

‘COMPLEX SYMPHONY ORCHESTRA’ McCurdy Studies Whether Kratom Can Reduce Opioid Withdrawal, Ease Pain

BY DANA TALESNIK

It’s a word now commonly spotted on smoke, vape and herbal shop signs across much of the country. But what exactly is kratom and is it safe to ingest?

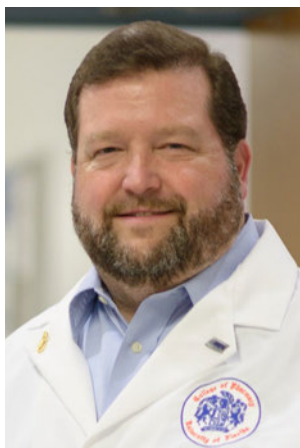
Kratom is a tropical evergreen tree, from the same family as the coffee plant, whose leaves can be consumed in various forms. Its active compounds reportedly produce a range of stimulant, pain-relief and mood-enhancing effects.

Dr. Christopher McCurdy, professor of medicinal chemistry at the University of

Florida (UF), became interested in the therapeutic potential of kratom from learning how it’s been used in its native region.

“Kratom has been used by field workers in Southeast Asia to relieve pain and as a stimulant to improve their work capacity in the hot, tropical climate,” he said.

“Also, when they would run out of opium—for those who used it—they would use kratom in a



Dr. Christopher McCurdy

SEE **KRATOM**, PAGE 6

MILITARY, CIVILIAN DIMENSIONS Stibbe Examines Effects of WWI Internment

BY ERIC BOCK

The internment of hundreds of thousands of soldiers and civilians during World War I gave governments a unique opportunity to experiment with different kinds of humanitarian assistance, said Dr. Matthew Stibbe, during a recent NLM History of Medicine talk. By studying the experiences of interned citizens in the 1910s, he hopes to gain insights into how isolation and uncertainty affect people, something that’s relevant today.

From 1914 to 1918, roughly 8 million to 9 million soldiers became prisoners of war, said Stibbe, professor of modern European history at the United Kingdom’s Sheffield

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Volunteer vets issue important reminder about campus wildlife. See p. 2.

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‘NO BETTER CHAMPION’ NIH Mourns Porter, Longtime Friend of Medical Research

“There is no better champion for medical research than John Porter.” When then-NIAMS director Dr. Stephen Katz made that observation in 2011, legendary legislator Porter had been retired from Congress for a decade already. However, he’d never paused his efforts to increase support for NIH and for the medical research enterprise at large.

Porter died on June 3 at age 87.

For 21 years, the Republican represented



NIH champion John Porter in 2014

PHOTO: ERNIE BRANSON

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Bldg. 1’s front lawn is once again awash in cyclists for Bike to Work Day.

PHOTO: MARLEEN VAN DEN NESTE

Bike to Work Day Back at NIH for 2022

NIH’s main campus in Bethesda was once again one of nearly 100 pit stops in the Washington, D.C., metropolitan area for this year’s Bike to Work Day, May 20. Forecast to be the hottest day of the year, BTWD dawned clear, but got muggy as thousands around the region pedaled to their job sites.

NIH’s first BTWD observance since 2019—when more than 550 people pre-registered to

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SHARE YOUR FEEDBACK

Take the Federal Employee Viewpoint Survey

The 2022 Federal Employee Viewpoint Survey (FEVS) is currently open and will close on Friday, July 22. The annual government-wide survey gives eligible federal employees an opportunity to provide confidential feedback about their work satisfaction, organization and its leaders, and work/life balance.



The FEVS is available to full- and part-time permanent, non-seasonal employees, on board on or before Nov. 19, 2021. Eligible employees should check their inboxes for email from OPM. Results from the FEVS are used by leadership to develop specific plans aimed at making your institute, center or office a better place to work by incorporating professional and coaching development programs, listening sessions, interactive social events and more. For details about FEVS, visit <https://hr.nih.gov/workforce/fevs> or email NIHFEVS@nih.gov.

COSWD Issues RFI to Develop DEIA Prize

Respond By July 28

NIH's chief officer for scientific workforce diversity (COSWD) is currently seeking suggestions on the development of a prize competition to reward and promote inclusive excellence. The outreach is an outcome of UNITE, which was established to address structural racism within the NIH-supported and the greater scientific community.

The potential prize would recognize institutions of higher education that have implemented successful, innovative interventions for enhancing faculty and student diversity, equity, inclusion and accessibility (DEIA). These elements are essential to ensure equity and eliminate structural barriers to success among students and faculty in biomedical research.

Initiating such a prize is part of COSWD's commitment to increasing and sustaining biomedical research workforce diversity through institutional culture change.

The primary goal in establishing a competition is to reward transformative interventions developed by



Deer graze on the lawn in front of the Clinical Research Center

PHOTO: DUSTIN HAYES, NEI

'KEEP WILDLIFE WILD'

Veterinary Volunteers Respond to Calls About Distressed/Injured Critters

Spring and summer are times when many wild animals on campus are busy raising their young.

The Wildlife Veterinary Volunteers Group wants to remind everyone to "Keep the Wildlife Wild" on NIH campuses while making sure that truly injured or distressed wildlife are cared for.

If you see any animal—no matter what species—that appears to be injured, distressed or acting aggressive, call the NIH Police non-emergency number (301) 496-5685. The NIH operator will call the volunteer veterinarian on duty to address the problem.

The group responds to calls about the Bethesda and Poolesville campuses.

The more information you can provide about the exact location of the animal, time found and activity of the animal, the better the team will be able to respond to the emergency.

institutions to create research environments that promote and value DEIA. A secondary objective is to highlight evidence-based best practices proven to create more inclusive environments for students and faculty.

Recently, COSWD issued a request for information (RFI) seeking comments it may use to inform the potential prize competition. The COSWD team would like to hear from stakeholders throughout the scientific research community, DEIA experts, researchers and interested members of the public.

COSWD particularly wants input on the following:

- Competition structure
- Strategies for sharing information about the competition

- Judging criteria
- Amount of time needed to develop a prize submission
- Ways to disseminate approaches that promote inclusive excellence
- Reasons for and potential barriers to participating in the competition

To learn more, visit <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-109.html>. All responses must be received by Thursday, July 28.

The COSWD team encourages everyone to take advantage of this opportunity to share thoughts on how NIH might recognize institutions that advance DEIA and create systemic change.

Send inquiries to: COSWDPrizeCompetition@nih.gov.

Can Good Hydration Reduce Risk of Heart Failure?

NIH researchers have found that staying well hydrated may be associated with a reduced risk for developing heart failure. Their research, which appears in the *European Heart Journal*, suggests that consuming sufficient amounts of fluids throughout life not only supports essential body functioning, but may also reduce the risk of severe heart problems later on.

Heart failure, a chronic condition that develops when the heart does not pump enough blood for the body's needs, affects more than 6.2 million Americans. It's also more common among adults ages 65 and older.

After conducting preclinical research that suggested connections between dehydration and cardiac fibrosis, a hardening of the heart muscles, NHLBI researcher Dr. Natalia Dmitrieva and her team looked for similar associations in large-scale population studies.

To start, they analyzed data from more



NHLBI researchers Dr. Natalia Dmitrieva and Dr. Manfred Boehm and their colleagues in the Laboratory of Cardiovascular Regenerative Medicine are looking at whether staying well hydrated can stave off risks of heart failure.

study. Approximately 11,814 adults were included in the final analysis and, of those, researchers found 1,366 (11.56 percent) later developed heart failure.

To determine potential links with hydration, the team assessed the hydration status of the participants using several clinical measures.

Looking at levels of serum sodium, which increases as the body's fluid levels decrease, was especially useful in helping to identify participants with an increased risk for developing heart failure. It also helped identify older adults at risk for developing both heart failure and left ventricular hypertrophy, an enlargement and thickening of the heart.

In a cohort of about 5,000 adults ages

“Serum sodium and fluid intake can easily be assessed in clinical exams and help doctors identify patients who may benefit from learning about ways to stay hydrated.”

—DR. MANFRED BOEHM

than 15,000 adults, ages 45-66, who enrolled in the Atherosclerosis Risk in Communities (ARIC) study between 1987-89 and shared information from medical visits over a 25-year period.

In selecting participants for their retrospective review, the scientists focused on those whose hydration levels were within a normal range and who did not have diabetes, obesity or heart failure at the start of the

70 to 90, those with serum sodium levels of 142.5-143 mEq/L at middle age were 62 percent more likely to develop left ventricular hypertrophy. Serum sodium levels starting at 143 mEq/L correlated with a 102 percent increased risk for left ventricular hypertrophy and a 54 percent increased risk for heart failure.

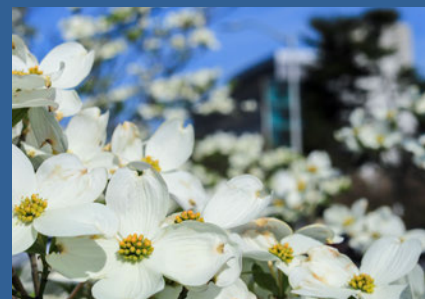
These early associations suggest good hydration may help prevent or slow the

progression of changes within the heart that can lead to heart failure.

“Serum sodium and fluid intake can easily be assessed in clinical exams and help doctors identify patients who may benefit from learning about ways to stay hydrated,” said NHLBI senior investigator Dr. Manfred Boehm, who leads the Laboratory of Cardiovascular Regenerative Medicine.

Fluids are essential for a range of bodily functions, including helping the heart pump blood efficiently, supporting blood vessel function and in orchestrating circulation. Yet many people take in far less than they need.

While fluid guidelines vary based on the body's needs, researchers recommended a daily fluid intake of 6-8 cups of water for women and 8-12 cups for men. **R**



ON THE COVER: Dogwood blossoms with Natcher Bldg. in background

IMAGE: DUSTIN HAYES, NEI

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Internment

CONTINUED FROM PAGE 1

Hallam University and 2019 NLM Michael E. DeBakey fellow.

The experiences of the POWs varied greatly, Stibbe noted. Some soldiers were forced into physical labor near the frontlines. Others spent their time at guarded camps in more comfortable conditions. Neutral countries like Switzerland detained soldiers who strayed onto their lands. Across Europe, the death rate for these prisoners was around 11 percent, with considerable variations from country to country.

About 800,000 civilians also experienced internment. When war was declared in 1914, hundreds of thousands of citizens on both sides were imprisoned in detention camps. British nationals living in Germany, for example, were seen as potential threats. These citizens were held captive, sometimes for the whole duration of the war.

“Military POWs were protected, in theory, by international legislation,” he said. “Captive states were supposed to treat captured soldiers from the opposite side according to the same standards as their own enlisted men, in terms of food, accommodations and access to medical care.”

Some civilian and military prisoners were also protected by the “reciprocity principle,” in which “captor nations would not mistreat prisoners because they wanted to protect the interests of their own subjects in enemy captivity.” Citizens interned by their own governments, however, had none of these protections.

Captives had political and military value, said Stibbe. They were not just “useless eaters,” although they were sometimes dubbed as such. Rather, they were bargaining chips, sources of intelligence and a labor force.



2019 NLM Michael E. DeBakey fellow Dr. Matthew Stibbe of United Kingdom's Sheffield University

Additionally, captor nations used POWs in propaganda to build support for the war.

Humanitarian organizations like the Geneva-based International Committee of the Red Cross campaigned for captor nations to treat civilian prisoners like military prisoners.

“There’s a dilemma there,” Stibbe argued. “If they were treated as military captives, civilians could experience disadvantages. They might not be able to excuse themselves from labor, for instance.”

Certain groups, such as the British Quakers, thought that if they organized good things for German captives in Britain, that would encourage Germans to do the same. For example, the Quakers lobbied universities in Britain to give scientific equipment to German scientists in internment camps. In return, the Germans gave scientific

equipment to detained British scientists.

As the war went on, countries began to standardize relief efforts, he said. Experts determined the amount of food, books and sports equipment each prisoner received. Neutral organizations like the Red Cross managed distribution of the packages.

“A lot of relief organizations decided that the typical prisoner was a literate, white male aged between 18 and 45,” Stibbe noted. “There’s a certain blindness towards the needs of particular groups.”

In response, Dr. Elisabeth Rotten, a Swiss citizen with ties to the Quakers, created an organization to help enemy aliens in Germany who were in distress. Rotten believed those “who were most distressed were not the people who were in camps” but “the wives and children,” Stibbe explained.


Exchange agreements were common. Soldiers with serious injuries were often traded. In 1917, some countries recognized that “barbed-wire disease,” an “umbrella term for mental health conditions observed in long-term captives,” could be grounds for exchange, he said.

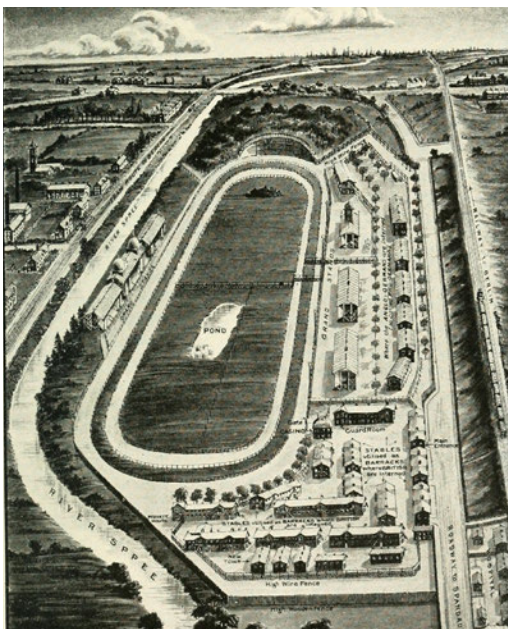
A Swiss medic named Adolf Lukas Vischer wrote a book about the disorder. He argued, “It doesn’t matter how good the conditions are in a camp. After a certain period of time, everybody in a prisoner of war camp will develop mental health symptoms, not just those who developed very obvious ones that necessitate their removal to a psychiatric institution.” He further stated no one knew what the psychological implications of long-term internment might be.

The idea was controversial. Some medical experts thought diagnosing prisoners with barbed-wire disease would encourage others to claim they had the condition so they could go home. The Quakers criticized Vischer because they thought sending food and materials for arts and crafts was a good thing.

“Captivity itself had overlapping military and civilian dimensions, purposes and features,” Stibbe said. “We cannot understand it holistically without understanding this overlapping of the military and civilian.”

To view the talk, see: <https://videocast.nih.gov/watch=44383>.

For more information about the NLM Michael E. DeBakey Fellowship in the History of Medicine, see: <https://www.nlm.nih.gov/hmd/get-involved/debakey-fellowship.html>. 



Stibbe showed this 1917 image of an internment camp of British prisoners near Berlin, from the book *In Ruhleben, Letters from a Prisoner to His Mother*.

IMAGE: WIKIMEDIA COMMONS

NEW PARTNERSHIP FORGED Implementing Interventions for Environmental Health Equity

BY JENNIFER HARKER

Environmental health scientists forged a new partnership with implementation scientists to discuss how, together, they might address challenges and improve environmental health equity, during a 2-day workshop held earlier this year.

Implementation science studies methods to promote adoption of evidence-based practices, interventions and policies to improve population health. The field is part of NIEHS's strategic plan—Promoting Translation: Data to Knowledge to Action—to encourage application of strategies to reduce or avoid environmental exposures and resulting health impacts.

Real-World Example

Dr. Lindsey Martin, a health scientist administrator in the NIEHS Population Health Branch (PHB), and Dr. Rick Woychik, director of NIEHS and the National Toxicology Program, offered a real-world example from the Clean Cooking Implementation Science Network that applied implementation science to promote uptake of clean cooking technology to reduce household air pollution (HAP).

Unsafe cooking practices lead to HAP around the world and disproportionately affect the health of women and children in low- and middle-income countries. Researchers are studying strategies to promote appropriate use of cleaner

cookstoves to replace HAP-generating instruments. Understanding the related individual, community, societal and policy factors is essential to supporting sustainable adoption.

Challenges to Implementation

“Could implementation science be the missing piece in addressing environmental health disparities through environmental justice research?” asked Dr. Melissa Smarr, a PHB health scientist administrator.

To achieve equity, barriers must first be worked through and understood. For example, structural racism may make implementation more difficult due to long-established interventions that might not serve all people equally. Therefore, de-implementation can be just as important a consideration, according to Dr. Rachel Shelton of Columbia University.

“We can introduce new programs and policies, but we also need to be thinking about how we de-implement programs, policies and

practices that are already in place and are harmful,” Shelton said. “This is a new and emerging area of implementation science.”

Power of Green

Living in green spaces, surrounded by



NIEHS's Dr. Lindsey Martin explained how implementation science and environmental health science can team up.

PHOTO: STEVE MCCAIV/NIEHS



A woman cooks indoors on a makeshift cookstove. Implementation science was used to promote uptake of an environmental health science intervention—clean cooking technology to reduce household air pollution.

PHOTO: MARVIN MINDER/SHUTTERSTOCK

trees and grass, improves cardiovascular health and reduces air pollution, according to NIEHS grantee Dr. Aruni Bhatnagar, who leads the Green Heart Study at the University of Louisville.

Expanding on the health effects of greening urban areas, Dr. Eugenia South, director of the Urban Health Lab at the Perelman School of Medicine at the University of Pennsylvania, explained that the hardest hit areas stand to gain the most from environmental interventions.

“Gun violence is not immediately an outcome that people associate with thinking about neighborhood environments and environmental health, but I really want to get people thinking about that outcome,” she said.

South's research suggests that revitalizing urban vacant lots with greenery resulted in a 29 percent reduction in gun violence and lowered self-reported depression by 41 percent.

'Never Too Early'

“A main takeaway is that it is never too early to think about implementation science,” Martin said. “From better understanding issues of feasibility to planning for sustainability, you could incorporate implementation science throughout the research pathway.”

The workshop featured panel discussions about four areas organizers say the fields of environmental health sciences and implementation science can grow together: environmental health disparities and environmental justice; prevention and interventions; climate change and disasters; community-engaged research.

“Equity is really the cornerstone and it needs to be front and center in how we think about science moving forward,” added PHB chief Dr. Claudia Thompson, in closing remarks.

Martin, NCI program director for implementation science Dr. Gila Neta and OBSSR health scientist administrator Dr. Dara Blachman-Demner cochaired the workshop, which was a joint effort by NIEHS, NHLBI's Center for Translation Research and Implementation Science, NICHD, FIC, NCI, NIMH, NIMHD, Office of Behavioral and Social Sciences Research and Office of Disease Prevention.

Kratom

CONTINUED FROM PAGE 1

little bit higher doses to help avoid opioid withdrawal.”

McCurdy wants to get to the root of the leaves’ chemical properties and pharmacologic effects. He asks, as does the title of his recent NCCIH Integrative Medicine Research Lecture, “Can a controversial tree help end the opioid crisis?”

Drug of Concern

Despite an FDA import alert, an estimated 2,000 metric tons of kratom enter the U.S. monthly, mostly from Indonesia, suggesting millions of users across the country. Though federally legal, kratom is banned or restricted in multiple states. The U.S. Drug Enforcement Administration has classified kratom as a drug and chemical of concern, pending further study.

“We know that very few deaths are



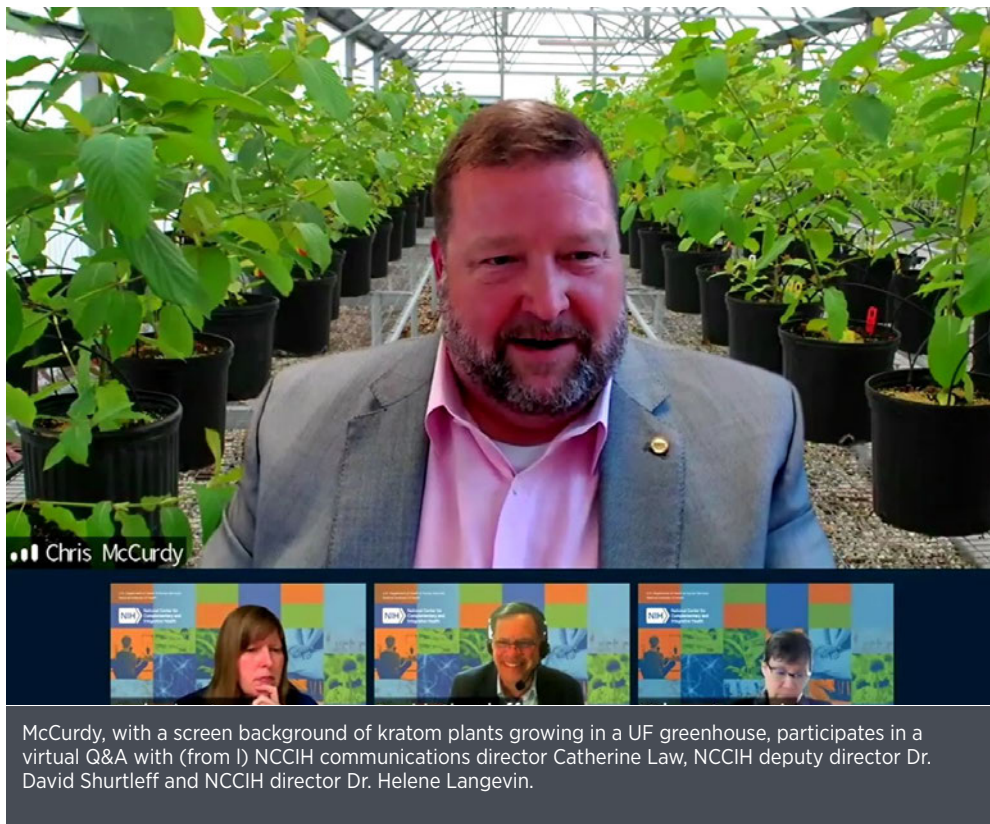
A sign next to an organics market in North Bend, Oregon

PHOTO: THE IMAGE PARTY/SHUTTERSTOCK

attributable to a kratom product alone, and for those that are, there could be extreme circumstances, in terms of overdosing, or it could be adulterated with synthetic compounds,” such as fentanyl derivatives or other novel psychoactive substances that are unknown or undetected, said McCurdy.

Traditionally, in Thailand and elsewhere in Southeast Asia, kratom is consumed as a brewed tea. The fresh leaves are cut and boiled for hours.

In the U.S., though, kratom arrives as crushed leaves or powder and can come in different forms: capsules, energy shots, even gummies. McCurdy is collaborating with UF’s Apopka campus to grow kratom trees and extrapolate the pharmacologic differences between fresh-leaf kratom and concentrated extracts.



McCurdy, with a screen background of kratom plants growing in a UF greenhouse, participates in a virtual Q&A with (from l) NCCIH communications director Catherine Law, NCCIH deputy director Dr. David Shurtleff and NCCIH director Dr. Helene Langevin.

“Collaboratively, we are trying to get a homegrown species to develop a product more similar to the traditional use for study in the U.S., [rather] than having to rely on these dried-leaf materials, which undergo post-harvest oxidation...and many times have changed the composition of the alkaloidal content,” he said.

Therapeutic Potential

Kratom has opioid activity, said McCurdy, “but I’m going to show you that it’s much more disruptive than just opioid activity. We’ve looked at it primarily as having the potential to replace several medications used during opioid detoxification.”

McCurdy points to kratom having adrenergic (stimulant); serotonergic (mood-enhancing); analgesic (pain-relieving) and anxiolytic (anti-anxiety) activity. “If you could combine all those into one product,” he said, “you might be able to improve medication adherence and completion of detoxification.”

Another plus is that

traditional kratom withdrawal tends to be mild. “It’s in the upper end of mild,” McCurdy said, “but it’s not in moderate and it’s certainly not in severe.” He’s working to get a standardized kratom product into clinical trials to evaluate its overall potential and therapeutic claims.

The Abundant Alkaloid

So far, investigators have isolated more than 40 alkaloids—organic compounds—in kratom. The predominant one, mitragynine



Kratom can be consumed in many forms, including brewed tea and capsules.

PHOTO: WASANAJAI / SHUTTERSTOCK



Dr. Brian Pearson of UF's department of environmental horticulture stands next to 1 of 100 in-ground kratom trees growing on the UF-Apopka campus. About 1,000 more are growing in a nearby greenhouse, allowing McCurdy to study the pharmacological properties of fresh-leaf kratom.

PHOTO COURTESY BRIAN PEARSON

(MG)—which gets its name from the plant's genus, *Mitragyna speciosa*—accounts for up to 66 percent of kratom's alkaloid content.

"It's the most abundant alkaloid in the plant, so it's the most easily extracted, isolated, purified and studied," said McCurdy.

MG occurs naturally in the plant. It's

traditional opioids, such as constipation and respiratory depression. "If you look at poison control center data," he added, "kratom overdoses resemble stimulants, not opioids."

In wild-type mice injected with a large dose of MG, McCurdy said the analgesic effect comes quickly, then dissipates after an hour. But this is just MG isolated.

★ ★ ★

"Kratom is a complex symphony orchestra of alkaloids, and what we generally tend to do in science is pluck each instrument out and listen to it at full blast and forget about the symphony it naturally occurs in."

-DR. CHRISTOPHER MCCURDY

★ ★ ★

considered a partial opioid receptor agonist, though McCurdy said he wouldn't lump it in the traditional opioid category.

"We've collected data to show it has much less abuse and dependence liability than other opioid analgesics," he said.

What's more, MG's chemical composition pushes away some adverse side effects of

"Kratom is a complex symphony orchestra of alkaloids, and what we generally tend to do in science is pluck each instrument out and listen to it at full blast and forget about the symphony it naturally occurs in," said McCurdy, urging listeners to take the data he presented in that context. "We're looking at these [elements] at full blast. These are big

doses [given to the mice]...To achieve that in humans taking kratom just straight, it would make them vomit long before they would get to that level of efficacy."

Ingesting kratom whole, through the tea leaf, has good analgesic effects but is less robust than taking straight mitragynine orally, which can be as potent as codeine or morphine in some cases.

"MG by itself is that loud trumpet it wants to be," he said. "It does not appear to have abuse or addiction potential and reduces morphine and heroin intake in rats. These are of course desired characteristics of candidate pharmacotherapies for opiate addiction and withdrawal."

Molecule of Concern

One of the three known unnatural alkaloids in kratom, 7-hydroxymitragynine (7-HMG), can form when drying the leaves and it also metabolizes in the body. Not seen in fresh-leaf kratom, 7-HMG has high selectivity at opioid receptors.


"That's why we're so concerned about this molecule," said McCurdy.

He said his studies found 7-HMG "more potently substitutes for morphine...indicating that 7-hydroxy is potentially an abusable and addictive compound."

However, 7-HMG is unstable in human plasma and, taken orally, it does not appear to cross the blood-brain barrier very efficiently. New research shows equally promising news about the amount of MG converted to 7-HMG in the body.

"This is some of the hottest new data, refuting some work that's come out saying that 7-hydroxy is responsible for kratom's analgesic effects," McCurdy said. "We don't believe that to be the case. We don't believe the amount generated through metabolism is pharmacologically relevant."

McCurdy's research to date suggests kratom could help curb the opioid epidemic and manage pain and has other potential applications yet unexplored.

"There's so much anecdotal evidence out there in treatment of cardiovascular disease, diabetes and other avenues we haven't been able to tread into yet," he said during the Q&A. "Legitimate users are fighting to keep kratom legal; it's revolutionary for them." 



In 2014, Porter and wife Amy celebrate completion of the research complex named for him at NIH.

PHOTO: ERNIE BRANSON

Porter

CONTINUED FROM PAGE 1

the North Shore of Chicago, northwest suburbs and eastern Lake County of Illinois in the U.S. House of Representatives, serving the 10th district from January 1980 until retiring in January 2001.

He was a member of the House

health-related programs of federal agencies such as NIH flourished.

In addition, Porter's commitment to the health and well-being of American citizens continued well after he left Congress. He chaired Research!America and served as vice chair of the Foundation for the NIH. He was a member of the Institute of Medicine



“Each one of us has to be involved. Let’s work together to put science and research at our country’s highest priority.”

-JOHN EDWARD PORTER



Appropriations Committee and chaired its Subcommittee on Labor, Health and Human Services, Education and Related Agencies. The committee had jurisdiction over all of NIH's health programs, as well as those of other health-related federal agencies.

Over the period of 1998 to 2003, Congress doubled the NIH budget. Porter was widely recognized as the lead architect of that “remarkable legislative achievement,” said NIH acting director Dr. Lawrence Tabak, addressing the Advisory Committee to the Director on June 9. “Mr. Porter was one of the greatest champions of NIH in the history of the agency. NIH has lost one of our most stalwart heroes.”

Congressman Porter's numerous achievements as a visionary public servant cemented his legacy. Under his leadership, influence and advocacy, the educational and

of the National Academy of Sciences and the boards of the RAND Corporation and the American Heart Association.

Porter received 10 honorary degrees and more than 275 awards, including the Mary Woodard Lasker Award for Public Service in 2000.



With Porter in 2019, NIH director Dr. Francis Collins unveils an exhibit about the ambassador for medical research.

PHOTO: CHIA-CHI CHARLIE CHANG

In January 2014, the National Academy of Sciences honored Porter with its esteemed Public Welfare Medal, “for being a tireless and effective advocate for scientific research over more than three decades, first in Congress and then in private life, thereby helping to maintain the preeminent status of biomedical research in the United States.”

Later that spring, NIH hosted a scientific symposium and a dedication ceremony to celebrate completion of the John Edward Porter Neuroscience Research Center (PNRC) on the main Bethesda campus. The 500,000-square-foot, state-of-the-art complex had been built in 2 phases and brought together 800 neuroscientists from 10 institutes and centers across NIH in an effort to spur new advances in understanding the nervous system in health and disease. PNRC's footprint nearly matched that of its namesake.

In prescient remarks at the time, Porter called on investigators to defend research to the public and announced plans for a national campaign to reach all Americans about the importance of science.

“Each one of us has to be involved,” he said. “Let’s work together to put science and research at our country’s highest priority. Now is the time to do it!” **R**

DEIA Town Hall Set, June 29

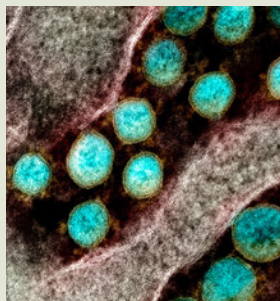
Join NIH acting director Dr. Lawrence Tabak on Wednesday, June 29 from 10:30 to 11:30 a.m. ET for a virtual Town Hall for all NIH staff, including employees, contractors, fellows and trainees to discuss NIH's diversity, equity, inclusion and accessibility (DEIA) efforts, share next steps on the NIH DEIA Strategic Plan and hear from Special Emphasis Program populations.

Also participating are Dr. Tara Schwetz, NIH acting principal deputy director; Dr. Marie Bernard, chief officer for scientific workforce diversity; Dr. Shelma Little, acting director, Office of Equity, Diversity and Inclusion; Julie Berko, chief people officer; and representatives of the following Special Emphasis Program populations: American Indian/Alaska Native, Black/African American, Asian/Native Hawaiian/Pacific Islander, Hispanic/Latino, sexual and gender minorities, people with disabilities and women.

Use this link to join: <https://bit.ly/3O6lqHc>. The meeting will include closed captioning and sign language interpreters. For other reasonable accommodation, contact Emma Wojtowicz (emma.wojtowicz@nih.gov, 301-451-2183) and/or the Federal Relay (1-800-877-8339).

Scientists Use Machine Learning to Better Identify Long Covid

An NIH-supported research team identified characteristics of people with long Covid and those likely to have it. Using machine learning techniques, scientists analyzed an unprecedented collection of electronic health records (EHRs) available for Covid-19 research to better identify who has long Covid.



Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient

IMAGE: NIAID

Exploring de-identified EHR data in the National Covid Cohort Collaborative (N3C), a centralized public database led by NCATS, the team found more than 100,000 likely long Covid cases as of October 2021 (as of May 2022, the count is more than 200,000). The findings appear in *The Lancet Digital Health*.

Long Covid is marked by wide-ranging symptoms, including shortness of breath, fatigue, fever, headaches, “brain fog” and other neurological problems that last for many months or longer after an initial Covid-19 diagnosis. Its symptoms mimic those of other diseases and conditions, often making it hard to identify.

The N3C data enclave currently includes information representing more than 13 million people nationwide, including nearly 5 million Covid-19-positive cases. The resource enables rapid research on emerging questions about Covid-19 vaccines, therapies, risk factors and health outcomes.

The new research is part of a related, larger trans-NIH initiative, Researching Covid to Enhance Recovery (RECOVER), which aims to improve understanding of the long-term effects of Covid-19, called post-acute sequelae of SARS-CoV-2 (PASC).

In the *Lancet* study, researchers examined patient demographics, health care use, diagnoses and medications in the health records of 97,995 adult Covid-19 patients in the N3C. They used this information, along with data on hundreds of long Covid patients from several clinics, to create three machine learning models.

In machine learning, scientists “train” computational methods to rapidly sift through large amounts of data to reveal new insights, patterns and clues.

The models focused on identifying potential long Covid patients among Covid-19 patients who were hospitalized and not hospitalized.

“Once you’re able to determine who has long Covid in a large database of people, you can begin to ask questions about those people,” said Dr. Josh Fessel, NCATS senior clinical advisor and a RECOVER scientific program lead. “Was there something different about those people before they developed long Covid? Did they have certain risk factors? Was there something about how they were treated during acute Covid that might have increased or decreased their risk for long Covid?”

The models searched for common features, including new medications, doctor visits and new symptoms in patients who were at least 90 days out from their acute infection. The research team hopes to use its long Covid patient classifier for clinical trial recruitment.

Study Looks at Antioxidant Effects on Dementia Risk

Some studies suggest that consuming high levels of antioxidants—compounds commonly found in vegetables and fruits that help protect cells from molecular damage—may help prevent the development of dementia.

In a new study, NIH researchers looked at associations between levels of certain antioxidants found in blood and the risk of developing dementia later in life. The compounds analyzed included carotenoids—antioxidant pigments found in plants—and some vitamins. The results were published in *Neurology*.

The team analyzed blood samples from more than 7,000 people between ages 45 and 90 who had enrolled in NHANES, an ongoing national study of nutrition, between 1988 and 1994. This data was linked with databases that tracked participants over an average of 16 years to find who later developed Alzheimer’s disease or other dementias.

Overall, the team found that people with higher blood levels of carotenoids were less likely to develop dementia. However, when the researchers expanded their analyses to include lifestyle factors such as smoking and diet, and socioeconomic factors like education and income, the benefit of higher blood carotenoid levels disappeared.

Looking at individual carotenoids, blood levels of some of them were associated with a reduced risk of developing dementia after adjusting for other health, lifestyle and social factors. However, the size of the effect was reduced by these adjustments. The potentially protective carotenoids were lutein and zeaxanthin, which are found in green, leafy vegetables, and beta-cryptoxanthin, found in some orange-colored fruits.



A new study examined associations between levels of antioxidants in blood and the risk of developing dementia later in life.

PHOTO: TOM WANG / SHUTTERSTOCK

In contrast, blood levels of the antioxidant vitamins A, C and E weren’t individually associated with dementia risk. Additional analyses suggested that high levels of vitamin A and E might actually counteract the effects of other antioxidants. The findings suggest that protective effects of some antioxidants may depend on the presence of other molecules in the body.

Around 6 million Americans are currently living with Alzheimer’s disease or another type of dementia, a number expected to rise substantially in the coming decades as the population ages. More targeted preventive strategies are needed to help people stay cognitively healthy as they age.—adapted from *NIH Research Matters*

Researchers Identify High Costs of Living with SCD

Americans ages 64 and younger with commercial health insurance who live with sickle cell disease (SCD) pay almost quadruple the out-of-pocket medical costs over their lifetimes—a total of \$44,000—as people living without the disease. And insurers pay \$1.7 million on average for each person living with SCD, according to new NIH-supported research.

The health care spending analysis—published in *Blood Advances*—highlighted the financial toll that SCD—an inherited blood condition—has on patients, families and the health care system.

To calculate the lifetime out-of-pocket medical costs for people living with SCD, researchers analyzed commercial health insurance claims filed between 2007-2018 by 20,891 people living with SCD and compared those claims to those filed by 33,588 people of the same age and sex who did not have SCD.

Researchers found that people living with SCD had more medical appointments, urgent care and emergency medical visits, and prescriptions as well as higher out-of-pocket medical costs, which averaged about \$1,300 annually.

SCD affects 100,000 people in the United States and millions worldwide. For more on this study, see: <https://go.usa.gov/xJCjd>.

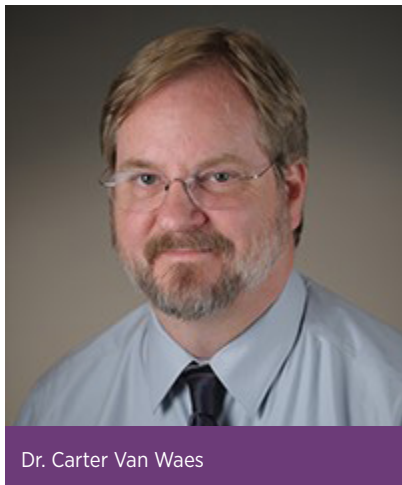
NIDCD Clinical Director Van Waes Retires

BY PATRICIA BLESSING

Dr. Carter Van Waes, clinical director and chief of the Head and Neck Surgery Branch (HNSB) and tumor biology section at the National Institute on Deafness and Other Communication Disorders, will retire on June 30.

Scientists, clinicians and colleagues honored his illustrious career at a symposium held May 13. NIDCD scientific director Dr. Lisa L. Cunningham presented Van Waes with the NIDCD Career Achievement Award for his outstanding leadership and scientific accomplishments. Many of the speakers were physician-scientists who were trained by Van Waes and spoke about how his mentorship influenced their professional careers. A common theme throughout the symposium was the inspiring role he played in training and nurturing future clinician-scientists and in advancing the NIDCD clinical research program.

“Dr. Van Waes’s early and continued leadership in NIDCD’s clinical program was instrumental in building the integrated clinical and basic research program that exists today,” said NIDCD director Dr.



Dr. Carter Van Waes

Van Waes earned a bachelor’s degree from Earlham College in 1980, followed by an M.D. and a Ph.D. in the immunology of cancer from the University of Chicago. At the University of Michigan, he completed an NIH postdoctoral fellowship in molecular biology of head and neck cancer in 1990 and his residency in otolaryngology-head and neck surgery in 1993. He joined the NIDCD Division of Intramural Research in 1993 as a senior staff fellow and was promoted to acting chief of the tumor biology section and acting NIDCD clinical director in 1995. He was selected for the permanent position as NIDCD clinical director and HNSB chief in 2003.

In the branch’s tumor biology section, Van

Waes led studies that centered on developing approaches for preventing and treating cancerous tumors that affect human communication. This basic science work built the foundation for collaborating with other NIH institutes to conduct clinical trials pioneering the use of genetic and molecular-targeted treatments and combined therapies using immunotherapies, radiation and chemotherapy for head and neck cancers.

Van Waes credits his academic mentors and colleagues at NIH and the many students and fellows in the clinical program for their

13,000 times. His work includes pioneering studies in head and neck cancer cell biology, immunology and genomics, with some of his discoveries translating directly to clinical studies and trials.

The cumulative body of work from HNSB and other laboratories provided an understanding of key genomic drivers of signal pathway and transcription factor networks in head and neck cancers, and ways these networks work to regulate the microenvironment that tumor cells create. Outlining these pathways from a systems biology perspective gave way to understanding how these networks and pathways were interacting at a molecular level.

These studies led Van Waes to work on the Cancer Genome Atlas (TCGA) program, which provided him with the opportunity to illustrate how genomic alterations fit within the pathways that he and others had previously defined.

Van Waes led a team of more than 50 TCGA researchers to compile research studies on the molecular characteristics that distinguish the genomic profiles of squamous cell carcinomas from the head, neck and other body sites. He, along with staff scientist Dr. Zhong Chen, now at the National Institute of Dental and Craniofacial Research, received the American Association for Cancer Research’s Team Science Award in 2020 for their work, which is critical to the development of more effective diagnoses and targeted treatment strategies for head and neck cancers.

Van Waes’s passion for mentoring and training the next generation of scientists was a constant force throughout his career. He was instrumental in developing the NIDCD clinical program into an environment that would attract surgeon-scientists eager for further training.

The Van Waes legacy continues today with the current NIDCD Otolaryngology Surgeon-Scientist Program, which provides opportunities for physicians to develop the skills necessary for cutting-edge, translational research on human communication processes in health and disease. He also mentored trainees in the NIH M.D./Ph.D. Partnership Training Program, the NIH Medical Scientist Training Program and the NIH Oxford-Cambridge Scholars Program. He tutored and mentored students and fellows in the NIH Clinical Research

“Dr. Van Waes’s early and continued leadership in the NIDCD’s clinical program was instrumental in building the integrated clinical and basic research program that exists today.”

—NIDCD DIRECTOR DR. DEBARA TUCCI

Debara Tucci. “The NIDCD is extremely grateful for Van Waes’s commitment to our institute over the past 29 years. His dedication to preclinical studies and clinical trials has led to the development of new therapies for the treatment of head and neck cancers that affect voice and speech and for inner ear tumors that cause hearing and balance disorders.”

robust contributions to collectively improving the treatment of head and neck cancers.

“The most gratifying experience in my career has been to see more patients live to raise their children, work, enjoy retirement and be able to communicate,” he said.

Over the course of Van Waes’s career, his research was published in almost 200 peer-reviewed journals and cited more than

Training Program and the NIH Medical Research Scholars Program.

Van Waes participated in civil rights marches from the time he was in a stroller, so it is not surprising that he was involved early in developing NIDCD programs to recruit and mentor trainees from backgrounds underrepresented in biomedical research.

In 1994, in collaboration with the then-National Center on Minority Health and Health Disparities, Van Waes and NIDCD deputy director Dr. Jay Moskowitz developed the NIDCD Partnership Program, which was designed to create research opportunities within the institute for diverse groups of trainees. The program was initially piloted with four universities and later expanded to allow applicants from anywhere in the country. He continued to value and promote diversity in his clinical program and hopes

that future initiatives will encourage more diversity in surgeon-scientist training programs.

Throughout his career, Van Waes received numerous awards for his contributions to diversity training programs, clinical care and research and scientific advances.

Past awards include the NIH Director's Award, NIH Clinical Center Director's Award for Excellence in Clinical Care, NIDCD Special Service Award for outstanding leadership as the clinical director in the establishment of a leading clinical program and numerous awards from professional organizations for head and neck cancers and clinical research.

In recognition of his outstanding leadership, expertise and mentorship, Van Waes will continue to serve NIH as a scientist emeritus.



Bernard Receives 2022 Hartford Foundation Award

NIH chief officer for scientific workforce diversity Dr. Marie A. Bernard was awarded the John A. Hartford Foundation Trustees Award for her many years of dedication to improving the lives of older adults through research, education and clinical practice improvement.

“Dr. Bernard has long been admired by the John A. Hartford Foundation, having been named to the first cohort of JAHF senior leadership scholars, chosen for their commitment to shaping the future of medicine and enhancing the health of older adults,” said foundation president Dr. Terry Fulmer. “She is ensuring diverse representation in the research workforce, addressing critical issues in geriatric care—especially Alzheimer’s disease—and has been a stellar educator and mentor to countless health care professionals. She is a true champion of older adults from all backgrounds.”

The award recognizes Bernard for her work enhancing diversity in the sciences, especially in her current role as COSWD. The COSWD Office’s mission is to be NIH’s thought leader in the science of scientific workforce diversity, using evidence-based approaches to catalyze cultures of inclusive excellence. Bernard also co-leads NIH’s UNITE initiative, which aims to identify and address structural racism within NIH and in the scientific community at large.

Established in 1929, the John A. Hartford Foundation has since 1982 awarded more than \$625 million in grants to enhance the health and well-being of older people.

Adults with Covid-19 Sought

NIMHD researchers are recruiting adults newly diagnosed with Covid-19 (within 72 hours). The study will collect physical health data using a temperature patch and digital wristband that will be provided. Collected data will be uploaded to an app using a smartphone and will help researchers better understand how Covid-19 progresses and its long-term effects in groups with different demographics and risk profiles. Contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #000315. Online: <https://go.usa.gov/x676m>.

Danzol Study Recruits Participants

NHLBI researchers are testing two low doses of danazol on individuals with short telomere disease and bone marrow disease, lung or liver disease. For more information, call the Office of Patient Recruitment (866) 444-2214 (TTY users dial 711). Online: <https://go.usa.gov/xnPym>. Refer to study #18-H-0004.

Healthy Women Sought for Study

NICHD is seeking healthy women to compare with women who have experienced implantation failure and/or early or recurrent pregnancy loss. Researchers want to look at the uterine lining, the endometrium, to understand its role in implantation and miscarriage. Contact the Office of Patient Recruitment, (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Online: <https://go.usa.gov/xzE5>. Refer to #000206-CH.

Adults with B-Cell Malignancies Sought

NHLBI opens a new clinical trial testing the drug NX-2127 for adults with relapsed/refractory B-cell malignancies. NX-2127 is an oral drug that degrades a protein in B-cell malignancies, Bruton’s tyrosine kinase, instead of inhibiting or blocking it like other drugs. NX-2127 may also stimulate the body’s immune T-cells to attack cancer cells. The study enrolls adults 18 years or older diagnosed with a B-cell malignancy that progressed after prior systemic therapies. Participation is at no cost and travel assistance may be available. Contact the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email: ccopr@nih.gov. Refer to study #000326-H. Online: <https://go.usa.gov/xuPDR>.

Have Psoriasis? CC Needs Volunteers

Do you or someone you know have mild to moderate psoriasis? Researchers at the Clinical Center are testing a form of vitamin B3 dietary supplement to help improve immune system function in the blood and skin of people with mild to moderate psoriasis. Treatments and research procedures are provided at no cost. Refer to study #20-H-0044. Online: <https://go.usa.gov/xdH2Y>. For more information, call the Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or email ccopr@nih.gov.



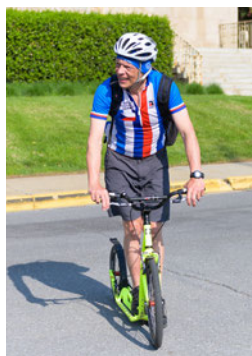
Above, Sean Cullinane (l) rocks the 2022 NIH souvenir T in cherry blossom pink. Below, it's got just two wheels and is leg-powered—count this scooter for BTWD!

PHOTOS: MARLEEN VAN DEN NESTE

Bike

CONTINUED FROM PAGE 1

bike to work on the designated day, this year's event seemed to be recovering in its own way from Covid-19. Safety precautions canceled the event in 2020 and 2021, interrupting its momentum from previous years. Participation in 2022 was also likely diminished as many employees remain on expanded telework schedules in the wake of the pandemic. Participants' enthusiasm remained high. They motivated by cycling's physical and mental health benefits as well as environmental benefits, according to several cyclists at the event.



"We had about 139 riders," said Frank Velez, NIDDK clinical research informatics analyst and NIH Bicycle Commuter Club (NIHBCC) president. "Our total mileage was 1,422 miles. We had 3 people tie for the longest ride in at 36 miles."

Riders from 17 institutes/centers, in addition to cyclists representing the Office of the Director, Office of Intramural Training and Education and Office of Research Services, checked in at NIH's pit stop in front of Bldg. 1. NCI had the highest number of unique commuters. The median commute was 8 miles and the average was 10.

"My commute was about 5 miles," said NIH acting principal deputy director Dr. Tara Schwetz, who pedaled from D.C. for BTWD. "I met up with Melissa Antman, who is on my team, and we rode most of the way together, going through some of the neighborhoods in Bethesda. We met around 9 a.m., and followed the bike route, so traffic wasn't really an issue. Last summer, I biked in almost once a week for several months. I

may start doing it again since the weather is better."

FIC deputy director Dr. Peter Kilmarx, a longtime bicycle commuter, noted the change in his routine over the past 2 years.

"Before Covid-19, I biked

every day year round," he said. "It's only about a mile from home to work across Old Georgetown Rd. Now I only come in once a week and I usually walk to get more steps, but I was in a hurry Friday, so I biked."

Since returning to work on site, NIHCC member Kathy Kranzfelder, director of NIDDK's Office of Communications and Public Liaison, bikes in once or twice a week from Gaithersburg (32 to 36 miles round trip). She was one of more than 20 NIHBCC members who volunteered to help sign in cyclists, hand out t-shirts and otherwise facilitate riders at the pit stop.

Kilmarx encourages "biking to work every day to improve health, reduce carbon footprint and pollution, relieve the parking burden on campus" and curtail overall traffic congestion in the region.

NIH'ers can find bicycling resources at: <https://ors.od.nih.gov/pes/dats/NIHBicycleProgram/pages/default.aspx>.

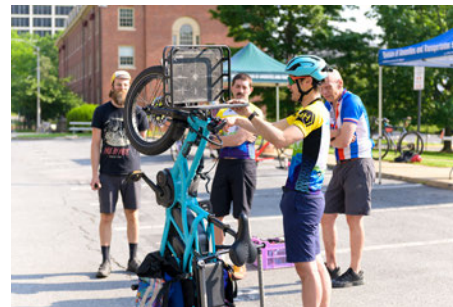
The League of American Bicyclists originated BTWD in 1956 to encourage bicycle commuting as a healthy and safe alternative to driving. NIH's observance is co-sponsored by NIHBCC and ORS's Division of Amenities and Transportation Services.—**Carla Garnett**



FIC deputy director Dr. Peter Kilmarx pedals to work.



Above, business is brisk at the sign-in table. Below, power pose on a beautiful day to bike to work



Above, a biker shows off a well-accessorized ride. Below, cyclists gather in front of Bldg. 1, after a 2-year BTWD hiatus.

