

The day-long symposium brought researchers from a broad range of disciplines together to share their AI-related research. It was sponsored by NIH's National Heart, Celi Cautions Developers, Lung, and Blood Institute and NIH Office of Intramural Research, in partnership with the Foundation for Advanced Education

in the Sciences

Electronic health records are the "de facto building blocks" of AI healthcare models, he said. Despite their importance, these records were never designed to be building blocks.

"Data is not an

objective representation of the world," Celi said. "It is a representation of the world as seen through the lenses of the observers."

National Institutes of Health

Anyone who trains AI models on electronic health records must be aware of bias, which can significantly impact a model's effectiveness and fairness. Healthcare AI

> models that don't account for bias often perform inadequately, compared to models that control for bias.

"You need to take caution when vou're using electronic health record data for developing AI," Celi warned.

There are medical devices that do not perform consistently across different populations. For instance, Celi's team found skin tone can affect the accuracy of a pulse oximeter's oxygen saturation reading. The

SEE AI, PAGE 5



"Those who are at the cutting edge of AI are convinced we are a year or two away from dumping a whole dataset into an AI model and asking it to write a full research manuscript," said Dr. Leo Anthony Celi, clinical research director and principal research scientist at the Massachusetts Institute of Technology's Laboratory for Computational Physiology. He spoke at a recent NIH AI symposium in Masur Auditorium.





ALSO THIS ISSUE

NIH to Fund Long-Term Health Studies in Aftermath of Ohio Train Derailment3 NIH Labs Compete in Freezer Challenge; Milestones6

ONE STEP CLOSER

Hammoud, Swenson Develop New PET Tracer for Fungal Infections

BY AMBER SNYDER

This story is part of our ongoing series on NIH makers and inventors.

Nothing worth having comes easy. Two NIH makers, Dr. Dima Hammoud



Dr. Rolf Swenson (I) and Dr. Dima Hammoud developed an imaging method for diagnosing invasive fungal infections.

and Dr. Rolf Swenson, are quite familiar with that adage. It took them almost five years of trial and error to develop a brand-new imaging method that will allow doctors to rapidly and accurately diagnose invasive fungal infections.

At least 1.6 million people globally die from fungal infections each year, a mortality rate surpassing that of tuberculosis, malaria, hepatitis and pneumonia. But diagnosing some of these fungal infections can be tricky

> because the available diagnostic methods are insensitive, nonspecific and/or invasive.

Immunocompromised patients are especially susceptible to fungal infections, and consequences may be fatal. Antifungal drugs can also have significant side effects, so doctors tend to avoid giving them before they confirm the type of infection. Confirming

NIH Research Festival Set

Mark your calendars. NIH will hold its annual Research Festival from September 9-12 in Bldg. 10. The event will feature lectures, posters and workshops. Vendors will exhibit on Sept. 11 and 12.

View the preliminary agenda: go.nih.gov/kZpI0mR.

As in years past, the Research Festival will feature poster sessions on the FAES Terrace. Poster abstracts are due by July 18. For the submission form, visit: go.nih.gov/244LIA4.

If you have questions related to this event, email researchfest@mail.nih.gov.



A poster session from the 2023 Research Festival

PHOTO: MARLEEN VAN DEN NESTE

The Doe Days of Summer



A doe walks behind Bldg. 31 seeking a shady spot. A four-day heat wave engulfed the region in June during which temperatures hovered around 100 degrees. PHOTO: BRAD MOSS

NIH to Launch Inaugural Strategic Plan for Autoimmune Disease Research

Autoimmune diseases encompass a diverse group of diseases that can affect nearly any part of the body and may manifest at any point in life. It is estimated that between 23.5 and 50 million Americans are living with autoimmune diseases, making them among the most common chronic conditions in the country.

While autoimmune diseases more commonly affect women, men often experience a more severe autoimmune disease course and face a higher risk



Bhattacharya Delivers Remarks at Aspen Institute

On June 24, NIH Director Dr. Jay Bhattacharya was interviewed by Stefanie Ilgenfritz, heath and science coverage chief for the *Wall Street Journal*, at the Aspen Institute in Aspen, Col.



At the event, Bhattacharya described his priorities for NIH, which include improving population health, fostering innovation, restoring public trust in science and ensuring the reproducibility of NIH-funded research results. Following the exchange, Bhattacharya took questions from the audience.

To watch the interview, see: http://bit.ly/4kXLXs5.



of mortality. Despite their high prevalence and serious impact, many autoimmune diseases remain understudied, and treatment options are limited. The breadth and complexity of autoimmune



diseases highlight the urgent need for a unified approach to better coordinate and accelerate research progress.

In 2023, NIH began to develop an agency-wide strategic plan for autoimmune disease research following creation of the Office of Autoimmune Disease Research within NIH's Office of Research on Women's Health. At that time, NIH formed the Coordinating Committee for Autoimmune Disease Research (CCADR), which includes representatives from across NIH institutes, centers, and offices.

Shaped with valuable input from the autoimmune disease community, this landmark plan sets a bold vision for establishing priorities, coordinating efforts, fostering collaboration and improving the lives of those living with and at risk for autoimmune diseases.

The first-ever NIH-Wide Strategic Plan for Autoimmune Disease Research will go live on Monday, July 21, at 1:00 PM ET. Visit https://orwh.od.nih.gov/OADR-ORWH/Strategic-Planning-for-ADR at launch time to watch a special introductory video and learn more about the future of NIH-funded autoimmune disease research.

NIH to Fund Long-Term Health Studies for Ohio Town after 2023 Train Derailment

NIH has launched a five-year, \$10 million research initiative to assess and address the long-term health outcomes stemming from a 2023 train derailment.

On Feb. 3, 2023, a 38-car freight train carrying hazardous materials derailed in the town of East Palestine, Ohio. Some of the train cars—which were carrying vinyl chloride, butyl acrylate, ethylene glycol, and benzene residue— caught fire and burned for days; some spilled their loads onto the ground. The chemicals traveled into local waterways and flowed for miles.

Following the derailment, emergency responders conducted controlled burns, which raised concerns about the airborne release of hydrogen chloride and phosgene. Since the accident, local, state and federal agencies, including NIH, have been part of a coordinated response to support the affected communities in Ohio and Pennsylvania.

Community members experienced and reported a range of initial health symptoms—including headaches as well as respiratory, skin and eye irritations—prompting concern about broader long-term impacts on maternal and child health as well as psychological, immunological, respiratory and cardiovascular effects.

"NIH is working to ensure that the people

of East Palestine and the surrounding communities are listened to, cared for and get the answers they deserve," said NIH Director Dr. Jay Bhattacharya. "This multi-disciplinary research program will focus on public health tracking and surveillance of the community's health conditions to support health care decisions and preventive measures."

The studies will focus on:

- Longitudinal epidemiological research to understand the health impacts of exposures on short- and long-term health outcomes, including relevant biological markers of risk
- Public health tracking and surveillance of the community's health conditions to support health care decisions and preventive measures.
- Extensive, coordinated communications among researchers, study participants, community stakeholders, health care providers, government officials and others to establish a comprehensive approach to address the affected communities' health concerns.

The deadline to submit research proposals is July 21. The studies will start this fall. For information on these research opportunities, see: https://go.nih.gov/yrXr4R6.

"The announcement today of the funding for long-term health studies for the people of East Palestine is great news for the community," Ohio Governor Mike DeWine said. "This funding will enable the people of East Palestine to have the peace of mind that comes from knowing that any potential for long-term health effects will be studied by the scientists at the NIH."

Rep. Dave Joyce (R-OH) said, "Programs like these, in coordination with other federal, state, and local partners, are critical to ensuring the impacted communities can move forward with the essential tools and knowledge to safeguard their long-term well-being. I look forward to continuing to work with the Administration and my colleagues in Congress to enact my bill, the East Palestine Health Impact Monitoring Act, and similar programs that advocate for the long-term recovery of the region."



ON THE COVER: A researcher holds a flask containing human cerebral organoids.

IMAGE: NIAID

The NIH Record

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An Environmental Protection Agency contractor conducts air monitoring during rail excavation after the 2023 accident. PHOTO: EPA



Imaging

CONTINUED FROM PAGE 1

a fungal infection, however, is invasive and time-consuming. Clinicians need a faster, easier way to diagnose them. Realizing the urgent need for a noninvasive fungal-specific imaging tracer, Hammoud and her team decided to develop a fungal-specific PET ligand.

"This [invention] was born from a need," Hammoud said. "Multiple patients who are successfully treated with chemotherapy and/or transplant end up succumbing to fungal infections because of their immunocompromised states."

As a senior investigator and radiologist with the Radiology and Imaging Sciences department at the NIH Clinical Center (CC), Hammoud often relies on structural imaging like computed tomography (CT) or magnetic resonance imaging (MRI) to make diagnoses. However, she noted, while she can identify a lesion on a patient's brain or lungs using CT or MRI, it's often difficult to pinpoint the actual cause—is it a tumor, an infection, inflammation? If it's an infection, what kind?

In her lab, Hammoud mostly relies on positron emission tomography (PET), a

technique which uses special molecules called ligands carrying radioactive tags—positron-emitting isotopes—to visualize certain tissues or processes of interest. Hammoud uses PET imaging mainly to better understand how certain infectious diseases affect different organs and interact with the immune system.

To develop a fungal-specific ligand, Hammoud and her team exploited already

existing fungal metabolic processes. They set out to develop radioactively tagged versions of certain molecules, mainly sugars, that are known to be used by fungi only. The idea is that when the fungus encounters those tagged sugars, it incorporates them, producing a radioactive signal on PET scan and confirming the presence of the fungus.

Hammoud and her team originally identified two promising sugars for this work: rhamnose and cellobiose. Working with Swenson, a synthetic organic chemist with NIH's National Heart, Lung and Blood Institute (NHLBI) Chemistry and Synthesis Center, and his team, the group labeled the molecules Hammoud identified with special PET isotopes so they can be tested in different infections.

The road to discovery was not straightforward, however. Their project, which began in 2019, encountered many obstacles right from the beginning. Developing the animal



Dr Jianhao Lai from the Hammoud lab prepares the small animal PET/ CT scanner for an imaging session.

models, spearheaded by staff scientist Dr. Swati Shah from Hammoud's lab, was very tedious and required multiple attempts. Logistical issues related to lab space and resources needed to be overcome, and the Covid-19 pandemic caused further delays.

"We decided to start with rhamnose because the chemistry was easier," Hammoud said. The tagged rhamnose worked well in the lab, but "in mouse models, the fungus wasn't taking the sugar in sufficient amounts to produce a detectable signal."

Hammoud, Swenson and their teams persevered, developing and testing multiple versions of tagged rhamnose and other existing ligands for almost two years. Eventually, they shifted their focus to cellobiose.

"It was our next best option," Hammoud recalled.

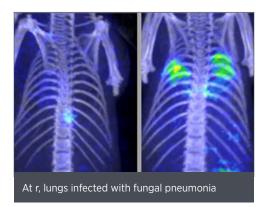
"Thankfully," Swenson said, "each of us wouldn't let the other give up."

They began the process again, with Swenson and his lab developing a practical synthetic method for the tagged cellobiose, and Hammoud and her team testing it first in the lab and eventually in animal models.

"The idea of cellobiose, which is composed of two glucose molecules bound together, is really cool," Hammoud elaborated. "In real life, only certain fungi can produce the special enzymes needed to break the bond between the two glucose molecules of cellobiose. Those enzymes are not present in bacteria or in mammalian cells. By adding a radioactive tag to cellobiose and exposing it to fungal infection, such as *Aspergillus*, the sugar is broken into two molecules which are then taken inside the fungus. This results in



From I to r, Rolf Swenson, Dima Hammoud, Falguni Basuli, Swati Shah, Neysha Martinez-Orengo, Jianhao Lai pose together last year after receiving NIH Director's Awards for their invention.



accumulation of the radioactive signal in the infection.

"If there is no fungus, on the other hand, cellobiose remains intact and is eventually excreted by the kidneys with no residual radioactive signal in the body."

The radiolabeled cellobiose was eventually proven in animal models to be a specific imaging ligand for certain invasive fungilike *Aspergillus*.

After so many failed attempts with other sugars, when Hammoud and her lab finally saw high radioactive signal localizing to the fungal infection on PET after injecting the tagged cellobiose, they thought it must be a fluke. But it was the breakthrough they were hoping for. She and Swenson published their work in August 2024.

Their next big goal is to test their findings in a human clinical trial. Cellobiose is an approved food additive and is also found in many vegetables but is minimally absorbed from the intestinal tract into the bloodstream. The collaborators are hopeful that it will be well-tolerated by humans.

The hopes of many of Hammoud and Swenson's colleagues at NIH are also riding on this research. Doctors at NHLBI and the National Institute of Allergy and Infectious Diseases (NIAID), for example, are excited about the potential for a fungal-specific imaging ligand.

"The reactions of our colleagues in the clinic and their enthusiasm for collaboration make all our effort worthwhile. At the end of the day, we all want to make a difference in the lives of our most vulnerable patients, namely those with weakened immune systems predisposing them to fungal infections," said Hammoud.

Both researchers repeatedly expressed their gratitude to the NIH intramural research program for providing the opportunity and the necessary expertise needed to carry on this type of high-risk/high-reward research work. Hammoud credited Dr. Cliff Lane of NIAID, founder of the Center for Infectious Disease Imaging (CIDI), former CC director Dr. John Gallin, who passed

away in 2024, and all her mentors for believing in her and supporting her efforts.

"They genuinely wanted me to succeed, and did everything they could to make it happen" she said.

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AI
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models don't just know that. "You need to give it context, he said."

Anyone who builds AI models must think about where the data came from, what instruments and devices measured the signals and who collected the data, he said.

AI developers must also be aware of how models influence human behavior. One of Celi's colleagues studied how an AI medical imaging tool affected the performance of

radiologists. The researchers found experienced radiologists performed worse after they began using the tool.

The radiologists were confident in their abilities until the tool began interpreting images differently. They realized the tool caught potential

abnormalities that they didn't. Afterwards, they were less confident and made more mistakes.

"AI will change the behaviors of users," Celi said. "When AI becomes more and more accurate, our tendency is to just hit accept, accept, accept."

Despite these challenges, Celi is excited about AI's potential. "We have an immense opportunity to start with a clean slate and truly improve the way we learn."

A few years ago, Celi began teaching courses in AI at MIT. Because the field is moving so fast, he teaches his students how to think critically.

"We need to teach our students how to ask the right questions, how to be able to evaluate those answers, how to know when their understanding of a problem is limited, how to seek help and how to seek other expertise to be able to come up with a good study design," he said.

Celi's team created several publicly available databases, including the Medical Information Mart for Intensive Care (MIMIC), a freely available, de-identified, electronic health record dataset. More than 10,000 papers have cited the database.

His lab regularly organizes "datathons," where experts from data science and health-care backgrounds come together to attend workshops and evaluate the performance of AI models in different medical fields. An

upcoming datathon will assess models for depression recognition. Patients, psychologists, social workers, psychiatrists and nurses will meet to evaluate the performance of the models.

Currently, Celi is measuring the impact of these events. He's found attendance

increases the chances scientists work with others outside their specialties.

They also bring together high school students and experts. They ask participants to read papers that have profound implications in the application of health AI. Then, they have a discussion.

"We ask students questions such as: What are the worst scenarios that could happen as a result of this? What should we do? What policies can we erect? What about guardrails and how do we change the incentive structure?"

By focusing on the ability to think critically, developers and clinicians alike will be able to take advantage of the promise AI healthcare models offer.

"There's so much energy around AI," Celi concluded. "I think we will be remiss if we waste that."

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NIH Labs Compete in the Freezer Challenge

Since its inception in 2017, the Freezer Challenge has encouraged labs to reduce

energy consumption, which reduces operating costs and environmental impact. While some participating researchers have received awards, all participants have attained better sample management and more reliable equipment.

Each year, thousands of labs from government organizations, universities and private companies compete to see who can reduce the most

energy consumed by the freezers in their labs. The challenge, co-hosted by My Green Lab and the International Institute for Sustainable Laboratories, is held from January through June.

This year, 87 labs participated in the NIH Freezer Challenge. Their combined efforts reduced energy consumption by more than 1,100,00 kWh, conserved 856 MTCO2e in greenhouse gas emissions and saved more than \$115,000 this year alone. There are thousands of freezers in service at NIH, yet this feat was accomplished by 87 labs. These results show the power each lab has to increase

freezer reliability while also protecting the environment.

The total costs and emissions from cold storage equipment is significant. Mechanical Ultra-Low Temperature (ULT) freezers are among the most energy-intensive pieces of laboratory equipment. Older, unmaintained

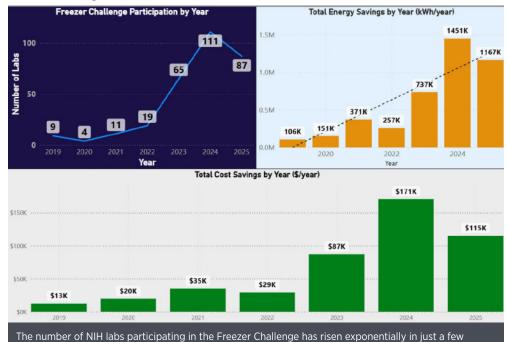
ULT freezers can be especially costly.

Challenge initiatives ranged from maintenance options, such as defrosting freezers, to laboratory best-management practices, such as changing the temperature setting of ULT freezers. Changing the temperature from -80°C to -70°C reduces the

amount of work the compressor does, which increases freezer reliability and reduces energy consumption by about 30%.

Within NIH, the National Institute of Environmental Health Sciences (NIEHS) boasted the most submissions with 21 labs participating. The National Center for Advancing Translational Sciences (NCATS) came in second with 12 submissions, and the National Heart, Lung and Blood Institute (NHLBI) came in third with 10.

For more information, see: go.nih.gov/ EooZTQt.



A researcher reaches into a ULT freezer.

Radiation Biostatistics Expert Retires

BY JENNIFER LOUKISSAS

Dr. Mark Little, senior investigator in the National Cancer Institute's Radiation **Epidemiology** Branch (REB), retired in June. Little is an internationally recognized expert in radiation biostatistics.



NCI's Dr. Mark Little

During his tenure in REB, Little focused on the study of ionizing radiation and risk of cancer, cataracts and cardiovascular disease, as well as solar ultraviolet radiation and risk of basal cell carcinoma, hemopoietic malignancies and brain tumors. He developed novel statistical models to estimate and account for measurement error, allowing for the identification of mechanisms of carcinogenesis and related radiobiological endpoints.

Little also served as the lead statistician in the UK-NCI study of cancer risk following pediatric CT exposure and assessed thyroid cancer risk in persons exposed in childhood to radioactive fallout following the 1986 Chornobyl accident.

Among his most important contributions were efforts to quantify the health risks in populations exposed to low and very low doses of environmental, occupational and medical sources of radiation. This aspect of radiation epidemiology is of considerable public health importance as most of the world's population experiences exposures in this range. Importantly, he developed methods to assess and address measurement error (in particular, shared errors) and explore the likelihood of dose thresholds.

Little studied mathematics at Trinity College, Cambridge, and obtained his doctorate in mathematics at New College, Oxford, both in the United Kingdom.

years, resulting in more energy and cost savings.

Taurine is Not a Reliable Aging Biomarker

Scientists at NIH have found that levels of circulating taurine, a conditionally essential amino acid involved in multiple important biological functions, is unlikely to serve as a good biomarker for the aging process. In blood samples from humans, monkeys and mice, scientists found that



PHOTO: PROSTOCK STUDIO/SHUTTERSTOCK

circulating taurine levels often increased or remained constant with age.

Longitudinal data revealed that within individuals, differences in taurine levels often exceeded age-related changes. Researchers also found that taurine levels were inconsistently associated with health outcomes across age, species and cohorts, suggesting that declining taurine is not a universal marker of aging. Instead, its impact may depend on individual physiological contexts shaped by genetic, nutritional and environmental factors. Results are published in *Science*.

Taurine recently gained popularity as a dietary supplement due to recent research that found supplementation with taurine improved multiple age-related traits and extended lifespan in model organisms (worms and mice). However, there is no solid clinical data to show its supplementation benefits humans.

Researchers measured taurine concentration in longitudinally collected blood from participants in the Baltimore Longitudinal Study of Aging (aged 26-100 years), rhesus monkeys (aged 3-32 years) and mice (aged 9-27 months). Taurine concentrations increased with age in all groups, except in male mice in which taurine remained unchanged. Similar age-related changes in taurine concentrations were observed in two cross-sectional studies of geographically distinct human populations, the Balearic Islands Study of Aging (aged 20-85 years) from the Balearic region of Mallorca, and the Predictive Medicine Research cohort (aged 20-68 years) from Atlanta, Georgia, as well as in the cross-sectional arm of the Study of Longitudinal Aging in Mice.

Researchers also found that the relation between taurine and muscle strength or body weight was inconsistent. Low motor function performance can be associated either with high or low concentrations of taurine whereas, in other cases, no relation at all is found between these variables.

NIH Researchers Identify Brain Circuits Responsible for Visual Acuity

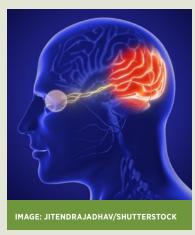
NIH researchers have identified which brain circuits are vital for visual acuity and how they are affected by damaged retinal cells.

While vision restoration therapies aim to replace or repair damaged cells in the eye, it is critical to understand how brain circuits involved in vision are affected by retinal cell loss. Study results suggest that targeting these circuits may be necessary for optimal vision recovery. The study was published in *The Journal of Neuroscience*.

Visual processing involves interactions between neurons in the eye and brain and is vital for sight. These pathways originate in photoreceptor cells in the retina that convert light energy into electrical signals, which are then transmitted to the brain's visual processing centers. Damage to retinal cells often affects sight. In a process known as neuroplasticity, the brain undergoes functional changes to adapt to a retinal injury or disease. A person who experiences vision loss, for example, may have a resulting "blind spot" in a portion of their field of view.

Current therapies target retinal cells; however, retinal cells are just the first step in the visual pathway.

Scientists aimed to understand how neurons downstream of the retina are affected by damage to retinal ganglion cells (RGCs), which receive signals from other retinal cells and transfer to the brain. RGCs connect to neurons in a relay center in the brain, known as the lateral geniculate nucleus (LGN), that transmits signals to the visual cortex, where those signals are processed into images. The study examined two types of LGN cells that respond to different types of visual information



and form parallel processing pathways: X-LGN neurons, which contribute to visual acuity, and Y-LGN neurons, which contribute to motion perception.

Researchers demonstrated the effects of retinal cell loss on the X and Y visual processing pathways using an animal model. Following injury to the RGCs in the retina, they found that X-LGN neurons didn't respond properly to visual stimuli, whereas Y-LGN neuron responses remained intact. These findings show retinal cell loss affects downstream visual pathways differently, suggesting higher sensitivity of visual acuity pathways to retinal degeneration.

Diagnostic Aid Can Assess Risk of Diabetic Foot Ulcer Recurrence

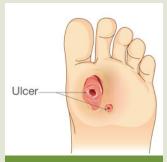


IMAGE: LOGO3IN1/ADOBE STOCK

An NIH-funded research team has identified a diagnostic aid with the potential to accurately predict the recurrence of diabetic foot ulcers that visually appeared to be fully healed. By measuring the skin's barrier function through a process known as trans-epidermal water loss, or TEWL, scientists were able to determine which wounds were more likely to reopen.

TEWL measurements are a major factor in burn care, where deep layers of the skin are often damaged. The findings suggest that full restoration of skin

barrier function should be incorporated into existing wound treatment standards to ensure complete wound closure and to better identify patients at risk of wound recurrence.

Scientists, collaborating through the NIDDK Diabetic Foot Consortium, evaluated more than 400 study participants who had a diabetic foot ulcer that appeared to be closed. They measured TEWL at the site of the foot ulcer and found 35% of participants with high TEWL (more water loss) reported a wound recurrence by 16 weeks, compared to just 17% for those with low TEWL (less water loss). Participants with higher TEWL were 2.7 times more likely to experience a wound recurrence than participants with low TEWL.

Diabetic foot ulcers are a major complication of diabetes where a break in the skin of the foot is often unnoticed by a patient due to nerve damage, known as neuropathy. They are the leading cause of non-traumatic lower-limb amputations, and untreated or unhealed ulcers significantly increase the risk of death. Wounds that appear to be healed on the surface may not be fully closed below the superficial surface of the skin, hampering the effectiveness of the skin's barrier function to keep in water and keep out pathogens, such as bacteria.



Above I, NIH'ers share energy conservation tips and procedures for proper disposal of chemical waste. Above r, staff from NIH's Office of Animal Care and Use host educational, interactive activities at their table.



Above, staff share wellness and stressmanagement tips; at right, colleagues enjoy rosemary and berry mocktails and promote NIH work-life resources.

Staff Explore Safety, Wellness Tips at Annual Fair

PHOTOS: MARLEEN VAN DEN NESTE

In June, Safety, Health and Wellness Day returned to the Clinical Center's south lobby. The annual fair raises awareness about safety and wellness concerns to help prevent and reduce work-related injuries and illnesses.

This year's fair featured posters, demonstrations, a stretch class and healthy treats. Exhibits included lab safety, radiation safety, energy conservation, fire prevention and Occupational Medical Services as well as a range of resources for when employees need advice and assistance—from child and family care to the Employee Assistance Program.

The fair was sponsored by NIH's Office of Research Services in conjunction with NIH's Recreation and Welfare (R&W) Association.







Above I, NIH Deputy Director for Management Dr. Alfred Johnson (standing third from I) greets members of NIH's Division of Fire and Rescue Services. At r, colleagues promote radiation safety.

