NIH Ebola Response

Ebola-Infected Nurse Discharged
BY LAURA STEPHENSON CARTER

A key element in the mission of the Intramural Research Program is to respond to public-health emergencies and this certainly has been realized in the Ebola epidemic. Beyond having had an Ebola vaccine ready for clinical trial before the onset of the recent West African outbreak, the NIH Clinical Center has long been prepared to accept Ebola patients. Its Special Clinical Studies Unit (SCSU) was recently called into action to treat Nina Pham, the Ebola-infected nurse who recovered from her illness and was discharged on Friday, October 24, 2014.

Pham works at Texas Health Presbyterian Hospital (Dallas) and was one of two nurses who became infected while caring for Thomas Eric Duncan, a Liberian national and the first Ebola patient diagnosed in the United States. He died on October 8, 2014. Pham was being treated at Texas Presbyterian until she was transferred to NIH on Thursday, October 16. The other nurse, Amber Vinson, was transferred from Texas Presbyterian to Emory University Hospital (Atlanta) and has also recovered.

Reporters and NIH staff, who had gathered for a press conference outside the Clinical Center, applauded and cheered when the 26-year-old Pham walked out of the building with Anthony Fauci and other members of her health-care team.

“I feel fortunate and blessed to be standing here today,” she read from a prepared statement. She expressed her thanks to God,

September 22, 2014: The government was open for business, unlike last year when the government shutdown forced the rescheduling of the NIH Research Festival from October to November. This year’s festival, celebrating “The Era of the Brain,” opened to a busy plenary session in Masur Auditorium (Building 10).

It’s “that time during the year when we bring together all of the amazing talents that exist here in this intramural program,” said NIH Director Francis Collins, to “develop

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The NIH intramural program has placed its mark on another Nobel prize. You likely heard that Eric Betzig of the Howard Hughes Medical Institute’s Janelia Farm Research Campus (Ashburn, Virginia) will share the 2014 Nobel Prize in Chemistry “for the development of super-resolved fluorescence microscopy” with Stefan Hell (Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) and NIH grantee William Moerner (Stanford University, California).

What you may not know is that Eric’s key experiment came to life right here at the NIH, in the lab of Jennifer Lippincott-Schwartz. In fact, Eric’s story is quite remarkable and highlights the key strengths of our intramural program: freedom to pursue high-risk research; opportunities to collaborate; and availability of funds to kick-start such a project.

Eric was “homeless” from a scientist’s viewpoint. He was unemployed and working out of a cottage in rural Michigan with no way of turning a theory into reality. He had a brilliant idea to isolate individual fluorescent molecules by a unique optical feature to overcome the diffraction limit of light microscopes, which is about 0.2 micrometers. He thought that if green fluorescent proteins (GFPs) could be switched on and off a few molecules at a time, it might be possible using Gaussian fitting to synthesize a series of images based on point localization that, when stacked, provide extraordinary resolution.

Eric chanced to meet Jennifer, who heads the Section on Organelle Biology in the National Institute of Child Health and Human Development (NICHD). She and George Patterson, then a postdoc in her lab and now a senior investigator in the National Institute of Biomedical Imaging and Bioengineering, had developed a photoactivatable version of GFP with these capabilities, which they were already applying to the study of organelles. Jennifer latched onto Eric’s idea immediately; she was among the first to understand its significance and saw that her laboratory had just the tool that Eric needed.

So, in mid-2005, Jennifer offered to host Eric and his friend and colleague Harald Hess so that they could collaborate on building a super-resolution microscope based on the use of photoactivatable GFP. The two had constructed key elements of this microscope in Harald’s living room out of their personal funds.

Jennifer located a small space in her lab in Building 32. She and Juan Bonifacino, also in NICHD, then secured some centralized Intramural AIDS Targeted Antiviral Program funds for microscope parts to supplement the resources that Eric and Harald brought to the lab. Owen Rennert, then the NICHD scientific director, provided matching funds. By October 2005, Eric and Harald had become affiliated with HHMI, which also contributed funds to the project.

Eric and Harald quickly got to work with their new NICHD colleagues in their adopted NIH home. The end result was a fully operational microscope, married to GFP technology, capable of producing super-resolution images of intact cells for the first time. Called photoactivated localization microscopy (PALM), the new technique provided 10 times the resolution of conventional light microscopy.

Another postdoc in Jennifer’s lab, Rachid Sougrat, now at King Abdullah University of Science and Technology in Thuwal, Saudi Arabia, correlated the PALM images of cell organelles to electron micrographs to validate the new technique, yet another important contribution.

Upon hearing of Eric’s Nobel prize, Jennifer said, “We didn’t imagine at the time how quickly the point-localization imaging would become such an amazing enabling technology, but it caught on like wildfire, expanding throughout many fields of biology.”

That it did! PALM and all its manifestations are at the heart of extraordinary discoveries. We think this is a quintessential intramural story. We see the elements of high-risk, high-reward research and the importance of collaboration and the freedom to pursue ideas, as well as NIH scientists with the vision to encourage and support this research.


The story of the origins of Eric Betzig’s Nobel prize in Jennifer Lippincott-Schwartz’s lab is one that needs to be told. I feel proud to work for an organization that can attract such talent and enable such remarkable science to happen.

Kudos to Eric and to Jennifer and her crew.
A talented clinician and clinical investigator in the National Heart, Lung, and Blood Institute (NHLBI), the late Elaine Sloand had a rare skill set that combined hematology with transfusion medicine and blood banking. Physicians rarely get that kind of dual training, but a new NIH fellowship program, named in Sloand’s honor, provides comprehensive training in the two fields.

Known for her compassionate and exuberant personality, Sloand affected many lives before her sudden death in December 2010. Her dual training enabled her to address a variety of issues that bridged patient care and laboratory procedures, ensure the safety of the blood supply during the AIDS epidemic in the 1980s, investigate post-transfusion human immunodeficiency virus activation, and discover interactions between antifungal medications and platelets. Her work also laid the groundwork for advances in individualized treatment of patients with certain bone-marrow disorders.

Yet, it’s rare for people to have the kind of dual training that Sloand had. At NIH as well as at other U.S. teaching hospitals, physicians would have to do two completely separate fellowships: a two-year hematology fellowship and a one-to-two-year transfusion medicine fellowship. Moreover, traditional hematology fellowships tend to emphasize blood cancers and give short shrift to the study of bone-marrow disorders and “benign” hematologic diseases such as anemias, clotting disorders, and sickle-cell disease. And few transfusion-medicine fellowships provide comprehensive training in the benign disorders even though the treatment for many of them may require transfusions of blood or blood products.

Recognizing the value and need for more clinicians with the kind of comprehensive training that Sloand had, NHLBI Hematology Fellowship Program Director Charles Bolan helped initiate a new three-year program—The Elaine M. Sloand Combined Fellowship Program in Hematology and Transfusion Medicine—which was approved by the NIH Graduate Medical Education Committee in 2011.

The first fellow in the Sloand program, Sandhya Panch, embodies Sloand’s spirit in her clinical acumen and caring practice. Bolan recruited Panch to the program because he recognized her potential as an outstanding physician with a drive to pursue clinically relevant questions and contribute to the future of patient care. Panch has excelled in this distinctive training opportunity, he said.

She spent the first year of the fellowship in the Department of Transfusion Medicine where she worked with Susan Leitman, the recently retired chief of the Blood Services Department. Panch helped identify factors in healthy donors that improved progenitor-cell mobilization for transplantation and in patients with severe combined immunodeficiency and chronic granulomatous disease, two life-threatening immune disorders. In 2013 and again in 2014, she received the American Association of Blood Banks Fenwal Award—the top fellowship achievement award in transfusion medicine and blood banking—for this work and other stem-cell characterization studies (Transfusion DOI:10.1111/trf.12854; Transfusion DOI:10.1111/trf.12830). She and Leitman are working on another article for Blood.

Panch’s second year was spent doing a clinical hematology clinical rotation, which involves caring for patients who are undergoing stem-cell transplantation and receiving drug therapies for leukemia and other bone-marrow malignancies. She also provides consultative hematology care. Now in the third year of her combined fellowship, Panch is conducting research in Cynthia Dunbar’s lab (NHLBI) on stem-cell mobilization and expansion using a non-human primate model.

“Her formal training in blood banking/transfusion medicine will give her a useful perspective about the practicality of new laboratory cell-processing protocols for clinical use in patients,” said Dunbar. This ability to bring practical insight to new therapies in hematologic disorders was a distinctive attribute of Sloand’s career, and this fellowship expedites that path for a new generation of physician-scientists, like the rising star Sandhya Panch.
“We care deeply about the next generation of scientists and health-care providers and people working at the interfaces of various disciplines,” said Sharon Milgram, director of NIH’s Office of Intramural Training and Education (OITE), during the seventh annual NIH Graduate and Professional School Fair.

The fair, held in July at the Natcher Conference Center (Building 45), aimed to guide that next generation as its members explored their choices in health-care careers. This year’s event showcased graduate, medical, public-health, psychology, and dental programs at 122 colleges and universities, and featured networking mixers and workshops on getting into different programs, interviewing, and career options. New this year were sessions on diversity that explored issues and opportunities for students of color, LGBT (lesbian, gay, bisexual, and transgender) students, disabled students, and parents and/or caregivers.

The fair attracted NIH postdocs and summer interns as well as local college students. Among the more than 1,100 participants were NIH Academy postdoc Johnetta Saygbe (NHLBI) and summer interns Felix Contreras (NINDS) and Brendan Marden (NIDDK).

Saygbe, who graduated from George Mason University (Fairfax, Virginia) with a B.S. in neuroscience, wanted to learn about M.D.-M.P.H. programs. She enjoyed networking with representatives from medical and public-health schools, gaining insights into career opportunities, and attending the workshop on getting into medical school.

She learned about the difference between traditional (allopathic) and osteopathic medical schools. The curricula of both schools are similar, but osteopathic schools emphasize a holistic approach to medicine based on the belief of treating the whole patient (mind-body-spirit) and trains students to use their hands to diagnose, treat, and prevent illness. “I loved the description of the hand as being another ‘modality for diagnoses,’” Saygbe said. The workshop “challenged me to consider innovative diagnostic modalities that could revolutionize medicine.”

Contreras and Marden, on the other hand, were less certain of their career goals. Contreras, who is a junior at Atlantic Cape Community College (Mays Landing, New Jersey) and majoring in neuroscience, is interested in science and health care. Marden, who is a junior at Emmanuel College (Boston) and majoring in biology, wants to help Native Americans in some way. Both saw the fair as an opportunity to learn about what institutions look for in applicants, obtain recruiters’ advice on applying to particular schools, and meet people from diverse backgrounds who have gone through the process of applying to graduate school. They concluded the fair was very informative and introduced them to new programs and nontraditional tracks.

“We knew neuroscience programs existed but [not] about getting your neuroscience degree and a master’s at the same time,” said Marden, referring to the concurrent Ph.D. in biomedical sciences/M.B.A. program offered by Pennsylvania State University (University Park, Pennsylvania).

“The fair helped me think outside the box,” added Contreras, who, like many students on the M.D. track, believed that private practice was the only option. The fair helped him realize that he could prepare for a career treating patients and doing research.

Contreras and Marden also enjoyed the new diversity sessions. “I liked hearing the stories, people explaining where they came from and how they got” to where they are now, said Marden. “It is possible for each and every single one of us to get [to wherever we want] as long as we work hard for it.”

In the session for students of color, participants discussed the advantages and challenges of wanting to attend graduate or medical school. Some attendees said their main challenge was being the first in their families to pursue higher education; others commented on the many resources available to guide students through the process.

The Graduate and Professional School Fair is only one of OITE’s many career- and professional-development services and events. To learn more, visit https://www.training.nih.gov.
From Hela Cells to Nanotechnology
NINR Celebrates 15th Anniversary of Its Summer Genetics Institute
BY ANDRIA CIMINO, NINR

The program begins simply enough—“What Is a Gene?”—but by the end of the intensive month-long training, participants in the National Institute of Nursing Research’s (NINR) Summer Genetics Institute (SGI) have covered a genome’s worth of molecular genetics material, including the many ethical, legal, clinical, and social issues that attend the advent of personalized medicine in the post-Human Genome era. NINR sponsors the tuition-free SGI, which is administered by the Foundation for Advanced Education in the Sciences, to provide nursing graduate students, faculty, and clinicians with a foundation in molecular genetics appropriate for use in research and clinical practice.

“SGI takes participants on a journey of discovery from HeLa cells to nanotechnology,” explained NINR Director Patricia A. Grady. “They explore the genetic basis for diseases both common, such as cancer and diabetes, and rare, such as fragile X syndrome (the most common cause of inherited mental retardation). They learn how to take a genetic history and how to counsel a patient about findings from a genetic test. But most importantly, they learn how to add pertinent genetic and genomic questions to their current research ideas.”

Participants also learn how to test their new genetic and genomic hypotheses. The course features lectures from world-class genetics and genomics experts and then immerses students in the lab for days of hands-on training in the latest ways to extract data from DNA, RNA, and mitochondria. Two-dimensional gel electrophoresis, mass spectrometry, polymerase chain reaction, and microarrays for characterizing global gene expression or analyzing chromosomal alterations are just some of the techniques they learn.

“The genetic and genomic knowledge base has grown so rapidly since the course first launched in 2000,” explains NINR Scientific Director Ann Cashion, who is an SGI alum. “We now send primers out before the course starts to ensure our SGI students arrive already familiar with the basics, so they can really internalize what they learn here and operationalize it once they get back to their own labs, clinics, and research programs.”

Participants are chosen based in part on their current research expertise: whether it indicates they will be ready to hit the ground running when they arrive, and who will most likely put what they’ve learned to immediate use when they return home.

The latest cohort of 25 joins more than 300 alumni who are making a difference in their communities—building programs of nursing research in genetics; disseminating the results of genetics-related research in peer-reviewed scientific publications and at scientific conferences; and integrating genetics content in nursing school curricula and practice.

As one student put it, “I learned another language and am leaving with a new vocabulary and understanding I can use in my research.”

Visit www.ninr.nih.gov/cgi to learn more about this outstanding research training opportunity and to apply for a spot at SGI 2015 (application period will open mid-November 2014).
WANT A GLIMPSE INTO THE National Library of Medicine’s (NLM’s) massive history of medicine collections that encompass millions of items spanning 10 centuries? Sure, you could visit the NLM in person, but there’s another way to explore some of its vast holdings that are in every form you can imagine—books, photographs, lantern slides, films, audio and video recordings, ephemera, portraits, lithographs, digital materials, and more—from the comfort of your home or office.

Check out NLM’s Circulating Now blog at http://circulatingnow.nlm.nih.gov. Launched on July 1, 2013, with new posts weekly, the blog conveys the vitality of medical history and its relevance to and importance for research, teaching, and learning about the human condition. Browse this dynamic window onto NLM’s historical collections by date or by topic, or stay current with it through NLM’s social media channels or by e-mail subscription along with over 280,000 followers.

“The blog is becoming a key way to give voice to the diversity of the collection,” said Jeffrey Reznick, chief of NLM’s History of Medicine Division. He and Elizabeth Mullen (NLM) developed and oversee the blog, which is written by a NLM employee, volunteers, student interns, and others. “The idea was to create something [that] was both more efficient and more dynamic… than traditional Web sites,” said Reznick.

Circulating Now weaves history with current events and has published to date more than 350 posts (about two a week), and covered a wide range of subjects that are included in the NLM collections: the Nuremberg Chronicle (“The Dance of Death”); Florence Nightingale (“The Lady Who Became a Nurse”); President James Garfield’s assassination (several postings); “Smoking in America: 50 Years On”; a recently discovered film showing President Franklin Delano Roosevelt speaking at NIH in 1940 (“Rare Footage of FDR at NIH”); and much, much more.

One of the more popular posts, “PTSD and Gene Kelly’s Lost Wartime Star Turn,” describes how, in 1945, the actor Gene Kelly directed and starred in a little-known and little-seen Navy training film called Combat Fatigue Irritability. The film has long been a part of the NLM collection and can now be viewed via Circulating Now, on the NLM Medical Movies on the Web project, and on the NLM’s YouTube channel. PTSD (post-traumatic stress disorder), which has gone by other names such as shell shock and combat fatigue, affects more than seven million people in the United States, soldiers and civilians alike. The blog also offers several posts featuring Kelly’s daughter, psychoanalyst Kerry Kelly Novick, who is interviewed about the film and PTSD.

Circulating Now not only represents NLM’s collections, but it also highlights collaborations with other institutions such as the Smithsonian, the Library of Congress, and the Wellcome Library in London. For example, to commemorate the centenary of World War I, NLM and the Wellcome Library joined together to release digital copies of documents that provide insight into health and medicine during WWI [“(Re)discovering the Great War”]. In addition, the blog highlights items that are on loan to other institutions, such as the poster illustrating “Man as Industrial Palace,” currently at the University of Pittsburgh’s University Art Gallery (“A Poster to Pittsburg”).

“History is appreciated by many who derive enrichment from exploring the past and understanding how it can inform the present and the future,” said Reznick. “Circulating Now is a wonderful platform that is helping us to open this national collection more widely for the benefit of the public.”

For questions about the Circulating Now blog, contact Elizabeth Mullen (woode@mail.nlm.nih.gov). To explore the blog, go to http://circulatingnow.nlm.nih.gov. Find posts mentioned in this article by entering their names into the search box. Readers might also be interested in the 2012 book Hidden Treasure, which also highlights the NLM collection: http://collections.nlm.nih.gov/HiddenTreasure.
Celebrating the Career and Legacy of William Coleman

Established Research Program in Minority Health
BY GERDA GALLOP-GOODMAN, NIMHD

William G. Coleman Jr., a distinguished researcher at NIH for 40 years, died of cancer on August 18, at age 72. He became the first permanent African–American scientific director in the history of the NIH Intramural Research Program (IRP) when he was appointed to direct the National Institute on Minority Health and Health Disparities’ (NIMHD’s) intramural research program in January 2011.

Over the course of his career, Coleman made seminal contributions to the elucidation of lipopolysaccharide biosynthesis, intrinsic gram-negative bacteria antibiotic resistance, and the pathogenic mechanisms and innate and adaptive immune response of Helicobacter pylori. H. pylori, a bacterium that causes infection in the stomach, is associated with gastritis, ulcers, and gastric cancers. These infections affect millions of Americans and are more common among Mexican-Americans and non-Hispanic blacks than in non-Hispanic whites.

Coleman continued his research while serving simultaneously as the scientific director at NIMHD and a senior investigator in the Laboratory of Biochemistry and Genetics in the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).

“Dr. Coleman’s groundbreaking research has played a valuable role in clarifying fundamental mechanisms associated with H. pylori infection,” said NIDDK Director Griffin Rodgers. “His legacy will endure as we learn more about peptic ulcer disease, gastric cancer, and other serious conditions associated with host-defense mechanisms and inflammation.”

He “pursued his important research with great passion and enthusiasm,” said NIMHD Acting Director Yvonne Maddox. “He also valued mentorship and dedicated himself to training future scientists to create a more diverse workforce.”

As NIMHD’s scientific director, Coleman had a set of priorities to develop mentorship programs, which he felt were critical for a diverse workforce, and to foster collaborations within the IRP to further NIMHD’s research on the factors that cause health disparities in underserved communities.

Under Coleman’s leadership, NIMHD’s intramural program focused on three scientific research areas for which there are significant health disparities: cancer, cardiovascular disease, and diabetes. “He realized that molecular, biological, clinical, medical, environmental, and lifestyle factors all converge to help explain health disparities,” said NIMHD Acting Deputy Scientific Director Kevin Gardner. “He also saw the synthesis of these approaches and disciplines as a major conduit to attract diverse investigators.”

Coleman oversaw the NIMHD’s Disparities Research and Education Advancing our Mission (DREAM) Program, which was established in 2009 to facilitate the preparation and transition of new investigators to become independent researchers. And, for more than 20 years, he mentored dozens of postdoctoral trainees, college students, and high-school students in his laboratory. Many of those trainees have gone on to become successful researchers, physicians, and educators.

“Dr. Coleman was a great mentor and an excellent boss,” said Lishi Chen, a former postdoc in Coleman’s lab who left NIH in 1996 and became a researcher at Memorial Sloan Kettering Cancer Center in New York. “He introduced me to the research of molecular biology and taught me a lot of advanced techniques and laboratory methods. I am grateful for his efforts.”

Coleman, who received a Ph.D. degree in microbiology and molecular genetics from Purdue University (West Lafayette, Indiana), came to NIH in 1974 for postdoctoral training in NIDDK’s Laboratory of Biochemical Pharmacology. In 1978, he became a tenured research microbiologist. He received numerous awards for his work, and for more than a decade, he taught several graduate courses at Howard University (Washington, D.C.).

He is survived by his wife, Belinda Seto, deputy director at the National Eye Institute, and his three daughters Melissa, Alicia, and Natasha.
new ideas about science, about collaborations, about ways to make progress in [an] even more creative fashion.”

And with 19 concurrent symposia and more than 250 posters (not to mention the ever-popular directors’ poster session and cooking contest, the “Taste of Bethesda” lunch, and the Vendor Tent Show), the 2014 Festival was set to “showcase some good science,” said Festival Co-Chair Michael Krause, scientific director of the National Institute of Diabetes and Digestive and Kidney Diseases. “I think we did that!”

The festival celebrated and highlighted a newly energized focus on neuroscience in the NIH intramural and extramural programs alike. “This has been a great year for neuroscience on the NIH campus for bringing people together,” remarked Festival Co-Chair Catherine Bushnell, scientific director of the National Center for Complementary and Alternative Medicine (NCCAM). This year marks the start of the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) initiative, a program meant to catalyze a fundamental understanding of the brain in health and disease through the development of novel technologies. Also during this year, the new Porter II Neuroscience building (Building 35) on the NIH campus opened, bringing together neuroscience researchers from many institutes.

The kickoff event for the Research Festival, the plenary session, included a presentation by Collins, an awards ceremony featuring the intramural Fellows Award for Research Excellence (FARE) program, and two presentations highlighting the neuroscience research being pursued in the NIH intramural research program (IRP).

In his opening remarks, Collins discussed four key areas of the NIH intramural and extramural programs: basic research, data and technology, from basic science discoveries to routine medical use, and preparing the biomedical research workforce. For each area, Collins discussed key programs and initiatives within and beyond the NIH, starting with the BRAIN initiative. For the first year, Collins said, the NIH has dedicated $46 million to the initiative, meant to revolutionize our understanding of the human brain and foster the development of new technologies to explore “how the circuits of the brain do what they do.”

A partnership with NIH’s Big Data to Knowledge (BD2K) program will accelerate the development of quantitative measures to help answer neuroscience questions by harnessing the massive amounts of data being produced in areas such as genomics, imaging, and health records. In addition, the Accelerating Medicines Partnership, a program joining NIH with nonprofit organizations and biopharmaceutical companies, aims to foster the translation of research to therapeutics for key targets such as Alzheimer disease, systemic lupus erythematosus, and type 2 diabetes.

And finally, Collins highlighted the NIH’s effort to expand the diversity of the biomedical research workforce, particularly increasing the contribution of underrepresented groups and encouraging early-stage investigators. Bringing the conversation back to the intramural program, Collins talked about how pleased he was that the IRP had initiated a long-term planning effort to determine where it should be in 10 years.

“We don’t just want to rearrange things a little bit,” he said. “We want to think big [and] should be aiming high [for] this remarkable program.”

After the presentation of the FARE, Women’s Science Advisors (WSA) Scholars, and Virology Interest Group awards, Antonello Bonci, scientific director of the National Institute on Drug Abuse, offered the first scientific presentation of the festival, covering his research into dopamine receptors and their role in addiction.

“I met these dopamine receptors 25 years ago, and I still love them,” Bonci said. Addictive drugs can cause long-term changes in neuronal activity. Bonci uses optogenetics, a technique that combines light and genetically encoded light-sensitive proteins to control cell behavior. He found that cocaine abusers have a lower than normal neural activity in specific areas of the prefrontal cortex, an area of the brain that controls executive functions and decision-making. With optogenetics, one can directly modulate the addictive behaviors by activating these neurons.

“Having these methods and use of optogenetics can really inform you about all the fundamental information you need,” Bonci said. “We don’t need to wait 15 years to figure out the mechanism. [W]e can use this data to guide and inform clinicians.”

In the final presentation, Mark Hallett, a senior investigator in the National Institute of Neurological Disorders and Stroke, discussed his research on movement disorders. Hallett has led the field in using neurophysiological methods to understand the neurology and physiology of movement disorders. He described his work with focal hand dystonia, the most common forms of which are “musician’s cramp” and “writer’s...
cramp.” Dystonia is a movement disorder involving abnormal muscle contractions, repetitive movements, and/or posturing. In focal hand dystonia, the muscle contraction often occurs in a single hand during a specific task.

He set out to explore the neurological basis for the disorder, focusing on two areas: “overflow,” or the movement of undesired muscles as well as the desired muscles, and the task specificity of the condition. Using transcranial magnetic stimulation, a technique that allows for the stimulation of particular areas within the motor cortex, Hallett studied the role of “surround inhibition.” He found that, normally, when a subject wishes to perform a movement—such as playing the piano—the desired muscles are activated while the surrounding muscles are inhibited; however, in focal hand dystonia, this inhibition is impaired, leading to unintended muscle contraction. In the piano player’s cramp, some of the fingers may develop abnormal postures while piano playing but not with any other task. Using functional magnetic resonance imaging, Hallett found reduced brain activity in “overlearned” motor programs.

“We hope that the understanding of the physiology…will lead to better treatments for the patients,” he said.

Over the course of three days, similar stories of basic and translational research, and everything in-between, were shared through posters, concurrent symposia, and lots of scientific interactions.

“We get so caught up in our little worlds—not interfacing with the people in your own group, much less the people down the hall or in a different building,” said Krause. The NIH Research Festival “is a way to get people out and about, and see what’s out there!”

Go to http://videocast.nih.gov/launch.asp?18629, to see a videocast of the plenary session. To read an article on Hallett’s work that appeared in the July-August issue of the NIH Catalyst, go to http://irp.nih.gov/catalyst/v22i4/human-motor-control.

SENIOR SCIENTISTS SHOW OFF THEIR POSTERS...AND BAKED GOODS
BY SOMA CHOWDHURY, OIR

Poster sessions at the NIH Research Festival are no longer the exclusive purview of the postdoctoral fellows. For the second year in a row, NIH’s scientific directors—and even a few institute directors—displayed posters at the festival and enthusiastically explained their research to anyone who would listen. And the directors generally displayed their culinary expertise in a cooking contest, too.

While explaining the pharmacokinetic behavior of the ATP-binding cassette subfamily G member 2 (ABCG2) transporter in the blood-brain barrier (“Direct Bioluminescent Imaging of ABCG2 Function at the Blood-Brain Barrier using the Specific Substrate D-Luciferin”), Michael Gottesman recollected how a 1983 poster session influenced his career. He met a fellow poster presenter, someone from the Massachusetts Institute of Technology (Cambridge, Massachusetts) whose poster showed a novel technique for cloning cells. The two collaborated, Gottesman adopted the technique in his research, his career took off, and he eventually became NIH’s Deputy Director for Intramural Research.

NCI Director Harold Varmus explained the roles of splicing-factor mutations in lung carcinomas and myeloid neoplasms (“Investigating the Roles of Splicing Factor Mutations in Lung Adenocarcinomas and Myeloid Neoplasms”). His research group is trying to understand the functional impact of splice variants of U2 auxiliary factor 65-kDa subunit in the pathogenesis of cancer using transgenic mice carrying the mutant allele and isogenic human bronchial epithelial cells carrying the splicing mutants.

When science is not keeping them busy, the directors are not afraid to get their hands dirty—in the kitchen. Along with traditional chocolate-chip cookies, oatmeal cookies, and chocolate-overload brownies, the budding chefs showcased the ethnic diversity of NIH’s scientific community by whipping up delicacies such as cannoli and biscotti, too.

Finally, the winners. “Who said pain doesn’t pay?” asked Gottesman as he announced the poster winner: NCCAM Scientific Director Catherine Bushnell for her poster on how chronic pain can have downstream effects beyond the pain itself (“Effect of Environment on the Long-Term Consequences of Chronic Pain”). Bushnell emphasized that pain may be reduced or prevented by making simple lifestyle changes such as practicing yoga or meditation.

Judging the directors’ culinary expertise was no easy task with so many delicious desserts to choose from. So the judges decided to declare two winners: NIGMS Director Jon Lorsch for his “high-risk low-impact cookies” and NIA Scientific Director Luigi Ferrucci for his biscotti di Prato (a cookie from his hometown in Italy).

To read poster descriptions, go to http://researchfestival.nih.gov/2014/posters.cgi. The directors posters are listed under Poster Session II.
Wouldn’t it be great to have X-ray specs (or some other gadget) that would let you look deep into a cell, so you could see each molecule dancing its way through the complexity of the cell membrane or cytoplasm? While super X-ray specs aren’t yet a reality, NIH researchers may have something close to it. Several described how they are finding better ways to view molecules at high resolution that allows them to see proteins at the nanoscale level.

To be able to see individual proteins on clathrin-coated pits on a cell membrane, Justin Taraska (NHLBI) combines the single-molecule fluorescence interference microscopy super-resolution light-microscopy technique with transmission-electron microscopy (TEM).

Richard Leapman (NIBIB) presented new electron-microscopy techniques for imaging cells and tissues in three dimensions. One technique was scanning TEM (STEM), which allows for imaging of thicker sections, and visualizing synapses in the retina and postsynaptic densities in hippocampal neurons.

Jordan Beach (NHLBI), a FARE Award winner, uses a combination of total internal-reflection fluorescence and structured-illumination microscopy to view the movement of different myosin isoforms and determine how these isoforms interact.

Greg Alushin (NHLBI) uses cryo-TEM and helical reconstruction to visualize vinculin, a protein involved in focal adhesions, when bound to actin fibers. He found that a small portion of the vinculin molecule moves, potentially revealing how vinculin interacts with the cytoskeleton.

Alasdair Steven (NIAMS) uses TEM in conjunction with STEM to study capsid, a newly discovered bacterial complex that resembles a viral capsid. He called this complex “superferritin” for its capacity to store more iron than traditional ferritins.

And finally, Sriram Subramaniam (NCI) highlighted recent advances that he and colleagues have made in cryo-electron microscopic studies of purified protein assemblies. He demonstrated how they are now able to visualize protein structures at near-atomic resolution thanks to new technologies for directly detecting electrons.

From the 2014 Research Festival session “Advances in Molecular Microcopy,” chaired by Sriram Subramaniam (NCI) and held on Tuesday, September 23, 2014.

TAKING THE LEAP...INTO BIOTECH FIRMS
BY JOSEPH P. TIANO, NIDDK

Several intramural investigators who left NIH to work in the biotechnology industry, or start their own companies, shared their stories.

Bruce Weintraub spent 27 years at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) before leaving to co-found Trophogen, Inc. (Rockville, Maryland) in 2001. While at NIDDK he cloned the human thyroid-stimulating hormone gene and recognized the importance of glycosylation (attaching carbohydrates to proteins) in hormone function. The discoveries and ideas he had at NIDDK formed the basis of Trophogen, which is developing glycoprotein hormone superagonists for human infertility and hormone-driven cancer treatments.

John Magnani co-founded GlycoMimetics, Inc. (Gaithersburg, Maryland) in 2013, after spending 10 years at NIDDK. Like Weintraub, Magnani is interested in the role of carbohydrates in disease: GlycoMimetics is designing therapeutics that mimic the structure and activity of naturally occurring carbohydrates.

Veronica Hall, who was a postdoctoral fellow at the National Cancer Institute for three years, credits NIH with inspiring and preparing her to succeed in the biotechnology industry. She joined Emergent BioSolutions (Rockville, Maryland) as a non-bench scientist specialist in 2008 and quickly rose to director of strategic development. She looks for innovative ideas, evaluates new technologies, and finds funding sources.

For six years, Scott Koenig worked on HIV and human T-cell lymphotropic virus type 1 while he was at the National Institute of Allergy and Infectious Diseases. In 1990 he joined Medimmune (Gaithersburg, Maryland) when the company was only two
years old and had fewer than 40 employees. He spent 11 years helping it grow as a publicly traded company, which subsequently became a subsidiary of AstraZeneca. In 2000, he co-founded MacroGenics, Inc. (Rockville, Maryland), which engineers antibodies to create therapeutic products.

If you are thinking about starting or joining a biotechnology company, heed Veronica Hall’s advice: “If you do not think you are qualified, remember that a Ph.D. is the only degree without a textbook telling you what to do and how to do it.”

From the 2014 Research Festival session “Commercial Development of My Research Discoveries: Still More Personal Stories from Former NIH Intramural Scientists,” chaired by Steven Ferguson (OD) and Todd Chappell (OD) and held on Monday, September 22, 2014.

**A (BRAIN) IMAGE IS WORTH 1,000 WORDS**
BY E. PETRUS (NINDS) AND S. ROYCHOWDHURY (NICHD)

**Imaging biomarkers that characterize neurological and psychiatric disorders are crucial for the accurate diagnosis and prognosis of brain disorders.** Several NIH researchers from different institutes presented their work at the Research Festival reflecting the latest developments in searching for imaging biomarkers of brain disorders.

Christopher Harris (a FARE winner in the National Institute of Neurological Disorders and Stroke) discussed his recent findings on the neural basis of goal-directed behavior in zebrafish. By using a genetically encoded calcium indicator called GCaMP6, he located specific neurons whose activity correlated with different types of movement including prey location and decision-making.

A different behavioral model was examined by Hanbing Lu (National Institute on Drug Abuse, NIDA) using functional magnetic resonance imaging (fMRI) in a rodent model of addiction. This study showed that after cocaine self-administration by a rodent, its brain undergoes an increase in plasticity specifically in the prefrontal cortex, anterior insular cortex, and dorsal striatum, which can serve as potential biomarkers at the circuit level.

Several other investigators also use fMRI to measure brain activity. Yihong Yang’s (NIDA) group did a study that emphasized the importance of brain network coupling (interactions between large-scale brain networks) in tobacco dependence: They found that brain-network coupling predicts acute nicotine abstinence-induced craving and cognitive deficits in smokers. Allison Nugent (National Institute of Mental Health, NIMH) described how fMRI scans revealed neural correlates underlying ketamine’s ability to provide faster relief than typical antidepressants in patients with severe depression.

James Blair (NIMH) uses fMRI to understand which brain regions are activated in different types of conduct disorder, a childhood behavior disorder characterized by aggressive and destructive activities such as defiant or impulsive behavior, drug use, and criminal activity. He hopes his findings will enhance diagnosis and help with treatments.

Karen Berman (NIMH) also uses fMRI to decipher neural abnormalities in Williams syndrome, a rare neurodevelopmental disorder characterized by cardiovascular disease, developmental delays, deficits in visuo-spatial processing, and a striking overly friendly personality. She found that people with Williams syndrome had decreased gray matter in the part of the brain linked to visuo-spatial processing, and they had abnormal structure and function in parts of the brain linked to social and emotional processes.

From the 2014 Research Festival’s session “Searching for Imaging Biomarkers of Brain Disorders: From Preclinical Models to Clinical Treatments,” chaired by Yihong Yang (NIDA) and held on Wednesday, September 24, 2014.
Win Arias (Clinical Center) has a knack for connecting the dots between advances in biology and their ultimate applications in the clinic. In 2001, he launched a program that does just that: the Demystifying Medicine seminar series, a course that features presentations by basic scientists, clinicians, and patients on major diseases and health conditions. This year for the first time, Arias offered Research Festivalgoers a sampling of his ever-popular program in hopes of enticing people to register for the 2015 session, which begins in January (http://demystifyingmedicine.od.nih.gov).

Craig Blackstone (National Institute of Neurological Diseases and Stroke) and William Gahl (National Human Genome Research Institute) are searching for answers to diseases of unknown etiology. Blackstone presented research on people with hereditary spastic paraplegias, a group of inherited disorders that are characterized by progressive weakness and spasticity (stiffness) of the legs. Using genetic sequencing, he was able to find mutations in a particular protein complex and subsequently uncovered how these proteins function in cells.

Gahl, who’s the director of the NIH Undiagnosed Diseases Program (UDP), also used genetic sequencing to discover the causes of some rare diseases. The UDP has been so successful that the NIH Common Fund started an Undiagnosed Diseases Network to encourage and train clinicians across the country to use genomic data to diagnose diseases.

Then National Cancer Institute’s Frank Maldarelli and John Coffin talked about their research on the human immunodeficiency virus (HIV) and antiretroviral therapy (ART) and how to respond to changes in the virus and the host.

Maldarelli presented an overview of HIV and its phylogeny, including the finding that HIV-1 is related to the simian immunodeficiency virus found in chimpanzees and that most likely humans first became infected by coming into contact with infected chimpanzee meat. Although 26 antiretroviral drugs can prolong life and prevent mother-to-child transmission of HIV, new cases of HIV infection still occur. Research on HIV is not nearly finished, he said.

Coffin explained why ART can only hold HIV infections at bay, but not cure them. ART blocks the formation of provirus (the virus genome that is integrated into the DNA of a host cell), but it has no effect on already-infected cells. In fact, should ART therapy be interrupted for as little as a week (even after years of therapy), those infected cells can cause the concentrations of HIV to return to pretherapy levels.

From the 2014 Research Festival session “Demystifying Medicine: A Sampler,” chaired By Win Arias (CC) and held on Tuesday, September 23, 2014.

THE CHALLENGES OF AGING
BY STEPHANIE COOPERSTEIN

Life expectancy is on the rise, but increased life span brings with it an increased burden of chronic disease and disability. Luckily, geriatric epidemiologists have made invaluable contributions to our understanding of the health status and functional trajectory of older individuals and have helped generate interventions to improve their lives. Several NIH researchers highlighted their aging-related research.

National Institute on Aging (NIA) Scientific Director Luigi Ferrucci argued for the need to “characterize and measure aging parameters and establish a list of candidate measures” in order to better understand disease and disability in the elderly and why frailer individuals are at a higher risk of developing comorbidity and disability.

“Age is the strongest predictor for most chronic diseases,” said Andrew Johnson (National Heart, Lung, and Blood Institute), who focuses on how the genetic and genomic underpinnings of individuals with cardiovascular disease affect their response to therapy. Using gene-expression studies, his team has predicted the “top 50 to 100 genes” identified with aging.
Michelle Shardell (NIA) described a new method to handle selection bias and incorrect conclusions in epidemiologic studies giving an example a case study of vitamin D and physical performance.

Charles Matthews (National Cancer Institute, NCI), who studies the relationship between physical-activity behaviors and cancer risk, is developing measurements that will better define the type and amount of physical activity needed to reduce the risk of developing cancer. This knowledge is critical for evidence-based public-health guidelines linking physical activity to cancer prevention and control.

FARE Award winner Elizabeth Yanik (NCI) presented research, based on an analysis of 2002–2009 Medicare claims and other data, that suggested that oral leukoplakia (white or gray plaques inside the mouth) is an early indicator for the risk of oral-cavity cancer in elderly adults. The earlier the diagnosis, she reported, the better a patient's chance of survival.

From the 2014 Research Festival session “Epidemiology of Aging,” co-chaired by Francesca Macchiarini (NIAID) and Evan Hadley (NIA) and held on September 22, 2014.

OH, THE PAIN OF IT ALL
BY LAURA STEPHENSON CARTER

Research Festival attendees heard from several NIH researchers who are conducting pioneering pain research.

“Pain and depression frequently co-exist,” explained Ted Usdin (National Institute of Mental Health), who found that, in mice with a temporary sciatic-nerve injury, depression and anxiety—as well as cellular changes in the hippocampus—persist for at least 30 days after the pain is gone. There seems to be signaling coming from somewhere other than the original pain source, said Usdin. “We are trying to figure out where.”

To figure out the neurobiology of pain, Kathryn Tabor (FARE Award winner in the National Institute of Child Health and Human Development) is using electric pulses to activate certain neurons that drive the rapid-escape response in zebrafish. The rapid-escape response is similar to the withdrawal reflex exhibited by higher animals in response to a pain stimulus.

Other researchers, such as Michael Iadarola (Clinical Center), are trying to figure out how to reduce pain. Iadarola described a clinical trial that is testing whether resiniferatoxin (RTX), a naturally occurring chemical from a cactus-like plant, can reduce the need for the opioids that are typically used to control certain types of pain. RTX works by destroying nerves that transmit pain information. “It’s too early to draw conclusions,” about the drug’s effectiveness, he said.

Scientific Director Catherine Bushnell (National Center for Complementary and Alternative Medicine) wrapped up the session by describing her institute’s focus on understanding the brain’s role in perceiving, modifying, and managing pain, with a special emphasis on nonpharmacological modulation of pain. She described one study that explored the mechanisms underlying reduced pain perception in yoga practitioners. Not only do yogis tolerate pain more than twice as long as individually matched control subjects, but they also have more gray matter in multiple brain regions. Bushnell also mentioned that other NCCAM researchers are exploring how, in mice, exercise and environmental enrichment may play roles in reducing the perception of pain.

From the 2014 Research Festival session “Moving Molecules from Model Systems to Medicine in Pain Research,” co-chaired by Alexander Chesler (NCCAM) and Yarimar Carrasquillo (NCCAM) and held on Tuesday, September 23, 2014.

READ MORE ONLINE AT:

Nature’s Drugs
BY LAURA STEPHENSON CARTER

Let’s Light Up the Brain
BY EMILY PETRUS, NINDS

Women’s Health: Bridging the Gap between Sex and Gender and between Race and Ethnicity
BY SOMA CHOWDHURY, OIR

Opening the Clinical Center’s Doors to Extramural Researchers
BY STEPHANIE COOPERSTEIN
to her family and friends, and to everyone involved in her care. “As a nurse, I have a special appreciation for the care I have received from so many people.”

Although Pham declined to take questions, the reporters had plenty for Fauci, who is the director of the National Institute of Allergy and Infectious Diseases (NIAID).

“How do you know that she’s virus-free?” asked one of the reporters.

“We know she is virus-free because we now have five consecutive negative PCRs,” said Fauci, referring to a test called a PCR (polymerase chain reaction), which detects bits of the virus’s RNA and is used to confirm an Ebola diagnosis. “We did five because this is a research institution. But that’s not the norm.”

Fauci went on to describe the kind of treatment Pham and other Ebola patients receive. It is important to “give them the kind of general medical support to allow their own body to be able to fight off the virus and essentially get rid of [it],” he said.

Supportive care includes providing intravenous fluids and electrolytes; maintaining blood oxygenation and blood pressure; and treating secondary infections if they occur. Pham also received plasma from Kent Brantly, the first person to be treated for and recover from Ebola in the United States—he was treated at Emory. People who recover from Ebola develop antibodies against the particular strain of the virus that infected them. It is not known, however, whether the transfusion played a role in Pham’s recovery.

“When you have so many separate factors...going into the care of this patient, it is virtually impossible to say that this is the thing that did it,” said Fauci. Clinical studies are needed to evaluate the efficacy of plasma transfusions containing anti-Ebola antibodies.

It didn’t hurt that Pham was cared for in NIH Clinical Center’s SCSU, which can accommodate up to two patients at a time and is designed to provide excellent clinical care and high-level isolation. It is staffed by clinicians trained in infectious diseases and/or critical care and in strict infection-control practices. The unit can provide routine to state-of-the-art intensive care. In terms of isolation, many redundant systems and precautions are in place such as special air-handling systems; cardkey restricted access; separate entrance and exit pathways for staff, including a shower prior to exit; and detailed protocols for clinical care and the handling of waste. Staff in direct contact with Ebola patients or specimens from them have received rigorous training in the use of personal protective equipment (PPE).

Pham was the second patient exposed to Ebola to be cared for at NIH. The first was an American physician who, while volunteering in an Ebola treatment unit in Sierra Leone, was potentially exposed and later developed a fever. He was admitted to NIH for observation on Sunday, September 28, 2014, tested negative for Ebola, and released on Tuesday, October 7, 2014.

The Ebola virus spreads in humans as a result of direct contact with blood or other body fluids (sweat, feces, vomit, semen, and saliva) from an infected, symptomatic person, contact with the body of a person who has recently died from Ebola, or through exposure to objects that have been contaminated with infected body fluids or secretions.

“When somebody gets exposed, the incubation period averages eight to 10 days, but the range is two to 21,” said Fauci. The problem is, in early stages, Ebola is “virtually indistinguishable” from the flu.

After five days, patients may develop gastrointestinal symptoms such as severe watery diarrhea, nausea, vomiting, and abdominal pain. In late stages of the disease, there may be organ-system failure. In addition to being able to care for Ebola-infected patients, NIH is conducting clinical trials on two Ebola vaccines, one of which was co-developed by NIAID and GlaxoSmithKline (Hanover, Pennsylvania), and will begin a third trial soon with another investigational vaccine that was developed in Canada. In addition, NIH intramural and extramural researchers have also been developing diagnostics and therapeutics such as ZMapp, which has been administered experimentally to several infected patients.

“Although I no longer have Ebola, I know it may be a while before I have my strength back,” said Pham. Fauci hugged her as she left the press conference. Before heading home, she made a stop at the White House, where even President Obama gave her a hug.

Chronobiology and Sleep

BY MATTHEW PAVA, NIAAA

The Scientific Interest Group on Chronobiology and Sleep (Chrono-Sleep SIG) has been resurrected and will serve as a scientific and technical resource for researchers in the intramural research program. Sleep and circadian rhythms represent fundamental, evolutionarily conserved processes that are being investigated by many intramural researchers in various institutes and centers. The SIG will facilitate discourse aimed at advancing sleep and circadian-biology research at NIH. This SIG will also provide a resource for intramural investigators who would like to begin incorporating measures and manipulations of sleep or chronobiological processes into their research.

The Chrono-Sleep SIG plans to have its inaugural meeting in early 2015 and to meet every month thereafter (dates and times to be determined). The SIG plans to host presentations from intramural and extramural sleep and chronobiology researchers. Trainees are strongly encouraged to participate. The SIG will compile and make available a membership list that will indicate members’ areas of technical expertise and research interests. This list will help to facilitate collaborations and reduce redundancies in problem solving that arise when investigators need to establish methods or protocols similar to work in another lab.

For more information, contact Matthew Pava (matthew.pava@nih.gov) or David Klein (kleind@mail.nih.gov). For information on joining the group and the LISTSERV, go to http://sigs.nih.gov/chronobiology. To read an article in the September-October 2014 issue of the NIH Catalyst about intramural researchers studying sleep, fatigue, and circadian rhythms, visit http://irp.nih.gov/catalyst/v22i5/sleep-perchance-to-research.

AWARDS

THE INSTITUTE OF MEDICINE (IOM)

On October 20, the IOM announced the names of 70 new members and 10 foreign associates during its 44th annual meeting. Election to the IOM is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service. Two NIH intramural researchers were elected: James Cimino (CC and NLM) and John O’Shea Jr. (NIAMS). Cimino’s primary research relates to clinical research informatics and clinical informatics, with special emphasis on biomedical-concept representation and automated-decision support. O’Shea discovered Janus kinase 3 (Jak3) and showed that genetic defects in its gene, Jak3, could cause severe combined immunodeficiency. His work led to collaboration with Pfizer, Inc., which generated a JAK inhibitor that is approved by the FDA for the treatment of rheumatoid arthritis.

NATIONAL MEDALS

NCI’s Douglas Lowy and John Schiller will receive the National Medal of Technology and Innovation, which along with the National Medal of Science is the nation’s highest honor for achievement and leadership in advancing the fields of science and technology. Lowy and Schiller made breakthrough discoveries that advanced the development of vaccines against human papillomavirus, the cause of almost all cases of cervical cancer. Roscoe Brady (NINDS) won this award in 2008. Winners of the National Medal of Science: Anthony Fauci (NIAID) in 2005; and Mortimer Mishkin (NIMH) in 2010.

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
ORI: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women’s Health
OTT: Office of Technology Transfer
CHRISTOPHER BAKER, PH.D., NIMH
Senior Investigator, Section on Learning and Plasticity, Laboratory of Brain and Cognition

Education: University of Cambridge, Cambridge, England (M.A. in neuroscience); University of Saint Andrews, Saint Andrews, Scotland (Ph.D. in psychology)

Training: Postdoctoral training at the Center for the Neural Basis of Cognition, Carnegie Mellon University (Pittsburgh); postdoctoral associate, Department of Brain and Cognitive Sciences and McGovern Institute for Brain Research, Massachusetts Institute of Technology (Cambridge, Mass.)

Came to NIH: In 2006

Selected professional activities: Reviewing editor, The Journal of Neuroscience; academic editor, PLoS ONE

Outside interests: Trying to keep up with three very active children

Web site: http://irp.nih.gov/pi/chris-baker

Research interests: My research aims to better understand how the structure, function, and selectivity of the cerebral cortex change with experience or impairment, even in adulthood.

I am using brain-imaging techniques to explore three avenues of research. The first avenue concerns the nature of perceptual representations in the human brain, focusing on complex visual stimuli such as faces, bodies, scenes, and words.

In the second avenue of research, I am investigating how experience and learning change the neural and cognitive representations of sensory input. For example, my section is exploring the neural changes that underlie our enormous capacity to learn to recognize new objects and make fine-grained discriminations among them.

The third avenue concerns how the cerebral cortex adapts after damage to either the peripheral or the central nervous systems. For example, we are trying to determine the impact of macular degeneration or amputation on cortical function and how it relates to conditions such as phantom-limb pain.

Elucidating the nature and extent of cortical plasticity is critical for understanding how the brain functions throughout life.

Before coming to NIH: Assistant professor in the division of infectious diseases, University of Iowa College of Medicine (Iowa City)

Came to NIH: In 1989 through 1991 for training; returned in 1997 as a staff clinician in NIAID’s Laboratory of Infectious Diseases; 2009 became a tenure-track clinical investigator

Selected professional activities: Member of the executive committee of the International Eosinophil Society; co-director of the Mali International Centers for Excellence in Research’s Filariasis Group

Outside interests: Spending time with family (including the dogs); traveling; and doing the New York Times crossword puzzle

Web site: http://irp.nih.gov/pi/amy-klion

Research interests: The Eosinophil Pathology Unit conducts basic and translational research related to the role of the eosinophil (a type of white blood cell) and eosinophil activation in disease pathogenesis. Our ultimate goal is to develop novel diagnostic tools and treatments for hypereosinophilic syndrome (HES) and other conditions associated with marked eosinophilia (a higher than normal concentration of eosinophils), including parasitic worm infections.

HES is a heterogeneous group of rare disorders in which eosinophils are responsible for the clinical manifestations. We
are using genetic and immunologic tools to identify and characterize new subtypes of HES, such as an autosomal dominant form of familial eosinophilia that has been mapped to chromosome 5q31-33 and a rare cyclic form of eosinophilia associated with angioedema. Our clinical trials using targeted therapies, including imatinib mesylate and monoclonal antibodies to IL-5 and IL-5 receptors, have provided insight into the etiology and pathogenesis of HES variants.

Eosinophilia is common in human helminthic infections and may be associated with pathologic sequelae that mimic clinical findings in HES, including tissue fibrosis and “allergic” manifestations. These manifestations may be produced or exacerbated by anthelmintic therapy.

We are assessing the safety and efficacy of chemotherapeutic agents that target eosinophils (or precursors) to prevent post-treatment reactions in loiasis, a filarial infection associated with eosinophilia after anthelmintic therapy. We are also exploring the role of eosinophils in post-treatment reactions in other helminthic infections.

**Research interests:** My goal is to understand branching morphogenesis and patterning in organ development, especially in the vascular and nervous systems, which are often patterned similarly. My lab is using a combination of high-resolution whole-mount imaging, molecular manipulations, advanced genetic perturbations, and in vitro organ-culture techniques.

During angiogenesis, a primary capillary network undergoes intensive vascular remodeling and develops into a hierarchical vascular branching network. We have shown that sensory nerves determine the arterial branching pattern in embryonic skin. This alignment facilitates access to oxygen and nutrients for the nerves. At the molecular level, two distinct mechanisms underlie the sensory nerve-artery alignment: Nerve-derived vascular endothelial growth factor A controls arterial differentiation, and nerve-derived C-X-C motif chemokine 12 (also known as stromal cell-derived factor 1) controls vessel branching and alignment with nerves.

We have also shown that blood vessels influence nerve patterns in the embryonic heart. After the hierarchical vascular network is thoroughly covered with vascular smooth-muscle cells (VSMCs), sympathetic nerves extend along the network and innervate large vessels to control vascular tone and help regulate blood pressure. Coronary veins serve as intermediate conduits that guide distal sympathetic axon projections via the secretion of nerve growth factor (NGF) by coronary VSMCs. Subsequently, venous VSMCs downregulate NGF expression, and arterial VSMCs begin to secrete NGF, which stimulates the axons to innervate coronary arteries.

Our studies demonstrate a unique concept for understanding branching morphogenesis and patterning: Blood vessels and nerves take advantage of one another to follow the same path. Ultimately we hope to understand the developmental programs of branching morphogenesis and patterning in the vascular and neuronal branching networks and how we can restart these programs in diseased organs to generate healthy new networks. We are fortunate to be in a collaborative research environment that allows us to use core facilities and involve colleagues who have invaluable expertise.

**Vipul Periwal, Ph.D., NIDDK**
Senior Investigator; Chief, Laboratory of Biological Modeling, Computational Medicine Section

**Education:** California Institute of Technology, Pasadena, Calif. (B.S. in physics and mathematics); Princeton University, Princeton, N.J. (M.A. and Ph.D. in physics)

**Training:** Research physicist, Institute for Theoretical Physics, University of California, Santa Barbara, Calif. (1988-1991); Member, Institute for Advanced Study, Princeton, N.J. (1991-1993)

**Before coming to NIH:** Assistant professor, Physics Department, Princeton University
**Came to NIH:** In 2003

**Outside interests:** Reading fiction, biking, skiing, listening to classical music, and visiting art museums

**Web site:** http://1.usa.gov/1pu1Un4

**Research interests:** In my lab, we use mathematical models to understand and predict the functioning of human and animal metabolism and, more broadly, biological systems relevant to human disease. An important focus has been on insulin resistance, a major risk factor for several common diseases including diabetes, heart disease, high blood pressure, and some forms of cancer. The mechanisms underlying insulin resistance are not completely understood.
At the NIH, we developed the first mathematical model of mitochondrial metabolism, taking into account reactive oxygen species (ROS) and their control. Metabolism leads to the production of ROS; ROS signaling is important in normal cellular functioning. In oxidative stress, the body’s inability to detoxify and repair damage as fast as ROS are produced may be associated with insulin resistance. We developed a theoretical framework for modeling the dynamic development of the entire fat-cell size distribution. Ours was the first mathematical model of dynamic fat-tissue development. We continue to investigate how dynamic changes in fat tissue relate to insulin resistance and diabetes.

Additionally, we developed the first mathematical model of the formation and growth in the pancreas of the islets of Langerhans, the crucial endocrine micro-organs that maintain glucose concentrations. We also developed the first mathematical model of liver regeneration—in rats—and then showed that the model applies with almost no essential changes in humans who have been liver donors.

Using high-throughput biomedical datasets, we are gathering information on basic mechanistic molecular interactions and mechanisms. We are predicting the activity of transcription factors from DNA sequences, finding collective modes in protein structures from sequence alignments, and determining molecular interactions from single-cell data. Improving the understanding of disease processes should help in the development of effective treatments that do not have harmful side effects.

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

**PETER WILLIAMSON, M.D., PH.D., NIAID**
Senior Investigator; Chief, Translational Mycology Unit, Laboratory of Clinical Infectious Diseases

**Education:** Loyola University of Chicago (B.S. in chemistry, minor in mathematics); Boston University, Boston (M.D. and Ph.D. in medicine and biochemistry)

**Training:** Residency in internal medicine at Georgetown University Medical Center (Washington, D.C.); fellowship in infectious disease in NIAID

**Before coming to NIH:** Professor of medicine, pathology, microbiology, and immunology at the University of Illinois at Chicago

**Came to NIH:** From 1989 to 1994 for training; returned in 2009 to head NIAID’s Translational Mycology Unit

**Selected professional activities:** Editorial boards of *Frontiers in Mycology* and *Journal of Mycology*

**Outside interests:** Medical and medical educational activities in East Africa

**Web site:** http://irp.nih.gov/pi/peter-williamson

**Research interests:** The Translational Mycology Unit seeks to understand the role of host-pathogen genetics in the outcome of fungal infections. We use an array of methods including fungal genetics, cell biology, immunology, and population genetics to identify and validate weak points of the host-pathogen interface that might facilitate personalized therapeutic intervention.

My laboratory focuses on the AIDS-related pathogen *Cryptococcus neoformans*, which kills over a half a million people a year in regions of Africa and Asia, as well as *Candida albicans*, a major cause of bloodstream infections in the United States.

Specifically, we are interested in how a pathogen such as Cryptococcus undergoes genetic changes to convert itself from an environmental colonizer to a human pathogen. When the pathogen invades the host, changes in the expression of virulence factors optimize the acquisition of nutrients including copper, iron and glucose, paralyze the host immune response, and protect the fungus.

We use mouse modeling as well as high-dimensional data analyses of human isolates from people with and without AIDS to understand the fine coordination among genes that determine pathogenicity and suggest novel new treatment strategies. We have also used clinical genetic studies of patients with *Candida albicans* infections and mouse modeling to identify and study a human gene whose expression levels predict death during treatment.

In addition, we are recruiting an unusual cohort of patients to the NIH Clinical Center who do not have an underlying immunodeficiency but have acquired severe meningitis from the fungus for no apparent reason. In a trans-institute initiative with the National Institute of Neurological Disorders and Stroke, we are seeking to determine the nature of host defects that might have resulted in infection as well as to identify novel methods for immunomodulation of the disease to improve treatment outcomes.

**STORYCORPS**

NIH’s Office of Science, Outreach, and Policy has partnered with NPR’s StoryCorps, a national oral-history project, to give patients, their loved ones, researchers, staff, and others in the community an opportunity to share their stories. For more information or to ask to participate, e-mail storycorps@nih.gov. For more details see the online Catalyst at http://irp.nih.gov/catalyst/v22i6/announcements.
THIRD ANNUAL DAVID DERSE MEMORIAL LECTURE AND AWARD
Tuesday, November 18, 1:30–3:00 p.m.
NCI-Frederick
Building 549 Conference Center
Walther Mothes (Yale University School of Medicine) will deliver the lecture “Seeing Is Believing–Visualizing Individual Steps of the Retroviral Life Cycle.” The event will be video- cast live at http://videocast.nih.gov.

WORKSHOP: REPRODUCIBILITY OF DATA COLLECTION AND ANALYSIS
Monday, November 24, 8:30 a.m.–4:30 p.m.
Lipsett Amphitheater (Building 10)
For agenda and to register, go to:
http://wals.od.nih.gov/reproducibility
This workshop will be the first of three on the important topic of reproducibility, the subject of recent editorials in leading scientific journals. Several world-class scientists will speak about important technologies in cell biology; a panel of editors from five journals covering cell biology will discuss issues with data reproducibility in the scientific literature. The purpose of these workshops is to educate intramural researchers about what advanced technologies can accomplish and the kinds of reproducibility problems that can arise. Videocast live: http://videocast.nih.gov.

THE ANITA B. ROBERTS FALL LECTURE
Thursday, December 11, 3:30–4:30 p.m.
Lipsett Amphitheater (Building 10)
Y. Peng Loh, section chief of NICHD’s Section on Cellular Neurobiology, will present “Neurotrophic Factor alpha-1: A Key Regulator of Neuroprotection, Depression, and Cancer Metastasis.” This seminar series highlights outstanding research achievements of women scientists in NIH’s Intramural Research Program and is dedicated to the memory of Anita B. Roberts, former chief of NCI’s Laboratory of Cell Regulation and Carcinogenesis. Individuals with disabilities who need reasonable accommodations to participate should contact Margaret McBurney at 301-496-1921 and/or Federal Relay, 1-800-877-8339, five days before the lecture.

WEDNESDAY AFTERNOON LECTURES
Most Wednesdays, 3:00–4:00 p.m.
Masur Auditorium (Building 10)

CLINICAL CENTER GRAND ROUNDS
Wednesdays, Noon–1:00 p.m.
Lipsett Amphitheater (Building 10)

DEMYSTIFYING MEDICINE 2015
Tuesdays, January 6–April 28, 2015
4:00–6:00 p.m.
Building 50 Conference Room
The “DeMystifying Medicine” course bridges the gap between advances in biology and their application to disease. Each class features presentations by a clinician, a researcher, and often a patient. Topics will include ADHD (January 6), dengue (January 13), new advances in cancer diagnosis and treatment (January 20), Ebola (January 27), tuberculosis (February 3), malaria (March 3), infertility (April 7), and more. For more information, visit http://demystifyingmedicine.od.nih.gov or contact Win Arias at ariasi@mail.nih.gov.

2014–2015 DIRECTOR’S SEMINAR SERIES
Fridays, 12:00–1:00 p.m.
Wilson Hall (Building One)
The speakers are recently tenured senior investigators. For questions, contact the Office of Intramural Research at 301-496-1921.

November 14: Joshua Milner (NIAID), “Pathogenic Pathways in Allergy Gleaned from Monogenic Diseases.” Future seminars on January 9, February 6, March 6, April 10, May 8, June 5.

FAES GRADUATE SCHOOL ONLINE REGISTRATION FOR SPRING TERM
December 1, 2014–January 23, 2015
Late registration runs till February 13, 2015
Open House: January 15, 2015
FAES Academic Center Terrace (Building 10)
The FAES Graduate School has over 120 evening courses (held mostly on the main NIH Bethesda campus). Courses are credit-bearing, cover fields relevant to the biomedical research community, and are open to the NIH community, other federal employees, and the general public. Tuition is $150–$450 per course. For more information, visit www.faes.org/grad, e-mail registrar@faes.org, or call 301-496-7976. The FAES office is in Building 10, Room 1N241 (close to Masur Auditorium).

OFFICE OF EQUITY, DIVERSITY, & INCLUSION LAUNCHES NEW WEB SITE
NIH’s Equal Employment Opportunity and anti-discrimination office is now the Office of Equity, Diversity, and Inclusion (EDI). EDI’s new mission statement is “We cultivate a culture of inclusion where diverse talent is leveraged to advance health discovery.” To learn about innovations at EDI, visit http://edi.nih.gov/.

THE NIH VOLUNTARY LEAVE BANK
Open enrollment: November 10–December 8
Membership period begins: January 11, 2015
The Leave Bank is a pooled bank of donated annual and restored leave available to eligible members. To become a member, access the Integrated Time and Attendance System (ITAS) during the open enrollment and enroll under “Leave Bank Membership.” If you are already a 2014 member, your membership will automatically continue into 2015, unless you opt-out during the open-enrollment period. The annual membership contribution is one pay period’s worth of annual leave accrual. To access ITAS, go to https://itas.nih.gov. For more information about the NIH Leave Bank, visit http://hr.od.nih.gov/benefits/leave/vlbp/default.htm. Direct questions to the NIH Leave Bank Office at 301-443-8393 or LeaveBank@od.nih.gov.

Read more online at http://irp.nih.gov/catalyst/v22i6/announcements.
This Art Nouveau–style window, depicting a waterfall, towers above a stairwell leading to what used to be a conference room on the fourth floor in the now-vacant Building 7. The building was once home to NIH scientists who worked on infectious diseases, identified new viruses, and developed vaccines against hepatitis, rotavirus, and adenoviruses (1947–2009). The conference room was built in memory of and named for one of those scientists—Wallace P. Rowe, who died of colon cancer at the age of 57 in 1983. Lab meetings were held there until 2001. Building 7—and the waterfall window with its matching balusters—is slated for demolition in 2016. Read more about Building 7 and its rich history in the September-October 2014 issue of the NIH Catalyst at http://irp.nih.gov/catalyst/v22i5/secrets-of-building-7). Anyone interested in rescuing the window should contact Christopher Wanjek (wanjek@od.nih.gov or 301-402-4274).