology (MIT; Cambridge, Mass.) led a group of researchers seeking to determine the relative contributions of young and old adult-born GCs in mice. GCs that are less than four weeks old are considered young. The researchers were able to halt the formation of new GCs with X-ray irradiation. But Tonegawa knew that blocking the function of the older cells, while leaving the younger ones intact, would be tricky. He created a transgenic mouse in which he blocked the output of the hippocampus's mossy-fiber pathway, so named for the GCs' mossy-looking axons. But how would he know whether he had successfully silenced the older GCs?

That's where the NICHD researchers came in. McBain was an expert in the hippocampal mossy-fiber pathway and was among the first to look at novel mechanisms of synaptic plasticity within it. Pelkey had played an integral part in the lab's discovery of a receptor that when activated weakens signaling between the dentate gyrus and inhibitory interneurons of the CA3 region; in its absence, signaling is strengthened. (*Neuron* **46:**89-102, 2005)

Tonegawa's group needed to "prove that the beast they made was in fact what they thought they [had] made," said Pelkey.

To test whether the mossy-fiber pathway had been silenced, Pelkey made electrophysiological recordings on neural tissue from Tonegawa's mice—some of which were genetically engineered and some not. McBain and Pelkey were blind to which mice were which. The results confirmed that the mossy-fiber pathway was indeed inhibited in the transgenic mice.

Meanwhile, the researchers at MIT and others at the University of California, Los Angeles, were "off doing their part of the puzzle, blind to what everyone else was up to," said McBain. Behavioral tests were conducted to assess pattern-separation and pattern-completion abilities in the experimental and control mice. To measure pattern separation, the researchers used fear-conditioning tests to see how well the mice distinguished between fear-inducing and safe situations. To evaluate pattern completion, the researchers used a standard reference-memory version of the water-maze task, in which the mice were trained to recognize full and partial cues to help them navigate to an underwater platform in opaque water.

Surprisingly, the DG, which had previously been associated only with pattern separation, was found to be responsible for both pattern separation and pattern completion. The adult-born dentate granule cells (a layer of tightly packed granule cells within the DG that produce mossy fibers) switch functions as they age: for the first four weeks they support pattern separation; then as they mature they facilitate pattern completion.

The discovery has implications not only for understanding how the brain stores new memories without forgetting the old, but also for treating mental-health disorders such as "epilepsies and stroke and stress and percussive head trauma," which, said McBain, "tend to have their impact largely inside the temporal lobe where the hippocampus resides." ●

MEGAN WYETH, NICHD

NICHD neuroscientists Kenneth Pelkey (left) and Christopher McBain were collaborators on a recent *Cell* study that links neuron age to the formation of memories.

Intramural Research Briefs

NEI: TWO DRUGS USED FOR AGE-RELATED MACULAR DEGENERATION ARE EQUIVALENT

Avastin (bevacizumab) and Lucentis (ranibizumab injection), two drugs used to treat age-related macular degeneration (AMD)—the leading cause of vision loss and blindness in older Americans—were compared head-to-head for the first time in a two-year clinical trial. In conducting the Comparison of AMD Treatment Trials (CATT), NEI researchers and their collaborators found that Avastin and Lucentis were equivalent in treating AMD. In AMD's advanced stages, abnormal blood vessels leak fluid and blood into the macula, the central part of the retina that allows perception of fine visual detail, and obscure vision. Avastin and Lucentis block the growth of abnormal blood vessels and leakage of fluid from the vessels.

Patients in the CATT trial were assigned to four treatment groups defined by drug (Avastin or Lucentis) and dosing regimen (monthly or as needed). At two years, visual acuity with monthly treatment was slightly better than with as-needed dosing, regardless of the drug. Overall, after two years, two-thirds of patients had 20/40 vision or better, compared with only 15 percent of patients retaining similar visual acuity with previous treatments. (NIH authors: M. Redford, F.L. Ferris; *Ophthalmology* DOI: 10.1016/j.ophtha.2012.03.053)

CC, NCI, NIBIB: STUDY FINDS METHODS TO IMPROVE TRANSPLANT CELL DELIVERY

A new technique for improving delivery of stem cells, developed by NIH researchers and others, may lead to better and faster tissue repair. Using noninvasive pulsed focused ultrasound (pFUS), in which high amounts of energy are delivered to a treatment site without affecting the surrounding tissue, the researchers enhanced the delivery of transplant cells in rodents. Energy generated by noninvasive pFUS stimulates tissue at the treatment site to produce mediators such as cytokines, chemokines, and growth factors. Normally, the production of these mediators is enhanced only during inflammation or injury. Because transplanted stem cells have receptors for these chemical agents, more chemicals attract more transplant cells to the desired site. By increasing the concentration of naturally produced chemical agents, the researchers saw eight to 10 times as many transplanted bone marrow stromal cells in a pFUS-treated rodent kidney than in a non-treated kidney. The use of pFUS to improve transplant cell delivery is a breakthrough in regenerative medicine with implications for sports medicine and military medicine. (NIH authors: A. Ziadloo, S.R. Burks, E.M. Gold, B.K. Lewis, A. Chaudhry, M.J. Merino, J.A. Frank; *Stem Cells* **30:**1216–1227, 2012)

NIAAA: KILLER T CELLS FOUND TO COUNTER OBESITY-RELATED DIABETES

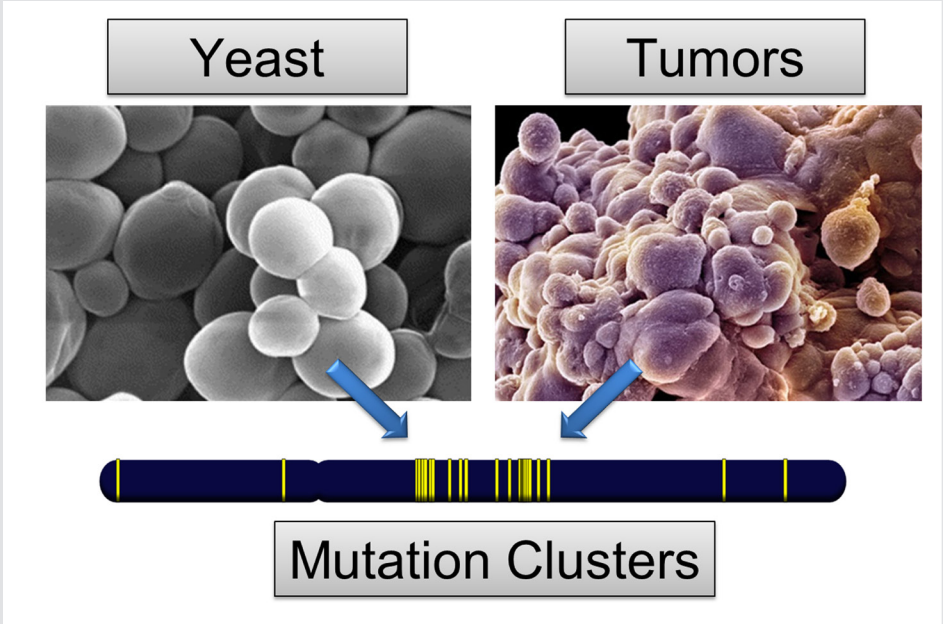
For years, researchers have known that obesity, type 2 diabetes, and inflammation are linked, but have not fully understood how. A study done by NIAAA researchers and others revealed that natural killer T (NKT) cells, essential to the human immune system, are a key piece of the puzzle. The researchers injected mice that were fed high-fat diets with alpha-galactosylceramide, a lipid known to specifically activate NKT cells. The injected mice exhibited decreased tissue inflammation, decreased insulin resistance, and increased glucose tolerance. Thus, though the mice were being fed a high-fat diet, their metabolic response was closer to that of mice being fed a healthier diet. The researchers plan to next alter the regimen of lipid treatment to see whether they can induce an even better effect in animals and identify compounds in foods that naturally activate NKT cells in humans. Their ultimate goal is to identify specific foods that obese people with diabetes could eat to achieve the positive effects seen in mice. (NIH authors: B. Gao; *J Biol Chem* **287:**13561–13571, 2012)

NICHD: TELEVISION VIEWING BY ADOLESCENTS ASSOCIATED WITH UNHEALTHY EATING HABITS

Television viewing and unhealthy eating habits in U.S. adolescents appear to be linked, according to a study performed by NIH scientists and others. The study authors used data from the 2009-2010 Health Behavior in School-Aged Children Study, a nationwide survey of 12,642 U.S. students in grades 5 through 10. Television viewing time was found to be associated with decreased consumption of fruit or vegetables daily and increased consumption of candy and soda daily, skipping breakfast at least one day per week, and eating at a fast-food restaurant at least one day per week. Further research is needed to clarify the independent contributions of TV viewing, food advertising, and TV snacking on dietary intake in U.S. adolescents. (NIH authors: L.M. Lipsky, R.J. Iannotti; *Arch Pediatr Adolesc Med* **166:**465-472, 2012)

FOGARTY, NIAID: STUDY SHOWS POOR-QUALITY MALARIA DRUGS POSE THREAT

Poor-quality antimalarial drugs lead to inadequate treatment and drug resistance and pose a threat to vulnerable populations. By studying survey data of the malaria drugs available across Southeast Asia and sub-Saharan Africa, NIH researchers found that from 20 to 42 percent are either poor quality or fake. The researchers also found that antimalarial drugs are widely distributed and self-prescribed, correctly or incorrectly, in the regions surveyed. Facilities to monitor the quality of antimalarial drugs are lacking, as are consumer and health-worker knowledge about the therapies. Of particular concern are signs of resistance to artemisinin derivatives, the most effective drugs against malaria, in western Cambodia. The findings indicate the need for a series of interventions to better define and eliminate poor-quality antimalarial drugs. (NIH authors: G.M.L. Nayyar, J.G. Breman, J. Herrington; *Lancet Infect Dis* **12:**488–496, 2012)



STEVEN ROBERTS, NIEHS

DNA mutations are thought to be rare events that occur randomly and over time, but NIEHS researchers have identified DNA regions in yeast and in some cancers that have a disproportionately high number of mutations that arose simultaneously. In yeast, the clusters are produced by exposure to environmental toxins; in cancers, they are produced through typical biochemical processes.

NIEHS: CELLULAR DAMAGE FROM NORMAL METABOLISM MAY CAUSE CANCER

NIEHS researchers and their collaborators have identified DNA regions in yeast and in some cancers that have a disproportionately high number of mutations. The findings represent an exception to the traditional view that mutations accumulate over time, and may explain one of the mechanisms behind cancer development. Team members subjected yeast to continuous damage by growing them in media containing the carcinogen methyl methanesulfonate (MMS). Normally, mutations occur haphazardly throughout the genome. But the researchers found that for approximately 70 yeast cells, certain DNA clusters contained more mutations than the rest of the genome. These clusters also exhibited a very unusual pattern, suggesting they were formed simultaneously in stretches of abnormally long single-stranded DNA.

The researchers next found that over half of 32 human tumor types examined had mutation clusters. But the cause of the mutation clusters wasn't environmental damage as it was in yeast. The DNA sequence surrounding clustered mutations suggested that specific proteins called apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like (APOBEC) cytosine deaminases, which inactivate viruses attacking the body, are also somehow damaging DNA. The study results suggest that antiviral drugs capable of stimulating APOBEC genes should be studied for potential long-term effects connected with enhanced mutagenesis. (NIH authors: S.A. Roberts, J. Sterling, C. Thompson, S. Harris, L.J. Klimczak M.A. Resnick, D.A. Gordenin; *Molec Cell* **46**:424–435, 2012)

NIAID: HIV-INHIBITING PROTEIN IDENTIFIED

NIH scientists and their collaborators have identified a new human immunodeficiency virus (HIV)–suppressing protein in the blood of people infected with the virus. In laboratory studies, the chemokine CXCL4 binds to HIV and thereby prevents it from attaching to or entering a human cell. Previously, four chemokines were known to function as HIV inhibitors. These chemokines, as well as CXCL4, may regulate the level of virus replication in infected individuals and thus the pace at which HIV disease progresses. According to the researchers, the site where CXCL4 binds to the outer coat of HIV seems to be different from other known vulnerable sites targeted by HIV-blocking antibodies and drugs. The researchers aim to better understand CXCL4's role in HIV disease and to determine whether the chemokine has a protective effect not only in laboratory studies, but also in people. (NIH authors: D.J. Auerbach, Y. Lin, H. Miao, R. Cimbro, M.J. DiFiore, M.E. Gianolini, A.S. Fauci, P. Lusso; *Proc Natl Acad Sci USA* **109**:9569–9574, 2012)

NIDA: VIDEO HELPS DIMINISH DRUG CRAVINGS

Viewing a five-minute video can remove memories of past drug use in former heroin addicts and ease cravings, according to a study done by NIDA researchers and others. Sixty-six people battling heroin addiction watched a video of people smoking and injecting heroin, which served as a quick reminder of past drug abuse. The study subjects then participated in "extinction sessions," in which they watched more drug-related videos and slideshows and handled fake heroin. Time between the reminder and the extinction sessions was varied: some people waited 10 minutes, others waited six hours. The researchers found that people whose memories were primed with the drug reminder 10 minutes before extinction reported less craving for heroin after seeing drug cues than did people who hadn't received the reminder. In contrast, people who waited six hours before undergoing the extinction did not get the same effect. The results suggest that there's something important happening in the 10-minute window right after the reminder. Further investigation is needed to clarify whether the effects persists under normal circumstances. (NIH authors: D.H. Epstein, Y. Shaham; *Science* **336**:241–245, 2012)

Graduate Partnerships Program

CONTINUED FROM PAGE 1

Research (DDIR) **Michael Gottesman**, who has hosted four GPP students in his lab. "These students become the catalysts for collaboration [among] investigators."

Working with graduate students can help principal investigators hone their mentoring skills, too. Mentoring graduate students "can be one of the most rewarding and intellectually satisfying experiences a PI can have," said Office of Intramural Training and Research (OITE) Director **Sharon Milgram**. "Support from ICs, partnership directors, and administrative staff has made [the GPP] a really positive force on campus."

A History of the GPP

Graduate students have been coming to NIH to work with its intramural scientists since the 1960s. NIH has never granted degrees itself, but in addition to encouraging students to work with its researchers, it has a long history of providing educational programs. In 1959, the Foundation for Advanced Education in the Sciences (FAES) was established as a nonprofit to promote scientific education and support biomedical research within the NIH intramural program. Each year, FAES offers nearly 200 graduate- and undergraduate-level courses that are accepted for credit at many universities. It also runs a bookstore, a music series, and an insurance program.

In the 1970s, NIH considered starting its own graduate school, but many investigators were concerned that the lack of infrastructure and experience would make it difficult to run a successful program. In the 1990s, then–NIH director Harold Varmus resurrected the idea of establishing a formal degree-granting program, but the Advisory Committee to the Director recommended against it. So Varmus and DDIR Gottesman proposed that NIH establish partnerships with universities whereby students could do their thesis work at NIH and earn their degree from an academic institution. In July 2000, the NIH GPP was launched to formally link the NIH intramural program with universities in the training of graduate students in the biomedical sciences. (See Gottesman's essay on page 2 for more on the GPP history.)

The GPP Today

Today, the NIH GPP offers structured and cohesive training experiences to expand opportunities for Ph.D. candidates both at and away from the bench while enriching the intramural program by giving faculty and postdoctoral fellows the opportunity to teach. Currently, there are about 500 graduate students from more than 100 domestic and international universities who are doing research at NIH campuses in nearly every institute and center (IC).

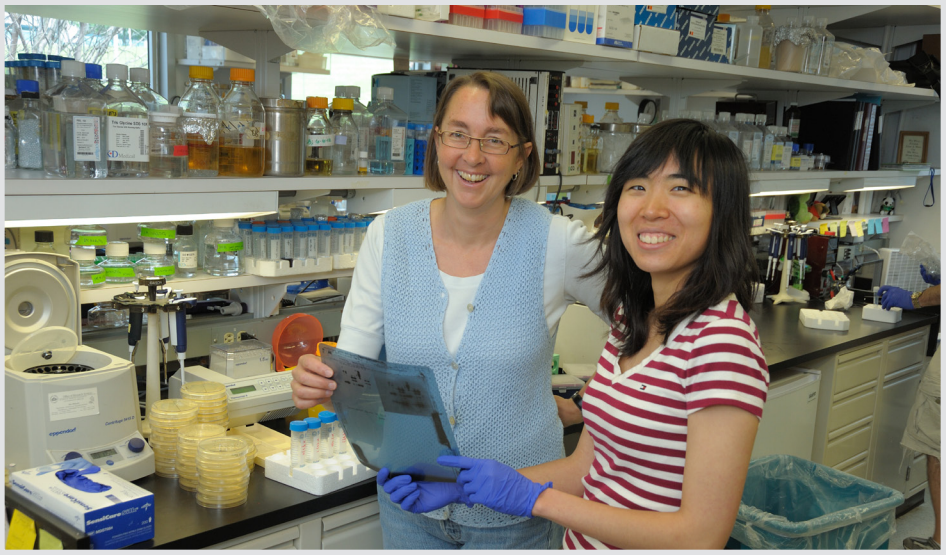
Students can enter the GPP through two mechanisms: institutional partnerships and individual partnerships. Institutional partnerships are established programs between the NIH and universities through which prospective students apply to begin their graduate education in the GPP. There are numerous institutional partnerships administered by the OITE and various NIH ICs. For individual partnerships, currently enrolled Ph.D. students (from domestic and international universities) establish agreements between their universities and NIH intramural investigators.

Compared with most graduate programs at universities, the NIH GPP offers a larger research environment and is spread across the 24 ICs that do intramural research. In addition, GPP students can participate in courses offered by FAES and OITE; attend workshops and activities held by their ICs; and participate in the Graduate Student Seminar Series in which they present their research to their peers and postdocs who provide critical feedback. Students also attend an annual GPP-sponsored retreat that is replete with science and professional- and career-development workshops. In January, students participate in the Graduate Student Research Symposium in which they showcase their research to the NIH community, listen to speakers, and attend the annual GPP graduation and awards ceremonies.

There are plenty of opportunities for non-science activities, too. Students can practice their leadership skills by participating in the Graduate Student Council (GSC). The GSC's Volunteer Committee organizes community service projects ranging from cooking dinner at the NIH Children's Inn to tutoring local children in a D.C. transitional housing program. The GSC also organizes social events and other activities and coordinates an after-hours seminar series.

On the following pages we highlight three graduate students and their NIH mentors. Some of the interviewers are GPP students themselves. **Katherine Bricceno** (**Gisela Storz** and **Xuefeng Yin**) and **Alexis Boyd** (**Mirit I. Aladjem** and **Augustin Luna**) are both graduate students at George Washington University (Washington, D.C.). Bricceno is getting a Ph.D. in biochemistry and molecular genetics and doing her research at NINDS. Boyd is getting a Ph.D. in immunoparasitology and doing her research at NIAID. **Monika Deshpande** (**Michael Lenardo** and **Austin Swafford**) is a postdoctoral fellow in NCI. **Meghan Mott**, is a postdoctoral fellow in NIAAA. ●

For more information on the GPP, including a complete list of institutional programs and instructions on establishing individual partnerships, go to https://www.training.nih.gov/programs/gpp. For more information on FAES, go to http://www.faes.org/.



ERNIE BRANSON

The scientist: Gisela Storz, Ph.D. (left)
Title: Senior investigator and deputy director, Cell Biology and Metabolism Program
Institute: NICHD
Came to NIH: In 1989 for training in NCI; returned in 1991

What qualities do you look for in a graduate student for your lab?
I look for students who are enthusiastic and take initiative because having a student with these qualities makes the research more fun.

What are the benefits—and challenges—of having graduate students in the lab?
Grad students are a pleasure to have in the lab; they are less jaded because they are at an earlier stage in their careers. Keeping track of university requirements can be challenging.

What is your strategy for mentoring?
My approach is the same for everyone. Students start working with others and then give more input on a project. As they sprout wings, I encourage them to be more independent.

How is mentoring rewarding and difficult?
It's rewarding to see people succeed. I didn't anticipate how much I would enjoy mentoring. The most difficult is learning how best to interact with each individual.

What advice do you have for those who want to improve their mentoring skills?
Be up front about expectations. It is also good to know what students want. It is easier to work together toward a common goal.

How can grad students get the most out of their relationships with their mentors?
Be enthusiastic and take initiative. I like students who read papers, come up with new ideas, and are thinking about the project.

The graduate student: Xuefeng Yin (right)
Hometown: Beijing, China
Education: B.S. in medicine, Peking University (Beijing)
Earning Ph.D.: In molecular biology from Peking University

What are your career goals?
I enjoy research—and the passion and enthusiasm that go into it—in an academic setting. I am also exploring other options and am considering doing postdoctoral fellowships in academia and industry.

What made you decide to do your graduate research at NIH?
I knew about the NIH's reputation for prestigious research and learned about the Graduate Partnerships Program from a professor.

What makes Dr. Storz a good mentor?
She enjoys mentoring and is very supportive of my transition from medicine to microbiology and to a new culture.

What got you interested in science?
While working in a lab as an undergraduate, I had my own project and became interested in how the cell works. I wanted to pursue further research in basic science.

What are the most exciting and challenging aspects of research?
It's rewarding to learn something new. It's challenging when my experiments aren't working and I can't get data.

What are your non-work interests?
I like to socialize with lab members outside of work. We played paintball, went to the Cherry Blossom Festival, and tried to go a Nationals game but it was rained out.

The laboratory: Xuefeng Yin and Maureen Thomason (from Georgetown University in Washington, D.C.) are the lab's first two graduate students. Storz's group made the serendipitous discovery of one of the first small, regulatory RNAs to be identified. Her lab works on the genome-wide identification and characterization of small RNAs in bacteria. Yin is studying two small membrane proteins that are thought to regulate transport and efflux pumps in the cell membrane.

CONTINUED ON PAGE 12

Graduate Partnerships Program

CONTINUED FROM PAGE 11

SOHYOUNG KIM, NCI

The scientist: Mirit I. Aladjem, Ph.D. (right)
Title: Senior investigator, Laboratory of Molecular Pharmacology
Institute: NCI
Came to NIH: In 1999

What qualities do you look for in graduate students for your lab?

The ability to understand an experiment; the intellect to follow a scientific question; open-mindedness about research; being independent and resourceful; and having a drive that comes from within.

What is your strategy for mentoring?

I encourage students to ask questions, make their own decisions, and interact with collaborators and other researchers by presenting at meetings and seminars.

What is rewarding—and difficult—about mentoring?

It's difficult, yet rewarding, to bring people to the point of being independent and able to think for themselves.

How can graduate students get the most out of relationships with their mentors?

Ask questions and listen. Try to understand how your mentor makes decisions. Mentors can teach about life in science in general and not just about specific research. Participate in the lab fully. Interact positively with colleagues so they will be willing to help you.

How have mentors helped you?

Three mentors served as role models and showed me how to balance my professional and personal life. I also learned how to manage a lab and how to approach the challenges of science.

The graduate student: Augustin Luna (left)
Hometown: Maysville, Ga.
Education: B.S. in biomedical engineering, Georgia Institute of Technology (Atlanta)
Earning Ph.D.: In bioinformatics from Boston University (Boston)

What are your career goals?

To find a position—in academia or perhaps industry—that merges mathematical modeling, pharmacodynamics, pharmacogenomics, and pathway analysis.

How did you select the lab you're in?

I wanted to do mathematical modeling so searched for labs doing work in bioinformatics, cancer, and aging. Mirit had received a postbac mentor award so I knew she would be a good mentor.

What makes Dr. Aladjem a good mentor?

She is very open to collaboration. She knows who can help me on technical computational issues and encourages me to talk to them and to go to conferences to meet others in the field. She also has the truest open-door policy of anyone I have ever worked for.

What got you interested in science?

When I was a child, my father had an accident in which he severed three fingers. Two were reattached, but never regained full mobility. That drove me to ask why; I wanted to advance knowledge in that area. As an undergrad, I took courses in cell and tissue engineering, which helped me appreciate that the lack of understanding of biological networks was a major problem in medicine.

What are the most exciting and challenging aspects of your research?

Figuring out how to integrate information—and contradictory findings—obtained from bioinformatics approaches to research.

What are your interests outside of work?

I enjoy art; I recently had an exhibit entitled "Random Walks" at Artomatic in Crystal City (Arlington, Va.). I also do volunteer work through NIH's Graduate Student Council and tutor minority students.

The laboratory: Augustin Luna is the lab's first graduate student. Aladjem studies the molecular regulation of cell growth, and her lab is part of a consortium made up of NIH researchers who are creating tools to describe protein interactions. Luna is collaborating with a co-mentor, Kurt Kohn, to develop a computer software program that will visualize signaling pathways and is developing a mathematical model to connect circadian rhythms to DNA repair responses.

MATT VOGT, NIAID

The scientist: Michael J. Lenardo, M.D. (right)
Title: Senior investigator; chief, Molecular Development of the Immune System Section, Laboratory of Immunology
Institute: NIAID
Came to NIH: In 1989

What qualities do you look for in graduate students for your lab?
I interview students in person. Often the students who get shortlisted are enthusiastic, open-minded, and smart.

What are the benefits—and challenges—of having graduate students in your lab?
Graduate students bring energy and enthusiasm. They are curious and open to taking on risky projects. The biggest challenge is finding money to pay them.

What is your strategy for mentoring?
I tailor toward individual needs. I encourage independent thinking, data-driven hypotheses, and getting input from everyone.

How is mentoring rewarding and difficult?
It's rewarding to watch the students grow and become independent thinkers. Training students is fun.

How can graduate students get the most out of relationships with mentors?
Work very hard. Take advantage of the resources available to you, have open lines of communications between your mentor and others in the lab, and learn a lot.

The graduate student: Austin Swafford (left)
Hometown: New Orleans
Education: B.S. in molecular biology, University of Texas at Dallas
Earning Ph.D.: In medical genetics and immunology from the University of Cambridge (England)

What are your career goals?
I have a passion for performing translational research and would like to develop a lab at a medical school or research hospital. I am particularly interested in engineering-targeted therapeutic agents.

What got you interested in science?
I was diagnosed with type 1 diabetes at age 8. Learning how to manage my disease was my first introduction to the complexities of biological systems. I wanted to understand biology so I could use it to improve the health and lives of others.

What made you decide to do your graduate research at NIH?
I was attracted by the flexibility and autonomy that would enable me to design my Ph.D. project. I was enthusiastic about the prospect of harnessing the experience and expertise from multiple sources.

How did you select the lab you're in?
Through a mixture of serendipity and seized opportunity. I scheduled a meeting with Dr. Lenardo because he was developing immunomodulatory therapeutics to prevent type 1 diabetes. The interview turned into a fantastic brainstorming session, and I fell in love with the project we laid out.

What are the most exciting—and challenging—aspects of the research process?
It's exciting to realize you may be doing something that no one has ever done before to gain insight into a phenomenon. It can be challenging to see the connection between the pipette and the patient.

What are your interests outside of work?
I enjoy playing Frisbee, soccer, and board games. I have been teaching myself the basics of Hebrew, Chinese, and Japanese to be able to communicate with people from diverse backgrounds and cultures.

The laboratory: Lenardo's laboratory is investigating the molecular regulation of T lymphocytes in order to develop novel means of diagnosis and immunomodulation for autoimmune diseases such as multiple sclerosis and type 1 diabetes. Lenardo has had more than a dozen graduate students in his lab. He also founded and directed two graduate partnership programs—the Oxford-Cambridge (England) program and the University of Pennsylvania (Philadelphia) immunology program. Swafford is currently examining the diversity of T cells in a mouse model of type 1 diabetes.

Recently Tenured

JAMES BLAIR, NIMH

WILLIAM DOUGLAS FIGG, NCI-CCR

JAMES BLAIR, PH.D., NIMH

Senior Investigator; Chief, Unit on Effective Cognitive Neuroscience, Mood and Anxiety Disorders Program

Education: University College London, London (B.S. in psychology, Ph.D. in psychology)

Training: Wellcome Trust Mental Health Research Fellow, Medical Research Council Cognitive Development Unit (London)

Before coming to NIH: Honorary scientist in the department of clinical neuropsychology at the National Hospital for Neurology and Neurosurgery (London); co-founder and leader of the Developmental Disorders group at the Institute of Cognitive Neuroscience, University College London; lecturer and senior lecturer in the department of psychology at University College London

Came to NIH: In March 2002

Selected professional activities: On the editorial board for several journals including *Biological Psychiatry and Social Cognitive and Affective Neuroscience*

Outside interests: Native plant gardening (20 percent of Maryland's native plants are represented in his garden); hiking; diving; enjoying movies

Research interests: I use functional magnetic resonance imaging (fMRI), psychopharmacology, and, more recently, molecular genetics to understand the neurocognitive systems mediating affect (emotion) in humans. The primary clinical goal of this work is to determine the computational impairments seen in different forms of conduct disorder. Conduct disorder—one of the most prevalent categories of mental-health problems of children in the United States—is a childhood behavior disorder characterized by aggressive and destructive activities such as defiant or impulsive behavior, drug use, and criminal activity. Until recently there has been relatively little attention paid to potentially differentiable forms of this disorder and the neurobiology of any of these forms.

Our work has shown that dissociable forms of conduct disorder can be identified and that they are associated with very different perturbations of neural circuitry. We have been able to develop fMRI biomarker tasks to index these perturbations to provide more precise indices of treatment. We are currently beginning studies to examine the extent to which currently available treatments do, or do not, "normalize" the identified pathophysiologies and hope to translate this new knowledge of the neurobiology into novel treatment strategies.

WILLIAM DOUGLAS FIGG, SR., PHARM.D., M.B.A., NCI-CCR

Senior Investigator; Head, Molecular Pharmacology Section, Medical Oncology Branch; Head, Clinical Pharmacology Program

Education: McWhorter School of Pharmacy, Samford University, Birmingham, Ala. (B.S. in pharmacy); Harrison School of Pharmacy, Auburn University, Birmingham (Pharm.D.); Columbia Business School, Columbia University, New York, and London Business School, University of London, London (M.B.A.)

Training: Internship in clinical pharmacy, University of Alabama Hospital (Birmingham); postdoctoral fellowship in clinical research and drug development, University of North Carolina at Chapel Hill (Chapel Hill, N.C.)

Came to NIH: In July 1992

Outside interests: Being a spectator and a participant in a variety of sports

Research interests: My laboratory is seeking to understand the pharmacology of new anticancer agents. We are targeting prostate cancer by inhibiting angiogenesis and regulating androgens. We are designing new agents to block key targets in the angiogenesis pathway. Using preclinical models (such as the rat aorta), we have identified several potential agents and are proceeding with preclinical testing of these agents in patients who have prostate cancer. We are also trying to identify agents that can inhibit the transport of androgens in prostate cancer cells.

We are also studying the drug thalidomide's effectiveness in treating prostate cancer tumors. We recently showed in cellular models of prostate cancer that thalidomide acts as an anti-androgen and therefore blocks the androgen pathway, which regulates the development of male characteristics. In collaboration with several academic institutions, we synthesized more than 187 thalidomide analogues and are moving several extremely potent angiogenesis inhibitors we have identified through clinical testing.

I also head the Clinical Pharmacology Program (CPP), which characterizes the clinical pharmacology of new anticancer agents that are entering the NIH Center for Cancer Research clinics; analyzes phase 1 and 2 clinical trials that are conducted within the NCI intramural program; and provides direct support for many studies performed in the extramural community. ●

NEW NIH WEB SITES LAUNCHED

NIH Center for Regenerative Medicine:
http://crm.nih.gov

Human Research Protections Program:
http://ohsr.od.nih.gov/

SPECIAL NIH DIRECTOR'S LECTURE
Wednesday, July 25, 2012
3:00–4:00 p.m.
Masur Auditorium (Building 10)
National Science Foundation Director Subra Suresh will give a lecture on basic research at the convergence of physical and life sciences with a particular focus on human diseases. For more information, contact Jacqueline Roberts (robertsjm@od.nih.gov or 301-594-6747).

MOLECULAR INSIGHTS ON AGING
Thursday July 12, 2012
1:00–2:00 p.m.
Masur Auditorium (Building 10)
NIH Director Francis Collins will deliver a seminar on recent developments in the field of progeria, a rare genetic disease that causes accelerated aging. Collins helped identify the responsible gene. The seminar, sponsored by the Geroscience Interest Group (GSIG), will be videocast at http://videocast.nih.gov. For reasonable accommodation, contact Felipe Sierra (Sierraf@nia.nih.gov or 301-496-6402). For more information on GSIG visit http://sigs.nih.gov/geroscience.

GRADUATE & PROFESSIONAL SCHOOL FAIR
Friday, July 20, 2011
9:00 a.m.–3:30 p.m.
Natcher Conference Center (Building 45)
Lister Hill Auditorium (Building 38A)
The fair includes more than 100 colleges and universities; workshops on making successful transitions and interviewing; and panels on getting into graduate and professional school and on careers in public health, pharmacy, and psychology. For more information and to register, visit https://www.training.nih.gov/gp_fair.

STEM CELL SEMINAR SERIES
September 4, 2012, 2:00–3:00 p.m., Lipsett Amphitheater (Building 10): Lorenz Studer, Director, Sloan Kettering Institute for Stem Cell Biology (videocast at http://videocast.nih.gov/)
September 18, 2012, 2:00–3:00 p.m., Building 50, Room 1227: TBD
For more information, contact nihcrm@mail.nih.gov.

PIONEER AWARD SYMPOSIUM
September 13–14, 2012
Doubletree Bethesda Hotel, Bethesda
Free and open to all; no registration required
Includes presentations by the 2007 Pioneer Award recipients; talks by selected recipients of the NIH Director's New Innovator Award; and poster sessions by Pioneer and New Innovator awardees. For more information, visit http://commonfund.nih.gov/pioneer/Symposium2012 or e-mail pioneer@nih.gov.

FRONTIERS IN BASIC IMMUNOLOGY
Thursday, October 4: 8:30 a.m.–5:00 p.m.
Friday, October 5: 8:30 a.m.–noon
Masur Auditorium and Lipsett Amphitheater (Building 10)
Abstract deadline: August 17, 2012
Learn about the latest findings in lymphocyte biology and signaling, adaptive and innate immune responses, and immunity and disease. Sponsored by NCI's Center of Excellence in Immunology. Registration is free, but seating is limited. To register and submit abstracts go to http://web.ncifcrf.gov/events/Immunology2012.

BEHAVIORAL AND SOCIAL SCIENCES RESEARCH RETREAT
Monday, October 22, 2012
9:00 a.m.–5:00 p.m.
Natcher Conference Center (Building 45)
The Office of Behavioral and Social Sciences Research will host this event featuring scientific discussions on behavioral and social sciences research. For more information, contact Dana Sampson (dana.sampson@nih.gov).

NCATS: DISCOVERING NEW THERAPEUTIC USES FOR EXISTING MOLECULES
NCATS has partnered with eight pharmaceutical companies and launched a collaborative program that will match researchers with dozens of pharmaceutical industry compounds that haven't been commercialized. Intramural research program investigators are eligible to compete for access to the drug candidates. Research support would need to come through the appropriate scientific director's intramural funds. Interested investigators must submit a pre-application by August 14 (http://grants.nih.gov/grants/guide/pa-files/PAR-12-203.html). For more information, visit ncats.nih.gov/therapeutics.html.

AWARDS

Gisela Storz (NICHD) has been elected to the National Academy of Sciences, one of the highest honors a scientist can receive. A major focus of her group has been the study of the bacterial and fungal responses to oxidative stress. As a result of the serendipitous discovery of the peroxide-induced OxyS RNA, one of the first small, regulatory RNAs to be identified, her lab shifted to the genome-wide identification and characterization of small RNAs in bacteria.

NIDDK Director **Griffin P. Rodgers** was elected to the American Academy of Arts and Sciences. His research contributed to the first effective therapy for sickle cell anemia. Other notable members of the 2012 class include actor and director Clint Eastwood, musician Sir Paul McCartney, and U.S. Secretary of State Hillary Rodham Clinton.

In recognition of her contribution to science and scientific interactions between Japan and the United States, **Keiko Ozato** (NICHD) received the Order of the Sacred Treasure, Gold Rays with Neck Ribbon, from the Japanese government. She has been the chair of the NIH-Japan Society for the Promotion of Science Fellowship from its inception in 1996 and has helped young Japanese scientists conduct high-caliber research with intramural PIs. She also helped organize a relief effort for biomedical researchers affected by the 2011 earthquake in Japan. NIAMS Director Stephen Katz received a similar medal, an Order of the Rising Sun, in 2011.

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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.

Samarendra Singh, a visiting postdoctoral fellow at NIDDK, took the photo on the right.

PHOTOGRAPHIC MOMENT

Sky Horizon

SAMARENDRA SINGH, NIDDK

Samarendra Singh, a visiting postdoctoral fellow in NIDDK's Laboratory of Molecular Biology, took this photo on an eerily overcast day in April. When he gets a break from researching how recombination activation genes mediate V(D)J recombination, Singh enjoys snapping pictures with his high-end Canon digital single-lens reflex camera, model 5D. The sculpture can be found below the Clinical Center on West Drive. It was selected to mark NIH's 1987 centennial anniversary. The sculpture "stands as a reminder of the accomplishments of NIH to the health of mankind and a salute to those who made those accomplishments possible." Constructed in 1986 by Louise Nevelson, 20th-century New York artist known for her abstract sculptures, Sky Horizon stands 30 feet tall and is made of the nonreflective material COR-TEN steel. The piece was dedicated to NIH in 1988 by the family of Edwin C. Whitehead, founder of the Whitehead Institute for Biomedical Research and the Technicon Corporation.

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