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Precision Psychiatry

Research Domain Criteria Leading the Way

BY MICHAEL LEHMANN, NIMH

Imagine you arrived at a hospital emergency room before the advent of modern medicine with intense abdominal pain. You could have had a stomach virus, kidney stones, appendicitis, or something worse. But because the doctors lacked the proper diagnostic tools and knowledge to identify your illness, the only thing they could do was treat your most prominent symptom—your pain.

For many with mental-health problems this scenario is still close to reality. There are no lab tests to diagnose what's wrong, so clinicians have no choice but to treat the symptoms—such as hallucinations in schizophrenia—but not the underlying disorder. And, like abdominal pain, each of the symptom-based diagnostic categories may include a diverse group of disorders.

Until recently, most mental-health diagnoses, treatments, and research have been structured according to definitions in the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*). The *DSM*, which was first published in 1952 and has been continuously revised and improved since then, uses clusters of symptoms agreed upon by psychiatrists to classify disorders into such categories as major-depressive disorder, autism, and schizophrenia. Although the manual is useful in that it provides a consistent terminology, it lacks the precision that derives from objective biological, behavioral, and socio-cultural information.

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Creating Devices for the Clinic

Deciding Which Seeds Are Worth Watering

BY LESLEY EARL, NCI

COURTESY CENTER FOR INTERVENTIONAL ONCOLOGY

Bradford Wood is using a fusion-imaging technique developed by NIH's Center for Interventional Oncology. The technique involves superimposing a magnetic-resonance-imaging scan on a real-time ultrasound image to create a detailed map of an internal area to be biopsied or treated. As Wood looks at a computer screen showing the map, he can guide the needle to the appropriate areas.

For every great idea—for every great solution to a problem—there are a thousand ideas that fall by the wayside, discarded along the path that begins at the first flash of insight and ends in a working solution. Translational medicine, in which an idea for a clinical solution is shifted from the laboratory testing ground to the public, often follows this twisty path, especially in the realm of developing new medical devices.

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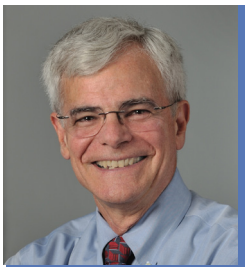


Data Sharing: Greater Than the Sum of All Parts

BY MICHAEL GOTTESMAN, DDIR

Aristotle's saying "The whole is greater than the sum of its parts" is as true today as it was in the mid-300s B.C.E., especially when it comes to sharing genomic and other kinds of biomedical data. When scientists can draw on huge repositories of research data, the discovery process is enhanced in ways not possible if they simply added up all the findings of individual studies.

Scientists can explore a wider range of research questions; improve the reproducibility and validation of research results; dig deeper into research questions than perhaps was done by the originators of the data; and advance the innovation of methods and tools for research. As a matter of principle and policy, NIH has long had an understanding with its investigators that data obtained using public monies would be widely shared with responsible individuals to accelerate the discovery process.

Although NIH and NIH-funded scientists are already required to share many types of biomedical data, until recently there has not been an explicit requirement for the development of data-sharing plans or the tools to implement these plans. The NIH as a whole, and the intramural program specifically, now have policies that cover both the sharing of genomic data (including human genomic data and data from all model systems) and the more general sharing of data derived from human subjects research or human specimens. These policies were recently sent to all principal investigators at the NIH and can be found at the following websites: http://gds.nih.gov and http://oma1.od.nih.gov/manualchapters/intramural/3016/, respectively.

You will be hearing directly from your scientific director or the person designated within your institute or center (IC) to be the point of contact on these data-sharing issues about your requirements for creating data-sharing plans under the Genomic Data Sharing (GDS) policy, which went into effect on August 31, 2015. Please also review the memos and *NIH Policy Manual* chapters you have already received about data sharing. In brief, the GDS policy contains the following basic requirements.

> Sharing data allows scientists to explore a wider range of research questions and improve the reproducibility and validation of results.

Sharing Human Data: IRP investigators must submit covered human genomic data and associated data (such as phenotype and exposure) to an NIH-designated repository. As was the practice under the NIH Genome Wide Association Studies (GWAS) Policy, NCBI's database of Genotypes and Phenotypes (dbGaP) will, in most cases, be the repository, although alternative repositories can be approved by your IC, and rare exceptions can be granted by the DDIR.

Registration: All human genomic data studies covered by the GDS policy must be registered in dbGaP by the time that data-cleaning and quality-control measures begin, regardless of which data repository will ultimately house and distribute it. Investigators should work with their designated genomic program administrator (GPA) to initiate the registration process.

De-identification: Before sharing, data should be de-identified according to current requirements.

Informed Consent and IRB Review: An institutional review board (IRB) will review study protocols and informed-consent materials to determine whether it is appropriate for data to be shared for secondary research use.

Institutional Certification: As was the practice under the NIH GWAS Policy, each IC must complete an institutional certification as part of the data-submission process. This document identifies whether human genomic data are being submitted for unrestricted or controlled-access use and ensures that certain provisions to protect the interests of research participants are satisfied.

The institutional certification should be completed by the investigator and signed by the scientific director. Whenever possible, the scientific director, or delegate, should send the institutional certification memorandum to the IC genomic point of contact before research is begun (see http://gds.nih.gov/Institutional_Certifications.html).

The human data-sharing (HDS) policy requires the development of data-sharing plans by October 1, 2015 (see chapter 3016 of the *NIH Policy Manual* at http://oma1.od.nih.gov/manualchapters/intramural/3016). Once again, your scientific director will explain the requirements, which initially will consist of data-sharing plans for all projects beginning preresearch scientific review after October 1, 2015.

The broader sharing of human data derived from our human subjects research at the NIH requires fastidious attention to the requirements of protecting privacy and consistency with all informed consent documents, as described in the *NIH Policy Manual* chapter 3016 on HDS.

At this time, a data-sharing plan for clinical trials might well consist of sharing with external collaborators and submitting data to ClinicalTrials.gov (as is required for all clinical trials conducted at the NIH), but for natural history trials and other clinical investigations, additional repositories may be necessary. We are exploring the possibility of adapting the Biomedical and Translational Information System to enable HDS as appropriate.

Please work closely with your scientific director and your IC contacts for further information and to determine whether your data are covered by the GDS and/or HDS policies. Thank you for ensuring that the very valuable data you obtain will be shared appropriately with the wider scientific community. ●

NEWS FROM AND ABOUT THE SCIENTIFIC INTEREST GROUPS

NEW SIG: DEVELOPMENTAL BIOLOGY

The Developmental Biology SIG seeks to foster and coordinate interactions among all NIH developmental biologists who use diverse experimental approaches and distinct model organisms. The SIG provides a collegial forum for investigators interested in the underlying principles of development and how they relate to human development and disease. The group hosts developmental biology workshops that feature keynote speakers and presentations by postdoctoral fellows. Workshops facilitate interactions among presenters and attendees, promote discussion, and solicit feedback on experimental observations. The SIG also provides mentoring to trainees. To join the LISTSERV (DEVELOPMENTAL-BIOLOGY@list.nih.gov), go to https://list.nih.gov/cgi-bin/wa.exe?SUBED1=DEVELOPMENTAL-BIOLOGY&A=1. For questions, contact the steering committee coordinator, Jurrien Dean (jurriend@helix.nih.gov).

NEW SIG: TRANS-NIH BIOMARKERS IN PEDIATRIC THERAPEUTICS

This SIG is pursuing opportunities for strengthening cross-disciplinary pediatric biomarker research at NIH while innovating beyond existing investments. Its goals are to provide leadership, vision, and support to promote a strong body of pediatric biomarker research funded by NIH; and to collect, evaluate, and disseminate scientific information and funding opportunities for biomarker research in pediatric therapeutics at NIH. Participants will include NIH program officials, intramural investigators, FDA regulators, and investigators from NIH networks. Industry scientists working in similar or complementary areas will be invited to participate in seminars and workshops. The group will promote trans-NIH funding announcements, host speakers, and support panels and minisymposia, national and international webinars, and group discussions. Activities will be coordinated by an interdisciplinary steering committee. The initial meeting of the steering committee will be in September 2015, and the first all-hands presentation and webinar will be on January 12, 2016, at 12:00 noon in room 9100/9104 (Rockledge II). To join the SIG, contact George Giacoia at giacoiag@exchange.nih.gov.

NEW SIG: PULMONARY VASCULAR DISEASES

The Pulmonary Vascular Diseases (PVD) SIG will foster cooperation among NIH intramural investigators and extramural communities who share an interest in basic and translational PVD research. The PVD SIG will facilitate interinstitute multidisciplinary synergistic collaborations and knowledge sharing. The group will provide a forum for developing PVD-related educational programs at NIH and regionally. The programs may include a combination of lectures, seminars, panel discussions, journal discussions, poster sessions, and more. The SIG also strives to provide peer-to-peer mentoring to trainees interested in PVD. The SIG will meet quarterly with the inaugural meeting scheduled for Wednesday, October 28, 2015, 4:00–5:00 p.m., in Room 2C145 conference room (Building 10). Anyone may attend. For more information and notices of meetings and events, join the LISTSERV (https://list.nih.gov/cgi-bin/wa.exe?A0=PULM_VASC_DIS-L) or contact Michael Solomon at Msolomon@CC.NIH.GOV.

NEW SIG: SINGLE-CELL GENOMICS

Many at NIH already have explored recent advances in nanotechnology and next-generation sequencing that make it feasible to sequence the genomes and transcriptomes of individual cells. The Single-Cell Genomics SIG will build upon this momentum by presenting a monthly seminar series with both internal and outside experts. The SIG also plans to run a monthly joint lab meeting to discuss technologically related issues. Potential future events include a scientific symposium and workshops. To join the LISTSERV (SINGLECELLGENOMICS-L), visit https://list.nih.gov/cgi-bin/wa.exe?SUBED1=SINGLECELLGENOMICS-L&A=1. Direct questions to co-chairs, Paul Liu of NHGRI (pliu@mail.nih.gov) and Mark Cookson of NIA (cookson@mail.nih.gov). ●

FROM THE FELLOWS

Curiosity of Curiologie

BY APRIL KILLIKELLY, NIAID

Two seventh-grade girls were intently watching three nightcrawlers (earthworms) positioned on a table between wet and dry paper towels. Which direction would they go, the girls wondered. Meanwhile, a previously sassy and nonchalant classmate peered over their shoulders and squealed, "O M G [oh my God], it moved!"

Thus began a typical Saturday morning science-enrichment session for middle-school students taking part in "Curiologie in the Classroom" (CiC) at the Shaw Campus of Center City Public Charter Schools (Washington, D.C.). CiC has been going strong since 2013, when a group of NIH trainees joined forces with a Shaw middle-school science teacher who wished to expose her students to more opportunities in science, technology, engineering, and mathematics (STEM).

The half-dozen CiC volunteers plan and facilitate science experiments for a group of 10 to 15 middle schoolers (grades 6–8). Initially, the volunteers paid for the science-experiment materials themselves. But soon CiC partnered with the nonprofit RESET (Raising Excitement for Science Engineering and Technology), which provided funding for materials as well as for field trips to a wildlife sanctuary and a science museum.

As CiC volunteers, we facilitate learning by drawing on our own experiences and encouraging the students to work independently and take ownership of their science. Our interactive experiments emphasize the biomedical sciences in such areas as human digestion, epidemiology, and animal behavior. Other topics have included physics (electromagnets, polymers), chemistry (chromatography), and earth science (viscosity, erosion).

In one experiment, the kids had fun building electromagnets. Each magnet consisted of insulated copper wire wrapped around a nail; the wire ends were attached to the terminals of a flashlight battery. The students measured the magnet's strength by picking up metal paperclips. We encouraged the students to experiment with the length and size of the coiled wire to vary the magnet's strength (the longer the wrapped wire, the stronger the magnet). They tried picking up the paperclips from various distances and used a compass to demonstrate the lines of magnetic force emanating from the electromagnet. It was gratifying to encourage the students to engage in the type of thinking and questioning that NIH scientists use.

"I notice a marked difference in the students who regularly participate in CiC," said Shaw science teacher Nina Barcelli. "CiC helps to empower students to feel confident in science, a discipline that can often be intimidating."

The National Science Teachers Association (NSTA) recommends a strong emphasis on middle-school-level science education and cautions that "if educators don't capture students' interest and enthusiasm in science by seventh grade, students may never find their way back to science" (http://www.nsta.org/about/positions/middlelevel.aspx). Programs such as CiC are consistent with the NSTA's position and aim to broaden the exposure of middle-school students to science topics, empirical questioning, and data collection.

The CiC has also begun working with underserved communities through the Homeless Children's Playtime Project (HCPP). HCPP provides weekly educational and play activities for children living in emergency and transitional housing. This summer, CiC started running

NINA BARCELLI

CiC volunteers run science-enrichment programs for middle-school and high-school students in Washington, D.C. Here middle-school students are building an electromagnet that can pick up metal paperclips.

evening science-enrichment sessions for middle-school and high school students at Washington, D.C.'s largest shelter, DC General. Our aim is the same as for the Shaw program—nurturing students' interest in science through experimentation with an emphasis on fun.

We will also continue our weekend work with middle-school students and coach them through scientific experiments like the one with the nightcrawlers. The worms, which prefer a damp environment, eventually gravitated toward the wet paper towels. Further testing revealed that the worms also liked dark spaces and did not like to be touched with a Q-tip. As to whether they enjoyed being the facilitators of science engagement…the results were inconclusive. ●

The author joined CiC in 2014. NIH Trainees who would like to volunteer with CiC can contact April Killikelly at april.killikelly@nih.gov. CiC is not affiliated with nor sponsored by NIH. Volunteers provide services during their free time.

Three-Minute Talks

A Short and Sweet Way to Communicate Science

BY SOMA CHOWDHURY, OD

Who doesn't want to brag about their research? But how quickly can you do it? On July 16, 2015, a good-sized crowd gathered in Lipsett Amphitheater (Building 10) to watch enthusiastic fellows creatively and accurately explain their research, capture and keep the audience's attention, use only one PowerPoint slide, and do it all within three minutes.

The Three-Minute-Talks (TmT) event evolved from the "Three-Minute Thesis" (3MT) competition that started in 2008 at the University of Queensland in Brisbane, Australia. The 3MT has since spread around the world, making its way to NIH last year: The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) hosted its own version, calling it TmT, with the support of NICHD Director **Alan Guttmacher** and Scientific Director **Constantine Stratakis**.

"Dr. Stratakis was the main moving force behind TmT," said NICHD Deputy Director, Liaison and Training, **Brenda Hanning**, who helped organize the event this year and last.

NICHD was already offering workshops on public-speaking and job-interviewing skills to their fellows. TmT turned out to be a popular way to enhance that training and focus on the critical importance of conveying complex science in an accessible way, to the public and even other scientists.

And this year NICHD joined with the National Human Genome Research Institute (NHGRI) and the National Institute of Dental and Craniofacial Research (NIDCR) to host the second annual competition. The pre-event training included a session with a representative from the Alan Alda Center for Communicating Science at Stony Brook University (Stony Brook, New York) and two coaching sessions with communication consultant Scott Morgan, author of *Speaking About Science* (2006). Out of the 30 fellows who participated in the competition, 15 were chosen as finalists for July 16 event.

"I think competing with other institutes this year added energy to the process," said Hanning.

"Everyone there gave a very dynamic talk," said NICHD investigator **Harold Burgess**, who was a judge for NICHD's semifinals competition and on hand for the finals. "They were really fun talks to go to."

The participants were judged on how clearly and concisely they described their research to a nonexpert audience. They were also evaluated on their presentation's logical flow, on how interesting it was, and on how well they explained the background, key findings, and significance of their work. And of course they had to do all that within three minutes.

Kathryn Tabor (NICHD), who won first place, described how she identifies misbehaving neurons in the acoustic-startle pathway in the brains of people with schizophrenia. Second-place winner was **Gustavo Sudre** (NHGRI), who talked about the human brain connectome's association with attention-deficit hyperactivity disorder. Third place went to **Melissa Harris** (NHGRI), who described the genetic modifiers responsible for age-related graying of hair in mice. The winners will receive training-travel support and have their talks professionally produced for video.

Tabor "made it very easy for people to understand why her work was important," said Burgess, who is also her supervisor. To that, Tabor added that "despite any butterflies, I know now that I will be able to describe the essentials of my work in an engaging [way]."

Ideas abound for next year's competition. The institutes plan to reorganize the judging with an electronic system and give the judges a little more time to reflect on each presentation (they had only a minute per presentation this year).

Burgess suggested encouraging the participants to give their talks with less reliance on their slide next time. "If you meet somebody at a dinner party or you are talking over a lunch during a meeting, you don't have a slide," he pointed out. "You just have three minutes to tell your story."

Hanning hopes that even more fellows will take up the TmT challenge next year. ●

Hope, Science, and Miracles

The NIH Children's Inn Celebrates 25 Years

BY JACQUELINE ROBERTS, OD

"Those of us who come here, our heart in our hand[s], [hope] for a miracle."

So said just one of the many grateful patients who come to be treated at the NIH Clinical Center (Building 10). The message rings true especially for families with children who have life-threatening illnesses and come to NIH hoping for a miracle. On June 18, the NIH Children's Inn, which houses children and families, celebrated its 25th anniversary with a symposium titled, "At the Intersection of Hope and Science: 25 Years of Advancing Medical Discoveries."

Since 1990, "nearly 12,000 children with serious, life-threatening illnesses have stayed at the Inn," NIH Director **Francis Collins** told the physicians, patients, and families who had gathered in Masur Auditorium (Building 10) for the symposium. They came to NIH in search of help when conventional medical treatments had failed to for their life-threatening and devastating diseases such as heart, lung, blood, bone, and growth disorders; mental illnesses; rare genetic conditions; many forms of cancer; and undiagnosed diseases. In most cases, the NIH was the last and best hope for a treatment or a cure. These children, said Collins, "have contributed to groundbreaking medical research" that has led to successful treatments.

The idea for the inn began to take shape in the early 1980s when **Philip Pizzo**, then chief of pediatrics at the National Cancer Institute, had a vision to create a homelike place on the NIH campus where families could stay while their children were being cared for at the Clinical Center. At the time, children's families were supposed to find local accommodations, but that didn't always work out.

"Families often wouldn't tell you about it, but they were sleeping in the waiting rooms or even in their cars," recalled Clinical Center Director **John Gallin**. "Many were eating primarily from vending machines that were in the hospital."

The establishment of the inn, however, mitigated these problems. "The NIH Clinical Center cares for a child's medical needs," said Gallin. "The inn tends to a child's heart, soul, spirit, and family."

The NIH donated two acres of land on which to build the inn; Merck and Company, Inc., donated the funds for the project. In June 1990, the NIH Children's Inn opened its doors to its first patients and their families. In the beginning the inn could host up to 36 families. In 2004, the inn was expanded to accommodate up to 59 families. In 2010, Woodmont House, which can host five families, opened just off-campus as a transitional home for families with children who were long-term patients but no longer in the acute phase of their illnesses. The families who have stayed at the inn or Woodmont House came from all 50 states as well as 86 countries.

"When the inn expanded, I was thrilled because that meant that more pediatric studies could take place," said Benjamin Banks, one of the former patients who spoke at the symposium. "More doors would be opened, and more answers would be found."

When the inn and Woodmont House are at capacity, the inn staff and NIH medical teams work with the families to find alternate accommodations. Families staying off-campus still have full access to all of the inn's programs and services. The inn "empowers the work done at the Clinical Center not only by providing the families a free place to stay, but [also] by reducing their stress and making their entire experience a little more bearable," said **Jennie Lucca**, chief executive officer at the Children's Inn. "NIH is their hope."

"What I loved about the Children's Inn was the camaraderie with the other children," said Banks. "It didn't matter if you were seven months old, seven years old, or like me, 17 years old. We were all friends."

The NIH Clinical Center and the Children's Inn aim to continue to provide the very best services and programs to the courageous children and families who come to NIH in search of miracles. ●

HOCHLANDER DAVIS PHOTOGRAPHY

The NIH Children's Inn celebrated its 25th anniversary recently with a symposium that attracted patients, clinicians, staff, and other supporters. The inn is a home-away-from home for families with children being treated at the Clinical Center.

Incidentally, another homelike residence at NIH is the Edmond J. Safra Family Lodge, which opened in 2005 and is for families and loved ones of adult Clinical Center patients.

CHINESE LEADERS GATHER WITH U.S. HEALTH OFFICIALS AT NIH

Chinese Vice Premier Liu Yandong and Li Bin, minister of the National Health and Family Planning Commission of the People's Republic of China, visited NIH on June 24, joining Department of Health and Human Services (HHS) secretary **Sylvia Burwell** and other HHS and NIH officials for a meeting on Ebola, research, and global-health security.

The officials were in Washington, D.C., for the sixth China–United States High-Level Consultation on People-to-People Exchange. This year marked the first time "health" was on the meeting agenda.

During the visit, HHS Secretary Burwell signed a memorandum of understanding with Minister Bin to promote closer cooperation, scientific discovery, capacity building, and exchange of information in the field of infectious diseases.

Bin and other guests visited the Clinical Center and were escorted to the Rehabilitation Medicine Department's Clinical Movement Analysis Lab. They were treated to a demonstration of a newly designed motorized "smart" robotic exoskeleton that will help children with cerebral palsy improve their ability to walk. ●

Excerpted from the July 2015 edition of the *Clinical Center News*: http://clinicalcenter.nih.gov/about/news/newsletter.html

ERNIE BRANSON

HHS Secretary Sylvia Burwell joined China's Vice Premier Liu Yandong (center) and the minister of China's National Health and Family Planning Commission, Li Bin, in signing a memorandum of understanding on infectious diseases.

KOROSHETZ NAMED NINDS DIRECTOR

Walter Koroshetz was named director of the National Institute of Neurological Disorders and Stroke by NIH Director **Francis Collins** at the June 11 meeting of the Advisory Committee to the Director. Koroshetz came to NIH in 2007 as NINDS deputy director and has served as acting director since **Story Landis** retired in October 2014.

"His deep grounding in clinical neurology and basic neuroscience research makes him the ideal candidate to lead NINDS into the future," said Collins.

Collins also recognized Koroshetz's role in the creation of StrokeNet, a national clinical-trial network for research in stroke treatment, prevention, and recovery; his role as point person for traumatic brain injury research at NIH; and being a co-founder of the NIH-Uniformed Services Center for Neuroscience and Regenerative Medicine.

Koroshetz came to NIH from Boston, where he served as vice chair of neurology and the director of stroke and neurointensive care services at Massachusetts General Hospital, head of its neurology resident-training program, and a professor of neurology—and co-director of the Neurobiology of Disease Course—at Harvard Medical School. ●

Excerpted from the July 3, 2105, edition of the *NIH Record*.

PÉREZ-STABLE TO DIRECT NIMHD

Eliseo J. Pérez-Stable has been named director of the National Institute on Minority Health and Health Disparities. He is expected to join NIH in September.

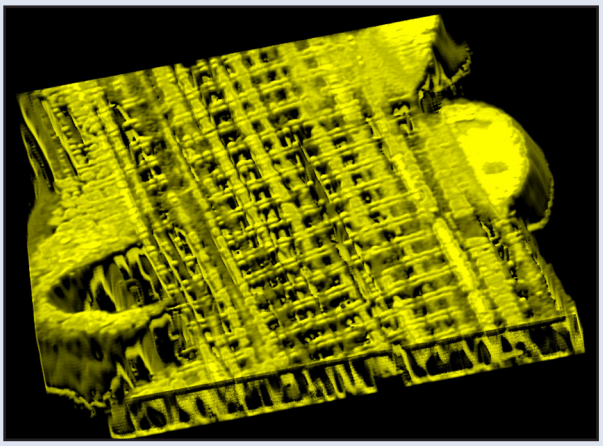
He will oversee the institute's $270 million budget to conduct and support research, training, research capacity and infrastructure development, and public-education and information-dissemination programs to improve minority health and reduce health disparities.

He comes to NIH from the University of California, San Francisco (UCSF), where he is a professor of medicine, chief of the division of general internal medicine, and director of the Center for Aging in Diverse Communities. The center works to alleviate health disparities with a focus on improving health care for aging minority populations and on diversifying the scientific workforce. He is also director of the UCSF Medical Effectiveness Research Center for Diverse Populations, which is addressing issues for African-Americans, Asians, and Latinos in the areas of cancer, cardiovascular disease, and reproductive health.

Pérez-Stable's research interests are improving the health of poor and minority patients, reducing health risks such as smoking in minority populations, and improving cross-cultural communication skills among health-care professionals. ●

Excerpted from the August 14, 2015 issue of the *NIH Record*.

Intramural Research Briefs



BRIAN GLANCY AND CHRIS COMBS, NHLBI

NHLBI, NCI: This high-resolution 3D microscopic image shows a network of interconnected mitochondria within a mouse muscle cell.

CC: ADVANCES MADE IN DIAGNOSING CORONARY HEART DISEASE

NIH Clinical Center researchers published a study that could help health-care professionals better identify, diagnose, and treat coronary-artery disease more quickly and effectively.

An indicator of the calcification of the heart's arteries can be seen through a coronary-artery calcium score from a CT scan. However, plaque that is still noncalcified, or soft, is not included in that score. The researchers believed that this type of plaque could also indicate an increased risk for the disease.

When researchers compared the calcium score of the hardened plaque with that of the noncalcified soft plaque, they found significant differences. Noncalcified plaque that had not yet hardened was associated with low-density lipoprotein ("bad cholesterol"), diabetes, and systolic blood pressure. These variables were not associated with the calcium score in low-risk, asymptomatic individuals. These results suggest that analyzing the different types of plaque, both hard and soft, gives more information about the risk of coronary-artery disease than just the calcium score. (CC authors: K. Rodriguez, A.C. Kwan, D. Vigneault, V. Sandfort, P. Pattanayak, M.A. Alhlman, M. Mallek, C.T. Sibley, and D.A. Bluemke, *Radiology* DOI:http://dx.doi.org/10.1148/radiol.2015142551)

NHLBI, NCI: HIGH-RESOLUTION 3D IMAGES REVEAL THE MUSCLE MITOCHONDRIAL POWER GRID

A new imaging study in mice overturned longstanding scientific ideas of how energy is distributed within muscles for powering movement. NCI and NHLBI scientists reported the first clear evidence that muscle cells distribute energy primarily by the rapid conduction of electrical charges through a vast, interconnected network of mitochondria—the cell's "powerhouse"—in a way that resembles the wire grid that distributes power throughout a city. The study offers an unprecedented, detailed look at the distribution system that rapidly provides energy throughout the cell where it is needed for muscle contraction. (NHLBI authors: Brian Glancy, Daniela Malide, Zu-Xi Yu, Christian A. Combs, Patricia S. Connelly, and Robert S. Balaban; NCI authors: Lisa M. Hartnell and Sriram Subramaniam, *Nature* **523**:617–620, 2015)

NEI: IN BLINDING EYE DISEASE, TRASH-COLLECTING CELLS GO AWRY, ACCELERATE DAMAGE

Spiderlike cells inside the brain, spinal cord, and eye hunt for invaders, capturing and then devouring them. These cells, called microglia, often play a beneficial role by helping to clear trash and protect the central nervous system against infection. But a new study by NEI researchers shows that they also accelerate damage wrought by blinding eye disorders, such as retinitis pigmentosa. The findings suggest that microglia may provide a target for new therapeutic strategies aimed at halting blinding eye diseases of the retina. (NEI authors: L. Zhao, M.K Zabel, X. Wang, W. Ma, P. Shah, R.N. Fariss, H. Qian, and W.T Wong, *EMBO Mol Med* **7**:989–1086, 2015)

NICHD: PLACENTA-ON-A-CHIP

NIH researchers and their colleagues have developed a "placenta-on-a-chip" to study the inner workings of the human placenta and its role in pregnancy. The device imitates, on a microlevel, the structure and function of the placenta and models the transfer of nutrients from mother to fetus. This prototype is one of the latest in a series of organ-on-a-chip technologies. (NICHD author: Roberto Romero, *J Matern Fetal Neonatal Med* DOI:10.3109/14767058.2015.1038518)

NIDDK, USDA: NIH BODY-WEIGHT PLANNER

The U.S. Department of Agriculture (USDA) and NIH have partnered to add the NIH Body Weight Planner to USDA's SuperTracker online tool as a resource to help people achieve and stay at a healthy weight. The planner's calculations reflect the discovery that the widely accepted paradigm that reducing 3,500 calories will shed one pound of weight does not account for slowing of metabolism as people change their diet and physical activities. (http://www.niddk.nih.gov/health-information/health-topics/weight-control/body-weight-planner/Pages/bwp.aspx)

NIEHS: RGS2 PROTEIN HELPS PREPARE HEALTHY EGG-SPERM UNION

NIEHS researchers and outside collaborators have discovered that the regulator of G-protein signaling–2 (RGS2) protein functions as a brake to suppress premature Ca2+ release in eggs that are poised on the brink of development. This is the first demonstration of the protein's significant role in fertilization. (NIH authors: M.L. Bernhardt, E. Padilla-Banks, C.E. McDonough, and C.J. Williams, *Development* **142**:2633–40, 2015) ●

Read expanded briefs online at http://irp.nih.gov/catalyst/v23i5/research-briefs.

Recognition of Brilliant Scientific Work

NIH's Two New National Academy of Sciences Members

BY SOMA CHOWDHURY, OD

It was an ordinary Tuesday morning for National Institute of Child Health and Human Development (NICHD) senior scientist **Alan Hinnebusch**, except his cell phone kept vibrating during his regular lab meeting. Annoyed, he finally answered it. It was his good friend and 1980s postdoc advisor calling to congratulate him on his election to the National Academy of Sciences (NAS). When Hinnebusch came out of the meeting, a celebratory cake awaited him, too.

Although Hinnebusch had an inkling that he and fellow senior scientist **Warren Leonard** (National Heart, Lung, and Blood Institute, NHLBI) might be elected to the NAS, he wasn't going to get excited until the news was confirmed. Leonard also had an inkling but officially found out when he arrived at work that Tuesday to find voicemails and e-mails already congratulating him on his election. Membership in the NAS is considered to be one of the highest honors that can be bestowed on a U.S. scientist.

The news was indeed confirmed that both had been officially named to the academy that Tuesday, April 28. On June 18, they were invited to present their research to their NIH colleagues at the "NAS Mini Symposium" in Masur Auditorium (Building 10).

Hinnebusch, who joined NICHD in 1983, heads its Program in Cellular Regulation and Metabolism. He studies transcriptional and translational control of gene expression, focusing on the regulation of amino acids and vitamin biosynthetic genes in the budding yeast *Saccharomyces cerevisiae*. This common yeast, used in baking and brewing, is a good model organism because it is a unicellular eukaryote with well-studied genetics and its pathways for messenger RNA (mRNA) and protein synthesis are similar to those in mammals. His most important discovery, he said, has to do with the way cells turn on the translation of genes encoding transcription activators while simultaneously reducing general protein synthesis to reprogram gene expression. In 1993, his lab showed for the first time how a modification of the translational machinery that slows down general protein synthesis stimulates translation of *GCN4* mRNA owing to specialized regulatory sequences (upstream open-reading frames) in its mRNA.

In mammalian cells, the same mechanism occurs and is commonly known as the "integrated stress response." It operates during heat shock and virus infections and, surprisingly, also exists in the nervous system to enhance learning and memory. There "still aren't that many examples of that type of fine control of gene expression at the translational level," Hinnebusch added. His lab continues to dissect molecular mechanisms governing the types and amounts of cellular proteins made in different circumstances.

Leonard came to NIH in 1981 as a postdoctoral fellow at the National Cancer Institute; in 1985, he established his own lab in NICHD; and in 1992 he moved to NHLBI. He studies the biology, signaling, and molecular regulation of a key family of cytokines, with study foci ranging from basic molecular mechanisms to human disease.

He is best known for his work on the interleukin (IL)-2 receptor and for the discovery of the genetic basis for X-linked severe combined immunodeficiency syndrome (X-SCID), also called the "bubble boy disease," in the 1990s.

IL-2, a cytokine produced by T cells, regulates the normal immune response. The IL-2 receptor is a complex expressed on certain immune cells and consists of different subunits, including one called IL-2R gamma chain. When Leonard was a postdoctoral fellow, he cloned the alpha chain. Later, he and his lab co-discovered the beta chain and that mutations in the gamma chain were responsible for X-SCID. They also determined that the gamma chain has a much broader role than initially realized. It is now known to be shared by the receptors for IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21.

"By connecting the gamma chain to other cytokine systems, we opened a whole new vision of the biology of these cytokines," Leonard said. He believes that this discovery is a prime example of basic research leading to a finding that has had great clinical implications.

His lab has continued to do exciting research over the years, he said. They cloned the IL-21 receptor and performed pioneering work on the IL-21 and the thymic stromal lymphopoietin cytokine systems as well as on a family of proteins called signal transducers and activators of transcription, which are critical mediators of cytokine signals.

Recently he published a paper on the first cytokine partial agonists, which "represents a new approach to both manipulating the actions of cytokines [and] learning more about them," Leonard said.

Both of the new NAS members emphasized that they were honored to be elected. It was a "recognition by peers at a very high level," said Leonard, whose celebration of his achievement at a French restaurant with his lab members was followed by many "mini-celebrations." ●

A videocast of the NAS Mini Symposium can be viewed (NIH only) at http://videocast.nih.gov/launch.asp?19073.

Looking Past the Glitz

Theodore Friedman: The Father of Gene Therapy

BY LAURA STEPHENSON CARTER

NIH alum Theodore Friedmann may be too modest to brag about his pioneering role in gene-therapy research, but the Japan Prize Foundation sure wasn't when it bestowed its prestigious prize on him and two other scientists earlier this year. The annual Japan Prize recognizes "significant contributions to the progress of science and technology as well as society to serve the cause of peace and prosperity of mankind." Since its inception in 1985, 83 laureates from 13 countries have received the prize and several have gone on to win the Nobel.

Friedman and French scientist Alain Fischer (Institut Imagine, Paris) were celebrated for the "proposal of the concept of gene therapy and its clinical applications." The third scientist, Yutaka Takahasi (professor emeritus at the University of Tokyo), was recognized for his contribution to the "concept of river-basin management and reduction of water-related disasters."

The Japan Prize Foundation "looked past the glitz and noise and went back in the history," said Friedman, who began his work on gene therapy at NIH in the 1960s and is now a professor of pediatrics and director of the Gene Therapy Program at the University of California at San Diego (UCSD, in La Jolla).

As the gene-therapy field was evolving in the 1970s and 1980s, "there was a lot of hype and controversy," said **Alan Schechter**, a senior investigator in the National Institute of Diabetes and Digestive and Kidney Diseases. He shared a lab with Friedmann at NIH and is still a close friend. "Ted has been active in the field—he convened meetings, wrote and edited books and continued to focus on ethical issues," said Schechter. But "he never held press conferences [and] never hyped."

RYAN PARKS, UCSD

It was Friedmann who in 1972 co-authored an influential *Science* paper that is considered important in the scientific beginnings of gene-therapy research (*Science* **175:**949–955, 1972). The article described the concept of gene therapy, proposed a way forward in research, and cautioned about the dangers and ethical issues surrounding gene therapy, too.

With a degree in chemistry (1956) and an M.D. (1960) from the University of Pennsylvania (Philadelphia), Friedmann came of age in the era of molecular biology. He was inspired by the likes of Francis Crick and James Watson, who had, in 1953, co-discovered (with Rosalind Franklin) the structure of DNA, a feat that won them the Nobel Prize in Physiology or Medicine in 1962; his medical school professor Colin MacLeod, who contributed to the demonstration that DNA encodes properties of genes; and British biochemist Frederick Sanger, who received the first of his two Nobel Prizes in Chemistry in 1958 for his work on the structure of proteins, especially that of insulin. (The second was in 1980 for his "contributions concerning the determination of base sequences in nucleic acids.")

"I wanted to learn more from the people pushing the frontiers of molecular medicine," Friedmann said in his Japan Prize lecture. So in 1963, he went to work with Sanger for a year at the University of Cambridge (Cambridge, U.K.). He met his future wife, Ingrid Stromberg, in Cambridge, too.

He returned to the United States to complete a residency in pediatrics at Harvard's Boston Children's Hospital. Still eager to learn more about protein chemistry, he made his way to the National Institute of Arthritis and Metabolic Diseases (NIAMD) in 1965, where he and Schechter worked with **Christian Anfinsen** and **Charles Epstein** on protein chemistry and protein folding. (Anfinsen went on to share the Nobel Prize in Chemistry in 1972 for his work on the enzyme ribonuclease and the way in which it folds to its biologically active form.)

Friedmann was anxious to apply what he'd learned to human genetics. After two years in Anfinsen's laboratory, he moved to NIAMD's Laboratory of Human Biochemical Genetics, where **J. Edwin Seegmiller** and Scottish researcher **John Subak-Sharp** were investigating uric acid and Lesch-Nyhan syndrome. Seegmiller had just discovered that a defect in the *HPRT1* gene causes the rare, hereditary syndrome that affects young boys and is characterized by neurological abnormalities, compulsive self-biting behavior, involuntary muscle movements, and the overproduction of uric acid.

In Seegmiller's lab, Friedmann made his first foray into gene therapy. "We wanted to fix the genetic defect in the children," Friedmann said. He and Subak-Sharp cultured some of the abnormal skin cells and exposed them to normal DNA. The genetic defect was corrected in a few cells—about one in a million.

"It was the first time that was done," said Friedmann. But "the process was inefficient." He wanted to find a way to genetically correct many more mutated cells, but he knew it wouldn't be easy. (*Nature* **220:**272–274, 1968)

In 1968, Friedmann left NIH for a visiting scientist position at the Salk Institute (La Jolla, California) and a faculty post at UCSD. At Salk, he worked with Renato Dulbecco, who had discovered that tumor viruses infected normal cells by carrying their DNA into them. "If we could teach the virus to carry normal genes—not tumor genes—we might be able to correct genetic abnormalities," Friedmann recalled thinking.

Dulbecco went on to share the Nobel Prize in Physiology or Medicine in 1975 for his discoveries concerning the interaction between tumor viruses and the genetic material of the cell. At this point, Friedmann was anxious to learn more about DNA and returned to Sanger's lab in 1976 to do that; they published several papers dealing with methods for determining DNA sequences.

Then Friedmann returned to UCSD to continue working on gene-delivery mechanisms and techniques to trick the virus into being a vector for therapeutic genes, especially for Lesch-Nyhan syndrome.

Meanwhile, scientists at NIH and elsewhere were starting to develop gene-therapy techniques,. There was a lot of excitement, but "Ted's contribution tended to get lost," said Schechter.

In 1995, then–NIH Director **Harold Varmus** commissioned a report that identified many concerns with the gene-therapy field. Varmus "didn't like what he saw, and he criticized the field sharply," said Friedmann. "The NIH director and others lost faith in us [and] chastised us."

Nevertheless, the news media eagerly promoted gene therapy until 1999 when 18-year-old Jesse Gelsinger, who was being treated for a genetic liver disease, died during a gene-therapy clinical trial at the University of Pennsylvania. His was the first death caused by gene therapy.

"We began to question the concept of gene therapy," Friedmann said. "Are we just fooling ourselves?" he wondered at the time.

But in Europe in the late 1990s, fellow Japan Prize winner Alain Fischer, at the Necker Hospital (Paris), was beginning to use gene therapy to treat children with X-linked severe combined immunodeficiency disease (SCID).

"Gene therapy wasn't a real field until the clinicians got busy," said Friedman. "Without Fischer, the concept would have wallowed around."

Unfortunately, five of the 20 children in Fischer's trials developed leukemia (one died) due to a component in the modified virus that was used to carry the corrective gene.

Since then, the technology has improved: Safer and more efficient gene-delivery viruses—such as the lentiviruses—have been found. More children with SCID have been successfully treated. Other diseases are now being approached with these methods, too.

In addition, clinical trials have suggested that gene therapy may be effective in treating certain forms of blindness, several childhood degenerative brain diseases, hemophilia, and other disorders. And new gene-therapy technologies—such as gene editing to correct mutant genetic sequences—are showing promise for the future.

Finally in the last decade, "I knew the [clinical] field was emerging," said Friedman, who is trying to establish a gene-therapy center at UCSD. "It was very gratifying."

And Friedmann found it gratifying to have had mentors who were the "greatest scientists of the last century"—Sanger, Anfinsen, Seegmiller, Dulbecco, and others. They were gentle, were interested in truth and science, and let their work speak for itself, according to Friedmann. "It takes a very special person to be that good," he said. "To emulate [them] is a challenge."

Friedmann certainly seems to have met that challenge. ●

THEODORE FRIEDMANN

Education: University of Pennsylvania, Philadelphia (A.B. in chemistry, 1956; M.D., 1960); University of Oxford, Oxford, England (M.A. in biology, medicine, and chemistry, 1995)

Training: Residency in pediatrics, Children's Hospital Medical Center, Boston (1960–1962); senior resident (1964–1965); teaching fellow, Harvard University, Cambridge, Mass.; research fellow in colloid science, University of Cambridge, Cambridge, U.K., laboratory of Frederick Sanger (1963–1964; 1976–1977); postdoctoral training, Salk Institute for Biological Sciences, La Jolla, Calif., with Renato Dulbecco (1968–1969)

Military: Captain, U.S. Air Force, 10th Tactical Hospital, Alconbury, England (1963–1964)

NIH: Laboratory of Chemical Biology, NIAMD, with Charles Epstein and Christian Anfinsen (1965–1967); Laboratory of Human Biochemical Genetics, NIAMD, with J. Edwin Seegmiller (1967–1968)

Current positions: University of California, San Diego (1969–present): professor of pediatrics; Muriel Jeanette Whitehill Chair in Biomedical Ethics; director, Gene Therapy Program; adjunct professor, Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, Calif.

Outside interests: Spending time with his family; playing piano

Creating Devices

CONTINUED FROM PAGE 1

The interdisciplinary NIH Center for Interventional Oncology—a collaboration among the NIH Clinical Center, the National Cancer Institute, and the National Institute of Biomedical Imaging and Bioengineering—was created in 2009 to foster just such translational work. The center develops targeted-imaging technologies to diagnose and/or treat various forms of cancer.

"Our process is definitely one that's hard to grasp," said center director **Bradford Wood**. The interdisciplinary approach favored in the center depends in part on developing or matching up tools that may have been intended for other purposes, and putting them together in novel ways to address an unmet clinical need. It's important to have "the resources, people and expertise on our team that might be able to build a match for that need," he added.

As a strategy to filter the most promising leads, Wood's group takes on many projects simultaneously, nurturing a variety of ideas to see which ones take off. "Deciding which of those seeds is worth watering and worth following through is both the hard part and the fun part of what we do," said Wood. "And those decisions are made as a group or by the technology itself."

That means that at any one time, the group is balancing projects at every stage, from fledgling ideas, to proof-of-concept prototypes, to devices and techniques that are in clinical trials or in the process of commercialization or translation to the community.

One of their best-known projects—now commercialized after clinical trials—is a new technique for image-guided prostate biopsies whereby physicians fuse two modes of imaging to locate possible cancerous tissue. Previously, in cases of suspected prostate cancer, biopsies were taken randomly and blindly throughout the prostate. Wood's group developed new software that superimposes a magnetic-resonance-imaging scan on a real-time ultrasound image to create a detailed multi-modality map of the prostate. The clinicians (Wood and **Peter Pinto**) can then use the map to guide the biopsy needle to suspicious-looking areas (identified by NCI Molecular Imaging Program partners **Peter Choyke** and **Baris Turkbey**) that are likely to be cancerous lesions. And although the exact clinical indications and roles are evolving, "the evidence seems to be pretty clear that this is an improved way to biopsy the prostate," said Clinical Center senior investigator **Ronald Summers**, who's working on automated ways of using MRI to diagnose or facilitate the diagnosis of prostate cancer.

COURTESY CENTER FOR INTERVENTIONAL ONCOLOGY

Close collaborations enable new perspectives on procedural medicine. In foreground: Peter Pinto (left) and Bradford Wood.

Another of the center's long-term projects involves using liposome nanoparticles as a chemotherapy drug-delivery system and applying heat to get them to release the drugs in the area of a tumor. Thermal-sensitive liposomes have been around for many years. Researchers would apply hot packs or other external heat sources over an affected area; when the liposomes traveled via the bloodstream to the heated area, they would melt and release their contents.

Wood's group, however, developed a more precise method: They paired the drug-bearing liposomes with radiofrequency ablation (RFA) or high-intensity-focused ultrasound (HIFU), which produces a small amount of heat in a narrowly defined space. So the drug is released at a high concentration exactly where it's needed most. The group has used the HIFU technique to deliver chemotherapy drugs directly to cancer sites in rabbit models, and RFA in patients (now in phase 3 international clinical trials). "We're still trying to fully understand the implications of HIFU hyperthermia," said Wood. "It improves oxygenation, which can cause more free radicals and can increase sensitivity to radiation. It also increases blood flow, so mechanical, thermal, and chemical synergy all increase drug delivery!"

The team has also pioneered other applications for image-guided drug delivery, including the embolization of beads that are both drug-eluting and imageable and are about 100 microns in size. The technology was co-developed with a CRADA (cooperative research and development agreement) public-private partnership and is being commercialized for release soon. These imageable drugs can be localized and tracked with navigation "video-game-like" X-ray software that makes use of fusion technology, similar to the prostate project, to compare drug dose to anatomy to tumor location.

The center's project mix includes new methods of combating bacterial contamination on catheters and other medical devices. "We had a bit of a crazy

idea to design an electrified catheter with super weak electric current to inhibit bacterial colonization," said Wood. Some bacteria form antibiotic-resistant biofilms that can colonize the catheters and cause life-threatening bloodstream infections. Drawing on knowledge from a variety of disciplines, Wood's group designed a device with a very low electrical current–low enough not to cause heart arrhythmias–and showed that a continuous current across the tip of the device could significantly reduce the formation of bacterial biofilms.

The Center for Interventional Oncology thrives on the interdisciplinary environment at the Clinical Center and draws on expertise from many academic and industry partners to develop its technologies. "Every day I learn something from a great enlightening conversation with somebody in a different discipline," said Wood. "You think, that's a cool unique way to think about the problem!"

"There are a lot of different paradigms for successful contributions in cancer diagnosis and treatment," said Summers. For the Center for Interventional Oncology, interdisciplinary team science "has been a successful approach."

Not every crazy idea ends up in patients or as a successful commercialized product. Wood's lab is full of failed contraptions that sit in the "device graveyard" without a clinical home. "We have a lot of projects that are high-risk and high-yield, in various phases of feasibility or proof of concept," said Wood. "Most of those will die a timely death." For example, there are multiple CT-integrated robots and carpentry-like devices in his closets that fit this description and were never judged to be clinically valuable or cost-effective.

But some of these "crazy idea" seeds will be watered and eventually blossom into working clinical solutions. ●

A videocast of Wood's May 13, 2015, presentation, "Video Game Medicine at the NIH: How Image-Guided Therapies Depend upon Interdisciplinary Translational Team Science," can be viewed at http://videocast.nih.gov/launch.asp?19000.

COURTESY CENTER FOR INTERVENTIONAL ONCOLOGY

The Center for Interventional Oncology, led by Bradford Wood, has pioneered a number of medical techniques including applications for image-guided drug delivery; pairing drug-bearing liposomes with radiofrequency ablation or high-intensity -focused ultrasound to make them more effective; and designing catheters to emit a low-level electrical current that would inhibit bacterial contamination.

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
NCBI: National Center for Biotechnology Information
NCCIH: National Center for Complementary and Integrative Health
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: Eunice Kennedy Shriver National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
OD: Office of the Director
OITE: Office of Intramural Training and Education
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health
OTT: Office of Technology Transfer

Precision Psychiatry

CONTINUED FROM PAGE 1

In an attempt at precision medicine for psychiatry, the National Institute of Mental Health (NIMH) launched the Research Domain Criteria (RDoC) initiative in 2009. RDoC provides a research framework for classifying mental disorders based on many kinds of objective measures instead of according to the traditional subjectively-based *DSM* groupings.

Despite decades of research, scientists have been unable to find any genetic or neurological evidence to support the breakdown of the disorders into the *DSM* categories. So far, no cellular or genetic signatures for any

"Our diagnostics are limited to symptoms clusters [so] we're not able to get any precision as to the underlying biology," explained NIMH Director Thomas Insel.

mental disorder have been discovered, nor has anyone developed reliable biomarkers, blood tests, or brain scans that match perfectly with a *DSM*-defined mental illness. NIMH is betting that the problem is the diagnostic system and that focusing on the biomarkers may provide diagnostic categories more useful for selecting treatments and improving outcomes. Because the focus of the field has been solely on understanding mental disorders as defined by the clusters of symptoms in the *DSM*, most current treatments have aimed at relieving symptoms rather than resolving the underlying pathology.

"Our diagnostics are limited to symptom clusters; we need the powerful tools of genomics and neuroscience for more precise diagnostics and better treatments," explained NIMH Director **Thomas Insel**. "We can reduce hallucinations, but we are not treating schizophrenia. We can relieve symptoms of depression, but that may not be treating the underlying disorder."

RDoC is already changing the way mental-health researchers approach the study of mental disorders.

"RDoC is about translating basic research into an understanding of psychopathology," explained NIMH clinical psychologist **Bruce Cuthbert**, who heads the RDoC project and runs educational webinars, workshops, and a forum for researchers to discuss RDoC issues. "What did the brain normally evolve to do? How does it do it? What goes wrong in these circuits [and] systems?"

Using the RDoC approach, scientists are trying to better understand mental illness by focusing on the convergence of biology and behavior and tying different aspects of behavioral, cognitive, and emotional functions to specific brain systems. The research is organized into five broad domains: positive valence (seeking and appreciating reward), negative valence (threat and loss), cognitive systems, social systems, and arousal and regulatory systems.

Some scientists are relying on an RDoC approach to investigate the biological underpinnings of anhedonia, the inability to seek or experience pleasure in normally pleasurable activities such as exercise, sex, and socializing. Anhedonia occurs in a variety of *DSM*-defined disorders—including depression, bipolar disorder, certain anxiety and personality disorders, and schizophrenia—yet there are no FDA-approved treatments for it.

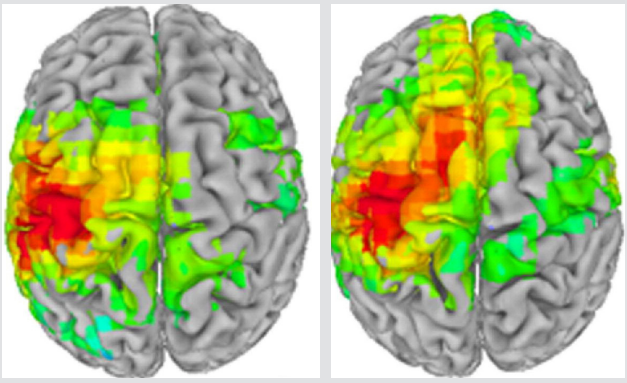
NIMH senior investigator **Carlos Zarate**, who is interested in developing novel medications for treatment-resistant depression and bipolar disorder, has linked

"RDoC is about translating basic research into an understanding of psychopathology," explained NIMH clinical psychologist and RDoC project head Bruce Cuthbert.

anhedonia to changes in brain activity. In one trial, his team administered ketamine to patients with bipolar disorder. Ketamine produces a rapid antidepressant effect within hours and lasts less than a week. But, surprisingly, the team found that it had an even an more powerful effect on anhedonia: Within 40 minutes of receiving ketamine, patients experienced a sharp reversal in anhedonia—and the effect lasted up to 14 days.

To determine which area of the brain was affected, Zarate's group used a brain-imaging technique called positron-emission tomography (PET). Earlier research that measured ketamine's antidepressant effects showed changes in the ventral striatum, a brain area linked to reward-seeking behavior. But when measuring changes in the hedonic drive, Zarate found that ketamine affected

Daniel Pine uses functional magnetic resonance imaging of the brain to determine whether a dysfunction in a particular brain circuit plays a role in children who have problems with stress and anxiety.



RHODA BAER

Carlos Zarate (far right) uses PET imaging techniques to measure changes in how the infusion of ketamine affects brain activity in a patient with treatment-resistant major depression. Brain images: (left) brain before ketamine infusion; (right) after the infusion of ketamine, different areas of the brain become activated.

another area of the brain—the dorsal anterior cingulate cortex, a region involved in reward processing, learning, and decision-making. The results were observed in patients who had bipolar disorder (a type of depression in which there are low moods as well as high moods and activity levels, or mania) and those with unipolar depression.

In related research, Zarate is trying to link anhedonia to changes in brain function in relation to attempted suicide. Suicide has been a relatively neglected area of mental-health research, according to Insel. "This year there will be more deaths from suicide, almost all related to mental illness, than from breast cancer or HIV or homicides," he said. "It's just phenomenal how great the morbidity and mortality is. It goes unrecognized."

Anhedonia plays a role in suicidal thoughts, according to Zarate, and ketamine can reverse them. "We'll be studying people with current suicidal thoughts irrespective of *DSM* diagnosis. Such participants may have prominent depression or not, or may primarily have an anxiety disorder or may not even have other prominent psychiatric symptoms as in the case of someone who has lost all their money in the stock market," said Zarate. "That way we will look at the biology of suicidal thoughts across psychiatric disorders." Because there is very little known about the brain circuits implicated in suicidal thoughts, Zarate and his team are planning to use multi-modal neuroimaging techniques to map brain areas involved with ideation (the process of coming up with new ideas) and to probe ketamine's rapid antisuicidal effects.

Ellen Leibenluft is also being guided by the RDoC approach as she uses imaging techniques to investigate brain mechanisms that mediate bipolar disorder and severe irritability in children and adolescents.

Anhedonia is also being studied by extramural researchers including former NIMH scientist **Jerzy Bodurka**, now at the Laureate Institute for Brain Research (Tulsa, Oklahoma). He is analyzing gene expression and using advanced imaging techniques to study how inflammatory cytokines may trigger dysfunction in brain circuits that control motivation and pleasure. In theory, if mechanisms of anhedonia could be identified, patients could be tested for them and treated, whether or not they have a *DSM* diagnosis.

NIMH senior investigator **Daniel Pine** uses the RDoC framework to investigate a process known as fear extinction, or the ability to deliberately ignore fear. He uses functional magnetic resonance imaging to study the connection between the basal lateral amygdala and ventromedial prefrontal cortex, a brain circuit involved in the ability to forget fearful memories. He believes that dysfunction of this circuit may occur in children who have problems with stress and anxiety.

Another NIMH senior investigator **Ellen Leibenluft** is also being guided by the RDoC approach as she uses imaging techniques to investigate brain mechanisms that mediate bipolar disorder and severe irritability in children and adolescents. "Irritability fits well as an RDoC construct," she explained. "It's dimensional—some people are pretty chill, others very irritable—and it cuts across many diagnoses: Children with anxiety, attention-deficit hyperactivity disorder, autism, [and] depression are irritable." Had she been guided solely by the *DSM*, she might have been looking at brain activity in association with a diagnosis. Instead, she's looking at how irritability affects the brain.

The RDoC was originally designed in the hope that researching mental diseases by dimensions—such as irritability, anhedonia, fear extinction, and other behaviors—instead of by symptom-organized diagnoses would generate a biological definition for mental disorders, and that in turn will facilitate the discovery of new treatments that target the underlying pathology.

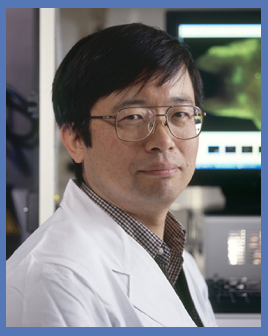
"It will give us much better guidance about what treatments should be given to which people," said Insel. "It really is precision medicine for psychiatry." ●

To learn more about RDoC, go to http://www.nimh.nih.gov/research-priorities/rdoc/index.shtml.

Recently Tenured


EDWARD GINIGER, NINDS


HORMUZD A. KATKI, NCI-DCEG


HISATAKA KOBAYASHI, NCI-CCR


KEIR NEUMAN, NHLBI


CHARLES VENDITTI, NHGRI

EDWARD GINIGER, PH.D., NINDS

Senior Investigator and Chief, Axon Guidance and Neural Connectivity Section, National Institute of Neurological Disorders and Stroke

Education: Yale University, New Haven, Conn. (B.S. and M.S. in molecular biophysics and biochemistry); Harvard University, Cambridge, Mass. (Ph.D. in biochemistry and molecular biology)

Training: Postdoctoral research in developmental neuroscience, University of California, San Francisco (San Francisco)

Before coming to NIH: Associate member, Fred Hutchinson Cancer Research Center (Seattle, Wash.)

Came to NIH: In 2004

Selected professional activities: Adjunct investigator, NHGRI; associate editor *PloS ONE*; associate editor (ad hoc) *PLoS Genetics*

Outside interests: Alpine mountaineering

Website: http://irp.nih.gov/pi/edward-giniger

Research interests: My lab studies neural wiring: how it is established during development and why it is disassembled during neurodegenerative disease.

In our studies of development, we focus on axon guidance, the process by which neurons send out axons to the correct targets. We first showed that the cell-surface receptor Notch, which is well known for controlling cell fates during development, has a second career: locally controlling the Abelson (Abl) tyrosine kinase signaling pathway in axons to direct their growth and guidance.

This finding has led to our conducting live imaging of single, Notch-dependent axons as they extend in their native environment in developing *Drosophila melanogaster*. To our surprise, we have found that axons growing in intact tissue have a morphology that is very different from what one sees in axons grown in culture dishes. In our current experiments, we are teasing apart exactly what each of the axon's cytoplasmic signaling proteins is contributing to its morphogenesis and movement.

In our neurodegeneration studies, we have been examining a mutant gene of *D. melanogaster* (called *Cdk5-alpha*) whose protein causes adult-onset neurodegeneration and a severely reduced lifespan. The protein disrupts the subcellular organization of neurons, leading to altered excitability, swollen axons, and eventually axonal and dendritic fragmentation. Remarkably, however, this mutation accelerates the absolute rate of aging in the fly. This mutation causes or exacerbates defects in innate immunity, stress sensitivity, and proteostasis. We are trying to understand the interplay between these two faces of *Cdk5*-associated neuropathology and their respective roles in human neurodegenerative disease.

HORMUZD A. KATKI, PH.D., NCI-DCEG

Senior Investigator, Biostatistics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute

Education: University of Chicago, Chicago (B.S. in applied mathematics and statistics); Carnegie Mellon University, Pittsburgh (M.S. in statistics); Johns Hopkins University, Baltimore (Ph.D. in biostatistics)

Training: Postbaccalaureate training at NIH's former Division of Computer Research and Technology (now CIT)

Came to NIH: In 1995 for training; in 1999 became staff scientist in NCI-DCEG; appointed principal investigator in 2009

Selected professional activities: Statistical reviewer for the *Journal of the National Cancer Institute*; associate editor for the *American Journal of Epidemiology*; member of the American Society for Colposcopy and Cervical Pathology

Outside interests: Reading nonfiction; biking; raising his three children

Website: http://irp.nih.gov/pi/hormuzd-katki

Research interests: My research focuses on developing and applying quantitative methods to epidemiologic findings to understand how they could be used for cancer screening and prevention. I am particularly interested in developing risk-based approaches to cancer screening.

I led a team that calculated cervical cancer risk for women with different combinations of human papillomavirus (HPV), Pap, and biopsy test results over time using data on 1.4 million women. These calculations are the foundation for the new cervical-cancer screening guidelines available in the official guidelines App (http://www.asccp.org/Bookstore/ASCCP-Mobile-App). These calculations are based on a new statistical model, called the logistic-Weibull model, that we developed.

I also lead a team to estimate the benefits and harms of undergoing computed-tomography (CT) lung-cancer screening. We developed new risk models for lung cancer and used them to identify a smoker's benefit (reduction in risk of lung-cancer death) and harm (risk of false-positive CT). We project that our risk-based approach to targeting CT lung screening might save 20 percent more lives from lung-cancer death over five years compared with screening the same number of smokers under current U.S. Preventive Services Task Force guidelines.

These risk-based approaches to cancer screening depend on the principle of "equal management of people at equal cancer risk." This principle ensures simplified and consistent management of people with different test results or risk factors, but with the same cancer risk. We are examining the limitations of this principle to develop a comprehensive intellectual approach to risk-based precision medicine.

HISATAKA KOBAYASHI, M.D., PH.D., NCI-CCR

Senior Investigator and Chief, Laboratory of Molecular Theranostics, Molecular Imaging Program, Center for Cancer Research, National Cancer Institute

Education: Kyoto University, Kyoto, Japan (M.D. in radiology; Ph.D. in immunology/medicine)

Training: Residency in radiology, Kyoto National Hospital (Kyoto); postdoctoral training in nuclear medicine and diagnostic radiology, Kyoto University

Came to NIH: In 1995–1998 as visiting (Fogarty) fellow, Nuclear Medicine Department, NIH Clinical Center; returned in 2001–2004 as a senior visiting fellow in the Metabolism Branch of NCI-CCR; in 2004–2015 was chief/staff scientist, and later chief/associate scientist, in NCI's Molecular Imaging Program

Selected professional activities: Serving on editorial boards for several scientific journals including *Bioconjugate Chemistry* and *Contrast Media and Molecular Imaging*

Outside interests: Spending time with his son by playing tennis and skiing in winter

Website: https://ccr.cancer.gov/Molecular-Imaging-Program/hisataka-kobayashi

Research interests: I am developing novel molecular-imaging and therapeutic agents and technologies for diagnosing and treating cancers. My group uses chemistry, pharmacology, physics, and engineering to focus on optical, radionuclide, and magnetic-resonance molecular-imaging methods.

To help physicians detect small cancers during endoscopic surgery, we created targeted activatable optical agents—including a sprayable optical-imaging probe—that turned on the signal only when they hit cancer cells. We have also developed instruments, cameras, and other agents for use during prostate-cancer surgery.

My group also has developed antibody-targeted photosensitizers to selectively treat cancer cells with light, a process that has been termed near-infrared photoimmunotherapy (NIR-PIT). Using a variety of antibody-photosensitizer conjugates, we have shown that applying near-infrared light causes dramatic, rapid immunogenic cell death in tumors that have been previously exposed to the conjugate. As the conjugate only binds to the target cells, cell death occurs only where the NIR light is applied. The adjacent normal cells and tissue are left untouched. We have also shown that NIR-PIT preserves the tumor vasculature so there is a dramatic increase in the flow through and permeability of tumor vessels. This increase allows up to 25-fold higher concentrations of nano-sized agents, including anticancer drugs, to reach the tumor bed.

Recently, we discovered that NIR-PIT induced a marked immunological response that may further aid in the treatment of head and neck, pancreas, lung, and colon cancers. The first clinical NIR-PIT trial for head and neck cancer patients targeting the epidermal growth factor receptor has been approved by the FDA and opened in the United States this year.

KEIR C. NEUMAN, PH.D., NHLBI

Senior Investigator, Laboratory of Single Molecule Biophysics, National Heart, Lung, and Blood Institute

Education: University of California, Berkeley (B.A. in physics and applied math); Princeton University, Princeton, N.J. (M.A. and Ph.D. in physics)

Training: Postdoctoral training at Stanford University (Stanford, Calif.); Human Frontiers Postdoctoral Fellow at the Laboratoire de Physique Statistique, l'École Normale Supérieure (Paris)

Came to NIH: In 2007

Selected professional activities: Editorial board member of *Biophysical Journal* and *Journal of General Physiology*

Outside interests: Spending time with his family; backpacking; cycling

Website: http://irp.nih.gov/pi/keir-neuman

Research interests: Enzyme mechanisms have traditionally been elucidated from experiments that involve thousands or millions of molecules. But such ensemble approaches don't reveal the complexities and features of individual enzymes. Single-molecule visualization and manipulation techniques, however, can probe distances

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Recently Tenured

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on the subnanometer scale and forces on the piconewton scale with millisecond temporal resolution. My laboratory develops and uses these techniques—including optical and magnetic tweezers and fluorescence imaging, in combination with conventional molecular biology approaches—to examine enzyme mechanisms and regulation at the molecular level.

Approximately two meters of DNA is crammed into a cell's tiny nucleus. The constraints of such a tiny space can contribute to complications during the chromosomes' replication, transcription, and segregation processes. We are deciphering the molecular mechanisms of enzymes called topoisomerases, which regulate DNA topology and are important drug targets. We hope to determine how chemotherapeutic and antibiotic agents can inhibit topoisomerase activity.

More recently, we have turned our attention away from the cell nucleus to study interactions between the structural protein collagen and the matrix metalloproteinase enzymes (collagenases) that degrade it. By studying the motion of individual collagenase enzymes as they degrade intact native collagen fibers, we have discovered a spontaneous periodic dynamic patterning of collagen fibers and elucidated the molecular mechanisms of fibrillar collagen degradation. Our findings may shed light on human pathological and physiological processes such as the rupture of atherosclerotic plaques and cancer metastasis.

Finally, we are developing fluorescent nanodiamonds as stable fluorescent probes for in vitro and in vivo imaging. We have applied a weak alternating magnetic field to demonstrate in vivo background-free imaging of fluorescent nanodiamonds. This promising technique could lead to advances in the depth and resolution of in vivo imaging with potential applications in biomedical optical imaging and diagnostics.

CHARLES VENDITTI, M.D., PH.D., NHGRI

Senior Investigator, Head, Organic Acid Research Section, Genetics and Molecular Biology Branch, National Human Genome Research Institute; attending physician, NIH Clinical Center

Education: Massachusetts Institute of Technology, Cambridge, Mass. (S.B. in biology); Pennsylvania State College of Medicine, Hershey, Pa. (M.D., Ph.D. in microbiology and immunology)

Training: Residency in pediatrics at Massachusetts General Hospital/Harvard Medical School (Boston); combined clinical and biochemical genetics fellowship at the Children's Hospital of Philadelphia/University of Pennsylvania School of Medicine (Philadelphia)

Came to NIH: In 2003 joined NHGRI as a member of the Physician-Scientist Development Program; in 2009 became a tenure-track investigator in the Genetics and Molecular Biology Branch

Selected professional activities: Board of Medical Advisors, Organic Acid Association; editorial board, *Molecular Therapy—Methods and Clinical Development*

Outside interests: Reading; bike riding with family; swimming; building bikes

Website: http://irp.nih.gov/pi/charles-venditti

Research interests: My lab studies the hereditary methylmalonic acidemias (MMA) and disorders of vitamin B12 metabolism—conditions that cause increased concentrations of methylmalonic acid and/or homocysteine to accumulate in body fluids. MMA is one of the most common inborn errors of organic acid metabolism. People with MMA suffer from multisystem complications ranging from developmental delay to metabolic stroke to end-stage renal failure. The American College of Medical Genetics recommends newborn screening for MMA.

My colleagues and I conduct clinical research aimed at defining the natural history of the MMAs and disorders of vitamin B12 metabolism. We also conduct laboratory studies that use metabolic, genetic, and genomic approaches to better understand the basic biology underlying these disorders.

By studying mouse models of vitamin B12–nonresponsive MMA, my group determined that mitochondrial dysfunction is a cardinal feature of the disorder and may underlie the tissue-specific manifestations seen in patients. In addition, we found that a large source of methylmalonic acid is skeletal muscle, which may explain the clinical observation of persistent MMA in patients after liver or liver-kidney transplantation.

We have also developed zebrafish (*Danio rerio*) models to study the metabolism of cobalamin (various forms of vitamin B12), specifically cobalamin C disorder (cblC; also known as methylmalonic aciduria with homocystinuria), a form of combined MMA and hyperhomocysteinemia and the most common inborn error of intracellular cobalamin metabolism. Its clinical manifestations range from intrauterine effects—such as congenital microcephaly—to cognitive deterioration in adulthood. Some patients develop progressive retinal degeneration that leads to blindness. We plan to use the cblC zebrafish model for genomic and proteomic studies in an effort to shed light on the human disorder.

We are also developing and testing gene therapy for MMA and cblC deficiency. For MMA, we have demonstrated that systemic gene delivery using adeno-associated viral (AAV) vectors effectively treats mice with MMA and provides long-term correction. We hope to perform a clinical trial at the NIH using AAV vectors to treat patients with MMA. ●

2015 NIH RESEARCH FESTIVAL

Wednesday–Friday, September 16–18
Masur Auditorium, Lipsett Amphitheater, and FAES classrooms (Building 10)
Website: http://researchfestival.nih.gov

This year's NIH Research Festival will feature the scientific initiatives outlined in the Intramural Research Program's long-term plan. There is a plenary session each morning: technology development; global-health emergency response; and chronic inflammation. The concurrent afternoon workshops will focus on gene- and cell-based therapies; microbiome and drug resistance; RNA biology and therapeutics; vaccines; natural products; and neuroscience and compulsive behaviors. For questions, contact Jacqueline Roberts at researchfest@mail.nih.gov or check the website.

NIH LIBRARY OPEN HOUSE

Thursday, September 17, 9:30 a.m.–3:30 p.m.
Friday, September 18, 9:30 a.m.–Noon
NIH Library (Building 10)
Updates at: http://nihlibrary.nih.gov/Pages/openhouse_2015.aspx

The open house, held in conjunction with the NIH Research Festival, will feature a demonstration of the data-visualization touch screen; outside experts who will discuss editing, scholarly publishing, and open-access issues and provide recommendations; presentations on tools, technology, and services such as 3D printing, bibliometric and portfolio analysis, bioinformatics software, data management, and custom solutions.

WEDNESDAY AFTERNOON LECTURES

Wednesdays, 3:00–4:00 p.m.
Masur Auditorium (Building 10)
Website: https://oir.nih.gov/wals

An exciting line-up of nationally renown scientists. Check the website for details.

Read more announcements online at http://irp.nih.gov/catalyst/v23i5/announcements.

NIH DIGITAL SUMMIT

Optimizing Digital Media to Reach Scientists, Clinicians, Patients, and the Public
Monday, Oct. 19, 2015, 9:00 a.m.–3:00 p.m.
Masur Auditorium (Building 10)
Registration required
Website: http://www.nih.gov/news/events/digital-summit.htm
Webcast (if you can't attend in person): http://www.videocast.nih.gov

The summit will explore how digital media are being used to communicate information on health and science. For up-to-date information, visit the registration website. For questions, e-mail Yasmine Kloth at Yasmin.kloth@nih.gov.

PLURIPOTENT STEM CELLS IN NEUROSCIENCE: RESEARCH AND APPLICATION

Monday Oct. 26, 2015, 8:30 a.m.–5:30 p.m.
Rooms 620-640, Porter Neuroscience Research Center (Building 35A)
For information and to register: https://meetings.ninds.nih.gov/meetings/PSCinNeuro

The symposium, presented by NINDS, will feature talks by Kristen Brennand (Mount Sinai, New York), Kevin Eggan (Harvard University, Cambridge, Mass.), Steven Finkbeiner (Gladstone Institute, San Francisco), Ron McKay (Lieber Institute for Brain Development, Baltimore), and Edward Wirth (Asterias Biotherapeutics, Menlo Park, Calif.). Contact Barbara Mallon for more information at mallonb@mail.nih.gov or 301-402-8246.

ADVANCING SCIENCE, IMPROVING LIVES

NINR's 30th Anniversary Scientific Symposium and Poster Session
Tuesday, Oct. 13, 2015, 8:00 a.m.–3:30 p.m.
Natcher Conference Center (Building 45)
For information and to register (required): http://www.ninr.nih.gov/30years

The symposium will highlight the accomplishments of NINR and its scientists and showcase the positive impact that NINR's science has had on the lives of millions of Americans.

POSTDOCTORAL RESEARCH ASSOCIATE (PRAT) PROGRAM

Accepting Applications
Deadline: October 2, 2015
Website: http://www.nigms.nih.gov/Training/Pages/PRAT.aspx

PRAT fellows conduct research in intramural labs. Before applying, applicants must identify a potential preceptor in an NIH intramural lab and develop a research proposal. PRAT fellows receive three years of stipend support and additional benefits such as health insurance, a travel allowance, and professional-development training activities, including a monthly seminar series designed for fellows. For more information, visit the website or contact Jessica Faupel-Badger at badgerje@mail.nih.gov.

PRAT 50TH ANNIVERSARY SYMPOSIUM

Friday, Nov. 6, 2015, 8:30 a.m.–4:30 p.m.
Natcher Conference Center (Building 45)
Registration requested (through Oct. 30): https://meetings.nigms.nih.gov/Home/Index/19247

This free, public, symposium will recognize the research contributions of PRAT alumni, highlight the role of the PRAT program in the careers of alumni, and provide an opportunity for PRAT alumni to network with each other and current fellows. The event will be videocast live at http://www.videocast.nih.gov.

SIG: TRANS-NIH BIOMARKERS IN PEDIATRIC THERAPEUTICS

"Application of Metabolomics to Provide Pediatric Biomarkers"
Monday, January 12, 2016, 12:00 noon
Room 9100/9104 Rockledge II and webinar

This SIG presentation will feature Susan Sumner (Director of the NIH Eastern Regional Comprehensive Metabolomics Resource Core at RTI International), who will describe potential applications of metabolomics in pediatrics biomarker development. For information, contact pharmcourse@circlesolutions.com or George Giacola at giacoiag@exchange.nih.gov . ●

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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.

READ THE COLOR EDITION OF THIS ISSUE (WITH MORE ARTICLES, AND EXPANDED VERSIONS OF THE ONES IN THIS ISSUE) ONLINE AT

http://irp.nih.gov/catalyst/v23i5

PHOTOGRAPHIC MOMENT

Bee Happy

SOMA CHOWDHURY

This honey bee (*Apis mellifera*) is dining on the nectar of mint flowers outside of Building 60, the Mary Woodard Lasker Center for Health Research and Education (a.k.a. the Cloisters). Although there are no known hives on campus, there are a number of beekeepers in the area. Bees will travel up to three miles to collect nectar and pollen. And they do love mint.

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

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