NIH RECORD

February 2, 2024
Vol. LXXVI, No. 3

REALIZING SCIENCE'S 'AMAZING POTENTIAL'

New Director Convenes 127th ACD Meeting

BY CARLA GARNETT

The advisory committee to the director (ACD) convened for two days late last year for the first time under NIH Director Dr. Monica Bertagnolli, who began by acknowledging the tremendous promise and challenges currently facing the greater biomedical science enterprise.

"Right now, we have an unprecedented opportunity to embrace and increase access to innovation," she said, after sounding the gavel on Dec. 14 to start the 127th ACD meeting, held in-person in Wilson Hall and online. "Has there ever been an environment like we are in right now? Fundamental science remains critical. You will hear a lot from me about application to the clinical environment, but please do not ever think that our commitment to fundamental science is wavering in any way. We just want to see that amazing potential coming out of our research laboratories get to people faster."

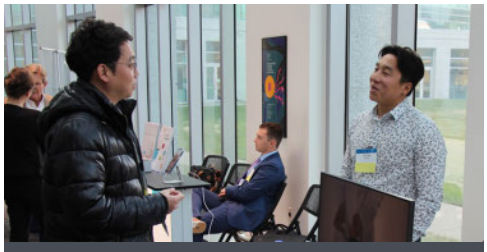
NIH Director Dr. Monica Bertagnolli (l) addresses the ACD as NIH Principal Deputy Director Dr. Lawrence Tabak looks on.

PHOTO: MARLEEN VAN DEN NESTE

Addressing one of the speedbumps to getting NIH research to the citizens it's meant to serve, Bertagnolli spoke briefly about ways to build back faith in the core work.

"I'd like to do everything I possibly can to help restore trust in science," she said. "I believe that means we have to directly engage people in science, promoting equity in science and leaving no one out. We will go far in restoring trust when people who stand to benefit from our research become our research partners, when we design studies that engage them and respect their needs, and when people see

SEE **ACD**, PAGE 6



Point-of-care tech research conference back in person. See story, p. 5.

ALSO THIS ISSUE

NIDCR Staffer Shares Experience in White House Leadership Program 2
French Public Health Leaders Visit NIH. 3
Point-of-Care Tech Research Conference Returns to Natcher Center 5
New NIH Climate and Health Scholars Announced 7
Digest. 9
Milestones 10
Seen 12

FOOD FOR THOUGHT

Ethnobotany Health Options Explored in Caribbean, Latino Diasporas

BY MYRANDA TARR

Dr. Ina Vandebroek

We are lacking scientific knowledge about the breadth and range of plants used as medicines, Dr. Ina Vandebroek lamented during a recent seminar, "Botanical Use for Health in the Caribbean and Mexican Diasporas," hosted by the Office of Dietary Supplements (ODS).

Vandebroek, an ethnobotanist at the University of the West Indies, Mona, in Jamaica, is working to bridge this research

SEE **ETHNOBOTANY**, PAGE 4

SYMBIOTIC OR SINISTER?

Sears Reveals Microbiome's Role in Colon Cancer

BY AMBER SNYDER

Dr. Cynthia Sears

How does colon cancer start?

According to research from microbial detective and Johns Hopkins University professor of medicine Dr. Cynthia Sears, microorganisms in the human gut microbiome may contribute to the development of cancer (oncogenesis). She revealed her findings in the hybrid lecture "Sleuthing the Microbiome Reveals Undercover Agents of Oncogenesis," which was also the 26th iteration of the annual Astute Clinician Lecture

SEE **SEARS**, PAGE 8

Rare Disease Day Scheduled for Feb. 29

Rare Disease Day at NIH will take place on Thursday, Feb. 29 from 9 a.m. to 5 p.m. ET in the Natcher Conference Center.

Each year, this NIH-wide event convenes people with rare diseases and their families, patient advocates, caregivers, researchers and clinicians for a day of presentations, personal stories and panel discussions. Topics this year will include reducing the lengthy diagnostic journey for people with rare diseases; advances in gene therapy; drug repurposing; and the role of artificial intelligence and organ-on-a-chip models to develop rare disease therapeutics.

To view the agenda and register, see https://go.nih.gov/8WBaPqN.

For those who wish to view the sessions remotely, the event will be livestreamed and available on archive through NIH videocast.

CCDI Hosts Webinar Set — Feb. 26

NCI's Childhood Cancer Data Initiative (CCDI) will host a webinar, "Developing Pediatric Cancer Data Standards." Tune in Monday, Feb. 26 from 2 to 3 p.m. ET as members from Data for the Common Good (D4CG) present pediatric cancer data standards and their contribution to the upcoming Childhood Cancer Clinical Data Commons.

The CCDI resource will allow researchers to access harmonized and standardized participant-level demographics and clinical data collected from multiple studies. Attendees will also have the opportunity to ask questions during the Q&A session.

CCDI webinars are free and open to the public, though registration is required to receive the event link. Register at https://rb.gy/emj35m.

For details on CCDI, including past event recordings, visit https://go.nih.gov/Jeoun1a. Visit https://events.cancer.gov/ccdi/webinar for information about or to enroll in any available events. Individuals with a disability who need reasonable accommodation to participate, email CCDIevents@mail.nih.gov as soon as possible.

OUT OF HER COMFORT ZONE

NIDCR Branch Chief Shares View from the White House

BY MICHAEL SOMES

NIDCR's Diana Rutberg spent a year in a White House leadership program.

Diana "Dede" Rutberg will never look at iron and steel—or the White House—the same way again after graduating from the White House Leadership Development Program. The whirlwind, year-long experience transformed her from chief of the Grants Management Branch at the National Institute of Dental and Craniofacial Research to one of a dozen or so temporary staff charged with implementing the recently launched "Made in America" office.

The office was designed to strengthen American manufacturing, create jobs and boost the economy. It requires all government-funded projects to use materials manufactured in the U.S. whenever possible. Rutberg needed to coordinate across numerous agencies to write policies that accomplish the program's goals while balancing the concerns of individual agencies.

The highly competitive leadership program required seven rounds of interviews. Rutberg is only the second NIH'er to participate in the eight-year-old program.

"I'd been at NIH for 20-plus years, always in grants management," said Rutberg, explaining why she considered applying for the program, "and it felt like it was the time to do something drastically out of my comfort zone."

She spent the first three or four months just getting acquainted with a body of information that was foreign to her.

"I was learning about iron and steel and construction materials," she said. "I had to digest all the information about Made in America and digest it quickly and accurately. I was drinking from a fire hose."

What did she learn about how the government functions?

"I really got a bird's eye view as well as an on-the-ground view of how the federal agencies work," she concluded. "It can be hard to develop broad policies because all of these agencies have their own purposes and goals, but it was really interesting to see how streamlined things could be if there was a specific mission and goal. It was refreshing to see [so many different agencies] come together and be collegial and share best practices."

President Joe Biden (standing, c) with leadership program participants

NIH Fellows Vote to Unionize

NIH fellows have organized into a union, the first fellow union ever within the U.S. federal government. NIH Fellows United-UAW comprises more than 5,000 early-career fellows including postbaccalaureate, predoctoral and postdoctoral researchers and clinical fellows.

A majority of NIH fellows who voted on Dec. 6 supported UAW representation. On Dec. 15, the Federal Labor Relations Authority then certified the vote to establish NIH Fellows United-UAW. NIH will partner with the UAW to understand member needs and engage in collective bargaining negotiations.

From l: Dr. Mireille Guyader, counselor for science and technology with the Embassy of France; Dr. Remy Slama, director of the Inserm Thematic Institute on Public Health; Dr. Elli Chatzopoulou, director of Inserm's department of national and foreign affairs; Dr. Didier Samuel, chair and chief executive officer of Inserm; and Dr. Matthew D. Hall, director of NCATS's Early Translation Branch.

French Public Health Research Leaders Visit NIH

Scientific collaboration crossed disciplines and borders late last year, as leaders from France's National Institute of Health and Medical Research (Inserm) met their U.S. colleagues in a tour of five NIH institutes, centers and programs.

Samuel holds two 1,536-well assay plates used to test drug compounds at NCATS's laboratories.

PHOTOS: TERRY RUDD/NCATS

Inserm Chair and Chief Executive Officer Dr. Didier Samuel and three colleagues—Dr. Elli Chatzopoulou, Dr. Remy Slama and Dr. Mireille Guyader—met with team members in the *All of Us* Research Program, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the Fogarty International Center, the National Center for Advancing Translational Sciences (NCATS) and the National Institute on Alcohol Abuse and Alcoholism.

On the tour, the Inserm officials visited NCATS's Rockville, Md., laboratories, where scientists demonstrated how NCATS uses innovative technologies such as 3-D tissue models to accelerate the development of new therapies.

"Biomedical research is much more transdisciplinary than it was, requiring cooperation among scientists, engineers, mathematicians, statisticians and others," Samuel told his NCATS hosts. "This is a big change and we have to find a way to merge all of these disciplines."

"Welcoming Inserm is a significant milestone that underscores NCATS's role as an integral player in fostering collaborative, multidisciplinary opportunities," said NCATS Director Dr. Joni Rutter. "Such opportunities allow us to showcase the depth of our translational science work at NIH."

MI Program Recruits

The NIH Management Intern (MI) Program vacancy announcement will be posted Mar. 4–13 at https://www.usajobs.gov/.

The NIH Training Center is recruiting a few outstanding NIH employees to participate in a competitive two-year internship program.

Management interns will gain insight into administrative career opportunities and develop a robust professional network of colleagues by rotating across NIH.

To register, send an email to mi_info@od.nih.gov and specify which event(s) you plan to attend:

- **Information Session 1**: Tuesday, Feb. 13, noon to 1:30 p.m., via Zoom
- **Information Session 2**: Thursday, Feb. 15, 2 to 3:30 p.m., via Zoom
- **Coffee with an MI**: Wednesday, Feb. 21, 11 a.m. to noon, via Zoom

For more information, visit the website: https://go.nih.gov/ISsjUCI.

ON THE COVER: *The Mobile Exam Unit or MEU, a high-tech research clinic on wheels, is a key part of the NHLBI's Risk Underlying Rural Areas Longitudinal (RURAL) Cohort Study. This long-term research project aims to uncover the roots of health disparities in the rural south, where adults have some of the highest rates of heart disease in the country. The MEU brings the region health technologies that enable researchers to get the information they need. February is American Heart Month.*

IMAGE: RURAL STUDY TEAM/NHLBI

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email nihrecord@nih.gov.

Editor:
Carla Garnett • *Carla.Garnett@nih.gov*

Associate Editor:
Dana Talesnik • *Dana.Talesnik@nih.gov*

Assistant Editor:
Eric Bock • *Eric.Bock@nih.gov*

Staff Writer:
Amber Snyder • *Amber.Snyder@nih.gov*

Subscribe via email: **https://go.usa.gov/x6mgQ**
Follow: **nihrecord.nih.gov/**

The NIH Record is recyclable as mixed paper.

National Institutes of Health
Turning Discovery Into Health

Graduate Research Symposium Set

The 20th annual NIH Graduate Student Research Symposium will be held in-person on Thursday, Feb. 15 at the Natcher Conference Center. The event will include poster sessions on dissertation research by NIH graduate students, a graduation ceremony for those who have recently defended their dissertations and presentation of the annual Graduate Partnerships Program Outstanding Mentor Awards. A keynote roundtable moderated by Dr. Sharon Milgram, director of the Office of Intramural Training and Education, will include NIH Director Dr. Monica Bertagnolli, Principal Deputy Director Dr. Lawrence Tabak and Deputy Director for Intramural Research Dr. Nina Schor. For details, visit https://www.training.nih.gov/me/graduate-student-research-symposium/.

Ethnobotanist Vandebroek studies the intricate relationship between people, culture and communities, and the use of plants as medicines.

Ethnobotany

CONTINUED FROM PAGE 1

gap by studying the intricate relationship between people, culture and communities, and the use of plants as medicines.

In a new study, Vandebroek examined individuals' knowledge and use of plants as medicines in four Caribbean and Latino (CarLo) communities in New York City—Dominican Republic, Mexico, Jamaica and Puerto Rico.

Why CarLo communities? Members of these communities represent one in four New Yorkers born outside mainland U.S. Immigrants moving to the city continue to use botanicals and traditional healers for a variety of reasons, including difficulties accessing health care, language barriers and cultural traditions and beliefs.

The use rate of plant medicines by CarLo communities throughout the entire U.S. can be up to 90%. Traditional medicine, rooted in and driven by cultural beliefs and experiences, coexists alongside and parallel to biomedicine.

Botanicals or medicinal plants are plants used in their raw or unprocessed form for a real or perceived benefit in treating physical, mental or spiritual illnesses, or the maintenance of good health and wellbeing. This includes plants that serve a major role as food and double as medicines. Medicinal plant use as a cultural tradition is active, dynamic and adapting to the current epidemiological context.

What Vandebroek found in her study was unexpected. Through surveys, each of the 400 participants named numerous botanicals they knew or used, totaling for each CarLo community to more than 200 different plants (or 527 species for the four communities); the majority of species were reported by less than five people each. Together, all participants reported 13,000 medicinal uses for these plants.

One key takeaway: plants are critical components for CarLo communities. Nine in 10 people in each community confirmed their confidence in the healing power of plants.

Some foods such as lemon/lime, ginger and garlic were mentioned by more than 20% of participants across CarLo communities along with their common medicinal uses—to help the common cold, stomach aches or hypertension.

"One must be careful not to transpose our own cultural understanding of common food plants and assume that it will be the species that we know," warned Vandebroek, who also currently serves as an honorary research associate at the New York Botanical Garden.

When looking at the diversity of botanicals, she said, there are rather uncommon medicinal uses for seemingly common foods. Some ate, ingested or infused ground avocado seeds to treat diabetes. Others used coffee as eye drops or simply put coffee grounds directly into the eye.

Ultimately, Vandebroek's study helped shed light on the diversity of ways CarLo communities use plants as medicines and why. Individuals may opt for medicinal plants over biomedicine because they see plants as safer and resulting in fewer side effects. Some people might consider plants to be natural and healthy, thus increasing the perception of effectiveness. Other cultural factors also play a role when folks decide between traditional (or ethno-) and biomedicine.

These communities turn to pharmaceuticals if herbal remedies do not work or are unavailable; if the illness is serious, painful or an infection; or as a necessity when a doctor recommends or prescribes medicine.

Many CarLo patients consider going to the doctor as merely a way to receive a diagnosis, not as a commitment to follow the suggested therapy. However, communities are ready and willing to work with providers to develop the right treatment path that is mutually acceptable.

What's important, Vandebroek stressed, is for medical professionals and other care providers to work in collaboration with patients and to take culturally informed understandings into account when determining the best plan to wellbeing.

"Patients appreciate that health care providers have open dialogue," added Vandebroek. "[It's] all about the relationship of trust."

For an archived version of the seminar, visit ods.od.nih.gov/Research/seminarseries.

Vandebroek examined people's use of plants as medicines in four Caribbean and Latino communities in New York City—Dominican Republic, Mexico, Jamaica and Puerto Rico.

Point-of-Care Tech Event Focuses on Partnerships, Speeding Translation

BY CHRISTINE LEHMANN

NIH recently hosted the first in-person conference for the Point-of-Care Technology Research Network (POCTRN) since the pandemic. Held at the Natcher Bldg., the meeting assembled under the theme "Research and Innovation Translation Partnerships in Point-of-Care Technologies."

The network was established in 2007 by the National Institute of Biomedical Imaging and Bioengineering (NIBIB) and currently has several NIH institute partners that support six technology and research centers. Each center receives a five-year award to develop technologies with clinical applications using a network model that enhances complementary strengths and builds multidisciplinary partnerships.

The conference brought together more than 200 POCTRN researchers, technology developers, clinicians and industry partners, as well as regulatory administrators, leaders of non-governmental organizations and investor networks.

Highlights included two distinguished keynote speakers—new NIH Director Dr. Monica Bertagnolli and Dr. Renee Wegrzyn, director of the recently created Advanced Research Projects Agency for Health (ARPA-H).

Dr. Tiffani Lash, conference co-chair and program officer in NIBIB's Division of Health Informatics Technologies, said the aim was to bring together key players to learn about available research resources, learn from recent successes and identify opportunities to develop collaborative research partnerships to accelerate the translation of point-of-care technologies.

Bertagnolli kicked off the event, commending POCTRN for the work that it did during the Covid-19 pandemic. She noted that the network established the Rapid Acceleration of Diagnostics (RADx) Tech program in record time and within months had products in people's homes that they could use to test themselves.

POCTRN conference participants visit exhibits during the technology showcase, which was held at the Natcher Bldg.

Bertagnolli also said POCTRN plays a critical role in moving the promise of NIH research into people's lives on multiple fronts.

"We can imagine a day when this network will be responsible for over-the-counter and point-of-care tests for many different conditions, including maternal health, fetal metabolic diseases, infections like hepatitis C and even neurological conditions," she said. "We know that we're not far off from seeing this resulting from your great work."

She also pointed out that POCTRN, with its focus on technology and partnerships, fills a critical gap between scientific discoveries and the quality of care that patients receive.

At the conference are (from l) Dr. Bruce Tromberg, NIBIB director; keynote speaker Dr. Monica Bertagnolli, NIH director; Dr. Tiffani Lash, conference co-chair; and Dr. Rebecca Richards-Kortum, panelist and principal investigator of a POCTRN center at Rice University.

PHOTOS: RAYMOND MACDOUGALL/NIBIB

NIBIB Director Dr. Bruce Tromberg picked up on the topic of translating research into clinical settings.

"At NIBIB," he said, "we're obsessed about data and the instrumentation producing it, aspects of standardization and how do we move ideas from the conceptual stage and benchtop into fully disseminated manufactured devices that impact public health."

Three panels discussed point-of-care technology innovations from clinical, industry and regulatory perspectives. Other panels explored collaborative partnerships, technology translation, validation and business models for commercialization and translation in low-resource settings.

Panelists from POCTRN centers and industry discussed how they have used the point-of-care technology and lessons learned from the pandemic to solve other health problems in areas such as women's health, nutrition, cardiovascular disease and heart, lung and blood disorders. Many of the innovations were presented during the rapid-pitch sessions and as exhibits in the technology showcase.

Participants also learned about available funding resources that could help move their innovations forward. This included an NIH preconference workshop featuring the Small Business Innovations Research program, and a forum highlighting both public and private sources of funding.

Keynote speaker Dr. Renee Wegrzyn, director of ARPA-H, talks about the agency's mission.

In her keynote talk, Wegrzyn described her agency's mission as "accelerating better health outcomes for everyone. There's a lot of great innovation in the world—we want to get it there faster—we measure progress as an agency by the impact we have on people's lives."

Wegrzyn also discussed some of the agency's new initiatives and the shared goals of POCTRN and ARPA-H.

She said that her goal was to have in place before the next public health crisis the necessary infrastructure that NIH and other HHS entities could use. This includes a national clinical trial network that would advance clinical readiness.

"We believe 90% of all Americans should have access to a clinical trial within 30 minutes of their homes," she said. "We're looking for solvers to help us close that gap." R

In Wilson Hall at the recent ACD meeting are (above, from l) Dr. Wafaa El-Sadr of Columbia University Mailman School of Public Health, Dr. Kafui Dzirasa of Duke University School of Medicine, Dr. Corey Moore of Langston University, Dr. Alexa Kimball of Harvard Medical Faculty Physicians and Beth Israel Deaconess Medical Center, (below, from l) Dr. Brian Mustanski of Feinberg School of Medicine at Northwestern University and Dr. Howard Chang of Stanford University.

ACD

CONTINUED FROM PAGE 1

that the results of our science make their lives better. We need to meet people where they are and reach out to people underrepresented in science."

Also on day one, the group was briefed on NIH's budget and legislative outlook as well as the UNITE initiative, the agency's think tank for addressing and eliminating structural racism in the workforce.

The final report of the day included recommendations from the working group on catalyzing development and use of novel alternative methods to advance biomedical research.

ACD day two entertained updates on the *All of Us* Research Program, Rapid Acceleration of Diagnostics initiative and NexTRAC—the novel and exceptional technology and research advisory committee, which provides both recommendations to the NIH director and a public forum to discuss scientific, safety and ethical issues associated with emerging biotechnologies.

• • •

"Right now, we have an unprecedented opportunity to embrace and increase access to innovation."

–NIH DIRECTOR DR. MONICA BERTAGNOLLI

• • •

Afternoon presentations included reports about NIH's response to the maternal mortality crisis and the future of ECHO, or Environmental Influences on Child Health Outcomes, now in its seventh year.

The two-day session closed with a report from the ACD working group on re-envisioning NIH-supported postdoctoral training. Attracting, nurturing and sustaining early-career investigators has become a top priority for NIH and the biomedical research community at large.

"We are heading into challenging times financially over the next few years," said Bertagnolli. "If you ask me what is the single thing that keeps me awake at night as new NIH director, it's the next generation and how we make sure we support them."

Recordings of both days of the ACD are archived online at https://videocast.nih.gov/watch=52608 and https://videocast.nih.gov/watch=52610. Find meeting materials at https://acd.od.nih.gov/meetings.html.

At left, Dr. Atul Butte of the University of California-San Francisco speaks at the ACD meeting. At right, in-person attendees gather for the first group photo opportunity with Bertagnolli (fourth from r).

NIH Welcomes New Class of Climate and Health Scholars

NIH has selected seven established scientists with expertise in climate and health to work on the NIH Climate Change and Health Initiative.

This class of climate and health scholars will become part of the cross-cutting NIH effort to reduce health threats from climate change across the lifespan and build health resilience in individuals, communities and nations around the world, especially among those at highest risk.

The diverse group of scientists went through a competitive selection process and will work with NIH staff until September 2024. Each scholar is currently employed at a major university or with a research-based organization but will be hosted by an NIH institute or center.

They will work with staff across NIH to share knowledge and help build capacity for conducting climate-related and health research. This is the second set of scholars.

2024 scholars are (above, from l) Dr. Laura Geer, Dr. Arnab Ghosh, Dr. Stefania Papatheodorou, Dr. Julie Postma, and below, Dr. Samendra Sherchan.

Meet the 2024 Scholars

Dr. Laura Geer
Associate Professor and Chair, Department of Environmental and Occupational Health Sciences, SUNY Downstate School of Public Health
Host: *All of Us* Research Program, NIH Office of the Director

Dr. Arnab Ghosh
Assistant Professor of Medicine, Weill Cornell Medical College, Cornell University
Host: National Institute on Aging

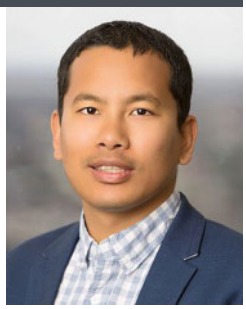
Dr. Stefania Papatheodorou
Lecturer in Epidemiology, Harvard TH Chan School of Public Health
Host: National Institute of Environmental Health Sciences

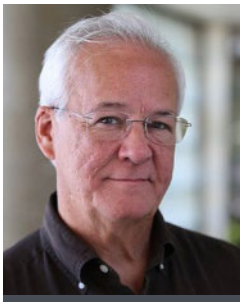
Dr. Julie Postma
Professor, Department of Nursing and Systems Science and Associate Dean for Research, Washington State University College of Nursing
Host: National Institute on Minority Health and Health Disparities

Dr. Samendra Sherchan
Associate Professor and Director of the Center for Climate Change and Health, Morgan State University
Host: National Institute of Allergy and Infectious Diseases

Dr. Ricardo Wray
Professor of Health Communication, Department of Behavioral Science and Health Equity, St. Louis University College for Public Health and Social Justice
Host: National Cancer Institute

Dr. Caradee Wright
Chief Specialist Scientist, Environment and Health Research Unit, South African Medical Research Council
Host: Fogarty International Center



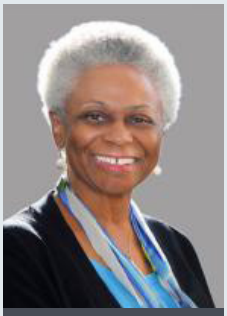


Above, Dr. Ricardo Wray; below, Dr. Caradee Wright

IMAGE: ICF/COSWD

Bernard Delivers King Lecture at UPenn Medical School

Asking "What would Dr. King say?," Dr. Marie Bernard, NIH chief officer for scientific workforce diversity, began her keynote address at the University of Pennsylvania Medical School's 10th annual Martin Luther King Jr. symposium.



Dr. Marie Bernard

A graduate of the University of Pennsylvania Medical School, Bernard used quotes from King to highlight NIH activities that foster an inclusive scientific environment. She spoke of how "we need different perspectives being brought towards science to ensure that we're getting the best science," to bend what King called the "arc of justice."

She also told the audience about the NIH UNITE initiative, the Community Partnerships to Advance Science for Society (ComPASS) and Faculty Institutional Recruitment for Sustainable Transformation (FIRST) programs, and Maximizing Opportunities for Scientific and Academic Independent Careers (MOSAIC).

Bernard thanked the many NIH staff involved in UNITE and at each institute and center for their passionate efforts to foster an environment of inclusion and belonging for all in the biomedical and behavioral science ecosystem.

As Bernard pointed out, King also said, "Human progress is neither automatic nor inevitable... Every step toward the goal of justice requires sacrifice, suffering and struggle, the tireless exertions and passionate concern of dedicated individuals."

For UNITE updates, visit https://www.nih.gov/ending-structural-racism/unite. To learn more about ComPASS, see https://commonfund.nih.gov/compass. FIRST and MOSAIC details are online at https://www.commonfund.nih.gov/FIRST and https://go.nih.gov/RTqwWDF, respectively.

Sears

CONTINUED FROM PAGE 1

Series. The series honors U.S. scientists who have observed unusual clinical occurrences and, by investigating them, have opened important new avenues of research.

Sears began her career as an infectious disease specialist studying gut infections, and now focuses on how microbiota and specific bacterial pathogens contribute to colon carcinogenesis. In her lecture, she sought to "give a framework for how we consider microbes in the pathogenesis of human colon cancer."

The gut microbiome consists of microorganisms—such as bacteria, viruses, fungi and archaea—that often have a mutually beneficial relationship with their host. However, Sears has discovered, changes in these microbes can alter the cells lining the gut (epithelial cells) in ways that make them more likely to become cancerous.

What causes changes to gut microbes? There are many factors, but one specific culprit Sears identified is antibiotic usage. Antibiotics are useful tools for treating infectious diseases, but, she said, doctors "must consider how antibiotic exposure over the lifetime [can be] an ever-evolving disease modifier, potentially with a high impact on disease development."

Using data from the United Kingdom Clinical Practice Research Datalink, Sears and collaborators matched colon cancer patients with healthy controls of similar backgrounds. The researchers found an increased association between the incidence of colon cancer and the patients' use of oral antibiotics more than 10 years prior to receiving a colon cancer diagnosis. Other studies have validated these findings. For Sears, these results highlight how antibiotic-mediated shifts in the microbiome may contribute to the development of chronic disease.

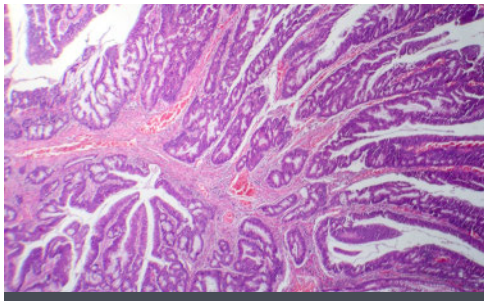
How do disruptions to the gut microbe population lead to cancer?

Sears discussed *Bacteroides fragilis*, a common bacterium in the colon that is typically harmless—unless it is a certain strain known as ETBF, or enterotoxigenic *B. fragilis*. ETBF is pro-inflammatory and tumorigenic by way of the *B. fragilis* toxin (BFT) gene it possesses. There is also a non-toxic *B. fragilis* (NTBF) that does not have BFT.

Not everyone with ETBF in their colon will have symptoms—it has been isolated in both healthy people and those with gastrointestinal disruptions such as diarrhea—but it is hypothesized that factors such as stress and antibiotic use may disrupt the gut microbiome and make ETBF more likely to induce inflammation.

Using a genetic mouse model permissive to colon tumor formation, Sears has found that a single oral introduction of ETBF causes rapid tumor formation—she could see evidence of microscopic tumors (microadenomas) one week post-inoculation. However, she has also found that if she deletes the BFT gene, "we obliterate all that tumorigenesis."

How does ETBF promote tumorigenesis on a cellular level?



Photomicrograph of colon adenocarcinoma

IMAGE: KATERYNA KON/SHUTTERSTOCK

The colon is lined with epithelial cells that are bound together with a protein called E-cadherin. BFT binds to the epithelial cells and splits E-cadherin. The now-separated epithelial cells undergo marked changes resulting in, for example, DNA damage, which makes cells more likely to become cancerous in the future.

Sears has a "hit list" of 11 bacterial species (including *B. fragilis*) that are "credible contributors" to colon cancer pathogenesis. But microbes can also work together as a grouping of microbial cells bound together by a matrix on the surface of the gut epithelium, known as a biofilm. Sears found that, in non-hereditary colon cancer, biofilms were often present on the tumor surface, within the tumor and also on the epithelium around the tumor.

Through her research, she has learned that biofilms can be pro-carcinogenic. Epithelial cells in the gut are coated with a double layer of mucus, but biofilms can sometimes penetrate the mucus and damage the integrity of the epithelial cells by cleaving

The gut microbiome consists of microorganisms—bacteria, viruses, fungi and archaea—that often have a mutually beneficial relationship with their host.

IMAGE: BEN SCHONEWILLE/SHUTTERSTOCK

E-cadherin, likely through a similar mechanism to *B. fragilis*. Interestingly, tumors on the right side of the colon are more likely to be biofilm-positive.

The notorious bacterium *Clostridioides difficile* (*C. diff*) may have something to do with that. *C. diff* infection can occur in people whose gut microbiome has been disrupted (typically as a side effect of antibiotic treatment), causing severe colon inflammation and damage.

Two toxins in *C. diff* (abbreviated TxA and TxB) are most strongly associated with disease in humans, and Sears has learned that TxB in particular "promotes biofilm invasion deep into colonic crypt cells," where stem cells that replenish the gut epithelium over a person's lifetime are produced. If the stem cells' genetic material are damaged, then they may develop mutations that could lead to cancer.

Sears tested this in a mouse model. One group of mice were infected with a TxB-positive strain of *C. diff*, while the other were infected with the same strain of C. diff, but with the TxB toxin removed. The latter group of mice still had the *C. diff* in their colons but did not develop tumors; in contrast, Sears said, "the [TxB]-positive community induced tumors...which [appear] to be driven by [the] singular virulence gene" that produces TxB.

Do the other species in biofilms also play a role in tumorigenesis? Sears and her collaborators are now investigating this.

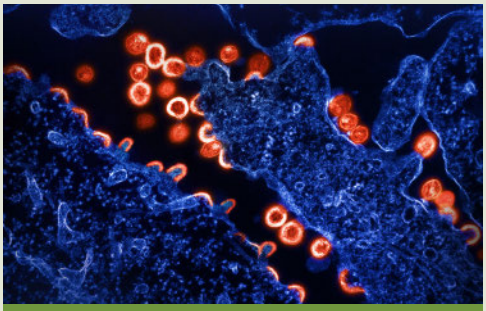
Early studies indicate that other bacterial species may help *C. diff* be "a chronic colonizer of the human gut," Sears said, but there is much more work to be done on the mechanisms of how this occurs.

She also wants to hone in on *C. diff's* linkage to colon cancer. It's a "totally new topic for the field," she observed, and one Sears is excited to explore more.

To watch the lecture, visit: https://videocast.nih.gov/watch=51118.

NIH-Developed HIV Antibodies Protect Animals in Study

Three different HIV antibodies each independently protected monkeys from acquiring simian-HIV (SHIV) in a placebo-controlled proof-of-concept study intended to inform development of a preventive HIV vaccine for people. The antibodies—a human broadly neutralizing antibody and two antibodies isolated from previously vaccinated monkeys—target the fusion peptide, a site on an HIV surface protein that helps the virus fuse with and enter cells.



Transmission electron micrograph of HIV-1 virus particles (red) budding and replicating from a segment of a chronically infected H9 cell (blue).

IMAGE: NIAID

The study, published in *Science Translational Medicine*, was led by NIAID's Vaccine Research Center (VRC).

Antibodies that target the fusion peptide can neutralize diverse strains of HIV *in vitro*, that is, in a test tube or culture dish outside of a living organism. The VRC isolated a fusion peptide-directed human antibody, called VRC34.01, from a person living with HIV who donated blood samples for research. Researchers also isolated two antibodies from rhesus macaques—a species of monkey with immune systems similar to humans—who previously had received a vaccine regimen designed to generate fusion peptide-directed antibodies.

The three antibodies studied each provided statistically significant protection from SHIV, and the effect was dose dependent, that is, highest in monkeys with greater antibody concentrations in their blood.

The study authors conclude that an effective HIV vaccine targeting the HIV fusion peptide likely will need to expand upon the concepts used in this study, by generating multiple varieties of fusion peptide-directed antibodies. This would increase the likelihood that the vaccine could maintain a preventive effect across the vastly diverse HIV variants in circulation.

Common Marker of Neurological Diseases May Play Role in Healthy Brains

Rendering of a synapse showing phosphorylated α-synuclein in pink "gluing" synaptic vesicles together.

IMAGE: ROY LAB/UCSD

Researchers have discovered that a protein called phosphorylated α-synuclein, which is associated with several neurodegenerative diseases such as Parkinson's disease and Lewy body dementia, is also involved in the normal processes of how neurons communicate with each other in a healthy brain.

The research, published in *Neuron*, was funded in part by NINDS.

Phosphorylation is a process where a phosphate ion is added to a specific amino acid, or building block of a protein, in this case the protein α-synuclein. This addition can change the shape of that protein, causing it to change its level of activity.

Most studies of phosphoryl-synuclein have studied its role in certain neurological disorders such as Lewy body dementia, where it builds up in protein clumps called Lewy bodies. These clumps are thought to be toxic to neurons, and a prevailing hypothesis is that the phosphorylation of the protein α-synuclein triggers these diseases.

"In most studies to date, the mere presence of α-synuclein phosphorylation is assumed to be a marker for pathology for certain [neurological] disorders," said Dr. Beth-Anne Sieber, NINDS program director. "Recently, there has been considerable interest in developing drugs that prevent α-synuclein phosphorylation as a way of treating these disorders. These findings challenge the current hypotheses about how these disorders may originate in the brain and may give insight into how we might better treat them."

Atlas of Placenta May Yield New Clues

An atlas revealing the activity of individual placental cells during childbirth offers insight on what happens at the maternal-fetal interface during term labor, according to an NIH-supported study. The work, led by researchers at NICHD, is published in *Science Translational Medicine*.

PHOTO: KIEFERPIX/SHUTTERSTOCK

The atlas provides a single-cell analysis of the human placenta and its surrounding membranes and is the first to use this method to understand the communication that occurs between maternal and fetal cells during the process of labor. Studying these processes aids understanding of typical labor and delivery at term, as well as preterm labor and delivery, which occurs before 37 weeks of pregnancy and is a leading cause of infant death and long-term disability.

The study team created the placental atlas by using single-cell RNA sequencing, which examines the activity and signaling patterns of individual cells. The atlas, based on samples from 42 term pregnancies, describes changes in gene expression patterns among the different cell types in the placenta and its surrounding membranes including both maternal and fetal-derived cells.

Researchers found that cells most affected by labor were in the chorioamniotic membranes, which surround the fetus and rupture as part of the labor and delivery process.

Scientists also found that fetal stromal and maternal decidual cells were particularly active in generating inflammatory signaling. These findings are consistent with previous research showing that inflammation (unrelated to infection) is important for sustaining labor.

The study is also a proof-of-concept that placental biomarkers present in maternal blood may be used to identify pregnancies at risk for preterm birth. Researchers used the atlas to classify cell-specific signatures of labor, which were detectable in maternal blood samples from term and preterm pregnancies.

NCI Senior Investigator Graubard Retires

BY JENNIFER LOUKISSAS

Dr. Barry Graubard, senior investigator in the Biostatistics Branch (BB) of the Division of Cancer Epidemiology and Genetics (DCEG) at the National Cancer Institute (NCI), retired earlier this year.

Dr. Barry Graubard

Throughout his career, Graubard focused on developing new statistical methodologies at the interface between biostatistics and survey sampling with a particular emphasis on cancer epidemiology, making fundamental contributions to the use of national population-based surveys to improve the representativeness of cohort, case-control, nested case-control and cross-sectional studies. These achievements have been internationally recognized through publication in the leading statistics journals and numerous awards.

In 1999, together with Dr. Edward Korn, a statistician in NCI's Division of Cancer Diagnosis and Treatment, Graubard published *Analysis of Health Surveys*, which remains the definitive textbook in the field.

Graubard has had a major impact on the use of population-based survey analyses within DCEG to improve study inferences. In this regard, he collaborated with dozens of investigators across almost all branches.

There are numerous examples of these successful partnerships, including the development of an absolute risk model for oropharyngeal cancer that is calibrated and validated to be representative of the U.S. population, the use of the accelerometer and mortality data from the National Health and Nutrition Examination Survey to show that increasing steps up to 8,000 per day substantially reduced mortality risk and an assessment of the effect of community immunity from the prophylactic human papillomavirus vaccine on rates of oral HPV infections among the unvaccinated U.S. population.

Later in his career, Graubard made important contributions to assessing health disparities in a population-based setting, developing novel techniques to evaluate the fraction of observed differences between advantaged and disadvantaged groups that can be explained by known factors. These methods are providing the basis for future health disparities analyses in DCEG and across the epidemiology research community generally.

Graubard has been an outstanding mentor to many current and former DCEG fellows. His former fellows hold prestigious appointments at major universities and at NIH—several in senior investigator roles. His dedication and excellence in mentoring have been acknowledged numerous times with the NCI Mentoring Award, the American Statistical Association (ASA) Mentoring Award and the ASA Jeanne E. Griffith Mentoring Award that recognizes and encourages mentoring of junior staff in the statistical community in federal, state or local government.

Before joining DCEG, Graubard had a long history of government service. In 1977, he began his career as a mathematical statistician at the National Center for Health Statistics, where he worked on network sampling methods to estimate prevalence of rare diseases and to estimate undercount in the 1980 census.

In a research post at the Alcohol Drug Abuse and Mental Health Administration (now, the Substance Abuse and Mental Health Services Administration), he evaluated serum-based diagnostic testing methods to identify patterns of abusive alcohol drinking. In the Biometry Branch of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, he worked on epidemiological studies of perinatal risk factors and adverse birth and early childhood outcomes.

In 1990, Graubard was recruited to the Biometry Branch in NCI's Division of Cancer Prevention and Control, where he led the development of statistical methods research to monitor tobacco consumption and smoking prevalence through time serial state-level sales data and the Current Population Survey for the evaluation of the NCI American Stop Smoking Intervention Study. In 1997, he was recruited to BB by Dr. Mitchell Gail, senior investigator.

Graubard is a fellow of ASA and of the statistics section of the American Association for the Advancement of Science. Among his numerous awards are the ASA and Biometric Society Snedecor Award for Applied Statistical Research and the Centers for Disease Control and Prevention Charles C. Shepard Science Award for Assessment and Epidemiology.

NINDS's Finkelstein Retires

BY SHANNON E. GARNETT

Dr. Robert Finkelstein, director of the Division of Extramural Activities at the National Institute of Neurological Disorders and Stroke (NINDS), has retired after a federal career spanning more than two decades.

Dr. Robert Finkelstein

"I'm ready to move on to the next phase of my life," he said. He officially retired on Dec. 30, marking 24 years of federal service.

Finkelstein's interest in science began at an early age with a fascination with astronomy.

"It was a long, winding road from there, but I eventually became interested in developmental neurobiology," he said. "I was particularly amazed by the evolutionary conservation of the genes that control development."

Finkelstein earned his bachelor's degree in physics from the State University of New York at Stony Brook and his Ph.D. in biology from the Massachusetts Institute of Technology, where he studied myc oncogene expression in teratocarcinoma cells. He pursued postdoctoral training at Harvard Medical School, studying the genetic regulation of nervous system development in the fruit fly.

Among other accomplishments, Finkelstein isolated and studied the first Otx gene—a master regulator of head and brain

development in flies and humans. He became an assistant professor in the department of neuroscience at the University of Pennsylvania School of Medicine (UPSM) in 1992, continuing his research on genes that control brain development in the fruit fly. He received tenure at UPSM in 1999.

Finkelstein joined NINDS in 1999 as a program director in the Neurodevelopment Cluster in response to a call to recruit program officials by then-NINDS Director Dr. Gerald Fischbach.

"I had just gotten tenure and renewed the grants that funded my lab, which gave me time to sit back and reflect on my interests," said Finkelstein. "Gerry made the job sound challenging and important, which is exactly what it turned out to be."

As a program director, Finkelstein developed many research initiatives and oversaw a portfolio of grants in neurogenetics, basic development, brain tumors, neurofibromatosis, Tourette syndrome and several neurodevelopmental disorders. He served as the first scientific team lead for the newly formed Neurogenetics Cluster.

In 2004, then-NINDS Director Dr. Story Landis appointed Finkelstein as extramural director. He became responsible for scientific planning and policy and coordinating the institute's extramural scientific programs.

At the time of his retirement, the Division of Extramural Activities included the NINDS Scientific Review Branch, Grants Management Branch, Administrative Services Branch, as well as the Training Office, Diversity Office and the Office of Research Quality. He worked closely with NINDS Director Dr. Walter Koroshetz and served as the executive secretary of the National Advisory Neurological Disorders and Stroke Council for 20 years.

"I'm proud of spearheading a large-scale analysis that revealed that NINDS funding for fundamental basic research had been plummeting over the years," said Finkelstein. "We developed a package of interventions that helped stem this decline, including pivotal statements and publications by the NIH and NINDS directors on the importance of basic science. I also led the development of the NINDS version of the R35 award, which I believe is having real impact on the field. But I'm probably most proud of working with many others to develop an open, interactive culture that makes NINDS a wonderful, stimulating place to work."

Throughout his career, Finkelstein helped organize and develop various workshops and symposia—many of which he chaired or co-chaired. He authored and co-authored multiple journal articles and represented the institute on numerous NINDS and NIH-wide committees, including the NIH High-Risk Research Roadmap committee/implementation group (which created the NIH Pioneer Award) and the NINDS extramural science committee. His work garnered him countless accolades and awards.

"In the 1960s—I'm showing my age—Joseph Campbell, a scholar of mythology, coined the phrase 'Follow your bliss,'" said Finkelstein. "At NIH, I've always championed investigator-initiated research—encouraging principal investigators to follow their interests, rather than trying to guess what ours are at NIH. I've applied that mantra to my own life as well and will continue doing so in retirement!"

In keeping with that mantra, relaxation and travel are at the top of Finkelstein's retirement agenda in the short-term. Having played in a rock band pre-Covid, he also plans to play more music and support various social justice causes close to his heart.

"I'll miss the people I've worked with tremendously," he concluded. "They are a wonderful bunch of talented and dedicated individuals. I want to thank my friends at NINDS and across NIH for their support over the years, and to remind everyone at NIH that what they do—no matter what it is—is critically important. It's too easy to forget that!"

Former NIDCR Director Slavkin Remembered

NIH mourns the passing of Dr. Harold C. Slavkin, who died on Dec. 22 at his home in California; he was 85. Slavkin had served as the sixth director of the National Institute of Dental and Craniofacial Research (NIDCR) from 1995 to 2000.

Dr. Harold Slavkin

Slavkin was a pioneer in craniofacial biology and contributed to its emergence as a multidisciplinary field. His efforts led to advances in dental-oral-craniofacial research as well as other scientific disciplines.

Slavkin arrived at the National Institute of Dental Research (NIDR) in 1995 from the University of Southern California School of Dentistry, where he was founder and director of the Center for Craniofacial Molecular Biology. His studies focused on the developmental processes underlying several congenital and acquired craniofacial and oral defects. He also created and chaired the nation's first Ph.D. program in craniofacial biology.

A true visionary, Slavkin began long-term planning as soon as he arrived at NIDR. He created a strategic plan that broadened the institute's research portfolio and led to the renaming of the institute in 1998 to NIDCR.

Under his leadership, the institute took the lead role in producing the first-ever Surgeon General's Report on Oral Health in 2000. He also oversaw development of NIDCR's strategic plan to reduce racial and ethnic health disparities—one of the first of its kind at NIH. Slavkin later expanded NIDCR's efforts to reduce oral health disparities for conditions such as childhood caries and oral cancer.

[See Slavkin reflect on his NIH experience in his own words for an NIDCR anniversary event in spring 2023, https://www.youtube.com/watch?v=4uCJEead3rY.]

"Dr. Slavkin will be remembered as a brilliant orator who effectively communicated his passion for research, his deep commitment to training future generations and his fierce advocacy for health equity," said NIH Director Dr. Monica Bertagnolli, in a statement to NIH staff.

Slavkin is survived by his wife, Lois, sons Mark and Todd, stepchildren Michael and Tracy, eight grandchildren and three great-grandsons.

NIH Goes Batty

It was early morning on Dec. 5 when a woman noticed a small grey bat clinging to the retaining wall on the NIH campus, near the visitor entrance. She'd seen it in that exact spot the day before. This time, she reported the bat's presence to NIH security at the nearby vehicle entrance.

Security Officer Eric Crutchfield's response made a big difference to the tiny creature. He called the NIH Police non-emergency number to notify the Wildlife Veterinary Volunteers (WVV), an NIH Intramural Research Program partnership led by Dr. Tom Thomas, a veterinarian in the Office of Research Services, Division of Veterinary Resources. Volunteers address wildlife concerns around the Bethesda campus.

"I got the notification around 9:30 a.m., but I couldn't get to the bat right away," said Dr. Ginger Tansey, the WVV veterinarian on call. "While I was preparing to go find the bat, I took a moment to look up the Maryland [Department of Natural Resources] website to confirm what we could do for this bat. The DNR page has a search function for wildlife rehabilitation specialists, who are federally and state-licensed professionals. It was important for me to find out who would be able to accept this bat, if it needed care. [Then] I called Second Chance Wildlife Center (SCWC), [a nonprofit that rehabilitates injured wild animals], and confirmed with them. Now, I could go rescue this bat, carefully."

Tansey then met Crutchfield at the gate and assessed the bat gripped to the wall.

"I could see the bat was slow, minimally responsive and its respiratory rate was very low," recounted Tansey. "This suggested hypothermia, and it was in the shade of a cold cement wall, so it could have been accidentally trapped in a cycle of hypothermia. I carefully grasped it by the scruff and wrapped it in a disposable paper towel with a hand-warmer."

Crutchfield was an eager observer. "This is the closest I've ever been to a bat," he said.

Tansey then placed the bat "burrito" into an NIH-approved animal transport box.

NHLBI veterinary technician Theresa Engels volunteered to deliver "Batman" to Second Chance. She said she has taken orphaned or injured wildlife to SCWC many times over the years.

On Dec. 13, the wildlife center shared the news that the bat had recovered and had been released three days earlier, when the ambient temperature was above 60˚F, which would allow the Silver-Haired Bat time to find a safe roost before temperatures dropped again.

Bat "burrito" inside an NIH-approved animal transport box

PHOTO: THERESA ENGELS/NHLBI

"She looked like a young (possibly first-year) bat that likely picked a bad place to roost and got caught out in the cold," said Hannah Wilson, SCWC clinic manager. "Activity and flight become difficult for them, if not impossible, when temperatures drop.

"Once we determined she was healthy, we waited for a warmer day to release her again so she could find a more appropriate hibernaculum for the winter," Wilson explained. "We get many bats in throughout the winter for the same reason (getting caught out in the cold and poor-roosting choices), or because their hibernaculums are destroyed by people. Once we get into the colder months, we often have to overwinter any bats that come in, as it won't get warm enough for them to fly again until spring. This bat got lucky and likely caught the last warm day of the season."

Tansey agreed. "I'm glad to have played a part in rescuing this little bat, and I hope she has a long and healthy life."

Engels said, "I have always had a soft spot for bats. I think they are really cute. I am glad I could help, and very happy that our little bat was healthy and able to be released back into the wild."

At left, an animal control officer holds a silver-haired bat. **PHOTO: JAY ONDREICKA/SHUTTERSTOCK** At right, Eric Crutchfield, an NIH security officer, stands at the retaining wall where the bat was found. **PHOTO: GINGER TANSEY/NEI**