

National Institutes of Health

IN THE ZONE

**Rathmell Leads Ambitious Charge Against Cancer**

BY DANA TALESNIK

When the call came, Dr. Kimryn Rathmell couldn't pass up the opportunity. Decades of experience, curiosity and drive all led her to this moment. In December, Rathmell became the 17<sup>th</sup> presidentially appointed director of the National Cancer Institute (NCI).

"This is an incredible period of time for cancer research in terms of having such amazing scientific talent, technologies to make more and faster discoveries that cure more patients, and an administration that's so supportive," she said during a recent interview.

Rathmell, a physician-scientist and oncologist who specializes in kidney cancer, most recently served as chair of medicine and physician-in-chief at Vanderbilt University. Deeply committed to research, innovation and patient care—and with longstanding ties to NCI—she took the helm shortly after Dr. Monica Bertagnolli left NCI to become NIH director.



Dr. Kimryn Rathmell

Incorporating to make an impact, Rathmell has hit the ground running to advance the goals of the reignited Cancer Moonshot toward ending cancer as we know it.

**Building Things**

As a child, Rathmell developed a passion for science, education and the inner workings of all things from her parents. Her father taught middle school earth science; her mother taught shop class.

"I grew up loving to take things apart and put them back together, just to get a sense for how they work," she said. "I also really enjoy solving a complex problem—from understanding how molecules interact in a pathway to how people interact in a system."

In talking with people around NCI and across the cancer community, "I'm applying that same fascination to understand how the parts fit together," she said. "It's helping me find organizational knots we can untangle, so we can make operations and collaborations smoother."

**Becoming NCI Point Guard**

Growing up as a tall girl in the Midwest,

SEE RATHMELL, PAGE 4

INTRAMURAL INVENTORS SERIES RETURNS  
**Making New Molecules for New Uses**

BY AMBER SNYDER

In celebration of Makers Month, the NIH Record introduces some intramural inventors.

Reverse munchies? That's what Dr. Malliga Iyer, principal investigator and acting chief of the section on medicinal chemistry (SMC) at the National Institute on Alcohol Abuse and Alcoholism (NIAAA), wanted to make as she pondered how to develop a drug to treat obesity and associated diseases (also known as metabolic syndrome disorders).

Iyer is a medicinal chemist, someone trained to design and synthesize



IMAGE CREDIT

SEE INVENTOR, PAGE 8

**Bike to Work Day Brings NIH Cyclists Together**

BY ERIC BOCK

A few hundred NIH'ers stopped by the "pit stop" in front of Bldg. 1 to celebrate Bike to Work Day (BTWD) on May 17. More than 265 registered cyclists dropped by NIH's station.



NIH cyclist and precious cargo arrive at BTWD.

According to the Metropolitan Washington Council of Governments, which sponsors BTWD in the national capital region, the event encourages commuters to choose a healthier lifestyle while also helping to reduce traffic congestion and improve air quality.

At the station in front of Bldg. 1, riders

SEE BIKE, PAGE 6



Police Day features demos. See story, p. 12.

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## Director Testifies at Senate Hearing on FY25 Budget Request

NIH Director Dr. Monica Bertagnoli, along with five other institute directors, testified on May 23 at a Senate appropriations subcommittee hearing on NIH's budget request for fiscal year 2025. Speaking before the subcommittee on Labor, Health and Human Services, Education, and related agencies in the Dirksen Senate Office Building, Bertagnoli—in her first appearance on Capitol Hill since last fall's confirmation hearings—and the NIH contingent discussed various topics including research on H5N1 bird flu, Long Covid and other infectious diseases and the opioid crisis, as well as NIH's role as a vital driver of states' economic wellbeing.

Accompanying Bertagnoli were institute leaders (shown below, from l) Dr. Gary Gibbons, director of the National Heart, Lung and Blood Institute; Dr. Richard Hodes, director of the National Institute on Aging; Dr. Jeanne Marrazzo, director of the National Institute of Allergy and Infectious Diseases; Dr. Kimryn Rathmell, director of the National Cancer Institute; and Dr. Nora Volkow, director of the National Institute on Drug Abuse.



At the recent Senate hearing on the 2025 budget request are (from l) NIH Director Dr. Monica Bertagnoli, appropriations committee chair Sen. Patty Murray and subcommittee chair Sen. Tammy Baldwin.

Led by appropriations chair Sen. Patty Murray (D-WA) and subcommittee chair Sen. Tammy Baldwin (D-WI), legislators acknowledged the country's difficult fiscal conditions, but also largely expressed strong bipartisan support for increasing NIH funding to the extent possible.



## ORWH Launches Strategic Plan for Women's Health Research

NIH's Office of Research on Women's Health (ORWH) unveiled the NIH-Wide Strategic Plan for Research on the Health of Women 2024-2028 during National Women's Health Week, marking a significant stride in NIH's commitment to prioritize and advance research on women's health.

In a video announcing the new plan, NIH Director Dr. Monica Bertagnoli underscores

the pivotal roles of NIH and ORWH in elevating women's health research. She emphasizes the significance of ensuring access to research and its benefits for all individuals. The plan's release coincides with a pivotal moment for women's health research, aligning with the recent White House Executive Order on Advancing Women's Health Research and Innovation.

The plan outlines five goals to guide and inform NIH-supported research on women's health over the next five years, leveraging a data-driven, iterative approach with robust community input. ORWH developed the comprehensive plan with contributions from various stakeholders, including

representatives from NIH institutes, centers and offices; and federal and community partners.

Recognizing the critical roles sex and gender play in research, the plan emphasizes the importance of understanding and addressing disparities in disease prevalence and severity affecting women uniquely. The plan also underscores NIH's commitment to advancing the careers of women in biomedical research. By fostering a supportive environment and investing in workforce development initiatives, NIH aims to empower women scientists who can help pave the way for groundbreaking discoveries in women's health.

To watch the video announcement, see [https://www.youtube.com/watch?v=\\_W9IWIGsI\\_Q](https://www.youtube.com/watch?v=_W9IWIGsI_Q). For plan details, visit <https://go.nih.gov/1c2W5qv>.

## Camp Fantastic BBQ Set for June 11

The annual Camp Fantastic BBQ will be held on Tuesday, June 11 on the south lawn of Bldg. 10 from 11 a.m. to 2 p.m. The yearly fundraiser, coordinated by NIH's Recreation and Welfare Association (R&W), helps defray costs so children with cancer can attend the camp and have a summer experience to remember.

The afternoon will be filled with food, live music, games, the weekly Community Market, a mini vendor fair and more. Commemorative BBQ shirts will also be on sale to raise funds this year; any that are left over can be purchased at the R&W store in Bldg. 31. Scheduled to offer eats for sale are Bangin BBQ, Malia's Kitchen, Catalyst Hot Dogs and SnoBlast DMV. Music will be provided by NIH's own ARRA (also known as the Affordable Rock 'n Roll

Act). All jam session enthusiasts are encouraged to attend the concert that features several of NIH's homegrown rock stars of science. Rain date is Wednesday, June 26.

## Seminar on 'Fostering Cultures of Inclusive Excellence' Scheduled

The Chief Officer for Scientific Workforce Diversity office is hosting its final Scientific Workforce Diversity Seminar Series event of the 2023-2024 season on Thursday, June 20, 1-2:30 p.m. ET. The virtual seminar "How Are Institutions Transformed to Foster Cultures of Inclusive Excellence?" will examine the benefits of inclusive excellence in the scientific workforce and barriers that institutions face in fostering inclusive cultures. Panelists will discuss strategies to enhance inclusion and create a culture of equity within the scientific workforce at academic institutions as well as methods for assessing culture change. For details, visit <https://go.nih.gov/nCAXv6H>.



## Bertagnolli Speaks at Columbia Mailman School Graduation

NIH Director Dr. Monica Bertagnolli gave commencement remarks at Columbia Mailman School of Public Health on May 14. The ceremony was held at Columbia University's Armory Foundation in New York City.



NIH Director Dr. Monica Bertagnolli speaks at the graduation ceremony.

The 2024 Class Day speaker and recipient of the Columbia Mailman Visionary Leadership Award, Bertagnolli addressed more than 750 graduating students, joined by their faculty, family and other guests. This year the school's master's and

doctoral graduates hail from 40 countries and 45 U.S. states and territories.

"You have chosen the most noble profession," Bertagnolli told the graduates, "one that brings tremendous good to the world by directing the power of science to the service of humanity."

Focusing on the "great joys together with the considerable challenges" of a career in public health, Bertagnolli described several areas where medical science has made extraordinary progress in recent decades, such as in developing treatments for hemophilia and HIV.

However, she pointed out, access to treatments for many similar debilitating and lethal conditions has not kept pace.

"Therapies that work can't be considered effective if they aren't accessible to people who need them," Bertagnolli emphasized, adding that society is "at the cusp of being able to cure deadly and debilitating diseases but still struggling with ways to ensure that our life-changing advances are available to all who need them."

Closing gaps in access requires a commitment to addressing all determinants of health, she said, concluding, "You are the new generation to take on the challenge of caring for everyone, with the wellbeing of all of society as your highest priority, and I have great confidence in you." **R**



At the graduation ceremony are (from l) Dr. Gary Miller, vice dean for research strategy and innovation, and professor of environmental health sciences at Columbia Mailman School of Public Health; Dr. Katrina Armstrong, CEO of Columbia University Irving Medical Centers; Bertagnolli; and Dean Linda P. Fried. The ceremony was held at Columbia University's Armory Foundation in New York City.

PHOTOS: LESLYE SMITH

## NIH To Pilot National Primary Care Research Network

NIH is investing approximately \$30 million over fiscal years 2024 and 2025 to pilot a national primary care research network that aims to integrate clinical research in everyday primary care settings. Called Communities Advancing Research Equity for Health™ (CARE for Health), the initiative seeks to improve access to clinical research to inform medical care, particularly for those in communities historically underrepresented in clinical research or underserved in health care.

CARE for Health™ is part of NIH Director Dr. Monica Bertagnolli's vision to deliver the best available scientific research to doctors on the frontlines of community health care and to expand opportunities for those communities to participate in clinical trials and studies. Bertagnolli describes her vision in more detail in a *Science* essay published June 6.

"Community-oriented primary care not only provides essential health services, but also engenders trust among those who lack confidence in recommended medical care or science," she writes. "In fact, greater availability of primary care services in communities is associated with fewer disparities in health outcomes and lower mortality.

We earn people's trust when they get access to the care they need and when they can see direct benefits from their participation in research."

Supported through the NIH Common Fund, initial awards are expected to be made in fall 2024 to organizations that serve rural communities and are already connected to existing NIH-funded clinical research networks. The goal will be to quickly establish the infrastructure for supporting research at select primary care sites.

Participating clinical sites can choose research studies based on health issues affecting and prioritized by their patients and communities. Patients can contribute to research that generates clinically meaningful results. Final study findings will be shared with research participants. Studies will seek to address common health issues, as well as disease prevention.

"The goal is to create a learning health system in which research informs clinical practice and clinical data informs research," said Dr. Tara Schwetz, NIH deputy director for program coordination, planning and strategic initiatives (DPCPSI). The Common Fund is a DPCPSI component. "As the program grows, sites and their communities will help design new clinical studies reflecting their specific health needs and results from those studies will inform the care they receive."



ON THE COVER: Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause TB. A NIAID phase-1 clinical trial found a freeze-dried, temperature-stable experimental TB vaccine was safe and stimulated an immune response in healthy adults.

IMAGE: NIAID

### The NIH Record

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Turning Discovery Into Health

## Rathmell

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Rathmell played basketball and developed a lifelong love of the sport. Her husband of 33 years, Jeff, also a cancer scientist, and two grown children are all big fans as well. Over the years, the game has shaped her career outlook as a scientist and leader.

“I’ve learned from basketball how practice and coaching are essential to building the skills and muscle memory that win games,” she said. “Winning happens when a team gets ‘into the zone.’ It’s thrilling to watch and even more thrilling to be in the game when that magic happens. I see my role as NCI director the same way—making sure we have the right mix of players, helping them work well together and bringing out the best in everyone so that same magic happens.”

Leading NCI, she’s now calling the shots. A big part of her strategy, she said, is listening.

Rathmell got a broad view of the cancer research landscape as a long-time NCI grant recipient, advisor and researcher in the Cancer Genome Atlas program.

“As NCI director, I now have a much broader view,” she said. “While the end goal of our collective work is straightforward, how the cancer research enterprise fits together and how NCI empowers that work is massive in scope and complicated.”

Listening to experts throughout NCI and beyond is pointing her toward the advances while showing her the potential to break through silos and enhance cohesion across this vast effort.

In taking on leadership roles, Rathmell admits she misses running a lab and interacting with patients. But “I carry with me each win and loss we experienced together,” she said. In guiding NCI, she’s grateful “to help scientists across the field have ‘aha’ moments that transform what is possible and translate them to wins for so many more patients.”

Last year, NCI launched a game plan.

### Reaching Moonshot Goals

“I’m a big believer in the National Cancer Plan, which has provided a much-needed roadmap to focus and align our nation’s collective efforts against cancer,” she said.

The Biden Cancer Moonshot set an ambitious agenda to cut the cancer death rate by 50% by 2047, a goal Rathmell deems realistic.

“We’ve already seen what science can

do, thanks to sustained strong investment in our work and the dedication of so many researchers, patients, families and advocates,” she said. “Having the energy and momentum from the White House is really valuable and it’s galvanizing people around our effort to achieve this goal.”

Rathmell reflected on how far we’ve already come, even for the most stubborn types of cancer. She recalled her first patient with renal medullary carcinoma, a rare kidney cancer with a three-month survival rate. The African-American teenager lived for a year following the experimental regimen, allowing him to graduate from high school.

“I came away from that experience knowing we had to make a difference for kids like him,” she said. “Now, we have a much better handle on this cancer’s biology” and new NCI-led clinical trials are underway.

“Collective action and advances in science and care have given kidney cancer a totally different outlook,” she said. And for many types of cancer, “now we have therapies that can extend life by years or even eradicate the cancers entirely.”

Rathmell lauded the new FDA approval of a cellular therapy for melanoma, the first such treatment approved for a solid tumor. Such advances pave the way for possible treatments for more solid cancers.

The best prognosis still comes from catching cancer early, before it becomes



HHS Secretary Xavier Becerra (l) congratulates Dr. W. Kimryn Rathmell (r) at the Jan. 10 swearing-in ceremony as her husband Dr. Jeffrey Rathmell looks on. HHS PHOTOS: AMY ROSSETTI

difficult to treat. Multiple efforts are now underway to develop tools for earlier detection, including an NCI-funded AI model that can identify pancreatic cancer more than 400 days before clinical diagnosis.

NCI also recently launched the Cancer Screening Research Network to evaluate other emerging technologies for cancer screening that ultimately could help many more people live longer.

### Championing Change

Rathmell is the second woman to serve as NCI director.

“I’d like us to get to the point that it’s not news or at all unusual when a woman is named to a top job in science,” she said.

Rathmell urges other women leaders to train and mentor future female leaders in science. “It can make such a difference when women early in their careers have a woman in a leadership role as a champion for them in their journey,” she said.

NCI remains committed to building a diverse and inclusive workforce, increasing research participation among



Rathmell (third from l), alongside her husband and daughter Dori, stands with Becerra (l), NIH Director Dr. Monica Bertagnoli (second from r) and NCI Principal Deputy Director Dr. Doug Lowy.

## First ‘Porter Day’ Celebrated, To Become Yearly Event

The NIH community recently celebrated the inaugural “Porter Day.”

Presented by the Porter Users Group and held in the Bldg. 35 atrium, the event aimed to celebrate science and foster community in the John Edward Porter Neuroscience Research Center (PNRC) by showcasing its people, science and art.

The event, held on Apr. 23—Shakespeare’s birthday, was conceptualized by a group of research fellows looking for a way to engage with their peers following the pandemic.

The afternoon featured a busy roster of activities: an art gallery displayed STEM-related artwork by talented NIH’ers; scientific



Columbia University neurobiologist Dr. Stuart Firestein gives the keynote presentation.

posters showcased the research of 80 PNRC research fellows; attendees enjoyed musical performances by classical pianist Dr. Tracey Rouault and Antonio Ulloa and Andrew Martinelli of the Latin Music Club; a photographer offered free professional headshots and more.

The main event of the afternoon, a keynote presentation by Columbia University neurobiologist Dr. Stuart Firestein, discussed the importance of ignorance, failure, uncertainty and optimism in scientific exploration. Firestein also moderated a panel discussion of NIH experts following the lecture.

PNRC officially opened in March 2014. The structure is dedicated to Porter, a former congressman and staunch supporter of biomedical research and the NIH mission, who passed away in 2022.

PNRC is a state-of-the-art facility that brings together neuroscientists from 10 institutes and centers across NIH to spur new advances in our understanding of the nervous system in health and disease.



A Porter Day gallery displays STEM-related artwork by talented NIH’ers in the PNRC.

PHOTOS: CHIA-CHI CHARLIE CHANG



Last fall, Rathmell (l) joined NIH Director Dr. Monica Bertagnoli (c) for a demonstration by NIDCD Stadtman Investigator Dr. Angela Ballesteros in her lab at the Porter Neuroscience Center.

underrepresented populations and identifying more ways to reduce cancer health disparities.


The National Cancer Plan is working to find and close the gaps. Eliminating inequities is one of eight overarching goals of the plan and a tenet within every goal.

“We don’t have enough people from all populations participating in research to produce the science that will provide equitable benefits to everyone,” Rathmell said. “That’s why ‘engage every person’ is one of the National Cancer Plan’s goals and one I very much take to heart.”

Another new screening program NCI launched may provide greater access to more people. The Self-collection for HPV testing to Improve Cervical Cancer Prevention (SHIP) trial network is assessing the effectiveness of people collecting their own samples to send in for HPV testing.

“Putting the ability to test directly into patients’ hands is a real opportunity to change the mindset around screening, bring screening to an entirely different group of patients and hopefully make a serious dent in disparities in cervical cancer incidence and mortality,” Rathmell said. “We’re continually looking at how we can do better to advance equity in every cancer arena.”

It’s a full court press and Rathmell is leading the charge to extend life and eradicate cancer.

“To me, progress against cancer is about people,” she said, “and a big puzzle piece is empowering the science and care workforce to do its best possible work. We need smart and dedicated people in every facet of what we do, and we need to ensure we have a pipeline of diverse talent, equipped to sustain and build on today’s advances.” 



More than 265 registered cyclists stopped by NIH's Bldg. 1 pitstop on Bike to Work Day 2024.

PHOTOS: MARLEEN VAN DEN NESTE

## Bike to Work Day

CONTINUED FROM PAGE 1

could grab a cup of coffee and a free T-shirt, have a mechanic do a bike check, register their bikes with the NIH Police Department and mingle with their fellow riders.

This year, NIH'ers biked 903 miles total. They saved 798 lbs. of CO<sub>2</sub>-eq emissions. The National Cancer Institute (NCI) had the most cyclists. The longest ride was 25 miles and the average commute was almost 6 miles.

"BTWD is a great time," said Joe Cox, chief of the Transportation Services Branch, Division of Amenities and Transportation Services (DATS), Office of Research Services. "Everyone always enjoys coming out. I see the same faces every year. Even some of the retirees come back."

Encouraging employees to cycle to work is a "no-brainer," he added. Biking to work also has environmental and health benefits. Additionally, bike commuters use less parking.

NCI's Steve Friedman has been biking to work for more than 18 years. He rides 13 miles each way.

"I don't drink coffee, so biking is a great way to wake up in the morning and get energized," he said.

For those interested in biking to work, spring is a great time to try. Friedman

suggested pedaling with a friend who cycles more often to pick up hints and tips. "Soon enough, you'll be riding on your own and looking forward to riding to work."

Friedman presented the annual Carl Henn Award to Sean Cullinane, DATS quality assurance specialist. Henn, who passed away in 2010, was a co-founder and president of the NIH Bicycle Commuter

Club (NIHBCC) and a dedicated environmentalist. The award is given to someone who exemplifies his values.

Cullinane has been a great supporter of the NIHBCC over the years, said Friedman. He's been a tremendous resource at events like BTWD. For the past seven years, he's also

worked with the club to craft cyclist-friendly policies and keep lines of communication open between DATS and NIHBCC.

He also works with the Department of Environmental Services to track emissions saved as a result of bike commuters.

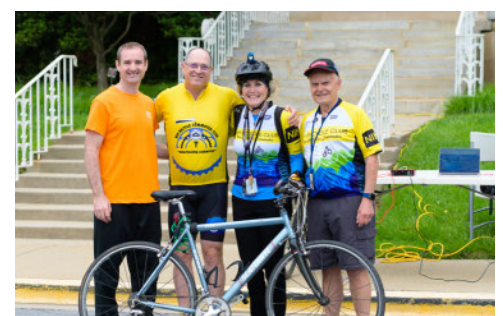
"Getting an award for bicycle advocacy means quite a bit to me," said Cullinane. "I



NCI's Steve Friedman (l) presents this year's Henn Award to Sean Cullinane of DATS.



Above, Bri Teiert of Bethesda's Terrapin Bicycle Club performs a bike check. Below, NIH Police Officer Kerin Cummings and the happy cyclist.



Above (from l), retired NIH Photographer Bill Branson (l), a longtime "non-polluter commuter," returned for Bike to Work Day; a bicyclist collects logo items; and a unique two-wheeler on display. Shown at right, Cullinane and NIHBCC members Friedman, Sarah Fowler and Ron Engle smile in front of Bldg. 1.



NIHBCC members and ORS staff stand at the BTWD pit stop. Shown are (from l) Friedman, Cullinane, Engle, Jeff Youmans, Joe Cox and Tammie Edwards.

grew up in the D.C. area and have been biking around since I was eight years old. I bought my first car when I was 35, so I've spent my life biking everywhere and as much as I can.”

Dr. Franziska B. Grieder of the Office of the Director wore her 2005 BTWD t-shirt. She hopes to see the return of the bicycle commuter subsidy, a \$20-per-month stipend for bikers who forgo a parking pass or transit subsidy. The allowance for cyclists ended Jan. 1, 2018 as a result of the tax reform package referred to as the “Tax Cuts and Jobs Act.”

Members of the NIH Police were on hand to help employees register their bikes with local law enforcement and Montgomery County. Registering a bike makes it easier to identify and recover a bike if it is lost or stolen.

Interested in commuting to NIH by bike? Visit <https://www.nihbike.com/>.



For some NIH'ers, BTWD is a family affair.



## ONE-STOP SHOP FOR IT SERVICES

### CIT Adds Customer Portal for NIH Staff

BY ROBERT WAXMAN

Finding information about IT services at NIH just got easier thanks to a new resource the Center for Information Technology (CIT) recently added for NIH staff—the CIT Customer Portal.

CIT provides a wide range of information and technology tools and services to the NIH community—computing services for scientific research, collaboration tools, high-speed network services, IT support, identity access and credential management, technology training and more. Now the Customer Portal provides a single access point for information about these resources in an easy-to-navigate format.

To make sure they got it right, CIT involved its customers from the start. Over seven months, CIT worked with staff across NIH, gathering input from different user groups and using the feedback to design the portal. The result is a one-stop shop that incorporates the wants and needs of NIH'ers.

The portal offers greater visibility into upcoming CIT projects and initiatives, an easier way to find and request services, and a better overview of the organization.

Since its launch in April, the portal has already received positive feedback from the NIH community.

“I really like the Upcoming Projects and also the CIT Working Groups [pages],” says Caitlin Allick, an IT specialist at the National Institute on Minority Health and Health Disparities. Allick finds the new site to be both helpful and engaging, noting that it “provides a lot more information to everyone, not just customers and users, but also the IT staff as well...It's a great first stop for anybody who needs IT services.”

#### Explore the Portal

To check out the portal, go to CIT's newly refreshed website at [cit.nih.gov](http://cit.nih.gov), and click the button labeled, “Log In To The CIT Customer Portal.” Use your NIH PIV card to log in.

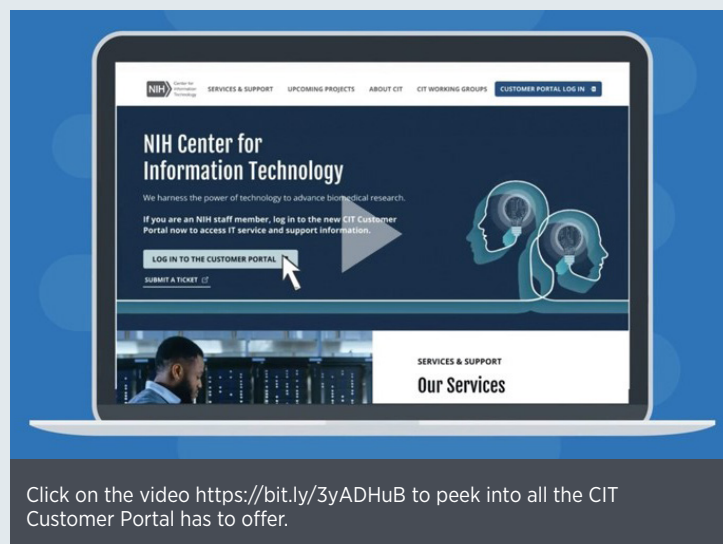
You'll see a personalized welcome message and menu options at the top of the page. Scroll down to see what's available or use the menus to find new resources like IT services and support, including the top ticket requests and knowledge base articles, answers to frequently asked questions, and best practices.

You can also find a calendar of upcoming projects and deployments that impact the NIH community and get information on CIT as an organization. Also, to help you get engaged and stay in-the-know, the portal provides information about CIT working groups that cover areas like cloud and scientific computing resources and collaboration tools, including the M365 suite.

#### Let CIT Hear from You

Like what you see on the portal or have suggestions? Let CIT know! To provide feedback, fill out the CIT Customer Portal Feedback Form at <https://bit.ly/4bDc1nu>.

Problems accessing the portal? Submit an IT Service Desk ticket at <https://myitsm.nih.gov/sp> under the category General IT Support and Website Inquiry.



Click on the video <https://bit.ly/3yADHuB> to peek into all the CIT Customer Portal has to offer.

## Inventor

CONTINUED FROM PAGE 1

molecules to create new drugs or improve existing ones. Her lab studies drug targets in the endocannabinoid system, with the goal of designing medications that could be used for treating obesity, diabetes, fibrosis and alcohol use disorders (AUDs).

The human body naturally produces endocannabinoids, which are named for their ability to induce effects mimicking the cannabinoid molecules found in the marijuana plant. These endocannabinoids regulate and control many vital bodily functions.

“We are looking at treating effects that are similar to those arising from marijuana consumption,” explained Iyer. One such effect, the “munchies,” occurs when certain compounds in marijuana (tetrahydrocannabinol-THC) activate signaling of a protein (receptor) in the hypothalamus called CB<sub>1</sub>. Overactivation of CB<sub>1</sub> causes an increased appetite, especially for palatable, highly processed foods and is also implicated in many pathological conditions.

Iyer wanted to “flip [this process] to use as an obesity treatment that would make people want to eat less.”

Tamping down the CB<sub>1</sub> overactivation offers opportunities to treat multifactorial



NIAAA's Dr. Malliga Iyer studies drug targets in the endocannabinoid system.

diseases, or diseases that are influenced by both genetic and environmental factors. Thus far, attempts to make a CB<sub>1</sub> antagonist have had mixed success due to unwanted side effects such as anxiety and suicidal ideation. Years of subsequent research

showed that if the CB<sub>1</sub> antagonist can exert its action away from the brain, it may offer renewed hope for treating multifactorial diseases with fewer side effects.

Iyer's lab is interested in developing safer and more efficacious drugs using a ‘designed multi-target approach,’ which seeks to synthesize safer CB<sub>1</sub> antagonist molecules that would suppress appetite and ameliorate associated diseases, all without the malaise seen from previous brain-penetrant drugs. Iyer has designed and synthesized two such molecules: MRI-1867 and MRI-1891, which ultimately became Zevaquenabant and Monlunabant. These compounds have shown to be effective in treating obesity,

diabetes and multiple organ fibrosis in animal models and are now candidates in human trials.

Other areas of interest for her lab include ways to make chemistry more environmentally friendly and improve the efficiency of the molecule synthesis process..

“We are interested in developing [methods for making chemical compounds] that are green and sustainable,” she explained.

Such methods could include minimizing use of hazardous solvents, utilizing benign reagents or even patenting new techniques to replace less efficient ones.

Iyer also sees opportunities for using artificial intelligence (AI) and deep learning to reduce the time it takes to go from designing a molecule to making a functional drug product. Sometimes the process requires making hundreds of molecules before finally landing on the right candidate, she said.

“Could we utilize AI to give us more knowledge-based decision making and take compounds to clinic [sooner]?”

Even as Iyer's lab monitors whether their CB<sub>1</sub> molecules reduce food intake, she and her colleagues are also looking to apply their development approaches to broader use. Iyer envisions a “single pill to treat many diseases.” **R**

## New RML Vivarium Opens for Research

A three-story, 120,000-square-foot vivarium (animal facility) opened in May at the Rocky Mountain Laboratories Comparative Medicine Center (RCMC)—a research complex run by the National Institute of Allergy and Infectious Diseases (NIAID)—in Hamilton, Mont.

RCMC's new vivarium is a centralized animal receiving and holding building that will support all biosafety levels of research throughout the RML campus and research projects on virology, bacteriology and viral diseases including work on SARS-CoV-2. The facility will provide expanded capabilities for studies with exotic species along with special imaging equipment and a multi-vector insectary.

A recent ceremony recognized the dozens of construction contractors and federal employees who have worked on building the vivarium, which began in November 2021. This climate-controlled facility replaces a 60-year-old building.

The new facility is a companion project to the expansion of NIAID's Dale and Betty Bumpers Vaccine Research Center (VRC) on NIH's Bethesda campus. The VRC's five-story addition is slated to open this summer.



Dr. Patrick Hanley (r), chief of the Rocky Mountain Veterinary Branch, describes how surgery will be performed in the new RCMC. NIAID Intramural Research Director Dr. Steve Holland (l) and Associate Director Dr. Meredith Shaffer take in the tour.



Above, NIAID Deputy Director Dr. Hugh Auchincloss (r) and Holland cut the ribbon outside the new Comparative Medicine Center on Apr. 11 at RML in Hamilton, Mont. Standing to Holland's left is Jim Parr, project senior contracting officer. Below, the new RCMC vivarium, now open, replaces a facility constructed in 1963.





## Scientists Discover How an Essential Nutrient Enters the Brain

Researchers have discovered that choline, an essential nutrient vital for brain health, is actively transported from the bloodstream into the brain by a protein. The findings may inform the development of new drugs that take advantage of this mechanism to treat brain disorders. The NIH-funded study was published in *Nature*.

Using brain tissue from mice and humans, researchers found that the protein, known as FLVCR2, was densely present in the blood-brain barrier, a tightly packed layer of cells that line the brain's blood vessels. Specifically, FLVCR2 was embedded in endothelial cells, which are specialized cells that control the flow of nutrients and small molecules from the blood to the brain. Additional experiments showed that FLVCR2 selectively recognizes and shuttles choline into the brain.

The blood-brain barrier is a protective cell layer that shields the brain from toxins, microbes and other harmful pathogens. The barrier also prevents many drugs that could treat neurological disorders from getting into the brain. Understanding how FLVCR2 interacts with choline and other molecules could help scientists develop drugs that mimic choline and use this molecular gateway to enter the brain.

To examine FLVCR2 at the atomic level, the researchers used a powerful technique known as cryo-electron microscopy to visualize the protein's three-dimensional structure and see how choline molecules bind to pockets inside FLVCR2, similar to a lock-and-key mechanism. They used the 3D model to run computational simulations that showed how the protein adapts and changes shape to release choline into the brain.

Choline is critical for regulating mood and overall brain and nerve cell health. Choline is also involved in the production of acetylcholine, a neurotransmitter that plays a role in learning, memory and muscle control.

Results of this study can help scientists understand the biology underlying diseases associated with abnormalities in the brain's blood vessels.

## Monoclonal Antibody Found Protective Against Malaria

One injected dose of an experimental malaria monoclonal antibody was 77% effective against malaria in children in Mali during the country's six-month malaria season. The findings come from a mid-stage clinical trial of an investigational monoclonal antibody developed by NIH scientists. Results appear in the *New England Journal of Medicine*.

"A long-acting monoclonal antibody delivered at a single health care visit that rapidly provides high-level protection against malaria in these vulnerable populations would fulfill an unmet public health need," said Dr. Jeanne Marrazzo, NIAID director.

The clinical trial assessed two dose levels, with 19% of the 300-mg-dose group and 28% of the 150-mg-dose group developing symptomatic malaria, providing protective efficacy of 77% and 67% against symptomatic malaria, respectively. Among children who received placebo, 81% became infected with *Plasmodium falciparum*, and 59% had symptomatic malaria during the six-month study period.

Malaria parasites such as *P. falciparum* are transmitted to people by mosquito bites. In 2022, the *P. falciparum* parasite caused a majority of the nearly 250

million estimated cases of malaria globally and most of the more than 600,000 malaria deaths, according to the World Health Organization. Most malaria cases and deaths are among children in Africa.

In 2020, scientists at NIAID's Vaccine Research Center isolated the antibody from a volunteer who had been vaccinated with an experimental malaria vaccine. The antibody was modified with a mutation that prolonged its durability in the bloodstream following administration.

The trial in Mali took place in two parts, first to assess safety in a small number of adults and children, and then in a larger clinical efficacy trial involving 225 children. The efficacy trial included healthy children ages 6 to 10 years, who received a 300-mg dose or a 150-mg dose or a placebo.

NIAID led the clinical trial in conjunction with the University of Sciences, Techniques and Technologies of Bamako, Mali, through NIAID's International Centers of Excellence in Research program.

## Researchers Find Cancer-Like Features in Atherosclerosis

Researchers have discovered that the smooth muscle cells lining the arteries of people with atherosclerosis can change into new cell types and develop traits similar to cancer that worsen the disease.

Atherosclerosis is characterized by a narrowing of arterial walls and can increase risk of coronary artery disease, stroke or kidney disorders. The NIH-supported findings could pave the way for the use of anti-cancer drugs to counteract the tumor-like mechanisms driving the build-up of plaque in the arteries, the major cause of cardiovascular disease.

"This discovery opens up a whole new dimension for our understanding about therapeutic strategies for the prevention and treatment of atherosclerosis," said Dr. Ahmed Hasan, NHLBI program director. "Previous research has suggested that atherosclerosis and cancer may share some similarities, but this association has not been fully described until now."

Using a combination of molecular techniques in mouse models and tissue samples taken from patients with atherosclerosis, researchers characterized the molecular mechanisms that drive the smooth muscle cells to transition into cancer-like cell types.

Researchers found increased rates of DNA damage and genomic instability—two hallmarks of cancer—in the converted smooth muscle cells of atherosclerotic plaque when compared to healthy tissue. Genomic instability is the increased tendency for DNA mutations and other genetic changes to occur during cell division.

Probing further, they also found that cancer-associated genes became more active as the smooth muscle cells were being reprogrammed into the cells that made up the plaque. Using a mouse model expressing a known cancer mutation accelerated the reprogramming and worsened atherosclerosis. Finally, treating atherosclerotic mice with the anti-cancer drug niraparib, which targets DNA damage, showed potential for preventing and treating atherosclerosis.

Understanding the molecular mechanisms that are driving the transition of smooth muscle cells can provide opportunities to disrupt tumor-like pathways and change how the cell behaves, in turn preventing or slowing progression of atherosclerosis.



A single dose of an injected monoclonal antibody provided high-level protection against malaria in children in an area of intense malaria transmission.

RICCARDO MAYER/SHUTTERSTOCK



Structure of the transporter protein FLVCR2 with a choline molecule (c).

IMAGE: ARNOLD LAB, UCSF

## NIDDK Remembers Research Pioneer Felsenfeld

BY LISA YUAN

“To focus on an experiment and to shut out everything else is one of the great pleasures,” said NIH Distinguished Investigator Dr. Gary Felsenfeld in his 2020 oral history.

During his more than 60 years at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Felsenfeld’s keen focus and enthusiasm for science never flagged. His long career was marked by monumental, lasting breakthroughs that transformed the field of molecular biology, particularly in relation to chromatin—the complex mixture of DNA and proteins that form chromosomes inside the nucleus of a cell.

Felsenfeld died on May 1 at age 94.

“Gary Felsenfeld was a creative and rigorous investigator who pioneered our current understanding of chromatin and the control of gene expression, among many other seminal contributions,” said Dr. Michael Krause, NIDDK scientific director. “His work earned the respect of his colleagues throughout his career, many of whom also became luminaries in the field, and his exalted reputation will persist for decades to come.”



Dr. Gary Felsenfeld

After graduating from Harvard College, Felsenfeld received his Ph.D. at the California Institute of Technology, where he studied with world-renowned chemist Dr. Linus Pauling. In 1956, Felsenfeld joined the Public Health Service and began work at the National Institute of Mental Health studying polynucleotides. There, he played a key role in discovering the first three-stranded nucleic acid molecule.

In 1961, Felsenfeld joined NIDDK as a founding member of the Laboratory of Molecular Biology, which shared in the discovery of the first erythroid-specific transcription factor. He became lab chief in the late 1990s and spent the next decade investigating chromatin boundary regions, eventually identifying the protein CTCF as a major genomic boundary protein. This discovery led to research on long-range interactions in the nucleus that affect insulin regulation in human pancreatic cells.

“Gary was the ultimate scientist—infinately curious, well-informed, analytical, rigorous and creative,” said Dr. Michael Gottesman, senior investigator at the National Cancer Institute, who served as NIH deputy director of intramural research from 1994 to 2022. “He was also a wonderful, caring human being who was a powerful advocate for the early-career scientists who worked with him, and a friend to his many colleagues.”

Throughout his career, Felsenfeld always gave credit to the NIH Intramural Research Program, which gave him the opportunity to spend countless hours doing what he loved most.

“At the NIH, I can work at my lab bench and experiment all day long...,” he said in a 2021 interview for the *NIDDK Director’s Update*. “The freedom to try unusual new



Shown in the Felsenfeld lab circa 1989 are (from l) Martin Gellert, Kiyoshi Mizuuchi, David Davies, Felsenfeld and Todd Miles.

PHOTO: NIDDK

experiments and explore out-of-the-ordinary ideas is something that is hard to find in the scientific world.”

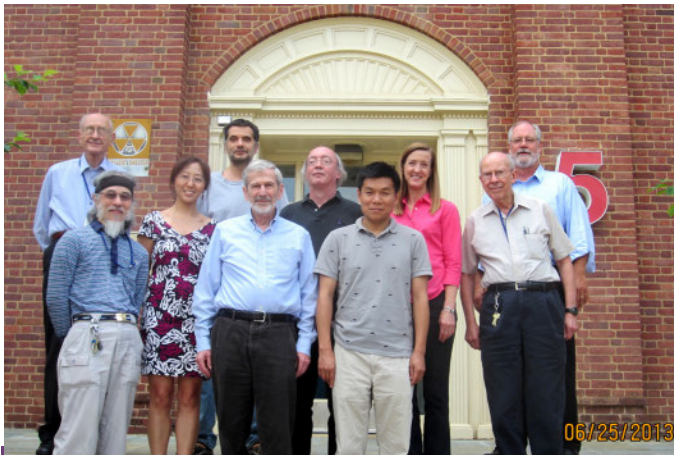
When he wasn’t solving complex scientific problems, Felsenfeld devoted much of his time to mentoring trainees, many of whom went on to become prominent leaders of research groups worldwide. He also published more than 250 primary research papers and garnered many awards.

“Gary embodied everything that is true greatness—as a scientist, colleague, mentor and friend,” said NIDDK Deputy Scientific Director Dr. Susan Buchanan, who’s served as chief of the Laboratory of Molecular Biology since 2014. “He will be remembered for his wry sense of humor, his optimistic perspective, his generosity, his wonderful friendship to so many of us and his illustrious career.”

NIDDK Director Dr. Griffin Rodgers also reflected on Felsenfeld’s extraordinary legacy:

“Next year marks NIDDK’s 75th anniversary, a time to celebrate the institute’s many scientific achievements. Gary’s contributions are among NIDDK’s most notable research advances throughout its rich history. He was a trailblazer in his field, an inspiration to so many and a beloved colleague who enriched the lives of all who knew him.”

Felsenfeld is survived by his wife, Naomi, children Sara, Adam and Dan; eight grandchildren; and one great grandchild.



Laboratory of Molecular Biology principal investigators in 2013

PHOTO: NIDDK LABORATORY OF MOLECULAR BIOLOGY

## Retired Rubella Researcher Parkman Is Mourned

Dr. Paul Douglas Parkman, an award-winning virologist whose research led to significant advances against rubella, died on May 7 at age 91.



Dr. Paul Parkman

A 1950 graduate of Weedsport High School, Paul attended St. Lawrence University under an accelerated pre-med program and received his B.S. from St. Lawrence and M.D. from the State University of New York Health Science Center in Syracuse in 1957. After interning at Mary Imogene Bassett Hospital in Cooperstown, he returned to Upstate Medical Center, specializing in pediatrics and serving as chief resident.

He joined the Army and in 1960, was assigned to Walter Reed Army Medical Center in Maryland as a virologist. During this time he began studying the rubella (German measles) virus.

Parkman was the first person to isolate the virus, which was the most critical step in developing the vaccine. He joined NIH in 1963 and partnered with Dr. Harry Meyer to develop the vaccine that would prevent infection and the resulting birth defects. Their vaccine started clinical trials in 1965 at the Arkansas Children's Colony and was licensed commercially in 1969.

In 1967, while working in the Laboratory of Viral Immunology in NIH's Division of Biologics Standards, the two scientists received an American Academy of Pediatrics E. Mead Johnson Award for their rubella immunity test and for the development of the first effective experimental vaccine against rubella.

As a result of their work, Parkman and Meyer held two rubella patents, which would have enabled them to profit from the sale of manufacturing rights. Instead, they assigned their patents to the U.S. Department of Health so that the vaccine could be distributed as quickly and affordably as possible, to as many people as possible. It was eventually incorporated with measles and mumps vaccines (MMR) and is now commonly administered as part of pediatric protocol.

He was also part of the team that received a patent in 1971 for the rubella immunity test. The Laboratory of Viral Immunology was, at the time, in Bldg. 29A on the second floor.

Parkman had a long and distinguished career, holding multiple positions at Walter Reed, NIH and the Food and Drug Administration and authoring more than 90 scientific papers. He retired in 1990 as director of FDA's Center for Biologics Evaluation and Research, and for many years continued to consult as an expert in his field.

Among his many accolades are letters of commendation from Presidents Lyndon B. Johnson and George H.W. Bush; the Joseph P. Kennedy, Jr. Foundation's International Award for Distinguished Scientific Research and the Department of Health and Human Services' Meritorious Award.



Parkman (l) receives an American Academy of Pediatrics Award in 1967.

"Few men can number themselves among those who directly and measurably advance human welfare, save precious lives and bring new hope to the world," reads the letter to Parkman from President Lyndon B. Johnson. "Through your accomplishments in developing an effective experimental vaccine against German measles, you and Dr. Harry Meyer have joined that tiny legion."

Parkman is survived by his wife of nearly 69 years, Elmerina Leonardi Parkman of Auburn, N.Y., and numerous members of the extended Leonardi family.

## Retired NHLBI Group Leader Ram Remembered

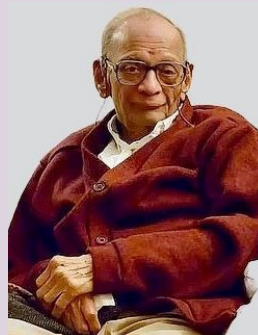
Dr. J. Sri Ram, who retired in 2005 from the Division of Lung Diseases (DLD) in the National Heart, Lung and Blood Diseases Institute (NHLBI), passed away on Mar. 2 at age 95. He first joined NIH in 1965 and spent the last 28 years of his career at NHLBI.

A native of India, Ram earned a Ph.D. in biochemistry at the Indian Institute of Science in Bangalore. Following in his father's footsteps, Ram embarked on a quest for knowledge that led him to migrate to the United States in 1953, where he furthered his studies at Fordham University in New York. He would spend the next 20 years in the United States, pioneering laboratory research at a variety of institutions. Ram enjoyed not only his work as a scientist, but also gained immense satisfaction from teaching.

Ram retired as group leader of the Training and Special Programs, Airway Biology and Disease Program.

During his time at NIH, he returned to the Indian Institute of Science in 1972, for a year, as a Fulbright visiting professor, teaching immunology and organizing workshops on immunochemical techniques.

Ram will be remembered for his dedication to research and his passion for groundbreaking scientific advancement.



"During his time in DLD, Dr. Ram advanced many significant basic science programs in asthma and COPD," recalled Dr. James Kiley, DLD director. "His efforts had a major impact on understanding lung biology and health."



Dr. J. Sri Ram, shown above receiving an NHLBI award from Dr. Helena Mishoe in 2005, spent nearly 40 years at NIH.

Kiley said Ram also made significant contributions to advancing minority investigators' careers and to efforts to reduce health disparities in minority populations. Ram developed an Academic

Award grant program to enhance the ability of physicians and other health care professionals to address disparities in the incidence, management and outcomes of cardiovascular, pulmonary, hematological and sleep disorders among various population groups in the U.S. in a culturally sensitive manner.

"He was a wonderful and kind man who was well liked by all staff," Kiley said. "He was generous with his time and willingness to help all succeed. He will be sorely missed."

Ram is survived by his wife of 75 years; two children, including daughter Kalpana Ram, who works at NIH's Center for Scientific Review; three grandchildren; and one great granddaughter.

## NIH Hosts Annual Police Day Event

PHOTOS: ERIC BOCK

NIH hosted its annual Police Day event on May 16 in front of Bldg. 1. Local, state and federal law enforcement agencies participated. The day featured K9 demonstrations, food trucks and other activities. During the event, NIH Police presented donations to the

Children's Inn at NIH and the Friends of the Patients at the NIH.

The yearly occasion is part of National Police Week, which honors police officers killed in the line of duty. In 1962, President John F. Kennedy signed a proclamation designating May 15 as Police Officers Memorial Day and the week in which that date falls as Police Week.



Lt. Myrical Gratton of the Maryland National Capitol Park Police mounted unit rides her horse in front of Bldg. 1 during NIH's observance of National Police Week.



Above, NIH Police Chief Cleveland Spruill Sr. (c) and Sgt. Matt Mehlhoff of NIH's Division of Police present a donation to Christine Brake, development manager for Friends of Patients at the NIH. CEO Heidi Williams and Housing Coordinator Kristin Grolig round out the team that runs day-to-day operations of Friends (<https://www.friendsatnih.org/>). Below, Spruill presents a donation to Aisha Campbell, director of resident services and family programming at the Children's Inn at NIH.



NIH Master Patrol Officer Sharai Farley and K9 partner Arca demonstrate several law enforcement maneuvers.



Shown on Bldg. 1's front lawn at Police Day are NIH Master Patrol Officer Rocky Toler and K9 partner Fury.