

Rothenberg Tracks T-Cell Education

BY RICH MCMANUS

When he goes off to university, the T cell is not like his other high-achieving classmates. Rather than breezing through in the standard complement of time, T cells are on a kind of M.D./Ph.D. track, lingering in the thymus for as many as 2 rigorous weeks before committing irreversibly to the T-cell profession, which they will then faithfully follow wherever they go in the body.

Learning to become an immune cell takes time and trouble, explained Dr. Ellen Rothenberg, Albert Billings Ruddock professor of biology at the California Institute of Technology, in the final Wednesday



Dr. Ellen Rothenberg discusses T-cell lineage.

Afternoon Lecture before summer break on June 27.

The T in T cell, like the H in Harvard, is not (necessarily) born to, but earned. Although the letter stands for thymus, seat of their learning, they actually arise in bone marrow. Arriving at the thymus

as precursors, they still have the potential to be lawyers, doctors or tech titans. But as the semesters roll by, exposure to classmates—including Notch pathway activators and a limited set of growth factors—induces T cells to relinquish all other options in favor of T-ness.

Neighborhood is hugely important to immune cell fate, just as zip code correlates with chances of being admitted to the Ivy League. “Cells adopt new gene expression patterns depending on their environment,” said Rothenberg, who studies T-cell development in mice.

She described the thymus as a “coercive environment” wherein precursor T cells are slow to commit while under constant bombardment by competing biological signals; such hazing can last up to 2 weeks. “They give up multi-potentiality in the process,” Rothenberg said.

SEE **ROTHENBERG**, PAGE 8

IN A HEARTBEAT

Don't Fear AEDs—You Might Save a Life

BY DANA TALESNIK

When someone collapses in sudden cardiac arrest, every moment counts. Using an AED (automated external defibrillator) and administering CPR (cardiopulmonary resuscitation) until medical help arrives can make all the difference. But would the typical bystander get over the initial shock of the situation to intervene?

AEDs, which assess heart rhythm and



Juli Egebrecht, CPR/AED instructor

SEE **AED**, PAGE 6

Workplace Civility Increases Productivity

BY ERIC BOCK



Dr. Christine Porath

“Civility pays.”

That’s the advice Dr. Christine Porath gave at a recent Deputy Director for Management Seminar Series lecture in Masur Auditorium.

“Being truly civil means doing the small things, like smiling and saying hello to

someone in the hallway or listening fully when someone is speaking to you,” said Porath, associate professor of management at Georgetown University’s McDonough

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Seated massage at Safety Day; see p. 2.

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Hopkins To Give Next ‘Mind The Gap’ Webinar

Aug. 22

The Office of Disease Prevention will hold a Mind the Gap webinar on Wednesday, Aug. 22 at 1



Dr. David Hopkins

p.m. with Dr. David Hopkins, who will discuss approaches to evidence synthesis in systematic reviews of public health interventions methods and the experiences of the community preventive services task force. The group develops guidance on community-based health promotion and disease prevention interventions using methodology developed by the CDC’s Community Guide Branch.

Hopkins is the medical officer with the branch. He joined the Community Guide in 1997 and has led systematic reviews of population-based interventions in tobacco prevention and control, asthma, diabetes, cardiovascular disease prevention, physical activity promotion and immunizations. He will accept questions during the webinar via WebEx and Twitter. In the latter case, use #NIHMTG.

Registration is required and can be accomplished at <https://nih.webex.com/nih/onstage/g.php?MTID=e458c8c43c51f351750201827dc0eef9f>.



Repairs Made to ‘Sky Horizon’ Sculpture

The large abstract sculpture near the Clinical Center’s north entrance recently got a facelift.

The “Sky Horizon” sculpture found at the end of West Drive was power-washed, given a fresh primer and a coat of paint, said Lillian Fitzgerald, curator of the Clinical Center Art Program.

Modern sculpture artist Louise Nevelson created the piece. The 25-foot high sculpture is an assemblage of steel beams and a variety of panels welded and bolted together.

The sculpture was dedicated to NIH in 1988. It originally belonged to the family of Edwin C. Whitehead, founder of the Whitehead Institute for Biomedical Research and Technicon Corp. In 2006, the family formally donated it to NIH.



Safety, Health, Wellness Celebrated

NIH’s 7th annual Safety Health and Wellness Day was held June 27 on the south side of Bldg. 10, drawing smiles and thumbs-up from many participants. The free event included fitness classes and assessments, dance classes, martial arts demonstrations and a dependent and elder care fair. There was also seated massage and virtual reality demonstrations (r, bottom), plus food trucks, information tables (r, above) and a farmer’s market. The event was sponsored by the Office of Research Services, Office of Research Facilities, NIH occupational safety and health committee, laboratory sustainability group and NIDDK.

PHOTOS: CHIA-CHI CHARLIE CHANG

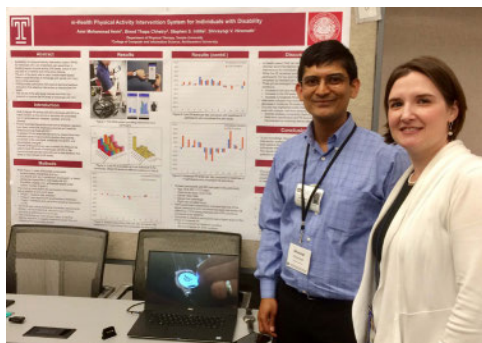


NIH Hosts mHealth Technology Showcase for Health Researchers, Device Developers

BY RAYMOND MACDOUGALL AND MEREDITH DALY

The mobile device in your pocket or on your wrist might help you pursue your own healthy lifestyle goals, but it also could contribute to new explorations into health interventions and public health research.

NIH hosted more than 300 university-based and industry technology developers, federal researchers and program staff eager to explore opportunities in health research using mobile technologies. The mHealth Technology Showcase—a recent 1-day meeting—provided the opportunity for developers and researchers to discuss ways to work together.

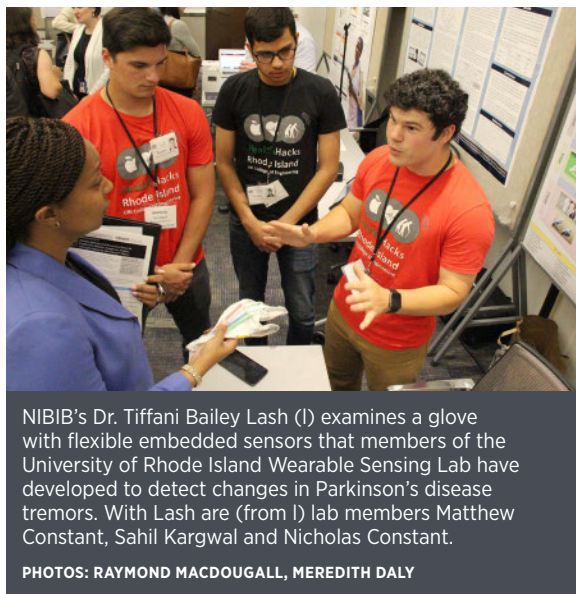


NICHD's Dr. Theresa Cruz visits a poster presented by Temple University's Shivayogi Hiremath, which depicts the Physical Activity Intervention System, a device to assist people in wheelchairs, specifically those recovering from a spinal cord injury.

Mobile health—or mHealth—has evolved over the past decade to encompass varied tools and strategies. The field now boasts wearable and mobile sensors for data collection, mobile apps for self-monitoring and intervention, software platforms for large studies, software tools for big-data analysis and an array of new biomarkers for research.

The range of mHealth tools makes it possible to measure dynamic changes in an individual's health state, as well as physical, biological, behavioral, social and environmental factors that contribute to health and disease risk in the wider community.

"Mobile health has been around since the 1940s, when it meant a truck with an X-ray machine going town to town screening for tuberculosis," said Dr. William Riley, director of the NIH Office of Behavioral and Social Sciences Research, during his keynote address. NIH's mHealth tech event, he added, gathered leading developers and designers together to advance the field.



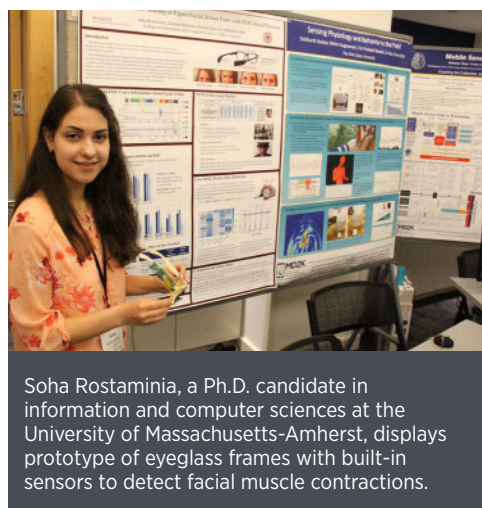
NIBIB's Dr. Tiffani Bailey Lash (l) examines a glove with flexible embedded sensors that members of the University of Rhode Island Wearable Sensing Lab have developed to detect changes in Parkinson's disease tremors. With Lash are (from l) lab members Matthew Constant, Sahil Kargwal and Nicholas Constant.

PHOTOS: RAYMOND MACDOUGALL, MEREDITH DALY

During the exhibition portion of the showcase, presenters demonstrated the latest technology and gadgetry, including assorted wearables—from wristbands to eyeglasses, smartphone apps and software for assembling and displaying data.

"The presentations were impressive, particularly devices designed to promote physical activity for people with disabilities," said Dr. Theresa Cruz, a program officer with NICHD's National Center for Medical Rehabilitation Research.

The MD2K (Mobile Sensor Data-to-Knowledge) Center of Excellence, led by meeting co-organizer Dr. Santosh Kumar of the University of Memphis, was instrumental in gathering colleagues in the field as presenters and speakers. The center includes participation by 11 universities and university medical centers and debuted in 2015 with NIH funding to develop hardware and software for



Soha Rostaminia, a Ph.D. candidate in information and computer sciences at the University of Massachusetts-Amherst, displays prototype of eyeglass frames with built-in sensors to detect facial muscle contractions.

compiling data from wearable sensors.

"Four years ago, when MD2K was created, it would have taken a dedicated research lab to run a single 50-person field study," said Dr. Timothy Hnat, MD2K chief software architect, discussing studies

his center has undertaken. "Now, our platform has been successfully deployed for 10 concurrent studies at independent locations throughout the United States."

These studies will enroll 2,200 participants and accumulate approximately 4.7 trillion data samples. "The largest of these studies supported 400 simultaneous participants in 3 separate sites," he said.

"We received an extraordinary response for the showcase from both the technology development and research communities," said Dr. Tiffani Bailey Lash, director of NIBIB's programs in connected health (mHealth and telehealth) and point-of-care technologies, who was part of the organizing committee. "It is important to work collectively to both take advantage of the array of mHealth technologies that are possible today, but also to think about the best ways to apply them in the future to gain answers to important health questions." **R**



ON THE COVER: A confocal microscopy image shows the developing face of a 6-day-old zebrafish larva.

IMAGE: OSCAR RUIZ & GEORGE EISENHOFER, UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

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Porath

CONTINUED FROM PAGE 1

School of Business. “It doesn’t mean you can’t have strong opinions, can’t disagree, can’t have conflict or can’t give negative feedback. It’s just do it civilly.”

Porath landed her dream job at the world’s largest sports management and marketing firm after she graduated from college. She saw firsthand one executive’s toxic behavior and how it affected the company’s employees at work and home. She resigned a year later and went to graduate school to study the impact of incivility in the workplace.

Incivility is disrespect or rudeness and “it includes a lot of different behaviors, from mocking or belittling someone, to excluding them, to texting while someone’s talking to you at meetings, to telling offensive jokes,” she explained.

The cost of incivility is high, Porath said. Instead of focusing on work, those who experience the behavior are far less motivated and are worried about future incidents. A few even leave their jobs. Sadly, employers are not aware of these behaviors because employees don’t report it. Some companies estimate that negative behavior costs millions of dollars in lost productivity.

Employees who witness incivility in the workplace are affected too, Porath noted. They become three times less likely to help anyone if they’re working around incivility. In hospitals, for example, not working together can have dire consequences for patients.

“Incivility is contagious. It’s a bug, it’s

★ ★ ★

“Saying thank you, sharing credit, listening attentively to people, humbly asking questions, acknowledging people and even smiling can have a great effect on others and, in turn, lift yourself up as well.”

-DR. CHRISTINE PORATH

★ ★ ★

a virus and we can catch it anywhere—not only at work, but at home, online or in our community,” she said. “It affects our emotions, motivations, performance and how we treat others.”

Most people admit to being uncivil because they are stressed. They also fear they’ll appear less leader-like if they act civilly. They wonder: Do nice guys finish last? Do jerks get ahead? Luckily, however, that’s not the case.

“If you’re civil, you’re more likely to be seen as a leader and you tend to perform better,” Porath said.

Most employees want their bosses to respect them, she noted. Those who felt respected said they are healthier, more focused, engaged in their work and are more likely to stay with the organization.

Some supervisors act uncivilly, unaware that they are doing it. Porath knew of one experienced doctor who admitted to being rude because his mentor acted disrespectfully and was rude to him. He didn’t think there was another way. Porath recommends that those who think they might act uncivilly ask others

for their perceptions of them. The good news is that it’s possible to change.

“Saying thank you, sharing credit, listening attentively to people, humbly asking questions, acknowledging people and even smiling can have a really great effect on others and, in turn, lift yourself up as well,” she said.

For those working or living in an uncivil environment, she recommends creating a “sense of thriving.” This means people look for growth opportunities, volunteer, ask a mentor for help, find meaning in work and build positive relationships.

To build a culture of civility, Porath advises hiring candidates who fit an organization’s culture, creating rules that encourage civility, recognizing those who behave civilly and providing feedback to employees who behave uncivilly.

“We will get people to give more and function at their best if we’re civil,” Porath concluded. “When we have more civil environments, we’re more productive, creative, helpful, happy and healthy.”

Bryan Cave’s Code of Civility

1. We greet and acknowledge each other.
2. We say please and thank you.
3. We treat each other equally and with respect, no matter the conditions.
4. We acknowledge the impact of our behavior on others.
5. We welcome feedback from each other.
6. We are approachable.
7. We are direct, sensitive, and honest.
8. We acknowledge the contributions of others.
9. We respect each other’s time commitments.
10. We address incivility.



“If you’re civil, you’re more likely to be seen as a leader and you tend to perform better,” Porath said.

PHOTOS: MARLEEN VAN DEN NESTE

NINR's Grady Discusses Nursing Science at UW

Dr. Patricia Grady, director of the National Institute of Nursing Research, recently spoke to nursing students, faculty and staff at the University of Washington School of Nursing.

Her talk focused on the state of nursing science and current trends and opportunities within the field, as well as NINR's vision for the future of nursing science.



Dr. Patricia Grady

She emphasized the training NINR offers including the Summer Genetics Institute, Symptom Methodologies

Boot Camp and Graduate Partnerships Program.

In her introduction of Grady, Dean Azita Emami noted the importance of nursing research and promoting the pursuit of Ph.D.s within the nursing community.

“Without Ph.D.-prepared individuals in the future, we are not going to have any nursing education...Without having educators to educate the next generation of nursing, that will be the devastation for the development of our profession and discipline.”

Grady echoed Emami in noting why research is so vital to the field. “I have always felt that we don't have enough of a research workforce...even at a steady incline we will not have enough of a research workforce to do everything important that needs to be done in any of our lifetimes. We need to keep building.”

Grady ended her talk with a bit of wisdom for the audience: “Research is fun and it's a way to make an impact that's going to last a lot longer than any of the rest of us.”

To learn more about NINR training opportunities, visit www.ninr.nih.gov/training/trainingopportunitiesintramural.

NIMH Holds 10th Axelrod Symposium

'JULIE'

NIMH recently hosted the 10th annual Julius Axelrod Symposium in remembrance of the NIH intramural Nobel laureate's scientific contributions and mentoring prowess. This year, the symposium honored 2015 and 2017 Society for Neuroscience Julius Axelrod Prize winners Dr. Pietro De Camilli and Dr. Moses Chao, respectively.

Chao has contributed significantly to the body of knowledge on nerve growth factors (NGFs) and receptor signaling. His lab seeks to identify the biochemical steps in trophic factor signaling and to understand how specificity is encoded in cell-cell communication in the nervous system. This work has yielded important discoveries in how neurotrophins nourish neurons, guide axons to form their proper connections and promote their survival.



On hand at the Axelrod symposium were (from l) NIMH director Dr. Joshua Gordon, fellows' awardee Dr. Amicia Elliott, Dr. Joseph Coyle, Axelrod prize winners Dr. Pietro De Camilli and Dr. Moses Chao, and NIMH scientific director Dr. Susan Amara.

Currently professor of cell biology, physiology and neuroscience and psychiatry at NYU's Skirball Institute of Biomolecular Medicine, Chao early in his career identified the p75 and TrkA receptors and demonstrated their roles in creating high-affinity binding sites for NGF. His team and collaborators then identified downstream mechanisms that account for how growth factors affect neuronal survival and synaptic plasticity. Over the past decade, he has uncovered novel aspects of downstream signaling for brain-derived neurotrophic factor and the TrkB receptor relevant to neurodegeneration, learning and memory.

When presenting the prize to Chao, SfN president Dr. Eric Nestler said, “In addition to his seminal research contributions in neuronal growth and signaling, his exemplary efforts in providing public service as a teacher and mentor make him a genuine leader in the field.”

For many years, De Camilli has studied steps involved in the release of neurotransmitters from synaptic vesicles and the re-formation of these vesicles inside nerve endings, elucidating key molecular mechanisms governing this cycle of membrane traffic. He has also contributed to our understanding of diseases of the nervous system that involve autoimmunity against synaptic proteins.

De Camilli is John Klingenstein professor of neuroscience and chair of the department of neurobiology at Yale University, as well as a Howard Hughes Medical Institute investigator, founding director of the Yale Program in Cellular Neuroscience, Neurodegeneration and Repair and director of the Kavli Institute for Neuroscience.

“The society honors Dr. De Camilli for his outstanding contributions to neuroscience, and especially to neuropharmacology, as well as his commitment to mentorship,” noted SfN president Dr. Steven Hyman in 2015. “Dr. De Camilli has mentored a large number of students and young researchers, both in his lab and beyond, who have gone on to have successful independent careers in neuroscience and related disciplines.”

In addition to the two keynote addresses, Dr. Antonina Roll-Mecak of NINDS's cell biology and biophysics section spoke on “How cells read and write the tubulin code.” Dr. Amicia Elliott, a postdoctoral fellow in NIMH's section on neural function, was presented the NIMH Julius Axelrod Memorial Fellows' Award (in basic science), which includes a travel award and \$10,000 to help defray research-related expenses. She spoke on use of light-sheet microscopy, which she built to study fruit flies, with the goal of finding out how neural circuits coordinate complex behaviors.

The symposium also included a data blitz session, where NIMH trainees Jakob Seidlitz, Dr. Jennie Garcia-Olivares, Dr. Stacey Kigar and Dr. Emily Finn gave short oral presentations of their work, and a closing poster session/reception that gave 27 trainees an opportunity to discuss their research with symposium attendees.



Trainees practice AED use on mannequins, seen above and below.

PHOTOS: DANA TALESNIK

AED

CONTINUED FROM PAGE 1

can send an electric shock to the heart, might appear intimidating to the untrained onlooker, but these portable devices are remarkably simple to use. Across NIH, on and off campus, there are 374 fully automatic AEDs, often located near elevators, including 94 in the Clinical Center alone.

“These devices are safe,” said Juli Egebrecht, director, basic life support training at NIH, who started teaching CPR in 1972 and has worked at NIH for more than 30 years. “They will only shock people who need it.”

Bystanders also need not worry, she said. The shocking field of the adhesive pads is surrounded by an insulated strip with minimal leakage.

“The hardest thing is to get over the initial ‘Oh my gosh’ situation,” said Egebrecht. “The AED talks with specific instructions and nags you until you do it.”

Annually, more than 18,000 Americans go into cardiac arrest in public places, and an estimated 1,700 lives are saved by bystanders using AEDs. A recent Johns



Hopkins study, partly funded by NHLBI and NINDS, revealed significantly higher patient survival rates when a bystander used an AED while waiting for emergency medical personnel to arrive. What’s more, many of those patients survive cardiac arrest with minimal disability.

All campus AEDs are inspected monthly, said Egebrecht. The unit chirps and flashes

• • •

“The hardest thing is to get over the initial ‘Oh my gosh’ situation.”

—JULI EGBRECHT

• • •

when the battery gets low. “For all the problems you might think could happen to a life-saving device,” she said, “people have done their homework and had the forethought to figure out how to keep them viable, active, easy and safe to use.”

A bystander’s first reaction to someone lying unconscious should be to check for responsiveness. If the person isn’t breathing or there’s an irregular pulse, or none at all, yell for help and dial, or ask someone nearby to call, 911.

When reaching for the door to an AED box, don’t fear the alarm. It’s not that loud and serves to alert people around you to an

emergency.

Next, grab the AED. Semi-automated AED models turn on at the push of a button; fully automatic ones turn on just by opening the lid; voice prompts then offer step-by-step instructions. There’s an enclosed pouch with scissors to cut the patient’s clothing and the talking AED coach tells you exactly where to place the two adhesive pads. The AED then analyzes the heart rhythm and will tell you whether a shock is advised.

At that point, it’s safe to start chest compressions while the AED is charging, says Egebrecht. After each shock, the machine prompts the rescuer to give CPR and chimes like a metronome so the CPR-giver can give compressions to the beat.

“By the fourth cycle of chest compressions, medical help should be arriving,” said Michael Dunn, an occupational health & safety manager at NIH who oversees NIH’s CPR training for non-medical personnel. “The best chance for survival is keeping the compressions going.

“But, if you don’t know what you’re doing,” warned Dunn, “go find someone who does. Don’t apply CPR if you’re untrained; you can do harm.”

Keeping blood circulating is critical, said Dunn. That’s why current CPR training focuses on chest compressions, not on giving breaths. “Keeping blood flowing extends the life of vital organs,” he said. “The longer you keep the vital organs alive, the better chance you have for recovery from a cardiac arrest incident.”

There’s no time like the present to learn CPR. NIH offers free CPR training to all interested personnel. Classes cover adult CPR and using an AED. Egebrecht teaches CPR to health care providers from current clinicians to trainees aspiring to get into a medical field. Dunn manages and leads lay responder classes for administrative staff.

To learn more or sign up, visit <https://www.ors.od.nih.gov/sr/dohs/safety/Training/Pages/aedlocations.aspx>.

For anyone seeking additional training, the American Heart Association offers Heartsaver classes that cover child and infant CPR, first aid and related training. See <https://cpr.heart.org>.

Said Dunn, “If you have CPR training, you’re considered one of the assets in your building who can save a life.” **E**



At left, co-organizer Dr. Catherine Stoney moderates a session on nonchemical stressors and atherosclerosis. At center, Dr. Danielle Carlin (r) and Dr. Michelle Olive describe the workshop's goal. At right, Dr. Cavin Ward-Caviness of the Environmental Protection Agency discusses the importance of genetic and epigenetic factors in susceptibility to atherosclerosis.

PHOTOS: MICHAEL GARSKE

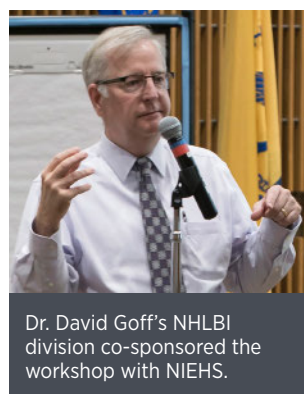
Atherosclerosis as a Model for Studying Combined Exposures

BY KELLY LENOX

In the first workshop of its kind, clinicians, psychologists and researchers gathered at NIEHS recently to explore approaches to studying combined health effects of exposures to both chemicals and nonchemical stressors. Organizers from NIEHS and NHLBI selected atherosclerosis as the model disease for the workshop because both types of exposures are known to play a role in its development.

"We know that lifestyle, nutrition, age and gender all affect atherosclerosis, but [how about] other things, such as psychosocial stress, lack of sleep or the chemicals we're exposed to on a daily basis?" asked Dr. Danielle Carlin, one of the lead organizers and a scientist in the NIEHS Hazardous Substance Branch. "There's evidence that arsenic, lead and cadmium contribute," she added. "Can we find specific mechanisms through which these factors interact with each other?"

Although the answers are far from clear, Carlin noted that inflammatory processes appear to be highly involved. She and two scientists from NHLBI, Dr. Michelle Olive and Dr. Catherine Stoney,



Dr. David Goff's NHLBI division co-sponsored the workshop with NIEHS.

led the organizing effort. They and others will prepare a paper on outcomes from the two days of presentations, discussions and brainstorming sessions for publication in a peer-reviewed journal.

Dr. David Goff, director of

NHLBI's Division of Cardiovascular Sciences, and Dr. Linda Birnbaum, director of NIEHS and the National Toxicology Program, welcomed attendees to the workshop. Birnbaum charged them with

determining approaches to studying biological mechanisms and interactions of both types of stressors with respect to atherosclerosis. The disease is dangerous because it results in constricted blood vessels and the potential for plaque to rupture, leading to a clot that can block blood flow. Furthermore, scientists know that the body may respond more intensely to a combination of chemicals compared with a single chemical.

Stoney was pleased by the intense focus of meeting attendees. "It was a very collegial group," she said. "They took their task very seriously, which gives a sense of how important the topic is." Participants enjoyed the interdisciplinary nature of the discussions. Olive said the meeting drew a unique mix of scientists, including cardiologists, comparative medicine experts, toxicologists, psychologists, immunologists, epidemiologists, public health scientists, systems biology experts, imaging experts, geneticists and chemists.

Not surprisingly, the exposures and mechanisms discussed were similarly broad and complex. Presenters highlighted chemical stressors such as ozone, fine particulate matter, nutrient deficiencies and metals, as well as bisphenol A and polychlorinated biphenyls. Geospatial data on heart disease mortality highlighted increasing geographic disparities.

Nonchemical stressors ranged from poverty, psychosocial stress and the built environment to sleep and circadian rhythm disruptions, depression, anxiety, infection and sedentary lifestyles. "Cytokines, bone marrow and the sympathetic nervous system are involved," said Stoney, highlighting inflammatory pathways addressed by many of the presenters. "When you're under a lot of stress, it triggers the bones to produce more inflammatory cells, which make their way into blood vessels and cause plaque formation."

On the chemical side, inhalation of particulate matter, for example, is linked to pulmonary oxidative stress and inflammation. Both eventually affect the heart. "There's definitely room for more research," said Olive. "For the paper, we'll invite each participant to reference the literature that supports known mechanisms." **R**

Smirnova Named Chief of CSR Review Group

Dr. Elena Smirnova is new chief of the Center for Scientific Review's genes, genomes and genetics (GGG) integrated review group. She had been acting chief of GGG since January 2018. Smirnova previously served as a referral officer and as scientific review officer (SRO) for CSR's cellular signaling and regulatory systems study section.

"Elena's exemplary grasp of policy, sound judgment and an unwavering focus on the quality of review make her the ideal choice for this important role,"

said CSR acting director Dr. Noni Byrnes. She also noted that Smirnova is well prepared for her new role due to her research background in basic cell and molecular biology, along with her years of experience handling reviews in the area of DNA damage/repair checkpoints, service as a referral officer for several IRGs including GGG and her leadership of trans-NIH Roadmap reviews in the areas of epigenomics and genome editing.



Dr. Elena Smirnova

Smirnova will oversee seven standing study sections and numerous special emphasis panels that review a broad range of NIH grant applications in fundamental and applied aspects of genes, genomes and genetics of humans and other organisms.

She earned a Ph.D. in biochemistry/biophysics from Heidelberg University in Germany. She did her postdoctoral training in the department of biological chemistry at UCLA School of Medicine. She then joined NICHD's Cell Biology and Metabolism Branch before joining CSR as an SRO in the cell biology IRG.

VOLUNTEERS

Healthy Volunteers Needed

NIAID researchers seek healthy volunteers, 18-60 years old, for a study at the Clinical Center to examine safety and tolerability of an investigational product targeting Ebola. You cannot get Ebola from this product. Financial compensation is provided. For more information, call 1-866-833-5433 or email vaccines@nih.gov. Read more online at <https://go.usa.gov/xQGpJ>.

Rothenberg

CONTINUED FROM PAGE 1

“This multi-step process involves a cascade of changes in the expression of different regulatory genes and resulting changes in global genome-wide activity,” she explained in a summary of her talk. “As the cells start their pathway to a T-cell fate, they come dangerously close to a gene-expression pattern typical of malignancy before they become safely locked into their T-cell identity.”

Just as some college students flirt with disaster before righting themselves, T cells go to some bars and clubs they might not want to frequent again. Rothenberg is keen to know how in development the T cell decides on its specific role rather than becoming a dendritic cell or an NK (natural killer) cell.

There are some 400 transcription factors vying for influence when precursor cells enter the thymus, Rothenberg said, but some are highly influential. One that is crucial to eventual T-cell fate is BCL11b, which is “needed for commitment, and correlated with commitment.”

In a conversation following her talk, Rothenberg explains: “Honestly, the part about this that is most fascinating to me is that these transcription factors (including BCL11b) are really very concrete little proteins that bind to DNA and work as part of gene-expression machines. Their own expression depends on turning on the genes that encode them, just like any other genes. And yet their functions, in the end, have these wonderful qualities that can transform the entire biological role of a cell. The challenge for all of us in molecular developmental biology is to figure out how these little agents carry out their roles in determining cell identity.”

Rothenberg and her colleagues have spent the past few years examining exactly how transcription factors explain “developmental causality” of the changes that take place in cells. To understand this, she and her colleagues can effectively do molecular surgery on the developing cells to remove particular transcription factors at specific stages and see what the effect is on the cells’ next moves.

It turns out that BCL11b becomes like the main party organizer, determining what kind of social contacts a precursor



Rothenberg’s talk capped WALs summer stint.

PHOTOS: CHIA-CHI CHARLIE CHANG


makes. Notes Rothenberg, “Some cells stay adolescent and don’t grow up, depending on transcription factors.”

Within the precursor cell’s nucleus, BCL11b can also act as a kind of traffic controller for other transcription factors, including Runx 1, determining their own choices of genomic binding sites, she added.

T cell precursors still have another couple of weeks of thymic school to go through, even after they commit to being T cells, Rothenberg noted in a conversation following her lecture. “In fact, the worst is yet to come. More than 95 percent of each generation of aspiring T cells get killed off in the thymus, so that only a chosen 5 percent can be sent to ‘grad/professional school.’”

The good news, Rothenberg concluded, is that T-cell lineage identity, once established, is robust. You can’t take away the diploma once it is awarded.

In a brief Q&A session that preceded a reception in the NIH Library, Rothenberg fielded a number of questions that so intrigued her that it seemed she could happily spend her own next semester working alongside stimulating NIH colleagues.

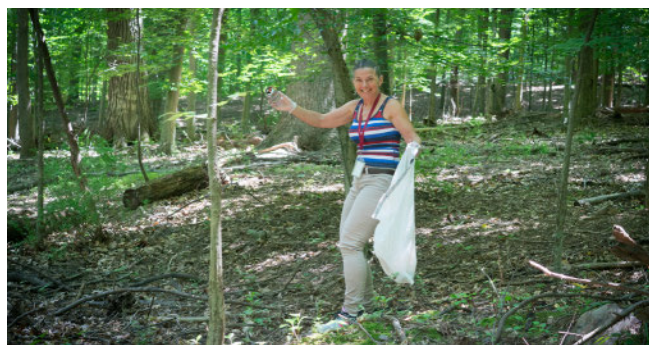
The full talk is available at <https://videocast.nih.gov/summary.asp?Live=28006&bhcp=1>. 

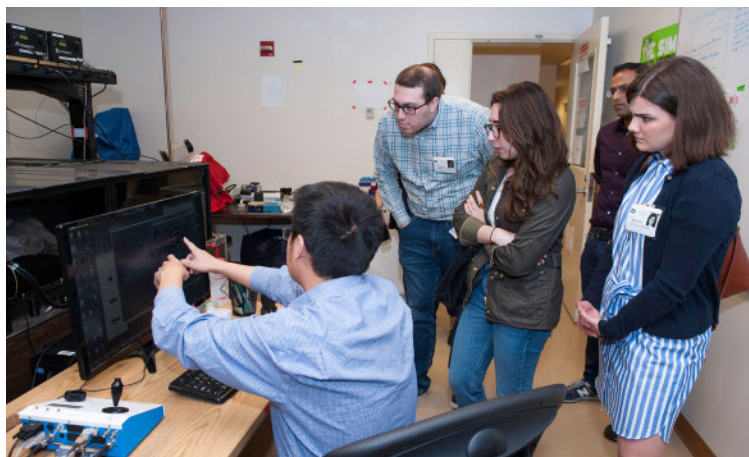


NIAID DEA Takes Care of Its Community

Staff from NIAID’s Division of Extramural Activities joined together on June 28 to pick up trash along the Fishers Ln.-to-Viers Mill Rd. bike path. The NIAID DEA liaison committee sponsored the walk and clean-up event as a team-building activity and as a way to give back to the local community. Everyone enjoyed a cool treat afterwards. Shown above are DEA staffers from the Grants Management Program, Office of Acquisitions, Office of the Director and Scientific Review Program; below are Jacob Rains, GMP intern, and Michelle Scala of OA.

PHOTOS: JACKIE CHRISTIE, BRYAN JOHNS





At left, congressional staff visiting NIH hear George Washington University researchers describe their development of portable and wearable sensors that can detect air pollution and tobacco smoke to help children with asthma. At right, staffers gather in NIBIB's high resolution optical imaging lab to learn how researchers are creating microscopes that can image the inner workings of cells in real-time.

Biotech Demonstrations Wow Congressional Staff

A group of 40 congressional staff recently visited NIH for a demonstration of technologies supported by the National Institute of Biomedical Imaging and Bioengineering. NIBIB acting director Dr. Jill Heemskerk reminded attendees that their visit coincided with Star Wars Day, welcoming them to learn about futuristic research projects—in various stages of development and with a range of applications for improving health.

The presentations included a tour of an NIBIB intramural research lab where senior investigator Dr. Hari Shroff and his team have developed a new microscope to study live biological processes at unprecedented speed and resolution. The group also toured the Advanced Imaging and Microscopy Resource Center, a trans-NIH shared resource that houses, operates, disseminates and improves non-commercial, prototype optical imaging systems developed at NIH.

Four table-top demonstrations showcased innovative technologies that address critical health problems:

- Johns Hopkins University researchers demonstrated a point-of-care device for diagnosing chlamydia, along with some other sexually transmitted diseases, in under 30 minutes. The rapid results available at a clinic or doctor's office allow treatment to begin immediately, improve patient management and reduce the transmission of infection. Currently, the device is approved in Europe and is in the process of FDA approval for use in this country.

- Representatives of Rivanna, a company based in Charlottesville, displayed a technology

supported by an NIH Small Business Innovation Research grant that uses a portable ultrasound scanning method to rapidly assess bone fractures. The device could be used by emergency room physicians and/or nurses to determine the best course of care and reduce long waiting times in the emergency room for X-rays. The company had previously received an SBIR grant to develop an ultrasound tool for assisting epidural placement, which is now FDA-cleared and available for use.

- George Washington University researchers demonstrated a technology developed through NIBIB's Pediatric Research using Integrated Sensor Monitoring Systems (PRISMS) program. This technology consists of a wearable tobacco smoke sensor and a portable air pollution gas monitor. Both sensors connect to a cloud-based informatics system for data storage, management and analytics.

- The winners of NIBIB's 2017 Design by Biomedical Undergraduate Teams (DEBUT) Challenge showcased the technology they are developing that uses advanced electroencephalogram readings to diagnose Alzheimer's disease at the first onset of clinical symptoms.



Congressional staff learn from Dr. Charlotte Gaydos (r) of Johns Hopkins University how a small device can diagnose sexually transmitted disease in 30 minutes.

The technology demonstration gave NIBIB-affiliated researchers the opportunity to show the legislative aides who attended how taxpayer dollars are being used to solve health problems and how NIBIB is fulfilling its mission to lead the development and accelerate the application of biomedical technologies to improve health.—
Christine Cooper

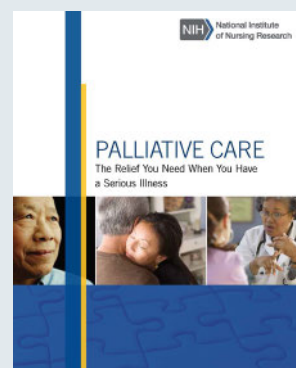
NINR Updates Palliative Care Brochure

NINR recently updated its brochure *Palliative Care: The Relief You Need When You Have a Serious Illness*. The revised publication is available in English and Spanish.

The brochure, originally titled *Palliative Care: The Relief You Need When You're Experiencing the Symptoms of Serious Illness*, has been revised to reflect the most recent research, terminology and practices.

The purpose of the brochure is to provide patients with serious illnesses and their families with clear, evidence-based information about what palliative care is, who it benefits and how it works. The brochure also addresses certain misconceptions about palliative care, such as that it is only for those nearing the end of life.

Download the brochure at www.ninr.nih.gov/PalliativeCareBrochure. To order free print copies, call (301) 496-0207 or send an email with your name, mailing address, phone number, email address and requested quantities to info@ninr.nih.gov.



Protein Affected By Rare Parkinson's Mutation May Lurk Behind Many Cases of the Disease

Mutations in the gene LRRK2 have been linked to about 3 percent of Parkinson's disease cases. Researchers have now found evidence that the activity of LRRK2 protein might be affected in many more patients with Parkinson's disease, even when the LRRK2 gene itself is not mutated.

The study was published in *Science Translational Medicine* and was supported in part by NINDS.

"This is a striking finding that shows how normal LRRK2 may contribute to the development of Parkinson's disease," said Dr. Beth-Anne Sieber, NINDS program director. "This study also identifies LRRK2 as an integral protein in the neurobiological pathways affected by the disease."

More than 10 years ago, researchers linked mutations in the LRRK2 gene with an increased risk for developing Parkinson's disease. Those mutations produce a version of LRRK2 protein that behaves abnormally and is much more active than it would be normally.

Despite its importance in Parkinson's disease, the very small amount of normal LRRK2 protein in nerve cells has made it difficult to study.

In the current study, the authors developed a new method for observing LRRK2 cells that makes them glow fluorescently only when LRRK2 is in its activated state. They have also used detection of fluorescent signals to demonstrate loss of binding of an inhibitor protein to LRRK2 when LRRK2 is activated.

Tickborne Diseases Likely to Increase

The incidence of tickborne infections in the United States has risen significantly within the past decade. It is imperative, therefore, that public health officials and scientists build a robust understanding of pathogenesis, design improved diagnostics and develop preventive vaccines, according to a new commentary in the *New England Journal of Medicine* from leading scientists at NIAID.

Bacteria cause most tickborne diseases in the U.S., with Lyme disease representing the majority (82 percent) of reported cases.

The spirochete *Borrelia burgdorferi* is the primary cause of Lyme disease in North America; it is carried by hard-bodied ticks that then feed on smaller mammals, such as white-footed mice, and larger animals, such as white-tailed deer.

Although there are likely many factors contributing to increased Lyme disease incidence in the U.S., greater tick densities and their expanding geographical range have played a key role, the authors write. For example, the *Ixodes scapularis* tick, which is the primary source of Lyme disease in the northeastern U.S., had been detected in nearly 50 percent more counties by 2015 than was previously reported in 1996.

Although most cases of Lyme disease are successfully treated with antibiotics, 10 to 20 percent of patients report lingering symptoms after effective antimicrobial therapy. Scientists need to better understand this lingering morbidity, note the authors.



Researchers have now found evidence that the activity of LRRK2 protein might be affected in many more patients with Parkinson's disease.

IMAGE: RYAN MCVAY/GETTY

Tickborne virus infections are also increasing and could cause serious illness and death. For example, Powassan virus (POWV), recognized in 1958, causes a febrile illness that can be followed by progressive and severe neurologic conditions, resulting in death in 10 to 15 percent of cases and long-term symptoms in as many as 70 percent of survivors.

Only 20 U.S. cases of POWV infection were reported before 2006; 99 cases were reported between 2006 and 2016.

The public health burden of tickborne disease is considerably underreported, according to the authors. For example, the Centers for Disease Control and Prevention reports approximately 30,000 cases of Lyme disease annually in the U.S. but estimates that the true incidence is 10 times that number. According to the authors, this is due in part to the limitations of current tickborne disease surveillance, as well as current diagnostics, which may be imprecise in some cases and are unable to recognize new tickborne pathogens as they emerge.

These limitations have led researchers to explore new, innovative diagnostics with different

platforms that may provide clinical benefit in the future.

Next-Generation ALS Drug Silences Inherited Form of the Disease in Animal Models

NIH-funded researchers delayed signs of amyotrophic lateral sclerosis (ALS) in rodents by injecting them with a second-generation drug designed to silence the gene superoxide dismutase 1 (SOD1). The results, published in the *Journal of Clinical Investigation*, suggest the newer version of the drug may be effective at treating an inherited form of the disease caused by mutations in SOD1. Currently, the drug is being tested in an ALS clinical trial.



An engorged deer tick, or *Ixodes scapularis*, can transmit Lyme disease.

IMAGE: NIAID

ALS destroys motor neurons responsible for activating muscles, causing patients to rapidly lose muscle strength and their ability to speak, swallow, move and breathe. Most die within 3 to 5 years of symptom onset. Previous studies suggested that a gene therapy drug, called an antisense oligonucleotide, could be used to treat a form of ALS caused by mutations in the gene SOD1. These drugs turned off SOD1 by latching onto versions of the gene encoded in messenger RNA (mRNA), tagging them for disposal and preventing SOD1 protein production.

Using rats and mice genetically modified to carry normal or disease-mutant versions of human SOD1, a team of researchers led by Dr. Timothy M. Miller of Washington University, St. Louis, discovered that newer versions of the drug may be more effective at treating ALS than the earlier one that had been tested in a phase 1 clinical trial.

Cancer Research Stalwart Rabson Dies

The cancer research and NIH communities are mourning the loss of long-time NCI senior leader Dr. Alan Rabson, who passed away July 4 at the age of 92.

With a distinguished scientific career that spanned six decades and included research on tumor virology and cancer pathology, as well as senior leadership roles at NCI, Rabson was highly respected at NIH and beyond.

Honored time and again for his commitment to science and to advancing cancer research, he was equally known for treating everybody he encountered—whether a member of Congress, a young researcher in training or a patient needing advice—with kindness and respect.

“There have been few people like Alan Rabson,” said NCI director Dr. Ned Sharpless. “The stories of his remarkable history at NCI, his immense dedication to his work and his love for his family are truly inspiring. It is no overstatement to say that we have lost a giant.”

Rabson’s wife of 59 years, Dr. Ruth Kirschstein, also was a highly respected and accomplished scientist at NIH. Kirschstein, who died in 2009, helped organize the research response to the AIDS epidemic and was the first woman to direct an NIH institute, leading the National Institute of General Medical Sciences for two decades.

The couple were known for their deep devotion to NIH and each other. In a 1998 interview, Rabson recounted: “I started [at NIH] by finishing my last



Long-time NCI senior leader Dr. Alan Rabson passed away July 4 at age 92.

PHOTO: BILL BRANSON

However, it was not to be. Washington, D.C., was simply too hot in the summer and there was no air conditioning at NIH, the eminent scientist explained in response to the young medical student’s request, so he usually worked in Berkeley, Calif., during those months.

During the Korean War, Rabson joined the PHS Commissioned Corps, studying virology at the Communicable Disease Center (now known as the

many people who participated in CC studies was simple: “We owed them the very, very best we could give them.”

Rabson was also legendary in his willingness to help people facing a cancer diagnosis to find the best options for their care, said NIH director Dr. Francis Collins. Whether it was a member of Congress or a young mother from the heartland, Collins recalled, Rabson always took time to understand the situation, build a relationship with the patient and family and help them sift through myriad possible clinical trials.

“Every year since 2012, the NIH Director’s Award ceremony has included the Alan S. Rabson Award for Clinical Care,” Collins said. “It goes to a deserving employee who demonstrates an exceptional commitment to assisting patients and their families who look to the NIH for help. Al’s half-century of service stands as the epitome of personal dedication to patient care at the National Institutes of Health.”

After 20 years in the pathology department, Rabson was named director of the forerunner to what is now NCI’s Division of Cancer Biology. During that time, he oversaw the division’s transition from an intramural research group that performed its own research to one that also managed the funding of cancer research performed by NCI-supported investigators at institutions across the country.

A Long-Time Leader and Role Model

The final stage of Rabson’s career at NCI began in 1995, when he was named deputy director of the institute by then-NCI director Dr. Richard Klausner.

“He came down to my office on the third floor and he said, ‘Would you be willing to be my deputy?’ And I said, ‘I can’t think of anything nicer,’” Rabson recounted.

Over the following several decades, he was asked by each new director to continue on in the deputy director role.

Current NCI deputy director Dr. Doug Lowy described Rabson’s invaluable service as a sounding board for each director and other NCI leaders on decisions both small and large as among his most important duties.

“He had an inimitable leadership style,” Lowy said. “When you talked with him, he spent most of the time trying to understand what you needed, so he could help you, rather than spending it figuring out how you could help him. He truly believed that if you were successful, he was successful.”

Rabson held clinical professorships at George Washington University and Georgetown University and received multiple awards from the Public Health Service for his clinical work and scientific contributions. He officially retired from federal service in 2015. That same year he was named a scientist emeritus at NCI. **R**

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“He had an inimitable leadership style. When you talked with him, he spent most of the time trying to understand what you needed, so he could help you, rather than spending it figuring out how you could help him. He truly believed that if you were successful, he was successful.”

—DR. DOUG LOWY

• • •

year of pathology training at the Clinical Center. My wife and I liked the place so much that we stayed here for the next 42 years.”

From Brooklyn to Bethesda

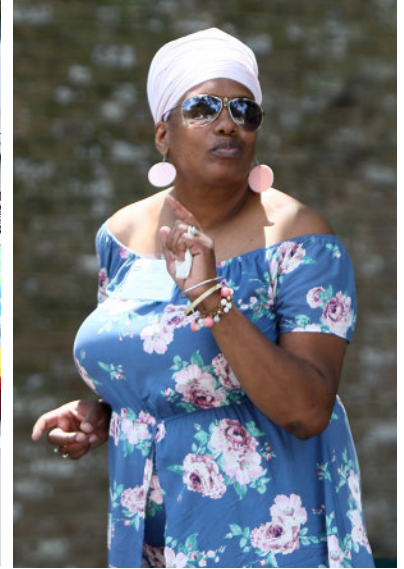
Born in Brooklyn in 1926, Rabson spent his first two decades mostly in New York, including completing his undergraduate degree at the University of Rochester and his medical degree at the State University of New York.

Remarkably, his first attempt to come to NCI was unsuccessful. Still in medical school, he applied to spend the summer at the institute working for well-known NCI biochemist Dr. Jesse Greenstein.

Centers for Disease Control and Prevention) and the University of Michigan, and pathology at the PHS Hospital in New Orleans.

He finally arrived at NIH in 1955, as a pathology anatomy resident. Rabson’s career at NCI began not long after, when he was recruited to study tumor-causing viruses and serve as a staff member in NCI’s pathology department at the Clinical Center.

For many years, the NCI Laboratory of Pathology performed the pathology for most of the NIH institutes conducting research at the CC. The mindset that Rabson and his colleagues had towards the



“At our Caribbean celebration, everyone is welcome,” said CANIH founder and president Althea Grey-McKenzie (l). “You don’t have to be from the Caribbean to join us.” Center, members of CANIH who call themselves the Fuego Dancers get down to a little reggae-Zumba. At right, an NIH’er moves to the music at CANIH Invigorate.

CANIH ‘Invigorate’ Celebrates Caribbean Culture

BY DANA TALESNIK

The sun emerged and a gentle breeze was blowing. It was the perfect day to take a cultural journey to the Caribbean.

On June 21, NIH’ers enjoyed regional Caribbean cuisine, music and dance on the Bldg. 31 patio at CANIH (Caribbean Association at NIH) Invigorate. The celebration, in its 11th year, featured foods from Haiti and Jamaica, reggae-Zumba, health and community information tables and international crafts.

“We called this year’s event CANIH Invigorate in an effort to support and motivate others to learn about Caribbean culture and food,” said CANIH founder and president Althea Grey-McKenzie, an event associate with the Foundation for Advanced

Education in the Sciences. “We’re restructuring the Caribbean Association here and, as we grow, we welcome the contributions of others to the group.”

The event, a collaboration with NIH’s R&W Association and the Caribbean-American Chamber of Commerce and Enterprise for the Greater Washington Area Network, donates proceeds to NIH charities. This year and last, CANIH donated to the Children’s Inn at NIH.

“This event supports the community,” said Grey-McKenzie. “It’s one way we give back.”

Grey-McKenzie started CANIH shortly after then-President George W. Bush signed a proclamation in 2006 designating June as National Caribbean-American Heritage Month. Having an official heritage month, she said, is a source of pride and gives the Caribbean-American community an opportunity to share their rich and diverse culture with the nation.

“We have done so much here to build the fabric of this country,” she said.

A native of Jamaica, Grey-McKenzie added, “I love the beauty, creativity and tenacity of Jamaica and its people. Our saying ‘*Wi liikkle, but wi tallawah*’—meaning we may be a little country, but we have huge aspirations—is how I share what makes us great.”

During the event, several CANIH members who dub themselves the Fuego Dancers led a reggae-Zumba workout. One of the dancers, Fiona Vaughans, is the treasurer of CANIH and has worked at NIH for 14 years. Originally from Jamaica, she came to the United States to pursue her doctorate in cybersecurity. She’s now an IT program manager at NCI. What does she miss most about Jamaica?

“I miss the gorgeous beaches and the peace of mind.”



ABOVE: CANIH members, including the littlest new member, visit with members of CACCE-GWAN, the Caribbean-American Chamber of Commerce and Enterprise for the Greater Washington Area Network. RIGHT: Attendees enjoy regional cuisine on the Bldg. 31 patio.



PHOTOS: CHIA-CHI CHARLIE CHANG