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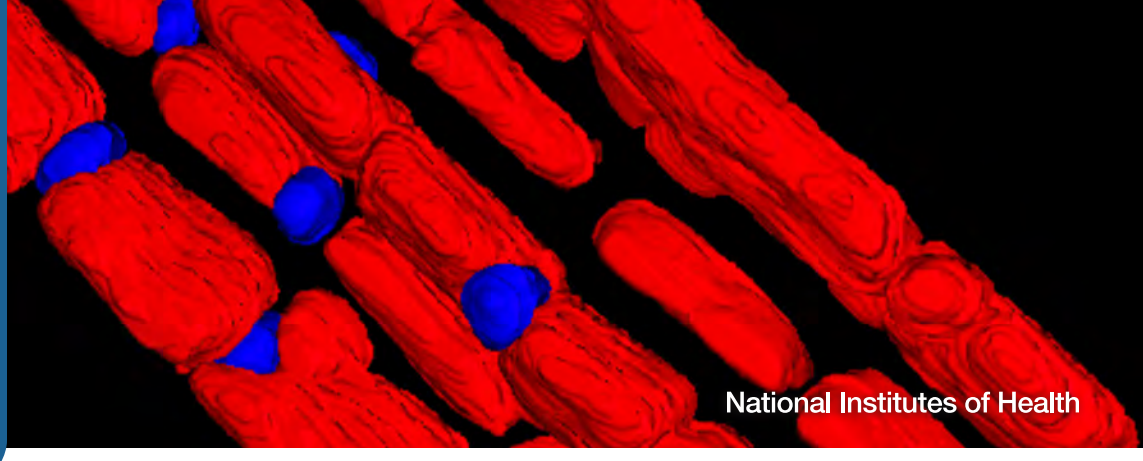


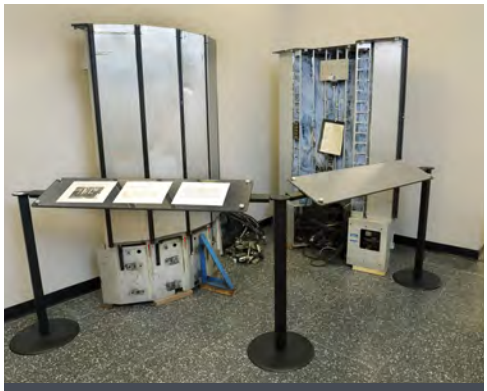
NIH Supercomputers Have Come a Long Way

BY DANA TALESNIK

Those tall, gray metal slabs nestled in the corner near the Bldg. 31 C-wing B3 elevators are not remnants of a defunct escalator. They are, in fact, a piece of fascinating history: NIH's first supercomputer—the Cray X-MP/22.

The Cray on display was the world's fastest supercomputer from 1983 to 1986, and the first one devoted solely to biomedical research. At capacity, it could perform 400 million calculations per second.

By today's standards, this Cray may seem rudimentary. But during the time it was used at NIH, from 1986 to 1992, "When you consider the alternative, sitting with paper and pencil or calculator, or even an abacus as at least one scientist did, this computer did quite a lot," said Michele Lyons, curator, Office of NIH History and Stetten Museum.



Not so super now: Exhibit on NIH supercomputing has modest debut.

The Cray X-MP/22, which had a price tag in the tens of millions of dollars, was the first supercomputer to contain dual processors that could be accessed simultaneously by one program. NCI's Laboratory of Mathematical Biology used the Cray to study molecular structure and conduct image processing, statistical analysis, basic DNA sequencing and crystallography.

How did this retired supercomputer come to rest in Bldg. 31? NIH's history office has more than 3,000 historical objects in storage and needs to move much of the collection this year, said Lyons. So they're trying to get as much on display as possible throughout the campus. Among the gems sitting in storage are paintings of distinguished NIH scientists, spectrometers, microscopes, DNA sequencers, an old giant centrifuge, lab clothing and hundreds of 20th century manuals.

When buildings are about to be demolished or renovated, history office staff swoop

SEE **SUPERCOMPUTERS**, PAGE 4

Surgeon General pays call on NIH; see p. 12.

ALSO THIS ISSUE

'RECALIBRATED WARRIOR'

Injured Veteran Shares Inspiring Story

BY DANA TALESNIK

A bad day at work usually doesn't have lifelong repercussions. When Travis Mills had a bad day at work—on Apr. 10, 2012—it would affect every day of his life going forward. Mills, a retired U.S. Army staff sergeant, lost all four limbs that day, during his third deployment in Afghanistan. Yet he's not just surviving, he's inspiring countless others through his

Travis Mills

SEE **MILLS**, PAGE 6

Abnormalities in Reward Processing May Underlie Depression, Outbursts

BY ERIC BOCK

Understanding how the brain processes rewards and threat might hold the key to treating depression and a childhood condition of severe and chronic irritability called disruptive mood dysregulation disorder (DMDD).

Dr. Argyris Stringaris

Depression is the leading cause of disability around the world, explained Dr. Argyris Stringaris, chief of the mood brain

SEE **MOOD**, PAGE 8

NIH Named NIOSH 'Total Worker Health' Affiliate

NIH is recognized around the world for its commitment to improving human health. The agency also cares about the well-being of its employees and others are noticing. The National Institute for Occupational Safety and Health (NIOSH), a research agency focused on the study of worker safety and health and part of the Centers for Disease Control and Prevention, recently named NIH a Total Worker Health Affiliate. To achieve this recognition, an organization must demonstrate an ongoing commitment to protect and promote worker safety, health and well-being.

Many familiar activities and collaborative efforts helped NIH achieve the honor, including Safety, Health and Wellness Day, Bike to Work Day, Take a Hike Day, the Institute Relay, the Wellness@NIH web site and newsletters sponsored by the NIH Health and Wellness Council, SafetyCast in a Minute videos, NIH Health in Buildings Roundtable, Spring into Wellness campaign and the Employee Assistance Program.

It doesn't stop with what NIH has already achieved. To maintain a leadership role in the federal sector and retain affiliate status, NIH must continue promoting injury and illness prevention;

conduct regular employee safety, health and wellness training; and sponsor educational forums and other outreach and employee engagement initiatives disseminating Total Worker Health research and findings.

Thanks to efforts by the Office of Research Services' Amenities and Transportation Services and Occupational Health and Safety Divisions in supporting a holistic approach to employee health and working with NIOSH, NIH secured this designation.

Sailing Association Open House, Mar. 8

The NIH Sailing Association will hold an open house on Thursday, Mar. 8 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln. Learn to sail and discover opportunities with NIHSA. There will be information about 6-week basic training classes, the club's racing program and social activities offered by NIHSA.

CRC Atrium Is Like Carnegie Hall

It is getting to be a rare event when the atrium of the Clinical Research Center does not host a performance of live music. Recently, six horn players (above) from the National Symphony Orchestra were joined by members of the NIH Community Orchestra horn section for a holiday sing-along. On Jan. 18, pianist Hui-Chuan Chen and violinist Kenneth Naito (r) performed Mozart's violin concerto No. 5, Brahms' violin concerto D major, 2nd and 3rd movement and Waxman's *Carmen Fantasie*. Chen has a Ph.D. from Johns Hopkins Peabody Institute and is on the faculty at the University of Maryland Baltimore County. Naito is a student at the Juilliard School Pre-College.

PHOTOS: DEBBIE ACCAME

A fee of $5 at the door includes pizza, drinks and snacks. Cash bar for beer and wine—$2 each. Look for NIHSA posters and flyers around campus. For more information, visit www.nihsail.org/.

NIH To Host Rare Disease Day Event, Twitter Chat

Rare diseases affect an estimated 25 million Americans. On Mar. 1, NIH will host an event to raise awareness about these disorders, the people they affect and current research collaborations.

Sponsored by the National Center for Advancing Translational Sciences and the Clinical Center, Rare Disease Day at NIH will take place from 8:30 a.m. to 4 p.m. in Masur Auditorium, Bldg. 10. The event will feature presentations, interactive panel discussions, posters, exhibits and tours of the Clinical Center. Admission is free and open to the public. In association with Global Genes, participants are encouraged to wear their favorite pair of jeans.

Learn more about Rare Disease Day at NIH at https://ncats.nih.gov/rdd. Visit https://events-support.com/events/NIH_Rare_Disease_Day to register and view the agenda. Be sure to follow the event on social media at #RDDNIH.

Prior to the event, NIH is hosting a Twitter chat on rare diseases on Friday, Feb. 23 from 1 to 2 p.m. The chat will feature NIH director Dr. Francis Collins and NCATS director Dr. Christopher Austin as well as representatives from the rare diseases advocacy community. Join in the conversation via #NIHChat.

Nurse Researcher Talks About Understanding, Treating IBS

BY DIANA FINEGOLD

NINR director Dr. Patricia Grady (l) with Dr. Margaret Heitkemper

If you or your loved one has ever been affected by irritable bowel syndrome (IBS), you are not alone. About 1 in 10 people in the United States has IBS and it is among the most-cited reasons for visiting the doctor. Additionally, 2 to 3 times more women than men seek a diagnosis for the disorder in most countries.

Dr. Margaret Heitkemper discussed IBS, its relation to other disorders and an intervention that she developed in "Symptom Science in Irritable Bowel Syndrome: Bench to Intervention," the final NINR Director's Lecture of 2017.

Heitkemper is professor and chairperson, department of biobehavioral nursing and health informatics, Elizabeth Sterling Soule chair in nursing, adjunct professor, division of gastroenterology and co-director, Center for Innovations in Sleep Self-Management at the University of Washington.

IBS is defined as a combination of abdominal pain and constipation, diarrhea or an alternating pattern of these problems. Currently, there is no universally accepted biomarker for IBS, but Heitkemper and her team are hoping their research will help identify one.

So what causes this common, chronic problem? Heitkemper uses the biopsychosocial model as guidance for researching this condition. The model outlines a range of factors that influence IBS, including genetics, epigenetics, psychological and environmental factors.

Although IBS is a stand-alone problem, Heitkemper showed that IBS often exists with many other chronic pain-related conditions and that symptoms can vary depending on sleep, stress and hormone levels.

Heitkemper was inspired to research IBS because of its "female predominance in most countries" and wanted to better understand why women seek a diagnosis for the condition and health care for their symptoms more often than men. She noted that the hysterectomy rate is three-fold higher in women with IBS than without, suggesting potential long-term consequences of the condition. Additionally, Heitkemper's research shows that "the presence of distress," such as anxiety, makes a difference in how women with IBS respond to pain.

Building on her understanding of IBS, Heitkemper developed and tested an intervention based largely on cognitive behavioral therapy. The intervention showed that behavioral therapy can be effective for approximately two-thirds of individuals with IBS. Later research also indicated that certain biomarkers may help in identifying those who are most likely to benefit from behavioral therapy. R

Barsevick Gives NINR Director's Lecture

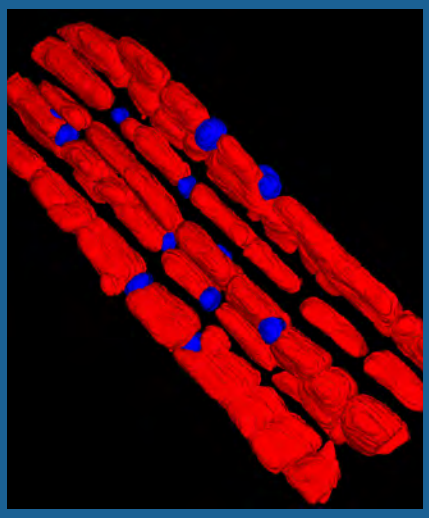
Mar. 1

Dr. Andrea Barsevick will present the first 2018 NINR Director's Lecture on Thursday, Mar. 1, from 11 a.m. to noon in Lipsett Amphitheater, Bldg. 10. In her presentation "The Science of Symptom Management," she will describe her research on cancer-related symptoms and quality of life.

Barsevick is a professor in the population science division of medical oncology at Thomas Jefferson University. She is known internationally for her research on symptom clustering during and after cancer treatment, particularly fatigue and its interactions with sleep disturbances, depressed mood and quality of life.

Barsevick is a fellow of the American Academy of Nursing and a past member of the National Comprehensive Cancer Network guidelines panel on cancer-related fatigue.

The NINR Director's Lecture series is designed to bring the nation's top nurse scientists to the NIH campus to share their work and interests with a transdisciplinary audience. The event is free and open to the public. For more information and to register, visit www.ninr.nih.gov/directorslecture.



ON THE COVER: *Mitochondria (red) in a mouse heart muscle and fat droplets (blue) as viewed under an electron microscope. February is American Heart Month.*

IMAGE: BRIAN GLANCY, NHLBI

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

Supercomputers

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in to save as many original, unique items as they can. When Bldg. 2 was demolished, Lyons and her colleagues took enough well-preserved equipment to reconstruct a vintage laboratory.

★ ★ ★

"Compared to the Cray, the Biowulf is actually simpler in some ways. The Cray was hand-wired. Biowulf uses commodity components in its circuitry. It's the equivalent of 4,000 computers comprising 90,000 core processors. The Cray X-MP had only 2."

–STEVEN FELLINI

★ ★ ★

"My dream is to put in a complete lab exhibit from each decade on each floor of Bldg. 31," said Lyons.

Walk up to the Bldg. 31 Cray and you'll see all the wiring, the computer boards soldered together and the cooling system. The history office plans to enhance the exhibit with a mirror, so passersby can see more of the internal wiring, an updated plaque and the original computer work benches. The office also has the old punch cards and paper tape, as well as drawings of the local network that connected computer terminals around campus.

NIH's current supercomputer is massive by comparison and operates at a mindboggling speed. While the Cray performed at 133 megaflops per second, the big beast known as Biowulf performs at 2 petaflops, or 2 thousand-trillion floating-point operations per second.

Its tall towers filling a large room in Bldg. 12, the Biowulf cluster is 15 million times faster than the Cray X-MP/22, said Dr. Steven Fellini, the supercomputer's systems architect and member of CIT's high-performance computing team.

NIH's intramural program uses the powerful cluster in large part for genomics studies—advanced DNA sequencing, whole genome analysis—as well as statistics, imaging and molecular modeling. Other NIH investigators use Biowulf to analyze brain MRIs, identify cancer targets, create algorithms to study disease and simulate the spread of pandemics.

"The Biowulf cluster is allowing scientists to do work they couldn't do otherwise," said Fellini.

During a recent winter afternoon, at 70 percent capacity, Biowulf was running 17,000 simultaneous jobs among 213 unique users across 20 institutes, with 3,000 jobs in the queue.

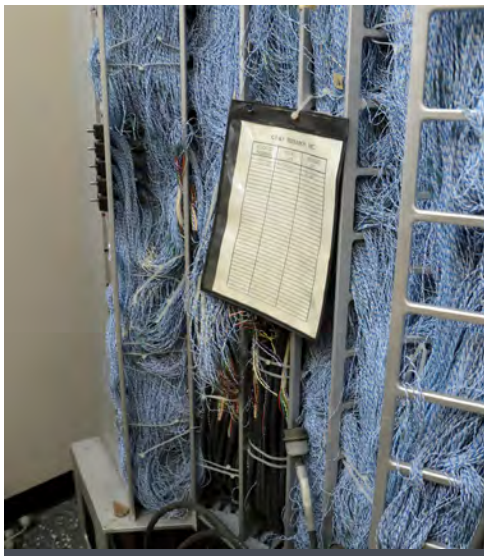
In fact, the Top 500 organization recently ranked Biowulf the 66th most powerful commercially available computer system in the world.

Almost 20 years ago, Biowulf began as a couple dozen boxes on a shelf and has expanded in phases. Biowulf now consists of many rows of computer towers, each with a customized refrigerator-like cooling system, all connected by 25 kilometers of fiber optic cable.

Fellini started his NIH career in 1980,

At the top of the page is the Cray X-MP used by NCI at Ft. Detrick, circa 1989. Above, CIT's Dr. Steven Fellini shows off the Biowulf cluster, which is 15 million times faster than the Cray.

PHOTOS: DANA TALESNIK, ERNIE BRANSON



Massive tangles of wire were connected by hand in the old Cray supercomputers.

working as a postdoc in a biochemistry lab. "I was using computers to do my data analysis and one thing led to another," he said.

Fellini continues to lead the team that built Biowulf from the ground up. In just over 3 years, Biowulf's computing capacity increased by 400 percent, from 18,000 to 92,300 core processors. The fifth expansion phase, slated for early next year, will add another 30,000 cores that will be housed in another room in Bldg. 12.

"Compared to the Cray, the Biowulf is actually simpler in some ways," said Fellini. "The Cray was hand-wired. Biowulf uses commodity components in its circuitry. It's the equivalent of 4,000 computers comprising 90,000 core processors. The Cray X-MP had only 2."

For anyone wondering where to unload biomedical relics, NIH's history office accepts donations; visit https://history.nih.gov/museum/donate.html. Lyons said the office is particularly interested in equipment from the 1980s to 2000s. They also regularly get requests for manuals, which sometimes are the only way to learn how older machines worked. The office has a large collection of 20th century manuals, all of which have been digitized.

"I'd be interested to know what's the oldest computer still being used on campus today," said Lyons. "And, if that person is planning on getting rid of it, we're interested!"

ON JAN. 19

HHS White House Liaisons Visit NIH

On Jan. 19, a delegation from the HHS Office of White House Liaison visited NIH to tour the Clinical Center and meet scientists from the National Cancer Institute. The group also toured the Children's Inn at NIH during the morning visit. Above, Dr. James Gilman (l), CEO of the Clinical Center, greets (from l) Heidi Stirrup, deputy director of OWHL and her colleagues Julie LeFevre, Tim Clark, David Mansdoerfer and Jacob Ashendorf. Below, NCI's Dr. Jack Shern (l) addresses the group in a lab as NCI deputy director Dr. Douglas Lowy (second from l) looks on.

PHOTOS: CHIA-CHI CHARLIE CHANG

Mills

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determination, humor and optimism.

Just don't call him wounded. "I hate being called wounded," Mills told the crowd during a recent Deputy Director for Management seminar in Masur Auditorium. "I prefer recalibrated warrior."

Mills is 1 of only 5 servicemen from the Iran and Afghanistan wars to survive injuries as a quadruple amputee. On that hot April day in Afghanistan, he and his troops strapped on gear to sweep the ground for bombs. They didn't find any until Mills tossed down his backpack, which landed on a bomb. The explosion nearly killed him and injured two other soldiers.

Speaking at NIH, he said, "I just hope I don't bomb this, because last time look what happened..." He paused for effect and smiled, inviting the crowd to laugh with him. "I'm gonna be like that bomb in 2012; it will be a surprise. You're not gonna see this coming."

Now, as a motivational speaker and international advocate for veterans and amputees, the gregarious Mills said, "I tell jokes to *disarm* the situation."

When the accident happened, medics rushed over to Mills, tying tourniquets around his four limbs to stop the bleeding. "In my head, I'm not going to make it," Mills recounted. "I've seen guys die from a lot less. I told my medics, 'Don't worry about me; you're not gonna save me. Go fix my guys.'"

The medics put Mills on a chopper to Kandahar where he was rushed into surgery, the first of which lasted 14 hours. He'd need more than 30 blood transfusions. "It's pretty incredible," Mills said. "Had they loosened one tourniquet, I'd have died within 3 minutes."

In those first days, upon realizing the extent of his injuries, Mills said he became withdrawn, embarrassed and angry. He doubted he could be a proper husband and father. How did an athletic, active guy from small-town Michigan wind up here?

But then he was transferred to Walter Reed National Military Medical Center, reunited with his wife Kelsey and baby daughter Chloe and his outlook began to change. He was further motivated by a visit from another quadruple amputee vet, Marine Cpl. Todd Nicely, who told Mills he would again dress and feed himself, walk and even drive.

With hard work, Mills eventually did relearn these skills. It took many grueling months of rehabilitation, some high-tech gadgets and a devoted medical team that included therapist Dr. Kerry Quinn, who sat in the front row of the lecture. "She's the whole reason I can walk again," Mills said.

At first, the pain was so debilitating, Mills needed ketamine to reset his nerves. Five weeks into recovery, he used his prosthetic hand to feed himself. Learning to walk was a more arduous process. He had to build up his hips and core just to sit up. After some time in a wheelchair, Mills strapped on prosthetic legs and began to walk. His legs have microprocessors that, each time he moves, make hundreds of internal adjustments to keep him upright. What's more, they're waterproof and have a Bluetooth remote to help him drive.

Five months after his injury, Mills walked a 5K in New York. The firemen who had invited Mills offered to push him in a wheelchair but Mills insisted on walking. He ached, bled and fell over at the end, but he pushed himself to finish the walk.

Mills is already plotting a good use for his prosthetic hand, which can clamp down with 25 pounds of pressure, perhaps even 35 pounds eventually. In 10 years, he said, when his daughter's date comes to the door, he'll shake the guy's hand and ask if it hurts. No? Let's try 35 pounds of pressure.

A quadruple amputee, Ret. Army Staff Sgt. Mills, now a motivational speaker and international advocate for veterans and amputees, shares his motto: "Never give up; never quit."

PHOTOS: CHIA-CHI CHARLIE CHANG

> ***"Life is all about perspective. I can't always control my situation, but I can always control my attitude."***
>
> ~TRAVIS MILLS

"I don't think my problems are more than anybody else's," says Mills. "I have a couple more steps in the morning, [putting on] my legs, then my pants."

Ellen, an audience volunteer, offers commands to demonstrate the voice-activation feature of Mills' prosthetic arm; when his hand repeatedly doesn't respond, Mills reveals his hand is not actually voice activated.

And, he quipped, his hand won't leave fingerprints.

As Mills grew stronger, the initial despair he'd felt after his accident dissipated. "I can reminisce about the 25 years I had with arms and legs and be grateful," he said. But he couldn't undo what had happened, so he realized there was no point in dwelling on the past.

"I learned I can still be active in society and do things with my family, adaptively," he said. "I really am happy and thankful for the life I get to live."

In addition to writing a memoir, *Tough as They Come*, and appearing in a Netflix documentary, *Travis: A Soldier's Story*, Mills started a nonprofit to assist other combat-injured veterans. The Travis Mills Foundation started out sending care packages overseas but has grown to hosting injured vets and their families at his foundation's Veterans Retreat in Maine, where guests enjoy adaptive recreational activities such as boating, biking and horseback riding.

Mills welcomed questions and, to prove that no topic embarrasses him, he said, "In case you're wondering, I've still got it...and it works." He then showed a photo of his son Dax, born in August 2017. The baby's name, he said, combines the first names of the medics who saved him, Daniel (Bateson) and Alexander (Voyce).

"Life is all about perspective," said Mills. "I can't always control my situation, but I can always control my attitude.

"I made it home," he said. Some of his friends didn't. "So for their memory, I'm going to keep living and I'm going to keep pushing forward. I realize it'd be a selfish slap in the face if I ever quit on myself."

A Starbucks Marketplace opened on Jan. 12 in the Clinical Research Center atrium. The new expanded eatery offers coffee, espresso, frappuccinos and a full complement of hot and cold beverages as well as hot meals, freshly baked pastries and snacks to go.

PHOTO: DEBBIE ACCAME

Starbucks Marketplace Opens in CC

Clinical Center visitors, patients and staff can now enjoy a Starbucks Marketplace in the Clinical Research Center atrium. The marketplace opened on Jan. 12, offering coffee, espresso, frappuccinos and a full complement of hot and cold beverages. If you're hungry, the marketplace offers a full selection of food options—from on-the-go hot meals, "better-for-you" snacks and kid-friendly favorites such as apple straws and protein bars, to Georgetown Cupcakes and other freshly baked pastries, muffins and cookies. In a rush? Multiple full-service registers and new self-service kiosks provide speedy service for appetites in a hurry.

The concept, brought to NIH by Eurest Dining Services in partnership with the Office of Research Services' Division of Amenities and Transportation Services, replaces the former Au Bon Pain space. A preliminary test phase allowed the team to assess the new facility, gain customer feedback and make final changes before the grand opening on National Wear Red Day, Feb. 2. With a full lineup of new features and flavors, the grand opening offered heart-healthy product samples and tastings available to support individual wellness goals.

Acting ORS Director Tim Tosten said the launch was a result of listening to customers. "They asked for it—we listened," he said. "We anticipate the Marketplace will become a popular destination point, with quick, convenient and healthy options to service one of the busiest locations on our campus."

Eurest Regional Vice President Ritu Dewan shared the enthusiasm. "We are so excited to be able to introduce this new concept into our service portfolio, as this program will drive great guest participation and satisfaction," she said. "We are confident that this move will provide significantly better options to meet the needs of the NIH community."

For more information, contact John Crawford, program manager, NIH Food Services, Retail and Concession Programs, (301) 402-8180 or crawfj@mail.nih.gov.

Mood

CONTINUED FROM PAGE 1

and development unit at NIMH, during a recent Clinical Center Grand Rounds lecture in Lipsett Amphitheater.

The incidence of depression increases in adolescence and young adulthood. He added, "It contributes to more disability than traffic accidents, self-harm, back pain and all sorts of common infectious diseases."

Forty percent of patients with depression do not respond to standard treatments such as selective serotonin reuptake inhibitors or cognitive behavioral therapy, said Stringaris. Of those who do respond, 25-40 percent of patients will relapse within a year.

His lab is studying two areas of the brain responsible for reward processing: the ventral striatum and the anterior cingulate cortex. Stringaris hopes to identify the neural circuits responsible for reward processing, with the goal of developing a drug to target the pathway.

In healthy volunteers, a reward, such as a piece of chocolate, triggers the release of dopamine, a chemical messenger that brain and nerve cells use to communicate feelings of happiness or satiety. Dopamine levels are highest when a person must wait for something or is surprised by something positive. However, when a person knows a reward is coming, he or she "won't be terribly surprised nor pleased and dopamine will not vary much."

In several studies, Stringaris has observed there is less activity in the striatum of patients who are depressed compared to healthy volunteers. This change begins in adolescence. This suggests there might be a causal relationship between reward processing and depression.

Dr. Melissa Brotman

In a clinical study, he's discovered that one anti-depressant, lurasidone, can increase activity in the parts of the brain that control reward processing. Although the results are preliminary, Stringaris believes the drug can affect the network involved in dopamine release.

Another condition, DMDD, is associated with abnormalities in reward and threat processing in children and adolescents, said Dr. Melissa Brotman, director of neuroscience and novel therapeutics in the section on mood dysregulation and neuroscience in NIMH's Emotion and Development Branch.

Stringaris hopes to identify the neural circuits responsible for reward processing, with the goal of developing a drug to target the pathway.

PHOTOS: CHIA-CHI CHARLIE CHANG

She said DMDD is "characterized by severe recurrent temper outbursts. These occur, on average, at least 3 times per week and they are inconsistent with the situation or developmental level" of the child.

Children with the disorder are irritable—"an elevated proneness to anger relative to peers"—and cranky most of the day, nearly every day. The irritability is pervasive; they are irritable around their peers, teachers and parents. Those who have increased irritability are at increased risk of suicide, anxiety and unipolar depression.

"Irritability is associated with abnormalities in reward processing, specifically responses to frustrative non-reward," she said. Possible treatments for DMDD include interpretation bias training and exposure-based cognitive behavioral therapy, commonly known as CBT.

Interpretation bias training helps children learn over time to not view ambiguous facial expressions as threatening. Youth who are irritable have trouble reading facial emotions.

In one experiment, Brotman asked children to look at photographs of an actor making a happy facial expression, an angry facial expression and then used a computer program to generate morphs with varying degrees of happiness and anger (i.e., ambiguous facial stimuli). Those with DMDD perceived the "ambiguous faces as more threatening." In another study, she demonstrated that irritable youth "rate neutral faces as more hostile and fear-producing."

Exposure-based cognitive behavioral therapy is widely used to treat anxiety disorders. In Brotman's novel application, patients are exposed to something that makes them irritable or frustrated in an attempt to help them learn to tolerate their emotional response.

In one example, Brotman worked with a young girl who exhibited temper outbursts and irritability whenever she was asked to complete her household chore of sorting laundry. During each therapy session, the girl's mother brought in clean laundry and gave it to Brotman to use in exposure exercises with the girl. Over the course of the treatment, the girl was able to sort the laundry with less and less anger. By the end, she was able to do her chore and move on to another task. Her ability to complete her household chore in session transferred to the home environment as well.

This approach, however, has only been tried in 10 cases. Currently, Brotman and her colleagues are expanding this work and exploring neural correlates using functional magnetic resonance imaging pre- and post-CBT.

Among recent Presidential Rank awardees are (from l) NLM retiree Betsy Humphreys, Camille Hoover of NIDDK, Kate O'Sullivan of NHLBI and Alex Rosenthal of NIAID. Honorees were recognized at a leadership summit held at D.C.'s Mayflower Hotel.

Presidential Rank Awards Honor Four from NIH

Three NIH'ers and one recent retiree were recognized with Presidential Rank Awards recently at an all-day leadership summit at Washington's Mayflower Hotel.

Betsy Humphreys, who concluded a distinguished career as deputy director of the National Library of Medicine last year, was one of 36 winners of the annual Distinguished Rank Award. That honor includes a bonus of 35 percent of base salary for extraordinary results achieved during a career.

Among the 115 winners of the Meritorious Rank Award, given for sustained accomplishment and resulting in a bonus of 20 percent of salary, are Camille Hoover, executive officer at NIDDK; Kate O'Sullivan, executive officer at NHLBI; and Alex Rosenthal, chief technology officer at NIAID.

The awards were hosted by the Senior Executives Association.

Former NCI Biostatistician Nam Mourned

Jun-mo Nam, formerly a biostatistician in the Division of Cancer Epidemiology and Genetics, NCI, died on Jan. 4.

He came to NCI in 1969 to work for Dr. John Gart in the mathematical statistics and applied mathematics section of the Biometry Branch. He retired from the Biostatistics Branch after a 43-year career, but came to the office regularly as a special volunteer until June 2017.

Nam was admired for his comportment and devotion to work and the NCI mission. He authored about 80 publications in biostatistical methods and the medical sciences. His statistical publications addressed efficient statistical inference, optimal study design, measurement agreement, sample size calculations and statistical genetics.

He was a member of the International Biometric Association and the American Statistical Association. In 2011, he received the Sustained Outstanding Contributions to Korean Scientists Engineering Association in America Award for lifetime achievements, presented by the Ministry of Education, Science and Technology of the Republic of Korea.

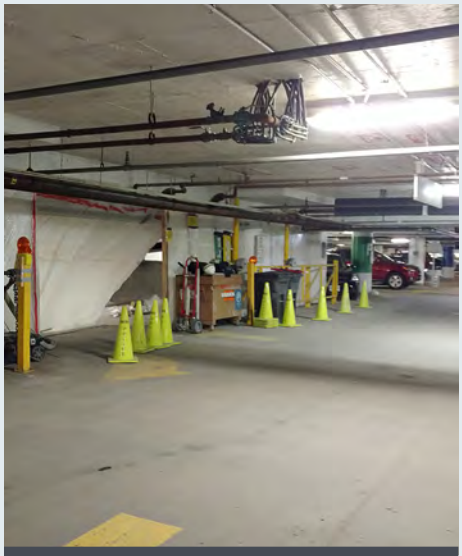
Besides statistical theory and methods, Nam was interested and knowledgeable about military history, particularly about World War II and the Korean War, of which he was a veteran.

Jun-mo Nam, a former biostatistician in NCI's Division of Cancer Epidemiology and Genetics, died Jan. 4.

FEEDBACK

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

Feedback: Beginning Wednesday, Aug. 9, 2017, the ramp connecting the P-1 level with the P-2 level of the ACRF underground parking garage in Bldg. 10 was to be closed for approximately 3 months. As of today, 1/8/2018, it is still closed. The project officer was emailed several times to find out when it will re-open, but the emails have gone unanswered. What is the time line for re-opening this area?



The refurbished underground ramp at Bldg. 10 is now slated to reopen sometime this month. Extreme cold and other weather-related conditions delayed some phases of repair.

Response from the Office of Research Facilities: The Office of Research Facilities apologizes for the lack of response to your previous inquiries. The latest projections have the ramp reopening by mid-February. Some concrete and steel fireproofing work is weather- and temperature-dependent and the recent period of extreme cold weather was not conducive for finishing this phase of construction, thus delaying the overall time line for completion.

DIGEST

A new mouse study links changes in the gut caused by a high-salt diet to impaired blood flow in the brain.

IMAGE: PIXHOOK/ISTOCK

Hold the Salt: Gut Reaction May Impair the Brains of Mice

We are often warned of the dangers of high levels of salt in our diet, yet the risks of salt consumption and the effects of salt on the body, including the brain, are not entirely clear. In a new mouse study, scientists link changes in the gut caused by a high-salt diet to impaired blood flow in the brain. This reduced blood flow can eventually lead to impaired cognition that could be reversed by changing back to a normal diet. The study, published in *Nature Neuroscience*, also provides molecular clues for treating these problems.

"For years researchers have wondered how a high-salt diet harms the brain," said Dr. Jim Koenig, program director at NINDS, which supported the study. "This mouse study provides a detailed cellular and molecular diagram for how the problems start in the gut and opens unexpected paths towards new treatments."

In this study, mice were fed a high-salt diet (HSD) containing 16 times the amount of sodium chloride typically found in their food. After 8 weeks, their brains showed a 20 to 30 percent reduction in blood flow compared to mice that ate normal food. This drop in blood flow was accompanied by the appearance of dementia-like symptoms, including defects in the ability of HSD mice to recognize objects, navigate a maze and properly build a nest. When the mice were returned to a normal diet, both blood flow and cognition improved, suggesting that the negative effects of excessive salt consumption could be reversible.

"The brain is extremely dependent on getting the right amount of blood at the right time. If blood flow isn't matched to what the brain needs, things go wrong," said Dr. Costantino Iadecola, director and chair of the Feil Family Brain and Mind Research Institute at Weill Cornell Medicine in New York City and senior author of the study.

In humans, high levels of salt in the diet has long been associated with high blood pressure, and increasing evidence has linked blood pressure and brain health. However, the blood pressure of HSD mice was not affected, suggesting a very specific and independent mechanism for the changes seen here.

"This study adds to our growing understanding of how the gut can modulate brain function," said Koenig. "From a public health perspective, the fact that these effects can be reversed by halting the ingestion of salt is very important and could help us improve health in areas where many people eat a high-salt diet."

NIH-funded studies have unveiled a new way that nervous system cells interact.

IMAGE: KIRSTY PARGETER/THINKSTOCK

Memory Gene Goes Viral

Two independent teams of scientists from the University of Utah and the University of Massachusetts Medical School have discovered that a gene crucial for learning, called *Arc*, can send its genetic material from one neuron to another by employing a strategy commonly used by viruses.

The studies, both published in *Cell*, unveil a new way that nervous system cells interact.

"This work is a great example of the importance of basic neuroscience research," said Dr. Edmund Talley, a program director at NINDS. "What began as an effort to examine the behavior of a gene involved in memory and implicated in neurological disorders such as Alzheimer's disease has unexpectedly led to the discovery of an entirely new process, which neurons may use to send genetic information to one another."

While Arc is known to play a vital role in the brain's ability to store new information, little is known about precisely how it works. In addition, previous studies had detailed similarities between the Arc protein and proteins found in certain viruses like HIV, but it was unclear how those commonalities influenced the behavior of the Arc protein.

The University of Utah researchers began their examination of the *Arc* gene by introducing it into bacterial cells. To their surprise, when the cells made the Arc protein, it clumped together into a form that resembled a viral capsid, the shell that contains a virus's genetic information. The Arc "capsids" appeared to mirror viral capsids in their

physical structure as well as their behavior and other properties.

"Beforehand, if I had said to any neuroscientist that this gene sort of acts like a virus, they would have laughed at me," said Dr. Jason Shepherd, an assistant professor at the University of Utah. "We knew this was going to take us in a completely new direction.

"This research highlights the fact that we often don't know where the cool discoveries are going to come from," he added. "We need to follow where the science takes us."

NIH Scientists Find Microbes on The Skin of Mice Promote Tissue Healing, Immunity

Beneficial bacteria on the skin of lab mice work with the animals' immune systems to defend against disease-causing microbes and accelerate wound healing, according to new research from NIAID scientists.

Researchers say untangling similar mechanisms in humans may improve approaches to managing skin wounds and treating other damaged tissues. The study was published online Jan. 18 in *Cell.*

Like humans and other mammals, mice are inhabited by large, diverse microbial populations collectively called the microbiome. While the microbiome is believed to have many beneficial functions across several organ systems, little is known about how the immune system responds to these harmless bacteria.

To investigate, NIAID scientists led by Dr. Yasmine Belkaid, chief of the mucosal immunology section of the Laboratory of Parasitic Diseases, observed the reaction of mouse immune cells to *Staphylococcus epidermidis*, a bacterium regularly found on human skin that does not normally cause disease. To their surprise, immune cells recognized *S. epidermidis* using evolutionarily ancient molecules called non-classical MHC molecules, which led to the production of unusual T cells with genes associated with tissue healing and antimicrobial defense.

In contrast, immune cells recognize disease-causing bacteria with classical MHC molecules, which lead to the production of T cells that stoke inflammation.

Researchers then took skin biopsies from two groups of mice—one group that had been colonized by *S. epidermidis* and another that had not.

Over 5 days, the group that had been exposed to the beneficial bacteria experienced more tissue repair at the wound site and less evidence of inflammation.

Belkaid's team plans to next probe whether non-classical MHC molecules recognize friendly microbes on the skin of other mammals, including humans, and similarly benefit tissue repair.

Eventually, mimicking the processes initiated by the microbiome may allow clinicians to accelerate wound healing and prevent dangerous infections, the researchers note.

Zika virus infection among pregnant women can lead to developmental problems in fetuses and newborns.

IMAGE: ISTOCK

Zika Infection During Pregnancy May Disrupt Fetal Oxygen Supply

Zika virus infection appears to affect oxygen delivery to the fetuses of pregnant monkeys, according to a small study funded by NIH. Researchers also observed a high degree of inflammation in the placenta and lining of the uterus, which can harm the fetal immune system and increase a newborn's susceptibility to additional infections. The study is published online in *Nature Communications*.

Zika virus infection among pregnant women can lead to developmental problems in fetuses and newborns. In the current study, researchers led by Dr. Daniel Streblow of the Vaccine & Gene Therapy Institute at Oregon National Primate Research Center, used non-invasive imaging to evaluate how persistent Zika infection affects pregnancy in five rhesus macaques. The team found that the virus induces high levels of inflammation in the blood vessels of the uterus and damages placental villi, the branch-like growths that help transfer oxygen and nutrients from maternal blood to the fetus. The researchers suggest that this damage may disrupt oxygen transport to the fetus, which can restrict its growth and lead to stillbirth, among other conditions.

The team observed evidence of fetal brain abnormalities in 2 of the 5 animals, but the researchers did not see any obvious signs of microcephaly. This finding, they reason, is consistent with previous studies that establish microcephaly as only one of a spectrum of Zika-induced complications. The authors call for additional studies to improve knowledge of how Zika virus causes infection during pregnancy.

VOLUNTEERS

Adults with Asthma Needed

NHLBI researchers seek adults with asthma to participate in a study to learn more about what causes persistent symptoms in some patients with asthma. To learn how to participate, call the Clinical Center Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more online at https://go.usa.gov/xnkTt. Refer to study 13-H-0059.

Patients with Kidney Cancer Needed

NHLBI researchers seek individuals with kidney cancer for a new treatment study using gene therapy. Gene therapy is a process of modifying a person's immune system to create tumor-fighting cells to recognize and kill their cancer. Only renal cell carcinoma patients who test positive for HLA-A 11:01 will be eligible to participate. Study-related procedures, tests and medications are provided at no cost. For more information, call the Clinical Center Office of Patient Recruitment, 1-866-444-2214 (TTY 1-866-411-1010). Read more online at https://go.usa.gov/xnfkz. Refer to study 18-H-0012.

Study Needs Overweight Men

NIDDK researchers are seeking overweight/obese men, 18-50 years old, to participate in a study looking at a potential link between consumption of processed foods and the development of metabolic syndrome. Participants will be required to remain in the hospital for 1 month on 2 separate occasions and eat only the meals provided by NIH during that time. Compensation is provided. To learn more, call the Office of Patient Recruitment at 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://go.usa.gov/xRRE7.

Healthy Volunteers Needed

NIAID researchers are seeking healthy volunteers, 18-50, to participate in a respiratory syncytial virus (RSV) challenge study at the Clinical Center. RSV is the most common cause of respiratory and lung infection in infants and older adults. Researchers will use what they learn to test new antivirals and vaccines in the future. Compensation is provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at https://go.usa.gov/xnpZD.

HIV Vaccine Study Needs Subjects

Vaccine Research Center researchers seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-444-1132 (TTY 1-866-411-1010) or email vaccines@nih.gov. Se habla español.

At left, Dr. James Gilman (l), CEO of the Clinical Center, greets newly confirmed U.S. surgeon general Dr. Jerome Adams. At right, Adams joins a briefing with NIH leadership, including NIAID director Dr. Anthony Fauci (l) and NIH director Dr. Francis Collins (r).

Above, Adams and Gilman take a look at a Commissioned Corps tribute wall in the Clinical Center 1st floor hallway highlighting the PHS response to Ebola in West Africa.
Below, during the briefing with NIH leadership, Adams shares a light moment.

Surgeon General Adams Visits NIH

On Jan. 18, U.S. surgeon general Dr. Jerome Adams visited NIH, meeting with NIH leadership and institute directors and with members of the Public Health Service.

He enjoyed a Bldg. 1 briefing hosted by NIH director Dr. Francis Collins and later visited the Clinical Center, where he was greeted by Dr. James Gilman, CEO of the CC. He also gathered for a group photo with members of the PHS serving at NIH.

An anesthesiologist, Adams is a Maryland native who most recently served as health commissioner for the state of Indiana.

PHOTOS: CHIA-CHI CHARLIE CHANG

Corps value: Adams (seated, third from r) gathers with NIH Commissioned Corps members and leaders of NIH's Office of Intramural Research, including assistant director Dr. Roland Owens (standing, l), deputy director Dr. Richard Wyatt (seated, l) and NIH deputy director for intramural research Dr. Michael Gottesman (seated, second from l). As surgeon general, Adams oversees the operations of the Corps, which has approximately 6,500 uniformed health officers who serve in nearly 600 locations around the world.