

'TRIALS OF BLDG. 10'

Documentary Showcasing CC Set to Air This Spring

BY ERIC BOCK

Most NIH'ers know about the extraordinary research happening inside the Clinical Center. Soon, the public will also know, thanks to a Discovery Channel documentary.

On May 18 at 9 p.m., the cable channel will begin a 3-part series *First in Human: the Trials of Bldg. 10*. Directed by John Hoffman and executive produced by Hoffman and Dyllan McGee, the film will chronicle patients, their families, doctors and researchers as patients undergo experimental treatments at the hospital.

Actor Jim Parsons will narrate the

documentary, which will air in 2-hour segments.

"The NIH Clinical Center's more than 60-year history has resulted in remarkable medical advances, from the first use of chemotherapy to treat cancer, to the development of the technique to keep the blood supply clean and safe from viruses," said NIH director Dr. Francis Collins. "For millions of patients around the world, it is known as the 'House of Hope.'"

At the CC, every patient is enrolled in a clinical trial designed to answer specific questions about the safety and effectiveness of a new treatment or how a disease progresses and, in some cases, to identify previously undiagnosed or new diseases. Most patients are enrolled in phase 1 trials—also known as first-in-human trials. In many cases, patients enrolled in these trials don't have any other treatment options.

Since it first opened in 1953, the CC has enrolled thousands of patients. The



A film crew from the Discovery Channel gets footage from the Clinical Center.

doctor-patient partnership has resulted in a long list of medical milestones, including the first use of gene therapy to treat a patient and

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OUT OF CONTROL

Breaking the Biological Cycle Of Addiction

BY DANA TALESNIK

The urge is strong to eat that cookie and perhaps another; you can't resist the temptation. Even before that first sweet bite, the anticipation has stimulated the reward system in your brain. Are we at all in control of our food cravings or are there more powerful forces at work?

The desire for certain foods, especially those high in sugar and fat, in some people can be almost as strong as for drugs of abuse. But while evidence shows addiction is a disease of the brain, "if we believe we are [in control], we are much more likely to have an impact



Dr. Nora Volkow

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NHLBI director Dr. Gary Gibbons and NHLBI communications director Dr. Lenora Johnson show their support for Wear Red Day and American Heart Month.

'SMALL CHANGES'

'Wear Red Day' Raises Heart Disease Awareness

From the looks of it, nearly everyone at NIH got the memo.

Donning red hats, dresses, shirts and even fancy red shoes, NIH multitudes fanned out across several campuses to celebrate

SEE WEAR RED, PAGE 6



Sound Science, NIH, Kennedy Center expand partnership. See story, p. 12.

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Win a 2018 FARE Travel Award

NIH fellows, win a travel award and enhance your CV. Submit an abstract by Mar. 16 to www.training.nih.gov/felcom/fare. The FARE competition provides recognition for outstanding intramural scientific research. Winners receive a \$1,000 travel award to present their research at a scientific meeting between Oct. 1, 2017, and Sept. 30, 2018. For more information, contact the FARE 2018 committee at FARE@mail.nih.gov.

Sailing Association Open House, Mar. 8 at FAES House

The NIH Sailing Association invites everyone to its open house on Wednesday, Mar. 8 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln. Explore your interest in learning to sail and discover opportunities for sailing with NIHSA. There will be information about 6-week basic training classes, the club's racing program and social activities offered by NIHSA. A fee of \$5 at the door includes pizza, drinks and snacks. Cash bar for beer and wine—\$2 each. Look for NIHSA posters and flyers around campus. For more information, visit www.nihsail.org/.

Workshop on Work/Life, Well-Being Offered for Supervisors

OHR and ORS continue to offer the free supervisory workshop *Work/Life @ NIH: A Supervisor's Guide to Enhancing Workforce Well-Being* in 2017.

This workshop, which was launched in 2016, provides an overview of workforce well-being and how it can benefit your organization; highlights the policies and programs NIH offers to promote workforce well-being; and provides supervisors with strategies to manage various workplace flexibilities. The workshop is led by NIH's own subject matter experts and has been approved for two Continuous Learning Points for supervisory refresher purposes.

Registration is available now in the Learning Management System. Register by searching for course ID #NIHWDR1003. The first session for 2017 is scheduled for Wednesday, Mar. 1 from 9 to 11:30 a.m. at 6710B Rockledge Dr., Rm. 1425/1427. Announcements for additional sessions will be released at a later date. Questions? Email Courtney Bell, ORS (bellcd@mail.nih.gov) or Kelly Peralta, OHR (peraltakl@nih.gov) for more information.

Circus Night Benefits Charities

Join the NIH R&W at 7 p.m. on Thursday, Mar. 30 as it celebrates the final appearance of the Ringling Bros. and Barnum & Bailey Circus at Verizon Center. For 20 years, R&W has been able to bring joy to patients and families at the Children's Inn, at-risk youth and others. Purchase your ticket at the R&W stores in Bldg. 31 (1st floor) or Rockledge or call (301) 496-2670. If you know of a group or organization that may be interested in purchasing a large quantity of tickets to the circus, have them contact David Browne at browned2@mail.nih.gov.



Progress Made on Water Tanks on Campus

Anyone familiar with the parade of dump trucks on campus in the past year already knows that much progress has been made on two huge new water tanks on the south side of campus, which comprise the Assure/Expand Chilled Water Capacity project. The TESS (above), or thermal energy storage system,

will hold 8 million gallons of chilled water and stand 100 feet high; it will help reduce peak power demand on campus. At right and below is the IWSS, or industrial water storage system, which will hold 5 million gallons of water. Like the TESS, it is 120 feet in diameter, but only 65 feet high. It will allow NIH to meet the need for water for a few days if a supply interruption occurs. Dirt taken from the massive excavation was used to fill in the site of demolished Bldg. 7, on the east side of Bldg. 10, according to the Office of Research Services. Both tanks are due for completion by this fall.



PHOTOS: BILL BRANSON





Dr. Lawrence Corey

3 p.m. in Lipsett Amphitheater, Bldg. 10. His talk, titled “Getting to an Effective HIV Vaccine: Perspectives on Progress,” will review the state of HIV vaccine development and describe current strategies to advance the field.

Since 1999, Corey has served as principal investigator of the NIAID-supported HIV Vaccine Trials Network (HVTN), which is dedicated to accelerating development of a safe and effective preventive HIV vaccine. The HVTN has built an international scientific collaboration of investigators in 12 countries on 5 continents.

Corey will discuss recent advances in identifying and manufacturing broadly neutralizing antibodies that target multiple, diverse HIV strains. Researchers are testing whether and to what extent infusions of these antibodies can protect people from HIV infection to help inform the design of novel vaccine candidates.

He also will explain how HIV vaccinology is at an important crossroads in defining whether protective non-neutralizing antibodies can be elicited with a vaccine. He will describe ongoing clinical trials in humans that aim to build on vaccine regimens that

have achieved protection in animal models, as well as regimens that aim to build on insights gleaned from a clinical trial conducted in Thailand that is the only human study to have demonstrated some efficacy for an HIV vaccine candidate.

Corey is past president and director of the Fred Hutchinson Cancer Research Center in Seattle and professor of medicine and laboratory medicine at the University of Washington. His laboratory has made major contributions to research on herpes viruses, HIV and viral-associated cancers.

The Hill lecture series is dedicated to the memory of former NIAID deputy director Dr. James C. Hill, who played a critical role in shaping NIAID’s HIV/AIDS research agenda during the early years of the epidemic. **R**

Annual Hill Lecture Features Virologist Corey on Progress Toward HIV Vaccine

Virologist and vaccine expert Dr. Lawrence Corey will deliver the 2017 James C. Hill Memorial Lecture on Tuesday, Mar. 14 at

Page To Speak in NLM Lecture Series

The next topic in the National Library of Medicine Informatics Lecture Series is “High-Throughput Machine Learning from EHR Data,” given by Dr. David Page on Wednesday, Mar. 8 from 2 to 3 p.m. in Lister Hill Center Auditorium, Bldg. 38A.

The widespread use of electronic health records and the many recent successes of machine learning raise at least two questions to be discussed in Page’s talk: How well can future health events of patients be predicted from EHR data, at various lengths of time in advance? And how can such predictions improve human health?

Page is a Vilas distinguished achievement professor at the University of Wisconsin. His primary appointment is in the department of biostatistics and medical informatics in the School of Medicine and Public Health, with another appointment in the department of computer sciences, where he teaches machine learning. He directs the Cancer Informatics Shared Resource of the Carbone Cancer Center and is a member of the Genome Center of Wisconsin.



Dr. David Page

MAR. 8



ON THE COVER: Scanning electron microscopy of collagen fibers

IMAGE: TOM DEERINCK & MARK ELLISMAN, NATIONAL CENTER FOR MICROSCOPY AND IMAGING RESEARCH

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

Documentary

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the first use of the antiretroviral AZT to treat AIDS.

“What was most powerful about embedding [film crews] in Bldg. 10 and following these trials was observing how the doctors and patients came to rely on each other in a true partnership to advance medicine,” said Hoffman, who also produced *The Weight of the Nation*, *The Alzheimer’s Project* and *Sleeplessness in America*. All three HBO documentaries featured NIH research.

“Clinical Center staff have much to be proud of when they come to work,” noted hospital CEO Dr. James Gilman. “Everything I’ve heard suggests this series bears that out. Since my arrival on campus, I’ve sensed the excitement around this broadcast. It’s a tremendous opportunity to educate about the NIH mission and biomedical research.”

After months of pre-production scouting and on-site information gathering, crews began filming in September 2015 and wrapped up their most intensive work in May 2016. Spot filming continues. More than 1,000 hours of footage have been collected; hundreds of staff, patients and their families have been filmed, said Justin Cohen, chief of the Clinical Center’s Office of Communications and Media Relations.

Before crews embedded with doctors and patients, they underwent training about patient safety and privacy, infection control and how to put on personal protective equipment, he added.

During filming, crews were always accompanied by staff from Cohen’s office and other IC communications offices or specially trained NIH staff acting as “filming ambassadors.” Sometimes, for instance, they had to troubleshoot for filmmakers or advocate for patients. Cohen called it “an extraordinary opportunity and a real team effort.”

Dr. Lauren Wood, clinical director of the Vaccine Branch in NCI’s Center for Cancer Research, was filmed for the show. She appreciated the time the crew took to get to know the people they were depicting. Discovery employees “were really committed to getting patients and their families’ stories” and “made an effort to be very respectful of patients,” she said.

The crew also focused on getting the science right and capturing “how exciting,



NCI’s Dr. Terry Fry consults with patient Bo Cooper about an upcoming CAR T-cell protocol in a filmed segment of the new Discovery Channel documentary about Bldg. 10.

PHOTOS: DISCOVERY CHANNEL

challenging and hard it is to do good science with patients,” Wood added.

She enjoyed seeing each crew’s transformation. At first, they were unfamiliar with NIH acronyms and medical terminology. As time went on, they picked up the vocabulary and asked great questions.

There were times when patients’ appointments changed at the last minute, but the film crew easily adapted, she recalled. Things went smoothly because there was real-time coordination between Discovery, the communications staffs of the CC and ICs “and what felt like an infinite number of emails,” she added.

Although she took part in filming, Wood hasn’t seen the documentary.

“I have seen not one thing,” she said. “I’m looking forward to watching it with everyone else and seeing the story unfold.” **R**

Durrant Named Director of CSR Division

The Center for Scientific Review has named Dr. Valerie Durrant to become director of its Division of AIDS, Behavioral and Population Sciences. She has been chief of CSR’s population sciences and epidemiology integrated review group since 2011.

Durrant will coordinate five integrated review groups, which review NIH grant applications for scientific merit: AIDS and related research; biobehavioral and behavioral processes; health care delivery and methodologies; population sciences and epidemiology; and risk, prevention and health behavior.

She is chair of CSR’s best practices committee and served as acting director of CSR’s Division of Neuroscience, Development and Aging in 2015. Durrant previously served as scientific review officer for the social sciences and population studies panel B study section.

Before coming to NIH, Durrant was a program officer at the National Academies’ committee on population. She directed studies on the transition from childhood to adulthood in developing countries that assessed the benefits of investing in youth in these countries.

Durrant holds a Ph.D. in sociology with an emphasis in demography from the University of Maryland. She was a Berelson postdoctoral fellow at the Population Council, conducting research on adolescents and on the influence of the status of women on infant and child mortality and children’s schooling in Pakistan.





Three NIH IC directors participate in Chat Day. NIAAA director Dr. George Koob smiles at the camera while NIDA director Dr. Nora Volkow (far r), with assistance from NIDA's Dr. Susan Weiss, and NIMH director Dr. Joshua Gordon (back l), with assistance from NIMH's Charlotte Armstrong, are busy answering questions from students across the nation.

Events Illuminate Drug, Alcohol Facts

National Drug & Alcohol Facts Week set an all-time record this year in the number of domestic and international events held during the week of Jan. 23-29. NDAFW, launched in 2010 by NIDA, and in partnership with NIAAA since 2016, is an annual health observance week for teens to shatter the myths about drug and alcohol use by connecting with health and scientific experts.

This year, more than 2,100 community events were held in all 50 states as well as 15 countries—the largest international reach ever. In addition, on Jan. 26, NIDA celebrated its 10th anniversary of Drugs & Alcohol Chat Day, a live online chat between teens and NIH scientists. More than 50 high schools participated from 50 states.

The directors from NIDA, NIAAA and NIMH were part of more than 60 scientists who participated in Chat Day this year, answering close to 2,500 questions from students across the world, including young U.S. airmen from Yokota Air Force Base in Tokyo, Japan. Online resources included several new drug-specific toolkits for event holders to use, a “shatter the myths” pledge card and the popular National Drug IQ Challenge, an interactive quiz accessible on mobile devices for teens to test their knowledge about drugs and alcohol.

Visit <http://teens.drugabuse.gov/national-drug-facts-week> for more information.



Teenagers from Imagine Prep Coolidge School in Coolidge, Ariz., share their “shatter the myths” pledge cards.

K AWARDEES

NIAID Holds K Workshop to Foster Science Leaders

The National Institute of Allergy and Infectious Diseases recently hosted its first career development award (K) workshop in Rockville with 63 NIAID-supported extramural K awardees participating and featuring key NIH staff.

Awardees gathered at the 2-day event to exchange information designed to help propel them into independent research careers. They were given guidance on applying for research project grants, conferred with NIH staff and provided feedback to NIAID on the effectiveness of its K programs.

NIAID makes a significant investment in each of its K01, K08, K22, K23, K25 and K99-mentored and transition awardees; the institute is motivated to see them reach research independence (e.g., attaining an R01). Participants were able to attend an array of sessions, including How to Design One's Research Career, Perceived Challenges to Transitioning to Research Independence, What Reviewers Look for in an NIH Research Grant Application, Roles of Program Officers and Scientific Review Officers and Other Funding Sources to Support Your Independent Research.

NIH launched its career development (“K” program) in 1957 to help develop the nation's biomedical research workforce. The K awards were designed to provide protected research time to promising investigators following the completion of their formal doctoral and postdoctoral training.



NIAID recently hosted its first career development award (K) workshop in Rockville. Sixty-three extramural K awardees attended the event.



Rubinstein Named Chief of CSR Review Group

The Center for Scientific Review has selected Dr. Amy Rubinstein as new chief of the oncology 1 basic translational integrated review group.

She has been scientific review officer for CSR's gene and drug delivery systems study section, which reviews grant applications across several institutes, with over a third focusing on cancer research.

“We are pleased that Dr. Rubinstein will take charge of this key review group,” said CSR director Dr. Richard Nakamura. “Since coming to CSR in 2008, she has proven to be a remarkable leader and mentor.”

He noted that she excelled as CSR's coordinator for the review of Small Business Innovation Research and Small Business Technology Transfer applications, co-chair of the trans-NIH SBIR shorten-the-cycle committee and leader of CSR's assessment of direct ranking and half-point scoring as alternatives to the current system for scoring grant applications.

Rubinstein earned a Ph.D. in biology from the University of North Carolina at Chapel Hill, studying the molecular genetics of pollen development in maize. She did her postdoctoral research at the Carnegie Institution of Washington, where she used the zebrafish model to advance research in multiple therapeutic areas, including angiogenesis in the context of cancer therapy. Rubinstein then helped form a start-up biotechnology company (Zygogen, LLC), which worked to design zebrafish assays for drug discovery. During her tenure there, she served as director and vice president of research.



“Small Changes for the Heart.” The annual campaign to kick off American Heart Month involves the entire NIH community. At left, Bldg. 31 cafeteria food services director Alayna Santiago shows off heart-healthy quinoa and black bean salad, specially prepared from an NHLBI recipe book. At right, a visitor at the Medical Center Metro station proudly shows off her Wear Red Day sticker.

PHOTOS: MARK SAMPSON

Wear Red

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National Wear Red Day on Feb. 3 and launch American Heart Month. Hosted by NHLBI, the event helps raise awareness about heart disease, the leading cause of death in the United States for both men and women.

This year’s theme, “Small Changes for the Heart,” encouraged people to make gradual

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Heart disease is the leading cause of death in the United States for both men and women.

• • •

changes to reduce their risk of heart disease. Taking the stairs instead of the elevator, eating less sugar and sodium and getting regular blood pressure screenings—all are examples of little changes that, cumulatively, can have big payoffs.

To get out this message and underscore the importance of a heart-healthy

lifestyle, NHLBI staff posted “National #WearRedDay” signs all over campus. They also handed out heart-shaped stickers at building entrances and at the Medical Center Metro station. NIH cafeteria staff wore red for the occasion and served menu choices that featured heart-healthy red foods such

as apples, beets and tomatoes. NIH experts were on hand to provide nutrition tips.

In addition to Wear Red Day, NHLBI celebrated American Heart Month in other ways throughout February.

On Feb. 8, NHLBI and *Woman’s Day* magazine co-hosted a panel in New York



Wearing red, members of the NHLBI Office of Science Policy, Engagement, Education and Communication gather for a photo.



NHLBI nutrition coordinator Kathryn McMurry (l) receives a visitor at the Bldg. 31 cafeteria display of heart-healthy foods and recipes.

City titled “The Power of Community: How local programs, businesses and faith-based organizations are innovating ways to fight heart disease in women.” The panel included representatives from a number of communities, including non-profits, medical and research groups.

A few NHLBI staff also attended the American Heart Association’s 2017 Red Dress Collection in New York City on Feb. 9. Founded by NHLBI, the annual fashion show helps bring needed awareness to heart disease in women. The show featured celebrity models in red designer dresses including Lucy Lawless, Diane Guerrero, Rachel Platten, Jeannie Mai, CCH Pounder, Maureen McCormick and Juliette Lewis. Actress Katie Holmes hosted the event.

On Feb. 24, NHLBI will join forces with the American Heart Association and *Woman’s Day* to host a Twitter chat to discuss heart disease, risk factors and research and how you can protect your heart. You’re invited to follow the discussion using #HeartChat.

You can also find more information about heart disease and prevention by visiting www.nhlbi.nih.gov. —**Mark Sampson**



The cafeteria at Bldg. 10 featured a special display of heart-healthy red foods.

PHOTO: MICHAEL AHMADI



New scientific staff members at NIMHD include (from l) Dr. Benyam Hailu, Dr. Beda Jean-Francois, Dr. Andrew Loudon, Dr. Priscah Mujuru, Dr. Richard Palmer and Dr. Meryl Sufian.

NIMHD Adds to Scientific Staff

The National Institute on Minority Health and Health Disparities recently added six employees to its scientific staff.

Dr. Benyam Hailu has joined the Division of Scientific Programs as a medical officer. He comes to NIMHD with experience as a general medical practitioner, project supervisor and researcher for a non-profit AIDS research project in sub-Saharan Africa.

He has worked at the Department of Veterans Affairs in Washington, D.C., and at the Food and Drug Administration. Hailu received his M.D. from Addis Ababa University and his M.P.H. from Bloomberg School of Public Health at Johns Hopkins University, with a concentration in infectious diseases.

Dr. Beda Jean-Francois has joined the Division of Scientific Programs as a health scientist administrator. She oversees a portfolio of research and training grants in the area of population science and community health. Prior to joining NIMHD, she was a social science analyst in the Center for Behavioral Health Statistics and Quality at SAMHSA.

Prior to that, she held faculty posts at the public school and university levels and served as a research psychologist with the Department of Defense. Her qualifications include a Ph.D. in applied developmental psychology and a master’s degree in education—specifically learning and reading disabilities.

Dr. Andrew Loudon is a program officer working in clinical and health services research within the Division of Scientific Programs, where he will help manage and develop the growing and diverse research portfolio.

Before coming to NIMHD, Loudon worked for 7 years as a scientific review officer at the Agency for Healthcare Research and Quality, where his responsibilities included providing policy direction and coordination for the planning and execution of the initial scientific and technical review of applications within the disciplines of health services research. He received his undergraduate degree in biology from Swarthmore College in 1990, and his master’s and Ph.D. degrees in genetics from Howard University in 1998 and 2001, respectively.

Dr. Priscah Mujuru is a health scientist administrator in the Division of Scientific Programs, Clinical and

Health Services Research Programs. Prior to joining NIMHD, she was an SRO at CSR and NICHD from October 2010 to January 2017. She earned a doctor of public health degree in epidemiology from the University of Pittsburgh, a master of public health degree in environmental health from Boston University, a B.Sc. in occupational hygiene from the University of the South Bank, England, and a bachelor of science in nursing degree from West Virginia University.

She also earned a nurse and midwifery state-registered education in England.

Mujuru is a board-certified occupational health nurse specialist and has collaborated with the Association of Occupational and Environmental Clinics to develop physical assessment tools for occupational health nurses. She has led programs that addressed a pipeline to health sciences careers in West Virginia youth from underserved and disadvantaged populations. She also led international projects in South Africa, Mozambique and Mali.

Dr. Richard Palmer joined the Scientific Review Branch in the Office of Extramural Research Administration as a health science administrator. He holds both a doctorate in public health and a J.D. degree and had been an associate professor and NIH-funded investigator in the Robert Stempel College of Public Health and Social Work at Florida International University.

In addition to serving as a scientific review officer, Palmer will contribute to OERA activities in extramural policy development and analyses and extramural scientific training and education, including the NIMHD Health Disparities Research Institute.

Dr. Meryl Sufian has joined the Integrative Biological and Behavioral Sciences Branch in the Division of Scientific Programs as a program officer. She came to NIMHD from the National Center on Advancing Translational Sciences, where she was a program director for the Clinical and Translational Science Awards Program.

Prior to that she worked in NCI’s Division of Cancer Control and Population Sciences.

Before joining NIH, Sufian conducted HIV prevention research and multi-site behavioral health intervention research with high-risk populations. She received a B.A. in sociology from Hunter College and a Ph.D. in medical sociology from the Graduate Center, City University of New York. **R**

Addiction

CONTINUED FROM PAGE 1

on our behaviors,” said NIDA director Dr. Nora Volkow at a recent Demystifying Medicine lecture in Bldg. 50.

Drugs and foods increase dopamine, a neurotransmitter in the brain associated with reward, triggering processes that lead to conditioning, which in those that are vulnerable can result in addiction, said Volkow. But the dopamine system also has a more primitive function, activating the body’s instinct to seek nutrients for survival and, working in conjunction with hormones and peptides, modulating hunger and satiety.

“So one could say it’s not that food produces addiction, but actually that drugs are hijacking a system that was developed by nature specifically to motivate behaviors needed for survival and to create habits,” Volkow said. “And drugs can more rapidly generate habits that are very difficult to break and also can result in compulsive behaviors more rapidly than food.”

Interestingly, recent studies have shown that dopamine levels didn’t necessarily increase, and sometimes decreased, when drug addicts took an illicit drug or when an obese person consumed food. “There is a marked suppression of the ability of the drug to increase dopamine in the brain of the person who is addicted,” Volkow said. What then would motivate an addict to continue taking the drug or a person to continue eating without the reward experienced upon its consumption?

The answer may lie in the old tale of Pavlov’s dog. The repeated administration of the reward—the drug or the food—creates a conditioned response, said Volkow. Animal and human studies have shown that repeatedly pairing auditory or visual cues with a drug or food will result in dopamine increases just with the presentation of the cue.

But it’s not just the expectation of reward. There’s another biological factor underlying addiction. “In individuals who are addicted to a wide variety of drugs—cocaine, methamphetamine, alcohol, heroin, nicotine—consistently we observed a decrease in the level of dopamine D2 receptors in the striatum of the human brain,” said Volkow.

The same held true in obesity research.



including self-regulation.

“If you damage the orbital frontal cortex [most ventral part of the frontal cortex], the cocaine abuser, the alcoholic, the meth abuser is not able to shift the preference of the drug reward for any other [preference],

Morbidly obese people had significantly reduced striatal D2 receptors, making them more prone to compulsive behavior. What’s driving this compulsion? The lower level of striatal D2 reduces the baseline activity of the frontal areas of the brain that are needed for executive function,

explained Dr. Kevin Hall, a senior investigator with NIDDK.

To help understand how radical weight loss affects the body, Hall’s team studied a group of contestants from the reality show *The Biggest Loser*. After months of extreme calorie cutting and daily intense exercise, during which contestants initially were losing a staggering pound a day, most of the weight they lost came from fat mass.

“These folks were able to preserve their lean tissue mass to an extraordinary extent,” said Hall.

Lean body tissue is the most metabolically active, so it came as a surprise that the contestants’ metabolic rate was falling dramatically despite their intensive exercise. After the competition, they couldn’t burn

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The more people try dieting, the more the body resists, recoiling like a spring to maintain its higher weight.
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even after it’s been consumed for hours,” she said. “The drug is going to be a main and fixed reinforcer.” This is different from normal function, when the orbital frontal cortex changes the value of the reward as a function of context, such as reducing the motivational value of food when we are no longer hungry, allowing us to focus our attention on an alternative behavior.

Despite our biology, Volkow asserted, “I do believe we are in control at many levels and we have the knowledge to recognize what environments may be pathological and dangerous because they will trigger automatic behaviors such as drug-taking or compulsive overeating.”

Although most conditioned responses are unconscious, Volkow said, our frontal cortex connects not only to reward centers but also to executive control circuits that help us predict situations and control, beforehand, our behaviors.

With obesity, however, there’s another biological process at work. If it wasn’t challenging enough to lose weight in the first place, especially for the obese, the body’s metabolism makes it even harder to keep the weight off. There’s a homeostatic mechanism fighting our weight loss efforts,

enough calories to maintain their slimmer size and had to dramatically reduce caloric intake just to maintain their current weight.

Six years after the competition, most contestants had regained at least two-thirds of the lost weight, much of it fat mass. But as their weight increased, their metabolisms didn’t recover.

The more people try dieting, the more the body resists, recoiling like a spring to maintain its higher weight. Metabolic changes are proportional to the amount of weight lost, said Hall, noting that *The Biggest Loser* is an extreme case; not everyone who diets experiences a huge metabolic slowing.

“The people who continue to experience the greatest metabolic adaptation 6 years later are the most successful at maintaining weight loss,” said Hall. “It’s somewhat encouraging that we may have some control over this process.”

As the obesity epidemic continues to grow, there’s a burgeoning need to promote healthier dietary choices. We can create an environment where obesogenic food isn’t so readily available, suggested Volkow. “And we can create health policy interventions that can protect the population from the adverse effects of very powerful food rewards.” **R**

Epilepsy Drug Discovered in Fish Model Shows Promise in Pediatric Clinical Trial

“Bench-to-bedside” describes research that has progressed from basic science in animal models that has led to therapies used in patients. Now, a study in the journal *Brain* describes what could be considered a direct “aquarium-to-bedside” approach, taking a drug discovered in a genetic zebrafish model of epilepsy and testing it, with promising results, in a small number of children with the disease. The study was supported by NINDS.

“This is the first time that scientists have taken a potential therapy discovered in a fish model directly into people in a clinical trial,” said Dr. Vicky Whittemore, NINDS program director. “These findings suggest that it may be

possible to treat neurological disorders caused by genetic mutations through an efficient and precision medicine-style approach.”

Dr. Scott C. Baraban, the William K. Bowes Jr. endowed chair in neuroscience research and professor of neurological surgery at the University of California, San Francisco, postdoctoral fellow Dr. Aliesha Griffin and colleagues used a zebrafish model of Dravet syndrome to test the drug lorca-serin and found that it suppressed seizure activity in the fish. Dravet syndrome is a severe form of pediatric epilepsy characterized by frequent daily drug-resistant seizures and developmental delays. It is caused by a genetic mutation, which Baraban’s group was able to introduce into the zebrafish to cause epilepsy.

Designer Compound May Untangle Damage Leading to Some Dementias

In a study of mice and monkeys, NIH-funded researchers showed that they could prevent and reverse some of the brain injury caused by the toxic form of a protein called tau. The results, published in *Science Translational Medicine*, suggest that the study of compounds, called tau antisense oligonucleotides, that are genetically engineered to block a cell’s assembly line production of tau, might be pursued as an effective treatment for a variety of disorders.

Cells throughout the body normally manufacture tau proteins. In several disorders, toxic forms of



A zebrafish model of Dravet syndrome, a severe form of pediatric epilepsy, may help scientists quickly find drugs for the disorder.

IMAGE: SCOTT BARABAN, UCSF

tau clump together inside dying brain cells and form neurofibrillary tangles, including Alzheimer’s disease, tau-associated frontotemporal dementia, chronic traumatic encephalopathy and progressive supranuclear palsy. Currently there are no effective treatments for combating toxic tau.

“This compound may literally help untangle the brain damage caused by tau,” said the study’s senior author, Dr. Timothy Miller of Washington University, St. Louis.

Grants from NINDS and NIA supported the research.

Antisense oligonucleotides are short sequences of DNA or RNA programmed to turn genes on or off. Led by Sarah L. DeVos, a graduate student in Miller’s lab, the researchers tested sequences designed to turn tau genes off in mice that are genetically engineered to produce abnormally high levels of a mutant form of the human protein. Tau clusters begin to appear in the brains of 6-month-old mice and accumulate with age. The mice develop neurologic problems and die earlier than control mice.

Injections of the compound into the fluid filled spaces of the mice brains prevented tau clustering in 6- to 9-month-old mice and appeared to reverse clustering in older mice. The compound also caused older mice to live longer and have healthier brains than mice that received a placebo. In addition, the compound prevented the older mice from losing their ability to build nests.

“These results open a promising new door,” said NINDS program director Dr. Margaret Sutherland. “They suggest that antisense oligonucleotides may be effective tools for tackling tau-associated disorders.”

Aspirin May Help Increase Pregnancy Chances in Women With High Inflammation

A daily low dose of aspirin may help a subgroup of women, those who have previously lost a pregnancy, to successfully conceive and carry



A daily low dose of aspirin may help some women successfully conceive and carry a pregnancy to term.

a pregnancy to term, according to an analysis by NIH researchers. The women who benefited from the aspirin treatment had high levels of C-reactive protein (CRP), a substance in the blood indicating system-wide inflammation, which aspirin is thought to counteract. The study appears in the *Journal of Clinical Endocrinology and Metabolism*.

Researchers at NICHD analyzed data originally obtained from the Effects of Aspirin in Gestation

and Reproduction trial. The trial sought to determine if daily low-dose aspirin could prevent subsequent pregnancy loss among women who had one or two prior losses.

For the current study, researchers classified the women into 3 groups: low CRP (below .70 mg per liter of blood), mid CRP (from .70 to 1.95) and high CRP (at or above 1.95). Women within each group received either daily low-dose aspirin or a placebo. In their analysis, researchers found no significant differences in birth rates between those receiving aspirin and those receiving placebo in both the low-CRP and mid-CRP groups. For the high-CRP group, those taking the placebo had the lowest rate of live birth at 44 percent, while those taking daily aspirin had a live-birth rate of 59 percent. Aspirin also appeared to reduce CRP levels in the high-CRP group.

Stem Cell Secretions May Protect Against Glaucoma

A new study in rats shows that stem cell secretions, called exosomes, appear to protect cells in the retina, the light-sensitive tissue in the back of the eye. The findings, published in *Stem Cells Translational Medicine*, point to potential therapies for glaucoma, a leading cause of blindness in the U.S. The study was conducted by NEI researchers.

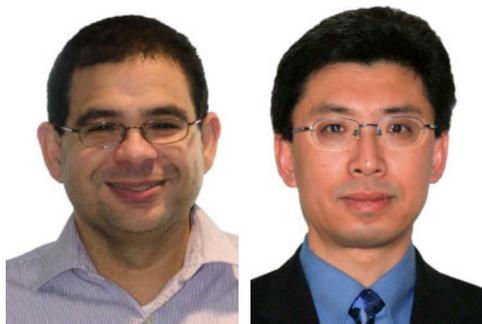
Exosomes are tiny membrane-enclosed packages that form inside of cells before getting expelled. Long thought of as part of a cellular disposal system, exosomes are packed, scientists have recently discovered, with proteins, lipids and gene-regulating RNA. Studies have shown that exosomes from one cell can be taken up by another by fusing with the target cell’s membrane, spurring it to make new proteins. Exosomes also facilitate cell-to-cell interactions and play a signaling role, prompting research into their potential therapeutic effect.

In his study, NEI postdoctoral fellow Dr. Ben Mead investigated the role of stem cell exosomes on retinal ganglion cells, a type of retinal cell that forms the optic nerve that carries visual information from the eye to the brain. The death of retinal ganglion cells leads to vision loss in glaucoma and other optic neuropathies.

Stem cells have been the focus of therapeutic attempts to replace or repair tissues because of their ability to morph into any type of cell in the body. However, from a practical standpoint, using exosomes isolated from stem cells presents key advantages over transplanting whole stem cells.

“Exosomes can be purified, stored and precisely dosed in ways that stem cells cannot,” Mead said.

Another important advantage of exosomes is they lack the risks associated with transplanting live stem cells into the eye, which can potentially lead to complications such as immune rejection and unwanted cell growth.



Dr. Luis Cubano (l) and Dr. Hongwei Gao recently joined the NIGMS staff as program directors.

NIGMS Adds Two New Scientific Staff

NIGMS recently hired two new program directors.

Dr. Luis Cubano is a program director in the Division of Training, Workforce Development and Diversity. He administers the Research Initiative for Scientific Enhancement program for students from underrepresented groups as well as other diversity-focused institutional research training grants.

Prior to joining NIGMS, he served as professor and associate dean for research and graduate studies at the Universidad Central del Caribe, in Bayamón, Puerto Rico. Cubano earned a B.S. in cellular and molecular biology from Tulane University, an M.S. in biology from the University of Alabama in Huntsville and a Ph.D. in biology from Kansas State University. He conducted postdoctoral research at Tulane University Medical School.

Dr. Hongwei Gao is a program director in the Center for Research Capacity Building, where he

manages Institutional Development Award (IDeA) Centers of Biomedical Research Excellence and IDeA infrastructure for clinical and translational research grants. He comes to NIGMS from Boston, where he was an assistant professor of anesthesia at Harvard Medical School and a senior scientist in the department of anesthesiology, perioperative and pain medicine at Brigham and Women's Hospital.

Gao earned his M.D. in a joint 8-year program of Nankai University and Tianjin Medical University, in China. He earned his Ph.D. in microbiology and molecular genetics at Michigan State University. He was a postdoctoral fellow in the department of pathology at the University of Michigan.

NINDS Alumnus Hessie Mourned

Bettie Jean Hessie, 78, who retired from the National Institute of Neurological Disorders and Stroke in 1999 after 34 years as a medical writer and consultant, passed away peacefully on Dec. 21, 2016.

Born in Comus, Md., she graduated *cum laude* from American University with a B.S. in distributed science-biology.

During her NIH career, she worked with authors and editors in the publication of more than 40 books in biomedical sciences and edited more than 1,000 journal articles, book chapters and abstracts, speeches and brochures. She also taught biomedical writing to NIH scientists from around the world.

Hessie also co-authored a book on antiepileptic



Bettie Jean Hessie

drugs. She served on the epilepsy advisory committee and helped organize the 15th Epilepsy International Symposium in D.C., in 1983.

She was a member of the American Medical Writers Association, Council of Biology Editors and the Washington Society for the History of Medicine.

In retirement, Hessie volunteered at Arena Stage and WAMU-FM. She also enjoyed traveling and attending National Symphony Orchestra concerts.

Former Medical Officer Cooney Mourned

BY JOSEPH J. BARCHI, JR.

Dr. David A. Cooney, a retired public health officer who had a 34-year career at NIH (1964-1998), died Oct. 8, 2016, from prostate cancer. He was 78 and lived in Bethesda.

A native of Arlington and Scituate, Mass., he attended Boston College High School and received his B.A. degree in classics and pre-medical sciences from the College of the Holy Cross in Worcester, Mass., in 1959. He subsequently earned his M.D. from Georgetown University School of Medicine in 1963. He spent a year in San Salvador, serving as a Public Health Service fellow in the department of microbiology at the Universidad de El Salvador.

After completing internship training in 1964 at Buffalo General Hospital in New York, he served as a senior investigator in the Laboratory of Toxicology at the National Cancer Institute from 1964 to 1969. After a 1-year postdoctoral fellowship in the department of pharmacology at Yale University School of Medicine, Cooney returned to NCI, serving as a staff scientist in the Laboratory of Toxicology from 1971 to 1976.

In 1977, he was appointed head of the biochemistry section in the Laboratory of Biochemical Pharmacology, where he served until 1988. The last decade of his career at NCI was as a supervisory scientist in the Laboratory of Medicinal Chemistry until his retirement in 1998.

Cooney spent most of his career studying anti-cancer and anti-HIV therapeutics. He studied the toxicology, pharmacology and biochemical pharmacology of both amino acid and nucleoside analogues.

Cooney's research accomplishments from the late 1960s into the early 1980s established him as a leading scientist in the fields of pharmacology and toxicology, especially relating to various families of anti-cancer drugs.

Most notable are his work on asparagine metabolism, asparagine synthase mechanism of action and inhibition as antitumor therapy; the toxicology and antitumor activity of FDA-approved drugs such as cisplatin, bleomycin and streptozotocin; and mechanism of action and pharmacology of anti-HIV dideoxy nucleosides.

The work on anti-HIV nucleosides in the mid-1980s saw collaborations with such NCI scientists as Drs.

NIDA's Rapaka Receives Service Award

NIDA's Dr. Rao Rapaka received the 2016 Distinguished Service Award at the American Association of Pharmaceutical Scientists annual meeting and exposition held recently in Denver. This is the first time a NIDA staffer has received the award, which recognizes distinguished service in advancing the pharmaceutical sciences through service to the AAPS.

Rapaka is chief of the Chemistry, Pharmacology and Physiological Systems Research Branch in the Division of Neuroscience and Behavior and has served as chair of the medicinal chemistry and drug design & discovery sections of AAPS. He has also served on its fellowship and program committees and journal editorial boards and has organized more than 30 AAPS symposia and AAPS-NIDA symposia. He was elected a fellow of AAPS as well as the American Association for the Advancement of Science. Rapaka has received several other awards from national and international societies, including the International Conference on the Science of Botanicals, International Cannabinoid Research Conference, International Narcotic Research Conference and the College on Problems of Drug Dependence (Michael Morrison Award).





Retired public health officer Dr. David A. Cooney

Samuel Broder, Robert Yarchoan and Hiroaki Mitsuya. The results of Cooney's research from the early HIV years until his retirement in 1998 labeled him as one of the few pioneers who identified the mode of action of numerous nucleoside reverse transcriptase inhibitors.

Two of the drugs he studied—dideoxyinosine (didanosine, Videx, Bristol-Myers Squibb) and dideoxycytidine (Zalcitabine, Hivid, Hoffmann-La Roche)—were later approved by the FDA and used as parts of combination anti-HIV regimens. Cooney won a PHS service award in 1991 for his contributions to development of these agents.

According to coworkers, Cooney touched a lot of lives with his fierce intelligence, distinctive wit and personal charm. He was extremely generous with his time, spending countless hours mentoring the many students (who ranged in age from early high school to late college) that he continuously had as interns in his section.

One thing that all of his friends and colleagues would agree on, "There was never a dull moment when Dr. Cooney was around." He kept the students and postdocs excited about their work, peppering them with questions to keep them on their toes while being spontaneous and unpredictable and keeping abreast of their lives outside the lab.

Cooney's generosity extended to his community, where he often cared for and supported those in need who were well outside his circle of professional colleagues.

In addition to his outstanding scientific contributions, he was a true "Renaissance man"—an accomplished musician, composer and writer. On his students' departure, Cooney often composed tributes to them, be it songs in a variety of musical genres (from jazz to rags to ballads) or poems rich with symbolism and heartfelt emotion.

"All of these traits made him a man who was brilliant yet selfless, frivolous yet focused, eccentric yet highly compassionate," noted a longtime colleague. "He will be truly missed by all who knew him."

Cooney is survived by sisters Mary Lou Manning of Rockville and Nancy Ryan of York Harbor, Maine; 19 nieces and nephews (and many more grand-nieces and nephews). Memorial contributions may be made to the NCI Gift Fund. **R**

Study on Depression, Repeated Doses of Ketamine Now Enrolling

Join a research study on depression. The purpose is to evaluate the rapid and sustained antidepressant effects of repeat doses of ketamine in the brain. Researchers want to learn how ketamine affects areas of the brain important in regulating mood and if there are unique signatures that could help predict who may respond to the drug. Also, investigators want to see if repeated doses of ketamine are safe and effective in treating the symptoms of depression. The study is enrolling eligible adults ages 18 to 65 with major depressive disorder. This inpatient study lasts 14-20 weeks. Procedures include a medication taper and drug-free period, taking repeated doses of the research drug, taking placebo, multiple brain imaging scans, transcranial magnetic stimulation and psychological testing. After completing the study, participants receive short-term follow-up care at NIH while transitioning back to a provider. There is no cost to participate. Compensation is provided. Study enrolls eligible participants from across the U.S. Travel arrangements are provided. Costs are covered by NIMH. To find out if you qualify, call 1-877-646-3644 (1-877-MIND-NIH), TTY 1-866-411-1010.

Patients with Leukemia Needed

NHLBI is testing if the two medications, pembrolizumab and decitabine, can be used to treat adult patients with relapsed/refractory AML (acute myeloid leukemia). Study-related medications, procedures and tests are at no cost. Travel may be reimbursed. For more information, call the Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read about the study at <http://go.usa.gov/x9PKv>. Refer to study 17-H-0026.

Study Seeks Healthy Older Adults

Healthy older adults, ages 55-70, are invited to participate in an outpatient research study investigating the benefits of tart cherry and aroniaberry supplementation on vascular health. The goal of the study is to determine whether the supplements improve blood flow and blood vessel function that can affect your heart. Eligible participants must be medication-free and in good general health. The study will be carried out in an outpatient clinic and includes 7 visits over 3-4 months. Compensation for the study is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 15-NR-0085 or visit www.clinicaltrials.gov.

Patients with Kidney Disease Needed

An NIDDK team seeks patients for a research study. Doctors are conducting a study evaluating the safety of an investigational drug, ManNAc (N-acetyl-D-mannosamine monohydrate, IND: DEX-M74), in patients with the following kidney diseases: focal segmental glomerulosclerosis, membranous nephropathy, minimal change disease. Compensation is provided for participation. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more online at <http://go.usa.gov/xkft4>. Refer to study 16-DK-0036.

Antidepressant Study Needs Volunteers

Depression, ketamine and alcohol researchers are evaluating rapid antidepressant effects in the brain. This inpatient study is enrolling eligible adults ages 21 to 65, who are free of other serious medical conditions, for 4-7 weeks as research participants. Procedures may include tapering off antidepressants, a medication-free period, 2 infusions of alcohol and 1 infusion of low-dose ketamine (an FDA-approved anesthetic) and 2 brain scans (MRI). There is no cost to participate. Compensation is provided. Study enrolls eligible participants from across the U.S. Travel arrangements provided and costs are covered by NIMH. After completing the study, participants receive short-term follow-up care at NIH while transitioning back to a provider. For more information, email moodresearch@mail.nih.gov, or call 1-877-MIND-NIH (1-877-646-3644), TTY 1-866-411-1222. Refer to protocol 14-M-0085, principal investigator Dr. Carlos Zarate, Jr.

Unipolar & Bipolar Depression Studies Recruiting

Studies are enrolling eligible participants ages 18-65 with unipolar or bipolar depression symptoms for a 2-3 month inpatient stay. Study compares ketamine, an experimental medication, to placebo and evaluates rapid reduction of depressive symptoms (within hours). For details, visit www.nimh.nih.gov/labs-at-nimh/join-a-study/index.shtml or call 1-877-MIND-NIH (1-877-646-3644), TTY 1-866-411-1010, email moodresearch@mail.nih.gov. Refer to protocol 04-M-0222.



ABOVE: At the 2-day January workshop launching the in-depth collaboration, NIH scientists Dr. Bob Finkelstein (l) of NINDS and Dr. Emmeline Edwards of NCCIH join NIH director Dr. Francis Collins and Kennedy Center Artistic Advisor-at-Large Renée Fleming, renowned soprano, for a discussion on music and neuroscience. At right, Dr. Isabelle Peretz of the University of Montreal addresses the assembly.

PHOTOS: ERNIE BRANSON



'SOUND HEALTH' NIH-Kennedy Center Initiative Expands

Through a new partnership, NIH and the John F. Kennedy Center for the Performing Arts will expand on an initiative that NIH has had with the National Symphony Orchestra (NSO) for several years called Sound Health. Scientists are already investigating how music can be used to help cancer patients fight anxiety about treatments, help children with autism learn communication skills and help people with Parkinson's disease walk in a steady rhythm. But there is much still to be learned.

Eminent scholars and researchers convened a workshop at NIH on Jan. 26-27 to discuss the evidence of how music is processed in the brain and used as therapy.

The new collaboration will broaden the scope of Sound Health to include current knowledge and understanding of how listening to, performing

or creating music involves intricate circuitry in the brain that could be harnessed for health and wellness applications in daily life; explore ways to enhance the potential for music as therapy for neurological disorders; identify future opportunities for research; and create public awareness about how the brain functions and interacts with music.

As a result of the workshop, NIH will identify areas of science that provide the greatest opportunity to validate current findings and advance knowledge about when and how music can be an effective treatment. Findings will be presented at a public event at the Kennedy Center on June 2-3 called Sound Health: Music and the Mind. The event will feature performances by the NSO and interactive presentations and discussions with some of the world's leading minds working at the intersection of neuroscience and music.

The NSO will continue to perform regularly for patients, doctors, nurses, visitors and staff at the Clinical Center.



Leading researchers, clinicians and music therapists working in music and neuroscience from 24 institutions in 3 different countries gathered to evaluate the state of the field, identify knowledge gaps and inform future research.