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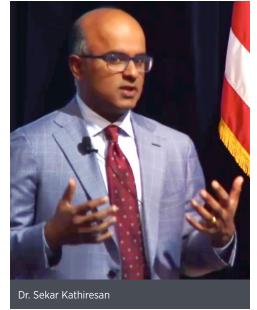
'SMOOTHIE, NOT FRUIT SALAD'

Role of Genes, Lifestyle Explored in Heart Attack

BY RICH MCMANUS

What if you knew you could spare yourself and your loved ones the devastation of heart attack-especially while you are still youngby paying attention to data you could have discovered at birth?

Owing largely to the massive amounts of data from large-scale genome-wide association studies funded by NIH and new population-based biorepositories such as the UK Biobank, scientists can now tease out the respective contributions of genetic predisposition and environmental exposure to the development of diseases, including heart attack.



In a Wednesday Afternoon Lecture on May 22 titled "Genes, lifestyle and risk for heart attack," Dr. Sekar Kathiresan, director of the Center for Genomic Medicine at Massachusetts General Hospital, director of the Cardiovascular Disease Initiative at the Broad Institute and professor of medicine at Harvard Medical School-at least until he gives all these up to become CEO of a company called Verve in mid-Julydescribed new avenues of preventing coronary artery disease, the leading global cause of mortality.

It has long been known that heart attacks run in families and that the younger the victim is, the more likely he or she drew an unfortunate inheritance. There are three main paths to one's genetic risk of myocardial infarction (MI), said Kathiresan: the monogenic model (4 genes stand out, especially FH, among a survey of many thousands, as conferring a 2- to 5-fold risk of MI); the polygenic model (common variant association studies have linked some 95 genetic loci to coronary risk. Summed up,

SEE KATHIRESAN, PAGE 6

COMPETING NEURONS

Neuroscientist Studies the Making of Memories

BY DANA TALESNIK

We've all had that light-bulb moment, suddenly recalling a memory, not even sure how we plucked it out of its latent state. Behind the scenes, there were all kinds of neurons. molecules and synapses at work.

Dr. Sheena Josselyn, senior

scientist at the Hospital for Sick Children in Toronto, has long studied what triggers the brain to make, retrieve and link memories.



Dr. Sheena Josselyn

SEE JOSSELYN, PAGE 8

PILLARS OF INSIGHT

Eurich Explores Why Self-Awareness Matters

BY DANA TALESNIK

Do you consider yourself an above-average leader? Do you think your staff and other

colleagues would agree?

When Dr. Tasha Eurich, an organizational psychologist, executive coach, researcher and best-selling author. asked the NIH audience assembled in Masur Auditorium to rate themselves as leaders, friends



and drivers, many proud hands were raised

SEE EURICH. PAGE 4



Horsing around at Police Awareness Day; p. 12.

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DiClemente To Give NIAAA Mendelson Lecture, July 11 in Masur

Dr. Carlo DiClemente will deliver the 2019 NIAAA Jack Mendelson Honorary Lecture on Thursday, July 11 at 1:30 p.m. in Masur Auditorium, Bldg. 10. His talk is titled "Is Relapse and Recycling Necessary for Recovery from Alcohol Use Disorder?"



DiClemente is an internationally distinguished scientist who has made groundbreaking contributions to our understanding of the process of human intentional behavior change. His research revolutionized the behavioral treatment and prevention of addiction and other health-related disorders.

He is co-developer of the transtheoretical model of behavior change (TTM), work which began in the field of smoking and addictive behaviors. The TTM is now used by researchers across multiple disciplines around the world, including alcohol treatment research, cancer prevention, HIV risk reduction and addictive behaviors.

DiClemente currently serves as professor emeritus of psychology at the University of Maryland, Baltimore County, and director of the MDQuit Resource Center, the Center for Community Collaboration and the Home Visiting Training Center at UMBC.

Graduate, Professional School Fair, July 17

The 12th annual NIH Graduate & Professional School Fair will be held on Wednesday, July 17 from 8:45 a.m. to 2:45 p.m. at Natcher Conference Center. The fair provides an opportunity for NIH summer interns (especially those in college) and postbacs, as well as other college students in the D.C. area, to prepare for the next step in their careers by exploring educational programs leading to the Ph.D., M.D., D.D.S., M.D./Ph.D. and other graduate and professional degrees. More than 200 colleges and universities from across the U.S. send representatives of their graduate schools, medical and dental schools, schools of public health and other biomedically relevant programs in the hope of recruiting NIH trainees.

The day will also include workshops on getting to graduate and professional school; M.D./Ph.D. programs; interviewing; and careers in public health, computational biology/bioinformatics, psychology and dentistry. Exhibits will be open from 9:45 a.m. to 1:45 p.m. A list of institutions planning to attend and registration information can be found at https://www.training.nih.gov/gp_fair.



CRC Atrium Rings with Music

The atrium of the Clinical Research Center resounded with music this spring, delighting staff, patients and visitors. On May 21, the National Symphony Orchestra Ensemble (below, I), featuring (from I) Julianna Nickel, flute; Sophia Kim Cook, piano; Robert Rearden, horn; and James Nickel, horn, gave a concert. On May 30, Chris Urquiaga (below, r), a local singer-songwriter and pianist who performs in English, Spanish and Portuguese, played an array of pop, R&B and Latin music. And on June 6, the University of Maryland Jazz Combo (above) presented a selection of jazz standards, old and new, bringing a sense of the classic and the contemporary to a live jazz setting. They are (from I) Jon Ozment, piano; Gerry Kunkel, guitar; Timothy Powell, saxophone; Joey Antico, drums; John Previti, acoustic bass. For a list of upcoming concerts, visit https://clinicalcenter.nih.gov/ocmr/music.html.

PHOTOS: DEBBIE ACCAME





Webinar on Design of Mobile Health Interventions, July 9



Dr. Predrag Klasnja

Join the Office of Disease Prevention for a Methods: Mind the Gap webinar with Dr. Predrag Klasnja on "Using Micro-Randomized Trials to Optimize the Design of Mobile Health Interventions." The event will take place on Tuesday, July 9 at 2 p.m.

Klasnja will describe how micro-randomized trials can be used to make data-driven decisions about how individual components of mobile health interventions should work to optimize their effectiveness.

He is an assistant professor in the School of Information at the University of Michigan and a scientific investigator at the Kaiser Permanente Washington Health Research Institute. He works at the intersection of human-computer interaction and behavioral science and studies how mobile technologies can help individuals make and sustain lifestyle changes needed to improve their health.

Register at https://prevention.nih.gov/education-training/methods-mind-gap/using-micro-randomized-trials-optimize-design-mobile-health-interventions. The webinar will be recorded and available on the ODP website within about a week.

Pobiner Takes Evolution Studies from Field to Classroom

BY MOHOR SENGUPTA

How did human beings evolve? Where did we come from? What did our prehistoric ancestors eat? And why is all that information relevant today? These are some of the questions that Dr. Briana Pobiner, keynote speaker at an NIDDK scientific conference, addressed recently.

Pobiner is a paleoanthropologist, research scientist and museum educator with the Human Origins Program at the Smithsonian National Museum of Natural History. She received a Ph.D. in anthropology from Rutgers University in 2007. Her area of research interest, which is evolution of meat-eating habits in humans, took her to Africa for field work on butchery with early stone tools. After having spent several months in the grasslands of Kenya, Pobiner has hypothesized that early humans often scavenged leftovers from kills by big carnivorous animals. In her talk, she shared her findings on the early food habits of humans before the advent of hunting.

There is evidence of meat in the diet of humans from as far back as 3.4 million years ago. However, hunting for food did not evolve until the invention of specific hunting tools, some half a million years ago. In the 3-million-year period in between these two events, prehistoric humans were predominantly scavengers, says Pobiner, who studied modern-day prey carcasses at the OI Pejeta Conservancy in Kenya. Our ancestor *Homo erectus* would get many of the calories it needed from the leftover flesh of a big prey animal, she said.

That we evolved from earlier human species, such as *Homo erectus*, is still an uncomfortable scientific proposition for many. At the Smithsonian, Pobiner also leads the Human Origins Program's education and outreach efforts. Her primary objective is to familiarize and interest the public in the concept of evolution.

These efforts have been successful in fostering

respectful dialogue to dispel common misconceptions about human origins. The Hall of Human Origins exhibit at the Smithsonian helps visitors think in a scientific way about evolution.

In the latter part of her talk, Pobiner focused on the Human Origins traveling exhibition that appeared in 19 public libraries across the U.S. from April 2015 to April 2017. The sites



Dr. Briana Pobiner
PHOTOS: CHIA-CHI CHARLIE
CHANG

were chosen deliberately, targeting some regions of the country where acceptance of evolution is a challenge. The exhibit welcomed people from diverse communities into science conversation and included workshops for teachers. Public response

That we evolved from earlier human species, such as Homo erectus, is still an uncomfortable scientific proposition for many.

to the initiative was encouraging, with 73 percent of the skeptical participants later reporting that they ended up enjoying the exhibit and about half of them saying they learned something new.

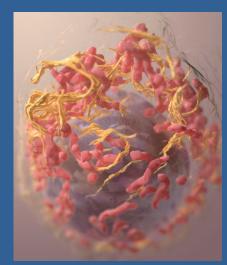
Another focus of the education and outreach efforts is to present the concept of human evolution in high school classrooms. This was a

challenge because fewer than 40 percent of high school students accept the theory of evolution, Pobiner said. Goals of the initiative were to create evolution-centered curriculum units and teaching resources for high school teachers. Classroom activities included discussion about evolution and promoted innovative methods, such as historical role play, which eventually became highly popular among students.

Understanding and acceptance of the science of evolution by these high school

students, some of whom had previously rejected the concept, has been a remarkable achievement of the education and outreach effort of the Human Origins Program. But there are large parts of society, predominantly among adults, where religious concepts overrule the acceptance of scientific findings. Pobiner admits it is not always possible to reach everyone.

In the Q&A session following her talk, it was asked, "How is the U.S. unique in science education?" Pobiner said the U.S. ranked second from last among 34 countries in acceptance of evolution, according to a 2005 survey. The U.S. is also the only country where an anti-science approach is politicized.



ON THE COVER: 3-D structure of melanoma cell derived by ion abrasion scanning electron microscopy

IMAGE: SRIRAM SUBRAMANIAM, NCI

The NIH Record

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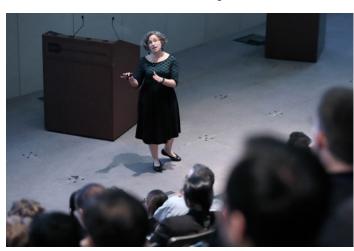






The NIH Record is recyclable as mixed paper.





Eurich

CONTINUED FROM PAGE 1

for "above average" in each category. It was a revealing exercise about the power of self-awareness.

"Most people believe they're above average on every socially desirable characteristic," said Eurich at a recent Deputy Director for Management seminar. Laughter then erupted when she said, "The least competent people are the most confident about their abilities and performance."

Almost everyone thinks they're self-aware but only about 10-15 percent of people have achieved the status. Having self-awareness, said Eurich, means fully knowing who you are—your values, passions, goals, personality, strengths and weaknesses—and understanding how others perceive you.

"People who are self-aware at work are better performers and more promotable," said Eurich. "They tend to be more respected and trusted co-workers and more effective leaders." Beyond the workplace, she added, they're generally happier in their personal relationships and tend to raise less narcissistic children.

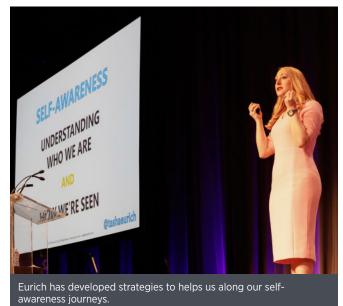
All around the world, in every age group, "We're all becoming more self-absorbed and less self-aware," she said. "We need to gently stop assuming we're already self-aware. Every one of us probably has more work to do than we think."

After working with senior-level leaders for more than a decade and surveying thousands of people, Eurich has developed strategies to help us along our self-awareness journeys. She outlined several pillars of insight, unique to each of us. The deeper we delve into them, the more we can cultivate our own self-awareness.

What are the values by which we live and work? What are our passions and aspirations? What environments give us energy? What are our patterns of behavior? How do we react to different situations and what thoughts and emotions underlie that behavior? What impact do we have on others?

Eurich then focused on the three pillars she considers especially important for leaders: our values, reactions and impact.

Identify your core values and find one that's the basis of your world, she said. Family. Health. Love. Service. Adventure.



Simplicity. Challenge. Knowledge...These are but a few examples. After identifying which are most important, check in with yourself periodically, she said. Did your behavior this week mirror your core values?

"When we're stressed, sometimes it's really easy not just to not reflect on our values and behavior, but to do the exact opposite," Eurich said. "Values are often aspirational. Just because it's a value doesn't mean we do it perfectly on a regular basis."

Eurich gained some new insights from conducting something akin to a self-awareness clinical trial, tracking 50 people she dubbed "self-aware unicorns," a group of admittedly unaware people who transformed themselves over time through coaching. They taught Eurich a few things, even upending common wisdom.

Such was the case for understanding reactions. Eurich thought she did. It seemed



"People who introspected were less happy, more stressed, more depressed, more anxious, less in control of their lives and less happy in their jobs," said Eurich.

logical to assume that making the best decisions in the moment requires us to be self-reflective. The unicorns and hundreds of other surveys revealed the opposite.

"People who introspected were less happy, more stressed, more depressed, more anxious, less in control of their lives and less happy in their jobs," said Eurich. It's not that introspection is a bad thing, she realized, but that most of us approach it the wrong way. Most of us ask why when we should be asking what.

"The more we ask why, the more we ruminate," she said.

Instead of asking why am I stressed, ask what alterable patterns can I find in my stress. Instead of asking why am I unhappy, perhaps ask what upsetting situations can I avoid.

"Why questions draw us to our limitations; what questions help us see potential," said Eurich. "Why questions can depress us and make us emotional. What questions help us to be more logical and action-oriented... and help us move forward."

Leaders also must consider the impact they want to have on others and how they want to be perceived by others. Asking for feedback can be daunting, but it's important for leaders to request and heed it.

Most unicorns listed 5 or fewer people they regularly came to rely on for feedback. They were picky about who to ask, said Eurich, acknowledging that sometimes feedback is not well-intentioned or helpful. Solicit feedback, she said, from loving critics—those you believe have your best interest at heart, but also those you believe will be truthful.

There's always room to grow and, in the process, said Eurich, "you're growing your self-compassion by seeing yourself more clearly." Go easy on yourself. Aim for incremental improvements. "Try to be as focused as possible and that's how you start to make dramatic improvements over time," she concluded.



NIDCR Celebrates Its History, Looks Ahead

BY ANNA MARIA GILLIS

NIDCR celebrated its origins and set its course toward 2030 during a recent craniofacial research symposium to mark its 70th year. "We were one of the first institutes," said Dr. Martha Somerman, NIDCR director. She described the "incredible epidemic of infectious disease of the oral cavity"—commonly known as tooth decay—that had disqualified men and women from military service in World War II as the impetus to form a dental research institute.

"Looking Back and Facing the Future: From NIDR to NIDCR," held in Lipsett Amphitheater on May 6, highlighted how science and clinical care have changed since 1948, when NIDCR's predecessor, the National Institute of Dental Research, was created by Congress. The symposium's speakers, a mix of NIDCR intramural and extramural scientists, covered craniofacial anomalies, tissue regeneration, skeletal development, wound healing, periodontal disease, salivary biology and other topics.

To more accurately reflect the institute's scope of research, "Craniofacial" was added to NIDR's name in 1998 during the tenure of Dr. Harold Slavkin, NIDCR's director from 1995 to 2000. He recounted some of the earliest work in the field by a Pennsylvania orthodontist named Dr. Herbert Cooper.

In Lancaster County, where he practiced, Cooper noticed many individuals with craniofacial deformities. "He felt overwhelmed," said Slavkin, so Cooper enlisted the help of the community's social services providers, pharmacists, pediatricians and speech and language professionals. With these people, he created care teams, and, in 1938, Cooper formed the Lancaster Cleft Palate Clinic.

Today, interprofessional health care teams are used around the world to help people with both



NIDCR director Dr. Martha Somerman and NIH principal deputy director Dr. Lawrence Tabak, who once led NIDCR

congenital and acquired craniofacial anomalies. The impact of these disorders is great, said Slavkin, dean emeritus of the Herman Ostrow School of Dentistry, University of Southern California. He said in the United States, a million people have serious craniofacial defects. He estimated that the total direct and indirect global health care costs for these conditions are around \$500 billion per year.

"Our face is our identity," said Dr. Yang Chai, a professor, surgeon and director of USC's Center for Craniofacial Molecular Biology. When there are defects, it affects quality of life.

To improve outcomes for people with cleft palate, a common birth defect, Chai's lab explores several research threads. Data from FaceBase, an NIDCR-funded resource for craniofacial researchers, helped Chai and his colleagues create a mouse model that has let them understand soft palate development. Critical for swallowing, breathing and speaking, the soft palate is often affected in patients with cleft palate.

His lab also has teamed up with biomedical engineers to make a 3-D printed scaffold that can be seeded with stem cells and placed into defective

bone to prompt its regeneration. In animal studies, this method has led to high-quality bone regeneration, said Chai. His goal is to use 3-D scaffolds to better repair cleft palates and other craniofacial defects in humans.

Like Chai, Dr. Chia Soo aims to improve the body's ability to heal. She and her colleagues at UCLA's School of Medicine have shown that a protein called fibromodulin is required for scarless tissue repair in rodents. Soo's group has spent the two decades since that discovery developing a fibromodulin-based peptide therapy that is currently being tested in clinical trials for its safety and efficacy for human wounds. If successful, the compound may be used to reduce scarring during surgery.

The study of rare diseases also could help scientists find better ways to treat common conditions. For example, NIDCR clinical investigator Dr. Niki Moutsopoulos and her colleagues have been evaluating patients with a rare genetic disorder called leukocyte adhesion deficiency type 1 (LAD1). People with the con-

dition are prone to frequent infections and develop periodontal disease at a young age.

Her team found that the periodontal lesions of people with LAD1 have an overabundance of immune cells called T helper 17 (Th17) cells. The researchers have tested a drug called ustekinumab that targets Th17 cells.

One 19-year-old patient with LAD1 had such severe periodontal disease that he had begun losing the bone supporting his teeth; Moutsopoulos wanted to find a way to save them. After receiving the drug, the young man's oral condition improved, as did an open lesion on his back. These findings are leading to insights into the mechanisms and potential treatments for the more common form of periodontal disease that affects up to half of U.S. adults.

Going forward, what do NIDCR's former and current directors hope for? For Dr. Lawrence Tabak, NIH principal deputy director and NIDCR's director from 2000 to 2010, it is to take full advantage of the power of data. "Our ability to collect and analyze data at scales that 8 to 10 years ago we could not have imagined is today a real possibility," he said.

Slavkin wishes to see more "evidence-based policy making," and the possibility that "all people have comprehensive, quality health care."

Dental, oral and craniofacial research is moving forward on many fronts, said Somerman, who outlined research priorities that emerged from the institute's strategic visioning initiative, NIDCR 2030.

She envisions a future where patients benefit from autotherapies that harness the body's ability to heal itself. She looks forward to the availability of more comprehensive salivary diagnostics, improvements in machine learning to speed diagnosis, increased understanding of the microbes that reside in us and more public-private partnerships to get treatments to patients faster.

By 2030, Somerman said, dental, oral and craniofacial health should "be understood within the context of the whole body," and precision health should be available for everyone.



PHOTOS: CHIA-CHI CHARLIE CHANG



Kathiresan CONTINUED FROM PAGE 1

these can equal the predictive power of the monogenic model); and somatic mutations that arise in the body over a lifetime.

Kathiresan and his colleagues have invented a polygenic risk score that one could theoretically learn at birth as a way of navigating away, throughout a lifetime, from the reefs and shoals of heart attack risk.

Like not a few other WALS lecturers, Kathiresan credits early training at NIH as crucial to his development as a scientist. He spent the summer of 1993 here, after his first year at Harvard Medical School, and "had a terrific experience, especially with respect to becoming a physician-scientist."

And like many other speakers, "Our science has been inspired by patients," he said. Kathiresan summarized the case of a 42-year-old man who suffered a heart attack and died 10 days later. Ironically, only 6 months earlier, the man had seen a cardiologist who calculated the victim's lifetime risk of MI as 1.7 percent, or "low," using a global risk score sanctioned by the American College of Cardiology and the American Heart Association.

Confident that he could surpass that woeful predictive capability, Kathiresan and colleagues set out to determine the average risk of MI by combining insights on the genetic risk of MI, countered by the genetic basis of resistance, or protection from, MI.

MI has two phases, he said. The first is chronic—decades of plaque buildup in coronary arteries. The second is when a tear forms on the inner wall of an artery on the surface of the heart. A clot forms, stopping

"Our science has been inspired by patients."

~DR. SEKAR KATHIRESAN

• • •

blood from flowing. If the blockage lasts for more than 20 minutes, necrosis sets in and heart muscle dies.

Although there are both heritable and lifestyle components of MI risk (and most risk of heart attack is from non-genetic causes, such as smoking, diabetes, high BMI, sedentary habits and other lifestyle factors), the best risk factor measures until recently have been lipoproteins—high-density (HDL, or "good cholesterol"), low-density (LDL, or "bad cholesterol") and so-called TRLs, triglyceride-rich lipoproteins.

However, Kathiresan and his colleagues have recently found that high levels of HDL are, in fact, not protective. Furthermore, medicines designed to raise HDL, in hopes of offering protection, have no effect on cardio-vascular outcomes. HDL is now considered a non-causal marker, no longer meriting the label "good." It simply marks a low level of TRLs. "We may have had it backwards for the last 30-40 years," Kathiresan said.



Statins are beneficial in lowering risk, whether from polygenic or monogenic causes, said Kathiresan. And lifestyle adjustments—not smoking, lowering BMI, eating properly and getting enough exercise and sleep—can cut risk by up to 50 percent. "DNA is not destiny here," he said.

Kathiresan predicts that within the next 5 years, people will know their polygenic risk score number as readily as they now know their LDLs.

He said that for most common, complex diseases such as heart disease and cancer, once one has teased out the contributions of heredity, lifestyle and somatic mutations, risk turns out to be "a smoothie [a blend of risk factors], not a fruit salad [separate and distinct driver pathways]."

He concluded with recent research results that may offer the greatest hope of all. Certain rare populations in the world carry a mutation to the APOC3 gene, which dramatically lowers triglyceride levels. Medicines are now being sought to do what this mutation accomplishes naturally.

Kathiresan acknowledges that his passion to make a difference in preventing MI has yet another personal dimension: his brother Senthil died 7 years ago of heart attack.

As he takes the reins at Verve this summer, Kathiresan has three major goals: interpret patients' genomes early in life, intervene with diet, exercise and medication and, perhaps most importantly, develop new treatments that mimic the effect of resistance mutations.

As NIH director Dr. Francis Collins had said in his introduction to the lecture, "Sek is the person I would most want to give a lecture on genes, lifestyle and risk for heart attack."



New Fellowship in Ophthalmic Genetics

The National Eye Institute is partnering with the International Council of Ophthalmology to offer a fellowship at NEI in ophthalmic genetics research.

This first such collaboration between the two organizations will bring to NEI an early-career clinician from a country designated by the World Bank as lower- or middle-income. The fellow will spend a year working in NEI's Ophthalmic Genetics and Visual Function Branch. NEI clinical director Dr. Brian Brooks will serve as the fellow's mentor.

The fellow will gain experience that is likely unavailable in his or her home country. For NEI, the fellowship is an opportunity to engage in "soft diplomacy," according to Dr. John Prakash, associate director for NEI international programs.

"Following this kind of experience, fellows will not only promote NEI," said Prakash. "They will become opinion leaders in their home countries and influence their government's policies. And the ultimate benefit will be to the patient population around the world."

NCI Workshop Explores Liver Cancer, Which Is on Rise

More than 150 investigators and clinicians with expertise in basic science, epidemiology, early detection and clinical research gathered at NIH recently to assess the state of the science regarding the progression of fibrosis to liver cancer. The objectives of the workshop "Liver Fibrosis to Cancer" were

Liver cancer incidence and mortality

1,200,000
1,000,000
800,000
400,000
2010
2015
2020
2025
2030

Opening remarks from NCI acting director Dr. Doug Lowy

to understand the mechanisms and epidemiology of viral and non-viral causes of liver fibrosis and the progression to liver cancer.

In the United States, liver cancer is the second most lethal tumor. The rate of death from liver cancer increased by more than 43 percent between 2000 and 2016, and the incidence has nearly tripled in the last decade. Most liver cancers occur in patients

with an underlying liver disease, mainly as a result of hepatitis B or C virus infection or alcohol abuse. However, non-viral conditions such as non-alcoholic fatty liver disease, metabolic syndrome, diabetes and obesity can amplify the risk of liver cancer and they may soon become a leading cause of liver cancer in the U.S.

NCI acting director Dr. Doug Lowy opened the meeting by detailing the scope

of the problem. "The mortality rate from liver cancer has continued to increase, and you'll notice that there has been a plateauing of the incidence. I think that, with the new epidemic of hepatitis C infection, if it is left untreated, we are going to see a continuing resumption in the increase in the incidence of liver cancer." He also discussed a collaboration between NIH and CDC that is designed to address barriers to care.

There was a special emphasis on opportunities for interventions that could combine

basic research with translational research (biomarkers, reversibility of fibrosis/cirrhosis, etc.).

The final session highlighted funding opportunities, clinical trials, SEER-linked registries and other NCI resources that may be useful to the liver cancer community.—

Audrey Wellons

NIBIB's Tromberg Takes in View from Hill

NIBIB director Dr. Bruce Tromberg marked his sixth month on the job with a visit to Capitol Hill, where he shared his vision for biomedical imaging and bioengineering with congressional members and staff. Rep. Anna Eshoo (D) of California's 18th congressional district and the Academy for Radiology & Biomedical Imaging Research, an organization instrumental in advocating



for NIBIB's founding and acclaiming its ongoing impact, hosted a June 4 welcome reception at the Cannon House Office Bldg. Eshoo sponsored the bill that became P.L. 106-580 and created NIBIB as an institute at NIH in 2000. More than two dozen





congressional members and staff attended the event to learn about NIBIB and its research. At left, Tromberg (I) and Eshoo meet with Rep. Bill Flores (R) of Texas' 17th district as NCCIH director Dr. Helene Langevin looks on in the background. Above at left, Tromberg chats with Rep. Lisa Blunt Rochester (D) of Delaware's at-large congressional district. At right, he meets with Rep. Rob Bishop (R) of Utah's first congressional district.

PHOTOS: NIBIB, LISA NOVITSKY

Josselyn

CONTINUED FROM PAGE 1

It's a field that provides insights into how we learn and could lead to interventions for cognitive impairments and neurodegenerative diseases.

"My lab is really interested in understanding how the brain encodes, stores and uses information," said Josselyn, who spoke at a recent NIMH Director's Innovation Speaker Series lecture at the Neuroscience Center. "We think this is a real fundamental goal of neuroscience."

Building on basic research, Josselyn's lab began searching for the long-elusive engram, or memory trace—a change in the brain when something is encoded as a memory. Previous researchers searched for it for years but couldn't pinpoint the engram to a specific spot in the brain.

To begin her quest, Josselyn ran a simple Pavlovian conditioning experiment on mice. After a quick shock followed by a tone, she placed the mouse in a different setting and played the tone again. The moment the mouse froze to the tone would indicate memory formation.

Research has shown that neurons in the lateral amygdala are involved in the memory trace. "They respond both to the tone and to the shock," said Josselyn. "Yet there's a surprisingly small number, about 20 percent, that seem to be necessary to encode any one given fear memory."

In humans, fear memories are sparsely encoded in the amygdala, leading Josselyn to question why certain neurons are chosen to be an engram team player while others get excluded. Her experiments revealed the highly competitive nature of neurons.

"Eligible neurons seem to compete against one another," said Josselyn. "The ones that win this competition and actually become part of this fear memory engram are the ones with the highest level of transcription factor CREB [cAMP response element binding protein]."

It turns out that CREB holds important clues to memory formation in part because it can increase neuronal excitability. These enthusiastic neurons are more likely to get recruited into the engram.

When CREB was increased in a small portion of random neurons, the mice froze more often, indicating better memory.



Josselyn's experiments reveal the highly competitive nature of neurons.

PHOTOS: MARLEEN VAN DEN NESTE

Josselyn's lab then overexpressed CREB in select neurons and, after the mouse learned something, shone a light to turn off those cells overexpressing CREB; these mice showed a memory deficit.

"We were very excited about this," she said. "It was the first hint we'd gotten our hands, or at least our viruses, on the engram...

Josselyn is also studying what might cause memory disruptions in Alzheimer's disease. In recent experiments, she injected mice with amyloid beta, peptides that can induce neuron degeneration and disrupt synapses, which are prevalent in the brains of Alzheimer's patients. She then injected the transgenic mice with a peptide that would restore the synapse, which returned memory in these mice. Other researchers have made similar strides with various molecular interventions in animal models, she noted, but to date none have succeeded in people.

In these experiments, Josselyn also had another curious finding. In wild type mice, the neural freezing signature, or memory recall, started with individual cells, then evolved into a coordinated network activity. This pattern completion scheme was disrupted in the transgenic mice but was restored after the intervention.

"We think that events are represented by patterns of activity in cells that are active during an event, an engram, and we think memory retrieval involves recapitulation of this pattern of sequences."

Josselyn said it's time to take what researchers have learned so far about genes and circuit dynamics and use computational tools to look at all aspects of behavior.

In people, recalling a memory is an active process that could change the underlying engram. "You can change a memory [every time] you recall it," said Josselyn during the post-lecture discussion. "You can extinguish it. You can strengthen it. You can pair it with something new. When you change it, it becomes plastic again."

One attendee asked about the possibility of manipulating traumatic memories.

"When we retrieve an older memory, the neurons important in the recovery of this memory are active," she said, "and I think that gives us a really cool time window to try an intervention."

"Eligible neurons seem to compete against one another."

~DR. SHEENA JOSSELYN



These findings lead us to conclude that lateral amygdala neurons overexpressing CREB at the time of training are somehow necessary, or indispensable, for the subsequent expression of that fear memory."

Further experiments elucidated how some memories might be linked. In one study, Josselyn found that if two fear memory events occurred within 6 hours of each other, they were allocated to the same population of neurons, which linked the memories. Other researchers are currently studying this phenomenon in people, using functional MRI.

"They're looking at fMRI codes in broad brain regions," Josselyn said. "We're looking at specific populations of a small brain region, but the goal is to link up these human and these mouse studies."



Scientists found that our brains are more sensitive to pitch, the harmonic sounds we hear when listening to music.

IMAGE: STOCKBYTE/GETTY

Our Brains Appear Uniquely Tuned for Musical Pitch

In the endless search for understanding what makes us human, scientists found that our brains are more sensitive to pitch, the harmonic sounds we hear when listening to music, than our evolutionary relative the macaque monkey. The study, funded in part by NIH, highlights the promise of Sound Health—a joint project between NIH and the John F. Kennedy Center for the Performing Arts, in association with the National Endowment for the Artsthat aims to understand the role of music in health.

"We found that a certain region of our brains has a stronger preference for sounds with pitch than macaque monkey brains," said Dr. Bevil Conway, investigator in NIH's Intramural Research Program and a senior author of the study published June 10 in *Nature Neuroscience*. "The results raise the possibility that these sounds, which are embedded in speech and music, may have shaped the basic organization of the human brain."

The study started with a friendly bet between Conway and Dr. Sam Norman-Haignere, postdoctoral fellow at Columbia University's Zuckerman Institute for Mind, Brain, and Behavior and the first author of the paper.

At the time, both were working at MIT. Conway's team had been searching for differences between how human and monkey brains control vision, only to discover that there are very few. Their brain

mapping studies suggested that humans and monkeys see the world in very similar ways. But then Conway heard about some studies on hearing being done by Norman-Haignere, who, at the time, was a postdoctoral fellow in the laboratory of Dr. Josh McDermott at MIT.

"I told Bevil that we had a method for reliably identifying a region in the human brain that selectively responds to sounds with pitch," said Norman-Haignere. That is when they got the idea to compare humans with monkeys. Based on his studies, Conway bet that they would see no differences.

A brain imaging study has found that the human brain strongly favors harmonic sounds over noise, compared to the macaque monkey brain. The results suggest that speech and music may have shaped our brain's hearing circuits. The two species appear to have evolved differences in the functional organization of brain regions involved in pitch perception.

Sleeping with Artificial Light at Night Associated with Weight Gain in Women

Sleeping with a television or light on in the room may be a risk factor for gaining weight or developing obesity, according to NIH scientists.

The research, which was published online June 10 in JAMA Internal Medicine, is the first to find an association between any exposure to artificial light at night while sleeping and weight gain in women. The results suggest that cutting off lights at bedtime

could reduce women's chances of becoming obese.

The research team used questionnaire data from 43,722 women in the Sister Study, a cohort study that examines risk factors for breast cancer and other diseases. The participants, ages 35-74 years, had no history of cancer or cardiovascular disease and were not shift workers, daytime sleepers or pregnant when the study began. The study questionnaire asked whether the women slept with no light, a small nightlight, light outside of the room or a light or television on in the room.

Scientists used weight, height, waist and hip circumference and body mass index measurements taken at baseline, as well as self-reported information on weight at baseline

and follow-up 5 years later. Using this information, the scientists were able to study obesity and weight gain in women exposed to artificial light at night with women who reported sleeping in dark rooms.

The results varied with the level of

artificial light at night exposure. For example, using a small nightlight was not associated with weight gain, whereas women who slept with a light or television on were 17 percent more likely to have gained 5 kilograms, approximately 11 pounds, or more over the follow-up period. The association with having light coming from outside the room was more modest.

Also, the scientists wondered if not getting enough rest factored into the findings.

"Although poor sleep by itself was associated with obesity and weight gain, it did not explain the associations between exposure to artificial light while sleeping

and weight," said

corresponding author Dr. Dale Sandler, chief of the Epidemiology Branch at NIEHS.

Sleeping with a television or

IMAGE: FATCAMERA/GETTY

light on may be a risk factor for gaining weight, study finds.

Vitamin D Does Not Prevent Type 2 Diabetes in People at High Risk

Taking a daily vitamin D supplement does not prevent type 2 diabetes in adults at high risk, according to results from a study funded by NIDDK. The Vitamin D and Type 2 Diabetes (D2d) study enrolled 2,423 adults and was conducted at 22 sites across the United States. These findings were published in the New England Journal of Medicine and presented at the 79th scientific sessions of the American Diabetes Association in San Francisco.



Taking a daily vitamin D supplement does not prevent type 2 diabetes.

IMAGE: ANILAKKUS/ISTOCK

D2d is the largest study to directly examine if daily vitamin D supplementation helps keep people at high risk for type 2 diabetes from developing the disease. The study included adults age 30 or older and assigned participants randomly to either take

4,000 international units of the D3 (cholecalciferol) form of vitamin D or a placebo pill daily. All study participants had their vitamin D levels measured at the start of the study. At that time, about 80 percent of participants had vitamin D levels considered sufficient by U.S. nutritional standards.

"Observational studies have reported an association between low levels of vitamin D and increased risk for type 2 diabetes," said Dr. Myrlene Staten, D2d project scientist at NIDDK. "Additionally, smaller studies found that vitamin D could improve the function of beta cells, which produce insulin. However, whether vitamin D supplementation may help prevent or delay type 2 diabetes was not known."

The study screened participants every 3 to 6 months for an average of 2.5 years to determine if diabetes had developed. Researchers then compared the number of people in each of the two study groups that had progressed to type 2 diabetes.

At the end of the study, 293 out of 1,211 participants (24.2 percent) in the vitamin D group developed diabetes compared to 323 out of 1,212 (26.7 percent) in the placebo group—a difference that did not reach statistical significance. The study was designed to detect a risk reduction of 25 percent or more.



Dr. Richard Chadwick listens to talks from mentees and collaborators at his retirement symposium in April.

NIDCD's Chadwick Retires

Dr. Richard Chadwick retired from NIH in April after 39 years of research and service. He spent the last 23 years at the National Institute on Deafness and Other Communication Disorders as chief of the section on auditory mechanics. He continues to serve as a scientist emeritus.

"Dr. Chadwick was one of the first researchers to study bioengineering as we know it today, promoting it internationally to spark interest in the budding field before it was standard curriculum at universities," said Dr. Andrew Griffith, NIDCD scientific director. "His unique and extremely collaborative approach to research has yielded fundamental discoveries about cell mechanics and fluid dynamics within the inner ear as well as other types of tissues and cells."

Chadwick began his career in mechanical engineering, earning a bachelor's and then a master's degree from Cornell University in 1966. He went on to earn a Ph.D. in aeronautics and astronautics from Stanford University in 1971. Chadwick then joined the engineering faculty at the Technion-Israel Institute of Technology, Haifa, Israel, in 1971, where he began to study the mechanical properties of the cochlea, the organ of hearing in the inner ear. He moved back to the United States in 1975 to work as a research fellow in chemical engineering at the California Institute of Technology before becoming an adjunct associate professor at the University of California, Los Angeles, in 1977.

Chadwick then joined NIH's Bioengineering and Instrumentation Branch in 1980, later leading the biomechanics group.

"When I first arrived at NIH, there was no perimeter gate; it was an open campus," Chadwick said. "However, the campus was not open about mixing engineering, physics and math with biology. There is much less resistance now. I hope I had something to do with it."

After NIDCD was established in 1988, Chadwick began collaborating with scientists at the institute, reentering the field of cochlear dynamics. In 1996, he transferred to NIDCD as a senior investigator and chief of the section on auditory mechanics. In 2006, Chadwick was elected as a fellow of the American Institute for Medical and Biological Engineering.

Chadwick was integral to the development and use of atomic force microscopy (AFM). He described how to use AFM with modeling to gain insights into soft tissues. He later pioneered a modified version of this technology called non-contact AFM, which allows researchers to study tissues without physically touching—and thus damaging—their delicate structures. With this method, Chadwick and his collaborators have been able to gain insight into the behavior of tissue, such as the tissue necessary for sound detection in the inner ear.

Chadwick's work has increased knowledge of the hearing process through an artful interweaving of mathematical, physical and biological approaches. One of his many research contributions was an insight into the structure of the cochlear spiral. The reason for the snail shape of the cochlea in mammals had been elusive. He and his collaborators used cues from famous architectural structures such as whispering galleries—where someone can hear another's whisper from across a large enclosed space, typically an area with curved walls—to show that the spiral curvature is critical to amplifying sensitivity to low frequency sounds.

Reflecting on his interdisciplinary work and life in general, Chadwick said that "there is an intersection between science and art. Both are intended to communicate a message and to make people feel something."

Chadwick has had a long history of mentoring and advocating for women in science. One of the speakers at an April retirement symposium in Chadwick's honor was Dr. Núria Gavara, associate professor at Queen Mary University of London. She was a postdoctoral fellow in the Chadwick lab and then became a long-term collaborator.

Gavara commented on the importance of being kind in the competitive world of biomedical research. "Being kind to those you supervise is not always easy. It is a choice. In this regard, Richard has been making the right choices for 40 years."

NINDS's Hart Retires After 30 Years of Federal Service

BY SHANNON E. GARNETT

In her career spanning 53 years, Nancy Hart has had many roles—some formal such as naval officer, nurse, professor and writer—and others perhaps not as formal, like CFC keyworker extraordinaire, stroke education champion supreme and overall NINDS outreach program cheerleader. On May 31, she added another title to the list—jubilant retiree. After 30 years of service in the federal government, 23 with NINDS, Hart has officially retired.

"After working fulltime since 1966, I thought now



NINDS director Dr. Walter Koroshetz presents Nancy Hart with a plaque thanking her for "her years of outstanding service, dedication, quidance and support."

PHOTO: ANDREA VAREA

is the time to start a new chapter in my life and do some things I haven't been able to do," said Hart.

A native of Bexley, Ohio (a suburb of Columbus), Hart graduated from Bexley High School in 1962 and earned her bachelor of science degree in nursing in 1966 from the University of Michigan School of Nursing. She began her career as a commissioned officer in the Navy Nurse Corps stationed at Bethesda Naval Hospital/National Naval Medical Center (NNMC), where she cared for wounded Marines returning from Vietnam.

"My father was a general practitioner and my mother and her three sisters were trained as nurses," said Hart. "I was fascinated to hear the stories my mother and aunts told about their nursing experiences and thought it would be a wonderful way to help and serve others. And I loved biology and chemistry in high school."

After serving a 3-year tour of duty and attaining the rank of lieutenant, she applied for a job at NIH and began working as a research nurse—first in cancer, primarily with leukemia patients, and later with patients being treated for manic depression.

In 1971, Hart earned her master's degree in health education and human growth and development from the University of Maryland. She began her teaching career in 1975, serving a year as an instructor at American University, where she created and taught a workshop on adolescent suicide. She left AU in 1976 to join the Catholic University staff as an assistant professor of pediatric nursing and human growth and development.

After leaving there in 1978, she became a nursing instructor at Suburban Hospital, where she developed programs designed to on-board new nurses and technicians and created seminars for diabetic patients and their families.

Hart joined Holy Cross Hospital in 1981 as a teaching specialist, creating the first diabetic

multidisciplinary health education program for the then-450-bed nonprofit acute care facility. From Holy Cross, Hart moved to work at Options and Choices where she was an advanced nurse clinician and educator, developing health education programs for clients across the country—covering a wide array of health issues from mental health conditions to gastrointestinal disorders.

Before coming to NINDS, Hart returned to NNMC as assistant director of the health promotions department. There, her efforts focused on creating and evaluating health promotion education programs for active duty, retired and civil service personnel. She joined NINDS on Nov. 24, 1996, as a scientific and medical coalition coordinator.

"I have always been passionate about prevention, so I wanted to work in an area where I could play some part in preventing stroke, and this job was a fantastic opportunity to do just that...and on a national level," Hart said.

At NINDS, she helped launch "Know Stroke. Know the Signs. Act in Time."—a nationwide educational campaign to increase awareness of new treatments and protocols for stroke. She also responded to stroke inquiries from the public, health professionals and Congress and for 11 years served as a key member of the NIH-wide Take Your Child to Work Day committee—taking the lead in soliciting NINDS scientists and staff to create educational and interactive activities for children.

Hart helped create the Unraveling the Mysteries of the Brain series—an NINDS science educational seminar series for nonscientists. She also served as the first coordinator for the newly formed Parkinson's disease coordinating committee and was a member of the NINDS social media team. She organized NINDS's efforts in the USA Science & Engineering Festival and Brain Awareness Week—an international campaign to increase public awareness of brain research.

Among Hart's most satisfying accomplishments was her work as coordinator of the Brain Attack Coalition. BAC is a group of professional, voluntary and government organizations dedicated to setting direction, advancing knowledge and communicating the best practices to prevent and treat stroke. In April 2017, Hart, a founding member, and BAC marked their 20th anniversary.

"Working with the BAC has given me the opportunity to work with a very diverse group of innovative, creative, dynamic people devoted to improving stroke care. And it is rewarding to think, perhaps, that I have made some contribution to improving the quality of life for people suffering from stroke and perhaps preventing a stroke from occurring," said Hart.

At their March meeting, BAC members presented Hart with a plaque thanking her for "her years of outstanding service, dedication, guidance and support. Her efforts have improved stroke care for millions of patients."

Throughout her career, Hart received numerous awards and accolades, including the Allene Van Son Diabetes Educators Award; several NINDS group merit awards for teamwork on stroke; and a special act group award for her role in the 2018 Stroke Twitter chat.

In 2011, Hart and colleagues won a gold Plain Language Award, a Blue Pencil Award and a NINDS Group Merit Award for concept development of an interactive exhibit—the Lobe-oratorium.

In retirement, Hart plans to decompress, relax and spend time with her daughter, son-in-law and four grand-daughters. In the fall she intends to take classes: "I am happiest when I am learning new things."

In parting, Hart offered words from the late Sen. Edward Kennedy: "For all those whose cares have been our concern, the work goes on, the cause endures, the hope still lives and the dream shall never die.' This quote has inspired me for many years. I kept it in a prominent place in my office so I could see it every day and will do the same in retirement."

Volkow Speaks, Receives Honorary Degree at UMBC

On May 23, NIDA director Dr. Nora Volkow delivered the commencement address at the University of Maryland, Baltimore County. Her speech honored graduates of the College of Natural and Mathematical Sciences, the College of Engineering and Information Technology and the Individualized Studies Program. In her address, Volkow inspired students to pursue career paths in the sciences. She also received an honorary doctor of science degree for her commitment to discovering innovative solutions to addiction.



Her full talk is available at https://youtu.be/XaFUXkUxgBY.

VRC Needs Healthy Volunteers

Vaccine Research Center researchers seek healthy volunteers, 18-50 years old, for a study evaluating an investigational vaccine that targets HIV. Compensation is provided. There is no risk of infection. To learn how to participate, call 1-866-833-5433, email vaccines@nih.gov or visit http://bit.ly/VRC-018.

People with Crohn's Disease Sought

NIAID is seeking individuals who have Crohn's disease where current or previous treatments have not worked to control symptoms.

Researchers are testing an investigational medication that may control the inflammation and symptoms of Crohn's disease. Study-related tests, medication and procedures are provided at no cost. Compensation may be provided for certain research-related procedures. Contact the Office of Patient Recruitment, 1-866-444-2214, prpl@cc.nih.gov (TTY for the deaf or hard of hearing: 1-866-411-1010). Read more at https://go.usa.gov/xNvGp. Refer to study 17-1-0101

Patients with Liver Disease Needed

NIDDK researchers seek volunteers to participate in a research study. For 30 weeks, participants will receive a medication called semaglutide (typically used for type 2 diabetes), aiming to improve their liver disease and help them lose weight. The study hopes to understand liver damage and its treatment in people with non-alcoholic fatty liver disease (NAFLD) or non-alcoholic steatohepatitis (NASH). Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010) or email prpl@cc.nih.gov. Read more at https://go.usa.gov/xmJ8q. Refer to study 19-DK-0072.

Suffered a Recent Head Injury?

NINR seeks research participants who have experienced a mild to moderate head injury in the last 30 days. The aim of the research is to explore why some people with a head injury go on to develop other conditions such as depression, post-traumatic stress disorder or post-concussion disorder. Compensation is provided. Contact the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010) or prpl@cc.nih.gov. Read more at https://go.usa.gov/xUaJ4. Refer to study 14-NR-0032.

Patients with OI Needed for Study

NICHD researchers seek individuals with osteogenesis imperfecta (OI) for study participation. Now enrolling children up to age 12 and people with OI of any age who were previously seen at NIH. For more information, call the Clinical Center Office of Patient Recruitment, 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010). Read more at https://go.usa.gov/xEYjh. Refer to study 18-CH-0120.

NIH Marks Police Awareness Week with Cookout, Exhibits

The NIH Police hosted their 27th annual NIH Police Awareness event on National Peace Officers' Memorial Day, May 15, on the front lawn of Bldg. 1. A number of local, state and federal law enforcement agencies attended, including units from the Metro Transit Police, Rockville City, Montgomery County, Gaithersburg, U.S. Park Police, U.S. Marshals and U.S. Department of Commerce. Several set up tables featuring examples of gear and equipment they use in their jobs.

The banner weather day brought out dozens of kids from the preschool/daycare communities at NIH who were delighted by visits with several K-9 officers and police on horseback. Children and adults both were also fascinated by gun-safety simulator drills and demonstrations of the remote-control robot used to handle suspicious packages.

"I didn't want to try it at first," said Sophia Grasmeder, a nurse in the Clinical Center's Office of Patient Safety and Clinical Quality, who was coaxed by coworkers into a practice exercise—retrieving a bomb, which was actually a tote bag—using the remote control robot. "I play Mario Kart [video game] with my son and my cart always ends up going around and around in circles and never getting anywhere. But this was much easier than a video game."

An NIH fire engine and other first responders as well as various NIH emergency management resources were also on hand at the event. The ever-popular cookout featured hot dogs, hamburgers, chicken and Italian sausages with onions and green peppers. NIH Police donate proceeds, about \$500 this year, from food sales. This year's charity supports families of police and firefighters who died in the line of duty. The organization is called Heroes, Inc., https://heroes.org/.

Police Awareness Week has been celebrated nationwide since 1962, when President Kennedy designated the memorial day to honor fallen law enforcement officers.



The event brought together a number of local, state and federal law enforcement agencies including units from Rockville City, Montgomery County and (above, r) Gaithersburg



Dozens of kids from the preschool/daycare communities at NIH are delighted by visits with police on horseback.



At the emergency management information table are (from I) NIH Police Deputy Chief Leslie Campbell; Mary Sparks, senior nurse manager, Office of Patient Safety and Quality Control; and David Haupt and Timothy Smith, both of the Division of Emergency Management.



At the grills are NIH Police Lt. Lawrence Brown (I) and Maj. Josh Minix. Proceeds from food sales, about \$500, were donated to Heroes, Inc., which supports families of police and firefighters who died in the line of duty.

PHOTOS: LISA HELFERT





At left, Ofcr. D. Kayal (I) of Metro Transit Police shows CC's Sophia Grasmeder how to use the remote control robot. At right, Ofcr. Dana Stroman (seated) of the Montgomery County Police Department talks with NIH Police Maj. Pamela Datcher.



Sgt. Alan Blaum with partner, K9 Copper, at the recent Police Awareness Week event in front of Bldg. 1