

Ancient DNA Is 'New Machine' For Peering into Human Past

BY RICH MCMANUS

"When we've been there 10,000 years, bright shining as the sun..." begins a verse of *Amazing Grace*. According to Harvard geneticist Dr. David Reich, who opened the 2016-2017 Wednesday Afternoon Lecture Series on Sept. 21, that's just about the time that ancient human DNA begins to loosen its tongue in order to testify to human origins and diaspora.

Reich's lab is taking samples mostly of European human remains dating back between 4,000 and 7,000 years and, using DNA sequencing machines that have gotten faster and cheaper over time, begun to learn the recipe for making a modern European.



Harvard's Dr. David Reich discusses ancient DNA at opening WALIS lecture.

"I work on human bones, mostly," said Reich, who called the ability to analyze ancient DNA "a new scientific instrument, developed in the last 5 or 6 years."

Combined with sophisticated mathematical analysis (including such tools as "statistical reconstruction" and "principal component analysis"), the industrial-strength sequencing technology used to study about 1,000 samples a year is yielding insights into how three main groups of humans—farmers, hunter-gatherers and ancient north Eurasians—intermingled to form a borderless biological identity.

"Three highly different ancestral populations combined to yield modern Europeans," said Reich.

Working in "clean" rooms under positive pressure, in order to avoid contamination with modern DNA from people and microbes, scientists in body suits work under fume hoods that are sterilized using ultraviolet light after use. They use low-speed drills to penetrate the surface of ancient bones and extract a powder that is then demineralized, and proteins are extracted. What remains is

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CFC kicks off at NIH. See story on p. 12.

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DEATH OVER DINNER Have You Had 'The Talk?'

BY DANA TALESNIK

Nobody wants to think about it, much less talk about it. Death is a scary subject; many people delay or avoid discussing their end-of-life wishes and concerns with loved ones. It can be daunting just figuring out how to begin.

"For many of us, talking about death feels suspiciously and superstitiously like letting death into the room," said Ellen Goodman, Pulitzer Prize-winning columnist and co-founder and director of The Conversation Project. Speaking at the NINR Director's Lecture Sept. 13 in Lipsett



Writer Ellen Goodman at NIH

SEE GOODMAN, PAGE 6



Runners sprint from the starting line in front of Bldg. 1. This year's top team set a course record: 12:07.

'AGING IN PLACE' NIA Teams Take First, Second In Instate Relay

BY ERIC BOCK

Practice pays off. That's the take-home lesson from the 33rd NIH Instate Relay.

In dominating fashion, NIA's "Charm City NeuRUNS" won the race. After months of practice, they finished the Sept. 22 event in a record time of 12:07. That shattered the previous record, set in both

SEE RELAY, PAGE 8

Symposium, Lecture Honor NIAID's Paul, Nov. 7 in Masur

On Nov. 7, NIH will honor the memory of Dr. William E. Paul, who passed away on Sept. 18, 2015, after having battled acute myeloid leukemia as well as B cell lymphoma. Paul had been chief of the Laboratory of Immunology, NIAID, beginning in 1970 at age 34 until his death.



Dr. William E. Paul

Paul will be remembered annually through an NIH Director's Wednesday Afternoon Lecture Series talk named in his honor. The first William E. Paul WALs lecture will be given by Dr. Laurie Glimcher at 3 p.m. in Masur Auditorium, Bldg. 10 as part of a one-day symposium sponsored by the NIH immunology and cytokine interest groups. Other speakers include Drs. Mark Davis, Ron Germain, Harold Varmus and Anthony Fauci.

Paul's groundbreaking contributions to the immunology field, including the discovery of interleukin-4, were demonstrated in more than 600 publications over half a century. He also played an important role in the establishment of the NIH Vaccine Research Center while he was director of the NIH Office of AIDS Research.

To register for the day-long event, visit <https://ncifrederick.cancer.gov/events/WilliamPaulMemorial/default.asp>.

Quartet's 28th NIH Season Under Way

The Manchester String Quartet recently opened its 28th season at NIH. There are 7 remaining dates in the 2016-2017 season, all Mondays at 12:30 p.m. in Masur Auditorium, Bldg. 10.

Future concert dates:

- Oct. 24 Schubert Quintet in C Major (1828)
- Nov. 21 Tchaikovsky Quartet #1 in D Major, Opus 11 (1871)
- Dec. 12 Brahms Quartet in c minor, Opus 51 #1 (1873)
- Jan. 23, 2017 Dvorak Quartet in E flat Major, Opus 51 (1879)
- Feb. 6 A sampler of miniatures
- Mar. 6 Dvorak Quartet in F Major, Opus 96 American (1893) & Ives Quartet #1 (1896)
- May 1 Schoenberg Transfigured Night (1899)

The series is supported by the Foundation for Advanced Education in the Sciences. For reasonable accommodation, contact Sharon Greenwell at (301) 496-1776 or sg115f@nih.gov.



NIH's Staff Race Medical Tent

Annually, on the weekend after Labor Day, the Montgomery County Road Runners Club sponsors the Parks Half Marathon, which finishes in downtown Bethesda. This year's medical tent was staffed by NIH volunteers, along with other area hospital volunteers. Shown are (from l) Dr. Stephanie Goff, Maureen George RN (department of perioperative medicine), Dr. Marjorie Perloff (NCI), Susan Redwood RN (nursing department- ICU), Karen Holcombe RN (DPM), tent director Dr. Julia Labovsky (DPM) and Martha Shepherd CRNA (DPM). "Race day was quite warm," said George, "so the medical tent was busy. In spite of the brisk pace, the NIH volunteers enjoyed giving back to the community."

NIH Veterans Day Celebration, Nov. 9

Join military and public health service colleagues in celebrating Veterans Day on Wednesday, Nov. 9 in Kirschstein Auditorium, Natcher Bldg. from 10 to 11 a.m. The event will include a military band, exhibits from veteran-oriented and uniformed services organizations and more. All are invited. NIH veterans and families of veterans are especially encouraged to attend.

This year's keynote speaker is Rear Admiral (ret.) Annie B. Andrews, who currently serves as assistant administrator for human resource management at the Federal Aviation Administration. Andrews' decorated naval career spanned more than three decades and included tours of duty in the Pentagon, the Naval War College and the Naval Recruiting Command.

Sign language interpreters will be provided. Individuals who need reasonable accommodation to participate should contact Byron Williams at williamsbj3@mail.nih.gov or (301) 496-5624 and/or the Federal Relay (1-800-877-8339). To find out more about how veterans contribute every day to the NIH mission, visit <https://jobs.nih.gov/veterans/vrf.htm>.

Community College Day Set, Oct. 28

Community College Day 2016 will be held on Friday, Oct. 28 from 8 a.m. to 4 p.m. at the Natcher Conference Center. Hosted by the NIH Office of Intramural Training & Education, the event provides community college students and faculty an opportunity to visit NIH and learn about careers/training opportunities in biomedical fields. Register at <https://www.training.nih.gov>.



NIH Showcases 'Super Suit' at White House Fashion Show

Dr. Michele A. Lobo (l), director of the Super Suits Program at the University of Delaware, and Dr. Alison Cernich, director of NICHHD's National Center for Medical Rehabilitation Research, show off one of Lobo's Super Suit designs, developed with NCMRR support. The modified onesie is a lightweight "exoskeleton" to help boost upper body movement in children with developmental difficulties. Lobo and Cernich featured the Super Suit during the White House Design for All Showcase in September. The event was a fashion show that celebrated inclusive design, assistive technology and prosthetics. Cernich, who gave the closing remarks, announced the launch of the NIH Research Rehabilitation Plan.

Challenge Spurs Ideas on Sickle Cell Awareness

A smartphone app, a social media campaign, a catchy tune—those were the concepts that took top honors after the National Heart, Lung, and Blood Institute challenged college students across the country to find innovative ways to raise awareness about sickle cell disease. The winning innovators recently presented their ideas at an NHLBI sickle cell disease research conference.

Teams from the University of Pittsburgh, Notre Dame University and Connecticut College came to NIH to show how their imaginative concepts could help spread the word about the often devastating blood disorder, the most common genetic disease in the United States. The disease affects about 100,000 people here and millions more worldwide. But much of the public remains unaware of the condition; the NHLBI Undergraduate Sickle Cell Disease Challenge, which ran from October 2015 to March 2016, was designed to help fix that.

The national call to action asked undergraduate students from various academic disciplines to form interdisciplinary teams so they could creatively collaborate.

Students from the University of Pittsburgh took home first prize with a smartphone app called Sickle Share. The app features basic information about the condition as well as video interviews of researchers and a link to a sickle cell support group.

“Knowledge, research and access were the goals of the app,” said team captain Loren Hampton, who studies psychology. “We wanted to help offer a central place for information, to highlight research efforts and provide support to access.”

Notre Dame’s team used the social media app Snapchat, which is popular among high school and college students, to grab the attention of the public. Their Snap Out Sickle Cell campaign, which took second prize in the challenge, was featured on Snapchat during World Sickle Cell Awareness Day, June 19.

Roland Rebuyon, a Notre Dame team member, said part of the goal was to inspire the next generation of scientists now exploring career options at college. “We wanted to show that clinical research can be fun and exciting,” he said.



Winning innovators at an NHLBI sickle cell disease research conference

Connecticut College took a more lyrical approach to help quash stereotypes about sickle cell disease. The third-place team wanted to reinforce the idea that the condition is inherited and not contagious. Their contemporary song *Blood Red Crescent Moon* uses scientifically accurate lyrics to explain the basics and address misperceptions about the condition.

“Our idea was to use music, use language, use poetry in a creative approach,” explained Joseph Donohue, who studied microbiology and music at Connecticut College. “And we wanted to use language that is precise and correct to invite people into this conversation.”

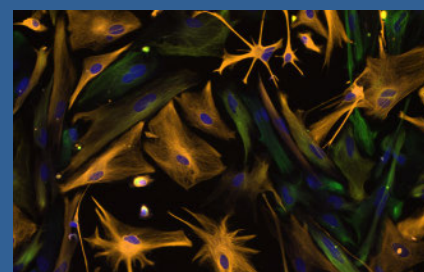
Donohue, with his scientific and artistic background, was a great example of the cross-disciplinary problem-solving approach the challenge hoped to spark, said Dr. Helena Mishoe, NHLBI associate director for research training and diversity. The challenge was a team effort led by the Center for Translation Research and Implementation Science in conjunction with other NHLBI offices and divisions.

“The challenge provided an opportunity to help educate communities, enhance students’ research skill sets and promote team science as it serves to enhance the lives of individuals with sickle cell disease,” Mishoe explained. “The hope is that widespread use of these tools will lead to greater knowledge and awareness of SCD.”

Mishoe said the winning teams will seek ways to improve the functionality of the respective tools and to expand access to larger audiences.

The challenge awarded each winning team a prize: first place \$7,000, second place \$5,000 and third place \$3,000 in addition to reimbursement of travel expenses for

each team up to \$2,000. To learn more about the challenge, visit www.nhlbi.nih.gov/news/spotlight/fact-sheet/nhlbi-novel-innovative-tools-increase-public-awareness-and-knowledge-sickle-cell-disease. **R**



ON THE COVER: *Photomicrograph of directed differentiation of multipotential human neural progenitor cells to astrocytes*

IMAGE: CAROL IBE & EUGENE MAJOR, NINDS

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NIH director Dr. Francis Collins (l) presents Dr. David Reich with a commemorative plaque at the first WALs talk of the 2016-2017 season. Joining them is Reich's brother Dr. Daniel Reich, a scientist at NINDS. The Reichs' parents also attended the lecture; their dad used to work at NIMH, making the event "a wonderful family occasion," said Collins.

PHOTOS: ERNIE BRANSON

Reich

CONTINUED FROM PAGE 1

then sequenced with modern machines that have gotten 10,000 times more powerful in the last decade, Reich said.

In 2010, four ancient samples were sequenced, he reported. Twenty or 30 more were sequenced in 2014. "In 2015, things went into hyper-drive, and several hundred samples were sequenced," said Reich. "We've sequenced more than 1,000 samples in our own lab—there's not enough time to publish" all the data they are collecting.

Indeed, on the day of the lecture, the *New York Times* ran a front-page story on studies of ancient DNA that included Reich's lab's work ("A Single Migration From Africa Populated the World, Studies Find").

Reich and his colleagues in this burgeoning new field are reconstructing human history a base-pair at a time and arriving at some general conclusions: West Eurasians from Europe to Iran "are genetically strikingly similar," as are East Asians from Korea to Indonesia, and Africans from Senegal to Zimbabwe.

"They are these massive mixtures of different populations," said Reich, who noted that genetics offers a new window onto the past to complement the traditional ones of archaeology and language.

The arrival of farming, probably from Turkey, or Syria, or Iraq, was a major driver of genetic mixture. It allowed populations to grow dense in single locales and prompted "huge movements of people," said Reich. "There was a large-scale migration from the near East."

He said there is evidence that Native Americans originated in part from a "ghost population" that inhabited northern Eurasia more than 15,000 years ago, and that also contributed to Europeans.

The genetic impact of this northern Eurasian population on Europe occurred around 4,500 years ago via the arrival of the Yamnaya steppe pastoralists, a group that made use of the wheel to extend the reach of herding; Reich quipped that they employed "mobile homes" to exploit the Russian steppe.

Large-scale migration led to the breakdown of social barriers, says Reich.

"Near-Eastern farming expansion and its after-effects homogenized west Eurasia," he said.

Reich and others in his field are using genome-wide association study data collected as part of medical studies to probe not just ancient history but also the biological impact of such crucial genetic traits as the ability to digest milk into adulthood, a mutation that conferred an important survival benefit. Complex traits such as height are also amenable: why are Europeans from the Netherlands and Croatia taller, and why are people in Portugal shorter? Reich described how genetic data shows that the

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"Three highly different ancestral populations combined to yield modern Europeans."

-DR. DAVID REICH


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ancestors of Portuguese experienced natural selection to get shorter after the arrival of farmers in Europe.

Students of DNA also aim to explain how modern traits have evolved over time, beginning with the Neanderthals 200,000 years ago in East Africa, who took 150,000 years to become behaviorally like us. "People 50,000 years ago had all of the mutations needed to do all that we do today," said Reich. But he says that the frequencies of these mutations likely changed in order to adapt to changing conditions.

He suspects that environmental and cultural changes were as significant as genetic adaptations as drivers of mankind's current capabilities.

"It is unlikely that there will be reductionist genetic answers," he said. "We must embrace the complexity."

The complete talk is available at <https://videocast.nih.gov/summary.asp?Live=19940&bhcp=1>. 

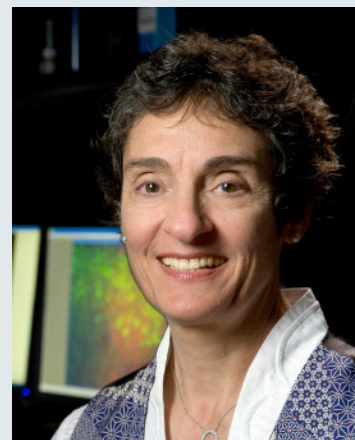
OCT. 25

Stanford's Shatz To Give NEI 'Audacious Goals' Seminar

Neurobiologist Dr. Carla Shatz will present "Saving the synapse: developmental critical periods and amblyopia" as part of the National Eye Institute Audacious Goals Initiative (AGI) Seminar Series in Neuroregeneration on Tuesday, Oct. 25 at 3 p.m. in Lipsett Amphitheater, Bldg. 10.

Shatz is the Sapp Family provostial professor of biology and neurobiology and the David Starr Jordan director of Bio-X, Stanford University's interdisciplinary biosciences program. She has devoted her career to understanding the dynamic interplay between genes and the environment that shapes brain circuits and modulates the visual system's neural plasticity. Among her notable work is the discovery that spontaneous activity of neurons *in utero* is crucial to establishing precise neural connections in the central nervous system. In addition, she has identified novel genes that regulate synaptic plasticity and pruning during critical periods of development.

The AGI series explores topics relevant to regenerative neuroscience and medicine, with special emphasis on the visual system. The AGI is a sustained effort by NEI to catalyze research toward new therapies for disorders that affect the retina and its connections to the brain. To learn more, visit www.nei.nih.gov/audacious/.



Dr. Carla Shatz

Grantee Shares Chemistry Nobel

The 2016 Nobel Prize in chemistry has been awarded to NIH grantee Sir J. Fraser Stoddart of Northwestern University. He shares the award with Dr. Jean-Pierre Sauvage of the University of Strasbourg, France, and Dr. Bernard L. Feringa of the University of Groningen, the Netherlands, for their design and production of molecular machines.



Sir J. Fraser Stoddart

PHOTO: NORTHWESTERN UNIVERSITY

The Royal Swedish Academy of Sciences said their work has "miniaturized machines and taken chemistry to a new dimension."

Molecular machines are tiny molecules with controllable movements that can perform a task when energy is added. The machines are a thousand times thinner than a strand of hair. These machines may be used in the development of new materials, sensors and create energy-storage mechanisms too tiny to be seen with the naked eye.

"Another application of these molecular machines could be delivering drugs within the body, for example, by applying them directly to cancer cells," said NIH director Dr. Francis Collins. "NIH is proud to have supported this work."

The National Cancer Institute began supporting Stoddart in 2010 and has provided more than \$2 million in funding.

Next Protocol Navigation Lecture, Oct. 24

The IRP Protocol Navigation Training Program Seminar Series will host a lecture to be held Monday, Oct. 24 from 11 a.m. to 12 p.m. in Lipsett Amphitheater, Bldg. 10. The program is a trans-NIH effort to develop resources and tools and to provide training for intramural staff and contractors involved in protocol development, writing, coordination and management. Shirley Rojas from NIH's Office for Human Research Protections will present "Reliance Agreements and NIH Human Research Protections Program Requirements for Collaborative Research." For more information, contact Marcia Vital, (301) 451-9437, vitalm@mail.nih.gov.



PHOTO: UNIVERSITY OF WISCONSIN-MILWAUKEE

NINR Director's Lecture Features Millon-Underwood

Dr. Sandra Millon-Underwood will present the fourth 2016 NINR Director's Lecture on Tuesday, Nov. 1 from 11:30 a.m. to 12:30 p.m. in Lipsett Amphitheater, Bldg. 10. In her talk, "Evidence-based Interventions to Address Health Disparities in Cancer," she will describe her research focusing on minority populations, including African-American women with breast cancer.

Millon-Underwood is a professor at the University of Wisconsin-Milwaukee. Her research focuses on cancer, including education, prevention, early detection and risk management. Her projects target at-risk and underserved urban, rural and island communities.

Millon-Underwood has served on the National Advisory Council for Nursing Research, the NIH Council of Councils, the National Cancer Advisory Board, the National Cancer Policy Board, the Department of Defense prostate cancer integration panel and the Wisconsin Women's Health Foundation expert panel. She was founding director of the UWM House of Peace Community Nursing Center, which provides wellness classes, intensive case management and support services for families dealing with cancer.

The NINR Director's Lecture series is designed to bring the nation's top nurse scientists to campus to share their work and interests with a transdisciplinary audience. Visit www.ninr.nih.gov/directorslecture for more information.

Goodman

CONTINUED FROM PAGE 1

Amphitheater, she made an impassioned plea for all of us to contemplate and frankly discuss end-of-life wishes with our families and doctors, before it's too late. NINR is NIH's lead institute on end-of-life and palliative care research.

"Most of us will face a cascading and confusing number of decisions as we and our loved ones come toward the end of our lives," Goodman said. "The health care improvements that have led us happily to [live longer] have also led us to this moment when we need to face this most difficult and crucial conversation, which we have avoided for too long."

• • •

"The health care improvements that have led us happily to [live longer] have also led us to this moment when we need to face this most difficult and crucial conversation, which we have avoided for too long."

—ELLEN GOODMAN

• • •

Today, 60 million Americans are over 55; that number is steadily rising. Meanwhile, half of all people older than 65 who are admitted to a hospital are unable to make decisions for themselves. "Americans haven't absorbed it emotionally, as part of our narrative," said Goodman. "We are told that 50 is the new 40, but how many of us are told that 60 is the new caregiver of the 85-year-old?"

When she became the caregiver for her elderly, ailing mother, Goodman faced medical choices on her mother's behalf "for which I felt wholly unqualified and unprepared, in fact, blindsided." When her mother died, Goodman began to meet with a small group of clergy, caregivers, media and others to discuss how they might make it easier for others to prepare for the inevitable. We need a bold change, she said, "so everyone's

end-of-life wishes are expressed and respected, and to see that more of the people we love will die in the way that they choose."

Determined to change the cultural norm and get people talking about this taboo subject, Goodman launched a public engagement campaign called The Conversation Project (<http://the-conversationproject.org>). Working in collaboration with the

Institute for Healthcare Improvement, the site features the Conversation Starter Kit, a colloquial guide with questions to ponder and discuss, from our values and concerns to who we'd designate to make end-of-life decisions if and when we cannot.

The Conversation Project also has information kits on how to talk with your doctor and how families of seriously ill children and those with dementia can start the conversation. A new guide will soon be posted on how to pick and how to be a health care decision-maker.

"We believe the starting point is around the kitchen table, with the people we love and who may be making decisions with us, or for us, when the time comes," said Goodman. With that in mind, the project recently released an e-cookbook, *The Endless Table*, containing stories and recipes from celebrity chefs.

In a 2013 Conversation Project national survey, 90 percent of respondents said talking about end-of-life care with their loved ones is important, but less than 30 percent had actually had the talk. Some 80 percent of people in a 2012 California HealthCare Foundation survey said they wanted to discuss their end-of-life wishes for medical treatment with their doctor, but only 7 percent reported having done so.

While the project aims to close this gap, Goodman said the health care system also needs to change. How many end-of-life treatments are futile or against the patient's wishes? In one California study, 1 in 5 ICU



NINR director Dr. Patricia Grady (l) presents commemorative plaque to Goodman, who urged people to share their end-of-life wishes.

PHOTOS: LISA HELFERT

patients received treatment the doctor in charge deemed ineffective or needless given the patient's dire state.

Many patients say they want to die at home, in comfort among their loved ones, but wind up dying in hospitals or nursing homes. Many doctors admit they're uncomfortable with, and untrained for, initiating the end-of-life conversation, so their patients' wishes remain unknown and unfulfilled, Goodman said.

If patient and family choices drive end-of-life decisions, she said, there's the potential to actually cut costs—both financial and emotional—while building trust with the health care industry and ensuring more humane deaths.

A polarizing debate has emerged over doctor-assisted suicide, but Goodman says it's not a useful one. "In Oregon, where doctor-assisted suicide has been legal the longest, only 1 in 500 deaths is with a doctor's prescription," she said. "We have to think about the health of the 499."

For too long, we've been in denial, not wanting to worry or burden our families, said Goodman. "And in our attempt to protect each other from the reality of mortality, we often end up alone and leave our survivors bereft."

Choose a health care decision-maker and have the conversation with your families, urged Goodman, long before there's a crisis. "Make it a priority to learn how to have these conversations. It's always too early until it's too late." **B**

Mutation May Explain Why Some Get More Severe RSV Disease

A mutation in the gene of a white blood cell protein contributes to the severity of respiratory syncytial virus (RSV) infection, according to a paper published in *EBioMedicine* by researchers at NIEHS and their collaborators.

RSV contributes to bronchiolitis, pneumonia, asthma and respiratory failure. It is also the leading cause of respiratory illness in infants, immunocompromised adults and the elderly.

The team used genome-wide association

studies in mice to identify candidate genes involved in RSV severity. The most promising gene, macrophage receptor with collagenous structure (MARCO), produces a protein that allows a particular type of white blood cell to fight infection. The finding was surprising because MARCO had not previously been associated with RSV.

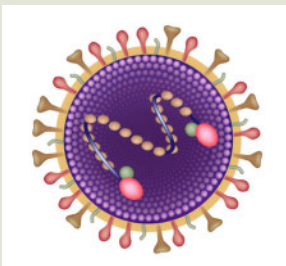
Mice with the MARCO gene knocked out experienced more severe symptoms from exposure to RSV, compared to wild-type mice. And effects in humans are strikingly similar. In two independent populations of children, infants born with a mutated MARCO gene exhibited more severe RSV symptoms than those with the wild-type gene.

"MARCO is an immune system gene that helps clear inflammation," said Dr. Steven Kleeberger, lead researcher on the study. "If the gene is mutated, it can't resolve the inflammation, so cells and mucus remain in the lung, blocking the airway."

Using information learned from mouse and human studies, the team hopes to develop a diagnostic tool to identify infants subject to severe RSV disease before they get sick. There is no vaccine for RSV and some of its health effects are irreversible, so preventing even a small number of RSV-induced asthma or pneumonia cases could have a huge impact.

Targeting Cardiovascular Disease Risk Factors May Be Important Across a Lifetime

New findings suggest that all adults, including those over 65, should be mindful of risk factors for cardiovascular disease. The results, published in the *Journal of the American Geriatric Society*, are part of the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which looks at stroke incidence in approximately 30,000 individuals. The REGARDS study is funded by NINDS.



RSV infection may cause mild, cold-like symptoms, or more serious symptoms, leading to hospitalization and even death.

"As life expectancy continues to increase, we need to improve risk factor prevention and management for stroke and heart disease across the lifespan, including for those adults over the age of 65," said one of the study authors, Dr. Claudia Moy of NINDS. "The latest findings from the REGARDS study reveal that no age group is immune to risk factors related to cardiovascular disease and that prevention efforts should target all adults."

In the current study, researchers examined individuals over the course of 10 years to determine how many developed risk factors known to be associated with stroke and heart disease. The study included a sample of black and white Americans, with more than half of the participants living in the Stroke Belt, an area of the southeastern U.S. where stroke mortality is higher than in the rest of the country.

"In addition to improving treatment and control of potent risk factors for stroke and heart disease, finding ways to prevent development of those risk factors may be a potential strategy to lower rates of cardiovascular disease across the age span, but especially in black Americans," said Moy.

Drug to Treat Alcohol Use Disorder Shows Promise Among Drinkers with High Stress

A new medication that targets part of the brain's stress system may help reduce alcohol use in people with alcohol use disorder (AUD), according to a new study by researchers at NIAAA.

"Medications have become an important tool for treating alcohol use disorders, but current medications are not effective for all people with AUDs," said NIAAA director Dr. George Koob. "We're committed to developing new medications to provide effective therapy to a broader spectrum of people with AUDs."

As reported online in the journal *Neuropsychopharmacology*, researchers led by Dr. Raye Litten, acting director of NIAAA's Division of Medications Development, conducted a randomized clinical trial of a new compound called ABT-436, which is designed to block the effects of vasopressin, a neuropeptide produced in the hypothalamus of the brain.

"Vasopressin helps to regulate the pituitary adrenal axis and other brain circuits involved in emotion," explained Litten. "As such, it plays a role in regulating stress, anxiety and their interaction with AUD."

Researchers found that participants receiving ABT-436 experienced more days of alcohol abstinence than those receiving the placebo. In particular, participants who reported high levels of stress appeared to respond better to ABT-436, in that both the frequency of their drinking and the number of heavy drinking days they experienced decreased.



NIGMS director Dr. Jon Lorsch (c) and institute staff members answer questions from students during Cell Day.

PHOTO: SOMA CHOWDHURY

NIGMS To Host 'Cell Day' Web Chat

On Thursday, Nov. 3 from 10 a.m. to 3 p.m., NIGMS will host Cell Day. This interactive web chat, focused on the cell, is geared toward middle and high school students but open to all. During last year's event, 23 NIGMS scientists fielded more than 300 questions about cell biology, biochemistry, research careers and related topics. To learn more about Cell Day, view past transcripts and register for the event, see www.nigms.nih.gov/cellday.

Workshop Details Pathways to NIH Leadership

In partnership with the NIH Office of Equity, Diversity, and Inclusion and the NIH Training Center, the NIH chapter of the Federal Asian Pacific American Council will host a leadership training workshop in Lipsett Amphitheater, Bldg. 10, on Thursday, Oct. 27 from 1 to 3 p.m. The purpose is to increase awareness of NIH leadership training opportunities and encourage participation in career development and advancement.

The workshop features presentations on three NIH leadership programs (mid-level, senior and executive) followed by a keynote speech on communication and leadership development by Dr. Belinda Seto, deputy director of the National Eye Institute. The workshop is open to all NIH employees with leadership aspirations.

It will be live-streamed at <https://videocast.nih.gov>. Registration is free and available at <https://respond.niaid.nih.gov/conferences/PathwaystoNIHLeadershipWS/Pages/default.aspx>.

Individuals who need sign language interpreters and/or reasonable accommodation to participate should contact Tyrone Banks at (301) 496-6301 or bankstc@mail.nih.gov or call the Federal Relay (1-800-877-8339).

For more information, contact Dr. Trinh Ly at tly@niaid.nih.gov or Dr. Jian Yang at jian.yang@nih.gov.



Relay first place: NIA's Charm City NeuRUNS include (standing, from l) Erez Eitan, Nate Ghena, Keelin Moehl, Julie Williamson and Ryan Spangler; in front is coach Dr. Mark Mattson. Relay second place: NIA's B'more Benchwarmers include (rear, from l) Sophia Raefsky, Natalie Plick, Caio Mazucanti and David Freeman; in front are Nicole Rumian (l) and Craig Myrum. Rumian didn't run, but she made sure everyone stayed on the course and cheered on the team, noted Raefsky. Relay third place: NIDCD's Calbindin Snap includes (from l) Kamren Hollingsworth, Nora Welsh, Mike Waltman, Czarina Ramos and Randall Harley.

Relay

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1980 and 1985, by 45 seconds. Their name will be engraved on the Allen Lewis NIH Memorial Trophy in the Bldg. 31 Fitness Center. NIA's "B'more Benchwarmers" placed second in 14:23 and NIDCD's "Calbindin Snap" came in third at 14:27.

Dr. Mark Mattson, chief of NIA's Laboratory of Neurosciences, coached this year's first and second place teams. Since May, the two squads did speed workouts on a high school track once a week. They also ran hills.

"Most of these kids have run track and cross country in college," said Mattson,

himself a competitive runner and former high school track and cross-country coach. Besides the weekly practices, team members ran 5-10 miles, 3 or 4 days a week, on their own.

This year, 112 teams participated in the relay, according to the NIH Recreation and Welfare Association's David Browne. As usual, team names didn't disappoint. Clever monikers included GOvaries, I-b-pro-fun, SNP It Snip It Good, Pokémon Go, Circuits Du Soleil, MIGHTYchondria, I Cannot Tell A-fib and Ignoring My Nociceptors.

Former R&W President Randy Schools explained the rules before the race on his bullhorn, as he has for decades. The first four

runners complete a half-mile loop around Bldg. 1 then hand off the baton to the last runner in an exchange area near the starting line. The final runner on each team must run the loop and then turn right at a chute to the finish line on the driveway between Bldgs. 1 and 2. Schools also reminded runners to "be safe and take your time" and encouraged runners to "stay fit all year long."

NCI's Dr. Harold Seifried played the traditional "call to the post" on his horn to assemble runners for the first heat. NIH director Dr. Francis Collins started the race with a whistle blast. Acting NIH deputy director for management Dr. Alfred Johnson whistled the start of the second heat.

A History of Speed

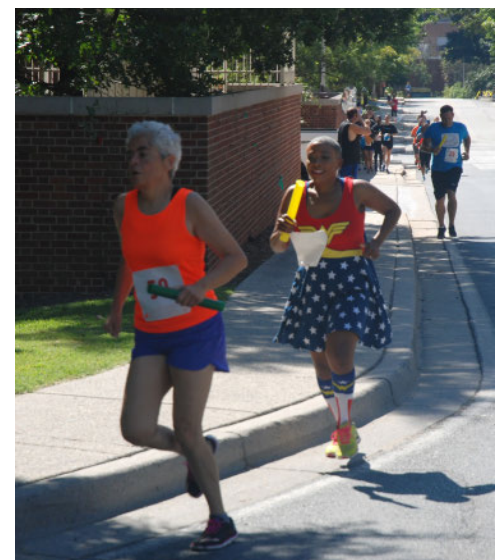
In its 33-year history, the NIH Institute Relay has included fast years and relatively slow ones. The race began as men-only, then for years included such categories as men, women, mixed and master's. The data below is for coed results only, which began in 1980.

Prior to the 2016 race, the two fastest years were 1980 and 1985, when the 2.5-mile course (believed to be the same for all events over the years) was completed in 12:52 (the 1985 result was, according to the *NIH Record*, an "unofficial" time).

In both 1992 and 1994, the winning coed team finished in 13:02.

No data exist for the 1986 race. All available years and times are:

2015.....13:23	2007.....13:54	1993.....13:13	1985.....12:52
2014.....13:33	2006.....13:59	1992.....13:02	1984.....13:21
2013.....13:56	2005.....14:04	1991.....13:32	1983.....13:22
2012.....13:31	2004.....14:16	1990.....14:47	1982.....No mixed results
2011.....13:05	2003.....14:20	1989.....13:08	1981.....15:09
2010.....14:02	2002.....14:27	1988.....13:25	1980.....12:52
2009.....13:50	1995.....13:34	1987.....13:13	
2008.....13:58	1994.....13:02	1986.....No data	



A runner in patriotic garb rounds the bend from Memorial Dr. onto Center Dr.

PHOTOS: DANIEL SOÑÉ, RICH MCMANUS



Dr. Harold Seifried of NCI's nutritional science research group plays "call to the post" on his horn, as he has done for years at this event.

"It's a fantastic event," said Johnson. "It's a great time to get outside, enjoy the weather and see all the runners come together and cheer for each other. I enjoy the camaraderie."

At the starting line, Joe Balintfy of NEI's "Eye Run Man" said his goal was to "have fun and not get hurt!"

Near the finish line, an original member of NIH Health's Angels running club, Jerry Moore, directed runners around the final turn and up the chute. He was one of the organizers of the first relay in 1978. Every year on the day of the relay, he emails his former teammates who now live around the



Candelario Zapata of the Division of International Services, OD, waves a poster touting the team from his office: DIScard, DISmember and DISstroy the Competition.



NIH director Dr. Francis Collins crouches to blow the whistle starting heat 1 of the NIH Institute Relay.

world. "The fact that it's lasted this long is incredible," he marveled.

When he last ran, Moore was on a team called "Runnin' on Empty." Despite the name, "We dominated it," he laughed.

Top 10 Teams

Charm City NeuRUNS	12:07
B'more Benchwarmers	14:23
Calbindin Snap	14:27
GRC	14:51
CamelGo	15:03
Proud Snail Hunters	15:08
FIC Globetrotters	15:12
Wurtz Possible Runners	15:18
Danio Runio	15:39
The Megalics	15:43

The first NIH Institute Relay was held May 24, 1978, and was won by "NIMH Shrinks" in 11:59, but that was a men-only team. For the race's first few years, men and women ran separately. Starting in 1980, mixed teams ran heats, except in 1982, when the event briefly reverted to single-sex. The relay was not held from 1996 to 2001 due to a major construction project along Center Dr.

Back in 1982, viewer interest was such that you could have watched a videotape replay of the race at a screening long after the event.

Schools expressed his appreciation for the help he receives each year from volunteers, R&W staff, the NIH Police, original members of Health's Angels, the Office of Research Services' Division of Amenities and Transportation Services and others who help make the relay possible. **R**

UW's Mooney To Speak at NLM

NOV. 2

The next talk in the National Library of Medicine Informatics Lecture Series, titled "Interpretation of Human Genomes and Identification of Impactful Variants Using Biomedical Informatics," will be given by Dr. Sean Mooney, professor, department of biomedical informatics and medical education and chief research information officer, UW Medicine, University of Washington, on Wednesday, Nov. 2 from 2 to 3 p.m. in Lister Hill Center Auditorium, Bldg. 38A.



Whole exome and whole genome sequencing is continuing to challenge researchers with a wealth of genetic variants of unknown disease effects. Mooney's group is investigating genomic and proteomic attributes that describe genetic variants in human genome sequences and then using those attributes to predict pathogenic variants that affect protein structure and function, mRNA processing and translation and transcriptional regulation. His team has built the MutPred suite of tools for discovering and characterizing pathogenic and pharmacogenetic variants from whole genome sequencing. Mooney received his B.S. with distinction in biochemistry and molecular biology in 1997 from the University of Wisconsin. He received a Ph.D. in 2001 at the University of California, San Francisco, and then an American Cancer Society John Peter Hoffman fellowship at Stanford University.

Falk Gives Astute Clinician Lecture

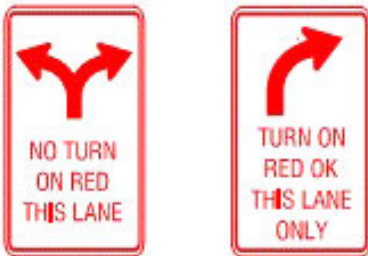
Dr. Ronald Falk will give the Astute Clinician Lecture as part of the NIH Director's Wednesday Afternoon Lecture Series on Nov. 2 at 3 p.m. in Masur Auditorium, Bldg. 10. He will present "Perspective on Autoimmunity: A View from the ANCA Vasculitis Looking Glass." Falk is an internationally recognized physician-scientist whose lifelong career has been the study of autoimmune kidney disease and antineutrophil cytoplasmic autoantibodies, or ANCA, vasculitis. For more than three decades, his research has led to a deeper understanding of the causes and conditions that may lead to the development of ANCA vasculitis. Falk graduated from Dartmouth College and earned his medical degree from the School of Medicine at the University of North Carolina, Chapel Hill. He is currently the Nan and Hugh Cullman eminent professor and chair of the department of medicine at UNC.

The annual Astute Clinician Lecture, established in 1998 through a gift from the late Dr. Robert W. Miller and his wife, honors U.S. scientists who have observed unusual clinical occurrences and opened an important new avenue of research. Sign language interpretation can be provided. For information or accommodation, contact Jacqueline Roberts at (301) 594-6747 or robertsjm@mail.nih.gov, or call the Federal Relay Service at 1-800-877-8339.

Have a question about some aspect of working at NIH? You can post anonymous queries at <https://nihrecord.nih.gov/> (click on the Feedback tab) and we'll try to provide answers.

Feedback: I noticed as I leave campus at Center and Old Georgetown that a new traffic light has been installed, but not yet uncovered. It shows that the left lane can be used for left or right turns and the right lane for right turns only. But, I also noticed a "No Turn on Red" sign by the right turn lane. Why are they doing this? Traffic will surely back up on Center, especially when the day care opens. There are plenty of times when no traffic is approaching that cars can easily turn right on red, especially off hours and weekends.

Response from the Office of Research Facilities: After a request from NIH, the Maryland State Highway Administration reviewed the history of the Center Dr. traffic control design and determined that the intent of the "No Right on Red" sign for Center Dr. onto Old Georgetown Rd. northbound was to only restrict vehicles from turning right from the left lane. They are proposing to replace the current signage with the following two signs, which apply to the corresponding right and left exiting lanes on Center Dr.



Feedback: Now that E-wing construction seems to be winding down in Bldg. 10, who takes care of the quirks that just never got done right? Examples: In the elevator lobby (C corridor) on the 2nd floor, one of the signs says that it's level B2 (not level 2), the automatic doors for the N corridor don't always work right on any of the floors (sometimes they open, sometimes they don't, sometimes they're stuck open, sometimes they phantom open). At least one of the floors has the sconces pointed up instead of down over a bulletin board (N corridor). Not major impacts, but enough to show that someone did not do a thorough walk-through to make sure everything was up to NIH standards.

Response from ORF: Thank you for your question. It should be noted, based on your comments, you are actually referencing the F-wing in Bldg. 10, not the E-wing. A thorough walk-through was indeed conducted and every item raised in this inquiry was noted by quality assurance staff and added to punch lists of follow-up work, prior to receipt of these questions. Each item has been tracked through what the F-wing team calls pre-final inspections and final inspections. These lists are forwarded to the contractor for completion in compliance with all design and specification requirements of the overall construction contract. All final inspections have not yet occurred.

In reality, with a project of this size and complexity, there is a small chance that minor issues may go overlooked. In a major, highly technical project, the focus goes from the larger systems down to the smaller items that may have little or no impact on the ability of the facility to be used for its intended purpose. One can expect that NIH will be working on issues for up to a year after "substantial completion." Warranty and correction work for latent deficiencies can go on for quite some time after occupancy.

However, the Office of Research Facilities has provided responses on the specific issues mentioned.

- Door systems:** The F-wing team, the NIH ORF Clinical Center facility maintenance door team and a contractor have been in a prolonged process of getting the doors to operate properly. They have been testing and checking door sets, their sensors, their operators and the overall operation. They have also identified some faulty door sets. While this repair work continues, some door leaf sets are left set to "open." Warranty work has to be scheduled in accordance with shutdowns to building systems, vendor schedules and arrival of required materials.

As an example, in late September, ORF had a shutdown of the fire protection system and the elevator call to floor 4 to test a remedy on a set of automatic doors. The result corrected the door swings. This technique will be applied to 14 other sets of doors. This will take, at minimum, 7 weekends as ORF can only correct, at most, 2 sets of doors per weekend due to shutdown requirements and the required work.

Daily damage also happens by careless vendors and jobbers. Even NIH staff crash into the doors with their carts. The automatic door controls are being adjusted regularly. Their systems are complicated and there are many of them. The

contractor on site went through the building testing and documenting door systems the week of Sept. 9. Warranty work is ongoing and new work is in the final stages of inspection, acceptance and quality control to activate the last few areas.

- Floor identifier signage in the elevator lobby:** The signage in question was found to be incorrect and was documented on the punch list prior to receiving this inquiry. On Sept. 9, a paper correction sign was placed over the signage until a new sign, ordered that day, arrived and could be installed. Apparently someone removed the paper sign. A new paper sign was mounted until the correct sign was received and scheduled to be installed on Oct. 6.

- The sconce-type lighting fixtures:** The sconces erroneously installed facing up on the 9th floor were identified on the punch lists by the quality assurance team and will be corrected. The electrical contractor has been notified and has scheduled a return visit and will take care of a number of electrical issues, including this one. The electrical contractor is no longer on the job every day and has to be scheduled to come in to correct items. Other lights found in that orientation were corrected as of Sept. 9.

Some of the lights above some boards are hand-adjusted, easy to reach and frequently someone will have a little fun and redirect their aim. Originally, there was to be important information installed on each floor on those illuminated boards. That directive was removed from the F-wing elevator lobby scope. ORF is investigating a way to have those lights only turned on when there is something to display.

The F-wing team welcomes any and all comments and is happy to respond and make corrections as necessary. They are proud of their work, never feeling like they are finished providing a higher level of quality.

2016 IN-FOCUS PHOTO CONTEST



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Several of Dr. Bevil Conway's pieces are on semi-permanent exhibit at NIH's Porter Neuroscience Research Center.

what vision is because our brains do it so effectively," Conway said. He uses color as a model for studying vision because "it connects a lot of the pieces of the puzzle. It's a low-level attribute involving a measurable physical stimulus, yet color also taps into a host of high-level cognitive and emotional functioning. Anyone who has ever seen a young girl enthusiastically favor the color pink has witnessed how color is imbued with the social cues of gender identity," he said.

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"We take it for granted that we know what vision is because our brains do it so effectively."

-DR. BEVIL CONWAY

• • •

"The LSR is one of the premier systems neuroscience research groups in the world," said Dr. David Schneeweis, NEI deputy scientific director. "Dr. Conway's innovative and groundbreaking efforts to understand how the brain processes information about color will fit perfectly. We are extremely excited to have him join the NEI IRP."

Conway earned his undergraduate degree in biology at McGill University before studying neuroscience at Harvard, where he completed a master's of medical science and earned his Ph.D. in neurobiology. After graduate school, he moved to Nepal to help launch the Kathmandu University Medical School, where he was director of education for physiology and pathophysiology of heart, lung and kidney. In 2003, he was elected a junior fellow in the Harvard Society of Fellows to pursue his combined interest in visual art and visual neuroscience. He also received a Humboldt fellowship to explore the functional organization of color circuits in posterior inferior temporal cortex before joining Wellesley College, and later also MIT.

When he is not in the lab, Conway is a professional painter and sculptor. Many of his works are displayed in private collections in Europe, Africa and North America and in the public collection of the Fogg Museum, the Boston Public Library and on semi-permanent exhibit at the Porter Neuroscience Research Center. [B](#)

Conway Joins NIH, Studies Color to Understand Vision

BY KATHRYN DEMOTT

Neuroscientist and artist Dr. Bevil Conway has joined NEI's Laboratory of Sensorimotor Research (LSR) as chief of the unit on sensation, cognition and action. Before joining NIH, he was associate professor of neuroscience at Wellesley College and a principal research scientist in the department of brain and cognitive sciences at Massachusetts Institute of Technology. His post at NIH is jointly affiliated with NINDS, NIMH and NIDA.

Conway investigates the neural basis for visual perception. He uses color perception as a model system for exploring how our brains process physical stimuli from our eyes. Much is already known about the encoding and transmission of signals from photoreceptors (the neurons in our retina that detect light) to the brain. Conway studies the neural mechanisms by which the brain decodes and processes signals from the retina.

"We take it for granted that we know

NIAAA Recruits Drinkers

NIAAA invites volunteers, 21-60 years of age, who drink more than 15-20 alcoholic beverages per week to participate in a study researching whether a medication reduces drinking. Research participation includes 4 outpatient visits that consist of alcohol self-administration, brain scans (MRI), blood draws and filling out questionnaires. Compensation may be provided. For more information, call (301) 827-0905. Refer to study 16-AA-0037.

Youngsters with Chromosome Variation Needed

The NIH Behavior and Brain Imaging Research Study is currently enrolling children and young adults (5-25 years old) with an XYY chromosome variation. Participation includes an initial 2-day outpatient visit and a visit every 2 years to the Clinical Center. Compensation, transportation, lodging and meal allowance provided. For more information, contact Jonathan Blumenthal at jb364e@nih.gov or (301) 435-4516.

Imaging Study Needs Males

NIMH is currently seeking healthy male volunteers, 5-25 years old, to participate in a study: Brain Imaging of Childhood Onset Psychiatric Disorders, Endocrine Disorders and Healthy Volunteers. There is one initial outpatient visit to the Clinical Center for a physical, blood work, cognitive testing and MRI scan of the brain and return visits every 2 years. Compensation is provided. For more information, contact Jonathan Blumenthal at jb364e@nih.gov or (301) 435-4516.

Study Seeks Healthy Adults

Healthy older adults ages 55-75 are invited to participate in an outpatient research study investigating the benefits of omega-3 oil and blackcurrant supplements 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 4 visits over 6 months. Compensation is provided. For more information, call 1-800-411-1222 (TTY 1-866-411-1010) and refer to study 14-NR-0034.

Combined Federal Campaign Kicks Off for 2016

PHOTOS: ERNIE BRANSON

A little rain did not dampen the spirits of hundreds of people gathered under a tent in front of Bldg. 1 on Sept. 28 to kick off the 2016 NIH Combined Federal Campaign, led this year by the National Institute on Drug Abuse. The annual fundraising launch featured NIH leadership, a guest speaker from The Theatre Lab, exhibits by more than 30 charities and half a dozen local food trucks.

The St. John's College High School color guard opened the event with the presentation of colors, which was followed by a performance of the National Anthem by NIH director and campaign co-chair Dr. Francis Collins, who played guitar, and Dr. Christopher Austin, director of the National Center for Advancing Translational Sciences.

Joellen Austin, NIDA executive officer, provided welcoming remarks and thanked coordinators, deputy coordinators and keyworkers for their help with this year's campaign. Collins noted it was Austin's birthday, to which she replied it was her "best birthday ever" to be able to share it with the enthusiastic group, many of whom were wearing light blue to show spirit and highlight this year's "Show Some Love" CFC color theme.

NIDA director and campaign co-chair Dr. Nora Volkow took the stage to thank everyone for their enthusiasm and support and emphasized that, through the CFC, we can show our generosity and demonstrate how "we are the institute of

hope." Volkow also mentioned that last year, NIH employees contributed more than \$2.3 million—the largest contributing agency within HHS—to benefit the more than 20,000 local, national and international charities participating in the campaign. She encourages NIH to beat that fundraising amount this year.

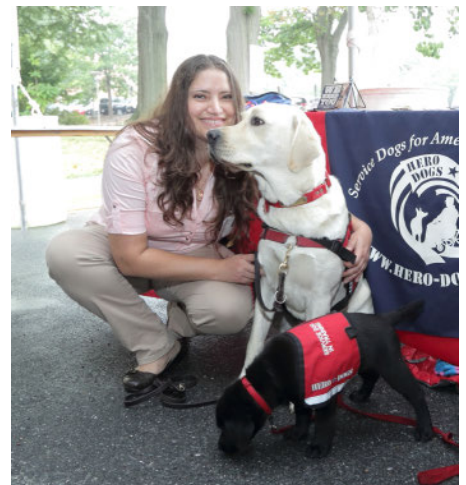
Collins spoke about the importance of the cherished tradition of making a positive impact on the lives of many people. He closed his remarks with, "Come on everybody, let's Show Some Love."

Guest speaker at the event was Deb Gottesman, co-founder and co-executive director of The Theatre Lab. She gave a presentation about how theater education can transform lives. She mentioned that one of her organization's highlights is to hold monthly theater workshops and events at the Children's Inn at NIH.

Following the presentations, attendees were able to have lunch, visit the Charity Fair tables and talk with representatives from dozens of charities, including the American Cancer Society, Mercy Health Clinic, Whitman-Walker Health, Aid for Africa, Global Impact, A Wider Circle and many other organizations.

The CFC is the largest and most successful workplace fundraising drive in the world. The goal for NIH is to donate \$2.24 million this year. Giving is easy and every dollar counts.

The deadline to donate to your favorite charities is Dec. 15. For more information on upcoming CFC events, links to charities and how to donate, visit the NIH CFC web site at <http://cfc.nih.gov>.



Above, NIH director Dr. Francis Collins (l) sings the National Anthem with NCATS director Dr. Christopher Austin at the CFC Kickoff on Sept. 28. At right (from top), NIDA director Dr. Nora Volkow's institute is the lead for this year's campaign, whose goal is \$2.24 million; a representative of Hero Dogs plays with pups at the event; Joellen Austin, NIDA executive officer, enjoyed her "best birthday ever" at the kickoff.

