THE NIH CATALYST

A PUBLICATION ABOUT NIH INTRAMURAL RESEARCH

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Feeding the Wulf: Biowulf Turns 25

NIH's Supercomputer To Enter a New Era of Support for AI and Other Complex Demands

BY CHRISTOPHER WANJEK, *THE NIH CATALYST*

Biowulf, NIH's premier high-performance computing (HPC) system, turned 25 this year. Yet unlike that Dell 486 you might have invested in during the 1990s (32 megs of RAM; yeah, that oughta be plenty), Biowulf is faster and has more capacity than ever before.

Indeed, Biowulf is the most powerful HPC system in the United States dedicated to biomedical research. The NIH Center for Information Technology (CIT), which maintains Biowulf, hopes to further enhance its capacity to accommodate a rapidly evolving landscape of artificial intelligence (AI) and machine learning (ML) demands, according to **Steve Bailey**, CIT's director of High Performance Computing Core Facility.

Today, Bailey said, Biowulf serves nearly 2,500 active users, including almost three quarters of the principal investigators in the NIH IRP. The majority of the usage is for genomics, followed by structural biology and imaging. **Adam Phillippy**, senior investigator and director of the NHGRI Center for Genomics and Data Science Research, is one such Biowulf user. His lab taps upward of 30 million central processing unit (CPU) hours per year.

With Biowulf, Phillippy and his colleagues were able to fully complete the sequence of a human genome in 2022, correcting errors introduced during the initial mapping, circa 1990–2003, and

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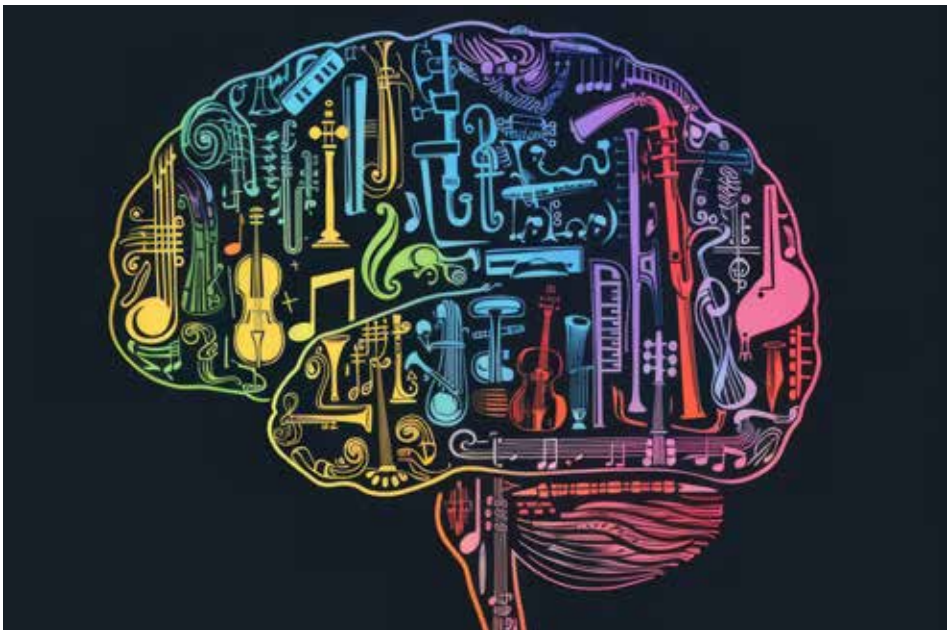
State of the Arts

A Mosaic of Medicine, Music, and Art at the NIH

BY MICHAEL TABASKO, *THE NIH CATALYST*



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Learn about how NIH scientists, staff, and clinicians integrate the arts into biomedical research, clinical trials, and the campus and clinical center environment.

When Bob Marley belted out that iconic opening line to *Trenchtown Rock*, "One good thing about music, when it hits you feel no pain," he was likely relating to the power of music to uplift the human spirit. But he may have been onto something more than the metaphorical.

Although it's no secret that engaging in music and the arts enhances the wellbeing of individuals and communities, science is only beginning to explain why. The NIH has long been a welcoming canvas for art in all its forms, well before the term neuroarts was coined. Consider the college-like Bethesda campus with its bucolic green spaces and a critical mass of artist-scientists and creative types. Tune into a performance by NIH-based

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In Science, the Arts, and Real-world Problem-solving, Creativity is Creativity

BY NINA F. SCHOR, DDIR

Have you ever wondered why so many of us in science, technology, engineering, mathematics, and medicine are avocational artists of one sort or another?

I daresay many on the campuses of NIH know me better for my music and poetry than my science! And what about the six-stringed artistry of **Francis Collins**, the line drawings of **Nora Volkow**, or the historical writings of **Jeremy Brown**?

Think, too, of the scientific art of Santiago Ramón y Cajal displayed in the Porter Neuroscience Building (Building 35). Indeed, in my seven years at NIH, I have met scientists and physicians who are dancers, singers, instrumentalists, writers, visual and textile artists, and photographers.

What is it about science that fuels the artistic muse? Or is it the other way around? Or does some proximate engine fuel both art and science independently and in equal measure?

I have thought long and hard about this for many, many years. How many of my colleagues have made career choices that, for a while, vacillated between science and the arts? I have come to a conclusion that is embarrassingly simple and perhaps trite: *Creativity is creativity.*

After all, what is the philosophical difference between the beauty and complexity of a restriction endonuclease that enables it to cut two strands of DNA at a palindrome and the way two "strands" of music exactly a fifth apart and phase-shifted a measure or two conspire to make a fugue? And how do they both differ from the symmetry and synergy in M.C. Escher's drawings or the aural appeal of "Le Monocle de Mon Oncle" by Wallace Stevens? The neurologist in me would say they differ only by the sensory network that is activated by them and that brings that impulse to whatever part of the brain it is that is fulfilled by creativity.

> "Don't be afraid to juxtapose science and art. They are two sides of the same wonderfully beautiful coin."
>
> — Nina Schor

This issue of the *NIH Catalyst* features the art that makes us all human. It also celebrates the 25th birthday of our Biowulf supercomputer (which is probably its 200th birthday in human years) and the amazing extravaganza that was this year's NIH Research Festival. The word "diverse" does not begin to capture the breadth of the people, the science, the presentation media, or the artistry of the week's events!

Finally, this issue features the power and synergy of the partnership between patients and the biomedical community, another generator of a uniquely creative whole. The Myositis Genetics Consortium brings together patients, families, clinicians, and scientists to better understand, diagnose, treat, and prevent this group of inflammatory disorders of muscle.

We happily and proudly close the 2024 calendar year with this creative exploration of the importance of interfaces between fields and communities. ●

A poem penned by Nina Schor:

PRAYER (DEMENT ME NOT)

When I am very old,
I pray the irony of the
Wool and linen that walk the streets together
Just before the Spring declares itself
Does not escape me.
I pray my annoyance at the
Scrape-whoosh-whirr of the snow plow ice salter
Persists into another slowly melting season.
And I pray I still remember mama's face vividly enough
That you look like her to me
Until my dying day.

"Prayer (Dement Me Not)" was first published in *Neurology*, the medical journal of the American Academy of Neurology.

A Tribute to the *NIH Catalyst* 'Founding Father'

In remembrance of John Gallin, 1943–2024

BY *THE NIH CATALYST* STAFF

CREDIT: NIH CC

John Gallin

John Gallin, an eminent clinician-scientist and longest-serving director of the NIH Clinical Center, died on October 10 at the age of 81.

Much has been and will continue to be written about Gallin's scientific legacy. Perhaps lesser known about his NIH contributions, however, is that he conceived the need for this very newsletter: *The NIH Catalyst*.

In fact, he pitched the idea in 1992 to then-director Bernadine Healy and found enthusiastic support from Lance Liotta, who had just been appointed DDIR and had told the NIH scientific directors that he hoped to serve as a catalyst to implement their ideas. Hence, the origin of the name of this newsletter.

"The *Catalyst* became more of a newsletter that chatted with the community," he told former *Catalyst* editor-in-chief Laura Stephenson Carter in a 2023 interview. "That was the goal—telling people who was there, what was happening. It's become a real part of the intramural program."

Gallin served for 52 years at NIH, with 30 of those years as an editor of the *Catalyst*. From its first issue in 1993 through the March–April 2023 issue, when he retired from the NIH, readers could often find his byline accompanying guest editorials that reflected his commitment to the scientific enterprise. He had written about strengthening partnerships outside of the NIH, the establishment of the first clinical research curriculum at the CC, and much more.

Throughout 182 issues of this newsletter, Gallin read each one thoroughly and provided discerning and illuminating feedback. We treasured him greatly and we will miss him dearly. ●

AN EXCERPT FROM *THE HISTORY OF THE NIH INTRAMURAL RESEARCH PROGRAM, 1984–2024*

Gallin was a man of many stories. Below is one such story about his interaction with President Bill Clinton in 1995, which very well may have led to the funding for the Clinical Research Center. This story is an excerpt from a book in progress about the history of the NIH Intramural Research Program, 1984–2024, by former-DDIR **Michael Gottesman** and **Christopher Wanjek**, OIR's director of communications.

In 1991, Bernadine Healy, the NIH director at the time, green-lighted a proposal to build a new clinical facility. The next NIH director, Harold Varmus, along with then-HHS Secretary Donna Shalala championed the project. But nevertheless, Congressional funding lagged—until Bill Clinton came to visit.

The year was 1995. President Clinton was to visit the Children's Inn on Saturday, August 5, followed by a quick show-and-tell at the Warren Grant Magnuson Clinical Center (CC). CC Director John Gallin was understandably anxious, given all his facility concerns. The night before the visit, Gallin awoke from a panic dream and was consumed by the worry that the CC's toilets might not be up to snuff, as was sometimes the case. What if the President needed to use one during his visit, he thought. In the middle of the night, Gallin drove to the NIH to inspect and indeed clean toilets.

The next day, President Clinton sat through a presentation on the 14th floor of the CC. The bathroom was clean; no problem there. After the presentation, Gallin was to escort him down the stairwell three floors to go on clinical rounds. He'd be alone with the President. What could he say about the true state of the CC and the predicament he found himself in the night before?

Flushed with courage, Gallin said, "Mr. President, this looks like a great hospital, doesn't it?" The President agreed enthusiastically. "Well," Gallin added, "it's falling apart, and we need a new building." President Clinton stopped on the stairs and said, "What are you talking about?" So, Gallin gave him his somewhat polished 30-second spiel and then went on rounds.

Gallin might have struck the right chord with President Clinton. Soon after, Congress approved $23 million in fiscal year 1996 for design of what was then called the Clinical Research Center (CRC) and then $90 million the following fiscal year to begin the construction. The project would cost approximately $600 million and would be named the Mark O. Hatfield Clinical Research Center in honor of the Republican Senator from Oregon who chaired the Senate Appropriations Committee and championed medical research. The CRC was added to the north side of the Building 10 complex. Construction began in earnest by 1999, led by Yong-Duk Chyun in ORF, and the exterior was largely complete by 2002. Dedication was on September 22, 2004, and patients then on the Magnuson side moved in soon after. ●

CREDIT: ONHM

Anthony Fauci, President Bill Clinton, Harold Varmus, and John Gallin tour the CC in 1995.

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musical ensembles such as the NIH Philharmonia or Affordable Rock'n' Roll Act. Pause and take in a tapestry of thoughtfully curated art exhibits that welcome inspiration and contemplation throughout the Clinical Center (CC), Building 10, and Porter Neuroscience Research Center, Building 35. For patients being treated at the CC or participating in clinical research, art therapy is often prescribed as a way to self-express and heal. Then there's the research uncovering precisely how the different components of art infiltrate our senses.

A medley of mechanisms

In 2017, NIH convened a first-of-its-kind workshop on music and health that brought together the likes of neuroscientists, researchers, music therapists, and other experts in the field to talk about the possibility of merging medicine and music together for therapeutic potential.

That meeting was an early step in the Sound Health partnership and cochaired by then-NIH director and musician-scientist **Francis Collins** and renowned soprano Renée Flemming, who cochairs the NeuroArts Blueprint Initiative. A resulting paper published in *Neuron* (PMID: 29566791) laid the groundwork to push the field forward. Soon after, the Trans-NIH Music and Health Working Group was formed and has since ushered along a newly focused wave of research into arts- and music-based interventions.

Nearly $40 million has since been invested into such research through Sound Health. The idea is that if an aligned research agenda could tease out the "active ingredients" in music and art, develop new technologies to reveal mechanisms by which those ingredients affect the body, and then design robust, reproducible studies to inform what an effective dose looks like—and for whom—then we might someday be able to prescribe artful engagement as a health behavior.

Speaking at the "Music as Medicine: The Science and Clinical Practice" workshop in December 2023, Collins delivered a keynote address on what has been accomplished since 2017, and the results are encouraging.

He highlighted NIH-supported studies that showed infants exposed to musical training could track changes in language tone better than infants not exposed to music (PMID: 36016666); that learning to play a musical instrument was associated with improved cognitive function and language development in adolescents (PMID: 36757558); and that learning to drum reduced hyperactivity and inattention in autistic children and resulted in measurable brain changes revealed by brain imaging (PMID: 35639696).

"I think a lot of this is the wave of the future of where we're going as to taking advantage of these really powerful technologies to not just make observations but actually understand mechanisms at the level of circuits in the brain," said Collins in his keynote address. "I would love to see us bring the fields of music therapy and neuroscience even closer together. That has been part of the dream all along; to make it possible for the remarkable things that music therapy can achieve to be better understood."

Quickening the tempo

"There's a lot of momentum that's building up," said **Emmeline Edwards**, director of NCCIH's Division of Extramural Research, and coauthor with Collins on the NIH Music-Based Intervention (MBI) Toolkit, which laid the building blocks of how to conduct high-quality studies on music-based interventions for brain disorders of aging (PMID: 36639235). "The MBI toolkit falls in place with the rigor and reproducibility policy at NIH," said Edwards, adding that feasibility trials are now underway to test how well the toolkit's guidelines are able to improve research quality.

The components of the MBI toolkit were designed to be translated to other art forms, according to Edwards. "We started with music and brain disorders of aging because we had the most data in that area," she said. "In phase two of Sound Health, currently happening now, we want to start investigating other art forms like dance and performing arts. We partnered with the National Science Foundation and the National Endowment for the Arts to do a workshop on the neural basis of creative movements, and we have a set of investigators working on that. This is the work that needs to be done before we design an intervention that makes sense."

SOUND HEALTH NETWORK

Learn more about the NIH Sound Health Network, the Trans-NIH Music and Health Working Group, and recent publications on music and the mind at https://www.nih.gov/sound-health.

The therapeutic potential of music and other art forms on pain represents another intriguing direction. "[Music and art] are noninvasive, low cost, and most people like interacting with the arts," said Edwards. "Maybe we could suggest that some of our investigators in the funded pain research networks program give talks in the IRP. That's something that we could stimulate and see where it goes."

Looking ahead, a primary goal in the arts-intervention field is to move toward the concept of social prescribing, already ongoing in Europe (PMID: 10735850) and in some local health departments in the United States (PMID: 36743160). "This is the blue-sky idea, to prescribe these art-based interventions in conjunction with conventional medicine," said Edwards.

New technologies have revealed how music might change the brain. **Yuanyuan "Kevin" Liu**, a Stadtman investigator in NIDCR's Somatosensation and Pain Unit, found that playing sound—any type of sound, from Bach to white noise—at a level five decibels over ambient levels suppressed pain in mice with inflammation pain (PMID: 35857536).

"Interestingly, [analgesia] can have a long-lasting effect," said Liu. "If you play music or sound for three days, the effect can last for an additional two days. That suggests it is not just that attention is shifted away from pain but that there could be long-lasting circuit-level changes."

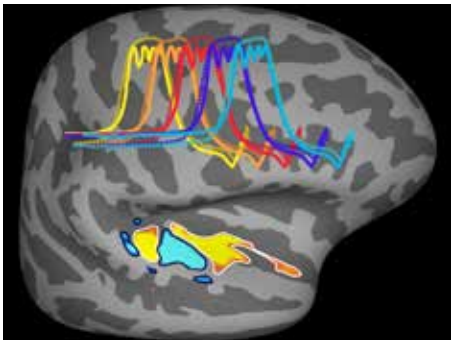
To find those circuits, Liu and colleagues used high-resolution electrical recording techniques to monitor how 5-decibel sound reduced activity in the auditory cortex of the brain. Viral tracers then tracked those cortical signals downstream to two regions in the thalamus known to process somatosensation and pain, providing anatomical evidence of the connection. Then, optogenetic and chemogenetic techniques were used to turn the corticothalamic circuit on or off, proving that the circuit is both necessary and required in sound-induced analgesia.

His paper has sparked two new directions. First, Liu is looking at the mechanisms behind how loud noise could exacerbate pain. Second, his team is exploring how music and sound could affect autonomic functions such as heart and breathing rate, which could give insights into mind-body control. Liu advocates for more communication between pain labs like his and clinicians using music as treatment.

"We really should encourage talk between basic scientists and clinicians who are working on this mind-body connection. What have they learned; do they see an autonomic change?"

From canvas to cortex

Mapping how the human brain integrates audio and visual inputs could give insight into how people (and other primates) experience art in different ways. For example, a Sound Health-funded project revealed that the human auditory cortex is uniquely tuned to pick up on harmonic tones compared with that of monkeys, suggesting a brain-shaping evolutionary role for speech and music (PMID: 31182868). That work was led by **Bevil Conway**, who is now a senior investigator at NEI's Sensation, Cognition, and Action Section.



CREDIT: BEVIL CONWAY LAB, NEI

This illustration from Conway's 2019 research shows the areas of the human auditory cortex that are uniquely sensitive to sound frequencies used in music and speech.

Conway's team also studies how visual perception and color are processed in the brain, using technology such as magnetoencephalography, which noninvasively measures neural electrical impulses. His lab revealed that people show similar neural patterns of activation in response to color, suggesting that how we humans perceive color is one thing we have in common (PMID: 33202253). Interestingly, warm hues such as red, orange, and yellow generated more specific patterns of brain activity than cool colors like blue and green, another finding likely due to evolutionary pressures, according to Conway.

Ideas of art are ultimately concepts, explains Conway, and his lab is aiming to understand the origin of concepts, using color as a model system. "The rainbow is continuous, but humans tend to carve it up into categories such as 'red,' 'orange,' and so on," he said. "These categories are examples of concepts, hallmarks of intelligent systems such as the human mind. We would like to know how concepts form, the extent to which they are innate, how we acquire new concepts, and how we update our concepts with new information. We think the same principles that apply to concept formation about colors will apply to concept formation about art, so understanding art better might therefore be instructive."

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CREDIT: CHIA-CHI CHARLIE CHANG

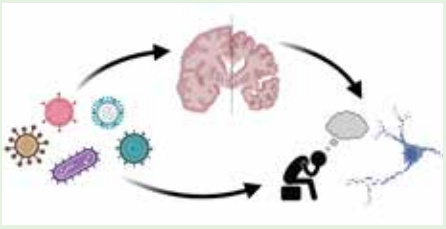
Francis Collins continues to pick up his guitar and advocate for more research into music-based interventions. "A lot of people are seeing this [research] as a window both into how the brain works, [and] how we can come up with something that would help people who are suffering from chronic pain or PTSD [post-traumatic stress disorder] without having to take a pill. Listen to the right kind of music; you'll be much better," said Collins during a guest appearance on the *Late Show with Stephen Colbert* on September 17. Shown here is opera singer Renée Fleming and Collins singing together at NIH during the 2019 J. Edward Rall Cultural Lecture.

Intramural Research Briefs

Read About Scientific Advances and Discoveries by NIH Intramural Scientists

NIA: INFECTIONS AND IMMUNE-SPECIFIC PROTEINS MAY INCREASE DEMENTIA RISK AND BRAIN ATROPHY

CREDIT: MICHAEL DUGGAN, NIA



NIA: Infections can promote the development of dementia and other negative neurocognitive outcomes (lower arrow) and can directly lead to brain atrophy and neurodegeneration (upper arrows).

NIA research suggests infections and varying concentrations of immune-specific proteins may contribute to increased dementia risk and brain volume loss in older adults. Although other scientists have found a link between infections and cognitive decline, this study identified the proteins involved and used a genetics tool to support the protein connection between infection, dementia risk, and neurodegeneration.

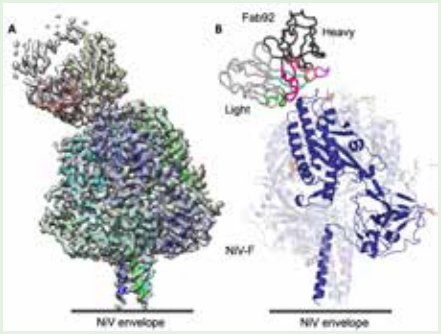
The research team was led by NIA tenure-track investigator **Keenan Walker** and NIA postdoctoral fellow **Michael Duggan**. They examined medical records of participants in the Baltimore Longitudinal Study of Aging (BLSA) looking for verification of infections from influenza, herpes, and other viruses as well as bacterial and fungal infections in the upper respiratory system, urinary tract, and skin. After separating plasma from approximately 1,200 blood samples obtained via the BLSA, team members measured more than 7,000 proteins in plasma. They then used magnetic resonance imaging to conduct brain scans on nearly 1,000 BLSA participants. The scientists processed the data using a technique called Mendelian randomization, an analysis that uses statistical genetics to estimate a cause for a particular outcome.

The scientists identified 35 immune-specific proteins that correlated with infection history and predicted patterns of brain atrophy that were specific to infections. Further investigation revealed that individuals who had infections on average 16 years earlier still had higher concentrations of damaging proteins and lower concentrations of neuroprotective proteins circulating in their bodies. The team theorized that genetic variability could provide the backdrop for infection susceptibility and altered immune protein regulation, both of which can contribute to increased dementia risk and brain atrophy. (NIH authors: M.R. Duggan, Z. Peng, J. Candia, T. Tanaka, C.M. Joynes, C.X. Alvarado, M.A. Nalls, J. Cordon, G.N. Daya, Y. An, L. Ferrucci, and K.A. Walker, PMID: 39143319)

[BY ROBIN ARNETTE, NIA]

NIAID: TREATMENT DEMONSTRATES PROTECTIVE EFFICACY AGAINST NIPAH VIRUS

CREDIT: NIAID, *JOURNAL OF VIROLOGY*



NIAID: The cryo-EM structure of the Nipah virus's NiV-F–Fab92 complex revealed where the mAb92 antibody binds to NiV-F, which could inform future therapeutics or vaccines.

Emerging cases of the lethal Nipah virus (NiV) in South Asia have prompted the World Health Organization to classify NiV as a priority pathogen. NiV is a highly pathogenic bat-borne virus that triggers severe neurological and respiratory diseases in humans and other animals. According to the CDC, the mortality rate in humans is 40–70% and treatment is limited to supportive care. Now, an international team led by NIAID researchers have found that a vaccination-derived neutralizing monoclonal antibody, mAb92, provides complete protection against NiV disease in hamsters (*Mesocricetus auratus*).

NiV is shed via the urine from infected large fruit bats, also called flying foxes (Pteropus genus). Humans can become infected through direct contact with fruit or sap contaminated with the virus, through exposure from infected animals such as pigs, or from contact with an infected human.

In a study led by **Vincent Munster**, chief of the Virus Ecology Section at NIAID's Rocky Mountain Labs, researchers tested the ability of mAb92 to target the NiV fusion glycoprotein (NiV-F), and found that interfering with NiV-F prevents the virus from attaching to and entering cells. Cryo-electron microscopy, or cryo-EM, analysis revealed precisely where mAb92 binds to NiV-F, thus providing a path for the development of therapeutics or vaccines.

The authors noted that in work by other research teams another monoclonal antibody, mAb102.4, offered protection against NiV and a similar virus, Hendra, in the African green monkey (*Chlorocebus aethiops*) and was safe in a phase 1 clinical trial in Australia. (NIH authors: V.A. Avanzato, T. Bushmaker, C.K. Yinda, K. Meade-White, R. Rosenke, T. Thomas, N. van Doremalen, G. Saturday, and V.J. Munster, PMID: 39240113)

[BY HÉCTOR CANCEL–ASENCIO, NINDS]

NIAAA, NINR, NIMH, NIDCD: DIET-INDUCED OBESITY LEADS TO GENETIC DIFFERENCES IN BRAIN REGIONS ASSOCIATED WITH EATING BEHAVIOR

A team of researchers from NIAAA, NINR, NIMH, and NIDCD's newly established NIH National Smell and Taste Center, along with external collaborators, have identified several genetic changes in the brains of obese mice associated with diet.

Obesity, characterized by an excessive accumulation of body fat, is linked to a range

of serious health issues. One major factor contributing to obesity is the overconsumption of high-fat foods, which are often rich in flavor and calories. The chemical stimuli from these foods can be particularly rewarding, leading individuals to eat more than necessary and, consequently, gain weight.

Recognizing this shift in eating behavior, NIH researchers suspected that genetic alterations might occur in the obese brain, reinforcing patterns of overconsumption. To explore this idea, they examined gene expression in obese mice fed a high-fat diet and compared the results with expression in controls. The study focused on two critical brain regions—the striatum and the olfactory bulb—that play a role in our eating behavior. In obese mice, 274 differentially expressed genes were identified in the striatum, along with 11 in the olfactory bulb. These genes were associated with inflammation and immune-related pathways, mitochondrial dysfunction, and reward.

"This [result] means that our diet is associated with gene expression differences in our brain," said **Rosario Jaime-Lara**, first author of the study, who was previously an NIH fellow at NIAAA and is now an assistant professor at the University of California at Los Angeles. "It also suggests that our diet may impact inflammation, the immune system, and reward pathways in the brain."

As obesity and related diseases increase worldwide, the authors note the importance of understanding modifiable risk factors, such as diet, and how they affect our bodies. "We hope that by understanding the underlying mechanisms and risk factors, we can better manage and prevent obesity and its comorbidities," Jaime-Lara said. (NIH authors: R.B. Jaime-Lara, C. Colina-Prisco, M. De Jesus Vega, S. Williams, T. Usdin, A. Kinkead, B. Brooks, Y. Wang, A.T. Franks, and P.V. Joseph, PMID: 39273278)

[BY MEAGAN MARKS, NIAAA]

NCI: FOTONOVELAS ARE PICTURE-PERFECT FOR TAILORED EDUCATION ON GENETIC CANCER RISK

Latinas are more likely than non-Latina Whites to be diagnosed with aggressive subtypes of advanced-stage breast cancer. Genetic cancer risk assessment is recommended for women at risk of hereditary breast and ovarian cancer (HBOC) and includes genetic counseling and testing (GCT). However, compared with non-Latina Whites, Latinas are less likely to receive GCT because of systemic and patient-level barriers.

CREDIT: NCI

NCI: Fotonovelas can be used as a culturally tailored tool to increase knowledge among Latina women at risk of hereditary breast and ovarian cancer.

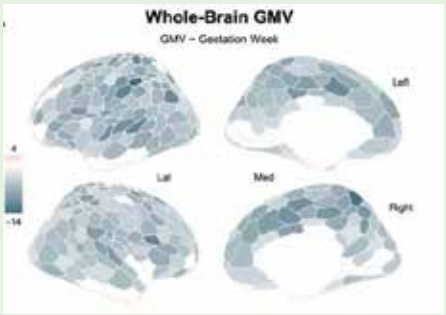
Fotonovelas, a well-accepted story-telling medium in Hispanic cultures, can be effective for communicating health education messages, an NIH-led study has found. A bit like a comic book but with real photographs, a fotonovela might include a short narrative, speech balloons, simple text, or engaging visual elements. Hypothesizing that fotonovelas, through storytelling, can help with learning and recalling information because of the reader's connection to a story, NCI researchers and their extramural colleagues developed and tested fotonovelas to increase awareness of GCT among Latinas at risk of HBOC. Content was drawn from an existing culturally targeted narrative video focused on improving GCT among the study's population.

The research team interviewed cancer patients and their relatives and found that the use of fotonovelas had several positive health effects. They reported an increased GCT self-rated knowledge from 50% to 60% in patients and from 63% to 100% in relatives, and an increased willingness to talk about cancer with family from 70% to 100% in patients and from 38% to 75% in relatives.

The team also identified and discussed six themes with participants and health workers, including perceived barriers to GCT. They concluded that fotonovelas could be used as educational tools to increase GCT awareness and cancer conversations among Latino families at risk of HBOC. They noted that, although their findings need to be replicated in a larger study, future research could explore ways to use fotonovelas for disseminating information about and access to GCT and cancer more broadly. (NIH authors: R. Barajas, M. Rotunno, and E. Gillanders, PMID: 39240499)

[SEPPIDEH SAMI, CC]

NIMH: STUDY REVEALS THE EFFECTS OF PREGNANCY ON THE BRAIN



CREDIT: *NATURE NEUROSCIENCE*

NIMH: A research team studied 26 magnetic resonance imaging (MRI) brain scans throughout pregnancy and found a widespread reduction in cortical gray matter volume. Darker colors represent regions of greater volume loss.

Neural changes that unfold in the maternal brain throughout gestation have not been well studied, but now a guide might be on the way: A team of researchers from the University of California at Irvine and Santa Barbara collaborated with NIMH scientists to map a human brain across pregnancy, which may provide better understanding of postpartum depression and similar neurological concerns.

Using precision magnetic resonance imaging, researchers mapped the brain of a healthy 38-year-old woman beginning three weeks preconception through two years postpartum. Corresponding author and neuroscientist Elizabeth Chrastil of the University of California at Irvine was the woman whose pregnancy—and brain—was followed in this study.

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Electronic Lab Notebook (ELN) Updates

BY JANELLE CORTNER, NCI; ANNA AMAR, OD; AND UTE REICHLING, NCI

As mentioned in the May-June issue of the *NIH Catalyst*, because of mandates (M-19-21 /M-23-7) that required the federal government to convert to electronic record keeping by June 2024, no new paper notebooks may be created going forward. NIH has adopted two different commercial electronic lab notebooks (ELNs): LabArchives, a general purpose ELN, and Signals, a chemistry-specific ELN. Both are available at no cost to NIH users.

Although 100% of NIH principal investigators have formally declared their ELN system of record, many groups have only recently completed training and onboarding. Legacy paper notebooks needed for scientific reference may continue to be managed in accordance with applicable records management requirements and do not need to be digitized. The following are a few more tips and some reminders as investigators embark on their new ELN journey.

The NIH policy on ELNs (OIR Sourcebook) states that a NIH lab notebook is a federal record that documents the complete research record in sufficient detail so the research can be reproduced by others (for example, why specific experiments were initiated, how they were performed, which biospecimens were used, what data and observations were produced, where the data are stored, or how the data were analyzed and interpreted).

Principal investigators and facility heads are considered "data owners" and are responsible for the overall management of content and access to data in ELNs. Data owners should maintain ownership of all notebooks used by their group members but may delegate most management functions to their account administrator or group members.

Use of other digital systems to store and analyze data does not normally replace the need for an ELN to serve as the central documentation hub. Exceptions to the need for an ELN include research that requires use of specialized documentation systems, such as clinical trials research, which are sufficiently comprehensive to meet the reproducibility standard. However, secondary reuse of clinical samples and data may require an ELN.

The ELN reproducibility standard is the same as any research documentation: Can a scientifically literate person with no prior knowledge of the project navigate the rationale, methods, experimental samples, results, analysis, and basis for the major conclusions entirely from the documentation provided in the ELN?

NIH ELN requirements have been designed to address the following.

- User-facing capabilities
- System security
- Records management
- Access and retention control of the ELN
- Federal records designation
- Investigator's index record of retrievable data sources

Guidelines for ELN data storage

Sensitive administrative information such as CVs, grant and contract information, banking information, financial disclosures, performance ratings, disciplinary actions, and grievances not needed for research should not be stored in an ELN. Intellectual property related to invention reports, patents, and preclinical studies should be stored in the ELN. Investigators are advised to use witnessing with validated signatures and page-locking capabilities as needed for these applications.

CREDIT: NCI

Screenshot of an activity feed of a LabArchives ELN.

Conditionally sensitive personally identifiable information, or PII, such as medical record numbers or image accession numbers may be used in the ELN when necessary to support clinical research. Investigators are encouraged to limit their use of conditionally sensitive PII to only the data elements required for their specific applications (for example, use age instead of birthdate when possible).

Clinical care and clinical trial data, genomic datasets, and large imaging datasets should be stored in appropriate platforms and systems designated by each IC. Use URLs or image thumbnails in the ELN to reference and link to the master data source(s). Smaller datasets such as those produced by laboratory instrumentation (for example, plate readers or flow cytometers) can be ingested into the ELN by uploading or via the application programming interface. If the lab or branch or investigator's policy is to retain master copies on a group drive, users are advised to note the URL of the master copy in the ELN and regard the ELN copy as an operational copy.

Investigators wishing to make changes to their ELN declaration or request accounts, or need training or other types of support assistance with ELNs should submit an ELN support ticket. Answers to many frequently asked questions about the use of ELNs at NIH can be found in the FAQ section of the NIH policy on ELNs. ●

STATE OF THE ARTS

CONTINUED FROM PAGE 5

At the CC's Rehabilitation Medicine Department, art therapist **Sarah Thuermer** recalls one of her international patients undergoing bone marrow transplant for severe aplastic anemia turned acute myeloid leukemia. The patient was struggling with depression, anxiety, and coming to terms with a new sense of self if her disease was cured.

"Patients use art to express, explore, and process emotions through their entire journey and to increase self-esteem and find identity beyond their illness," said Thuermer, who taught her patient how to create masks using symbols and colors as a form of self-expression. "On her very last day, she made a beautiful mask about hope and growth; and on the back, she wrote meanings to each symbol that she created and what each color meant."

Art therapy can reduce psychological distress (PMID: 34898951) and arts-based programming has been shown to enhance the mood, health, resilience, and wellbeing of people living with chronic health conditions (PMID: 38384874). From acrylics to photography, art therapy centers around each patient's emotional needs and mental health goals, according to Thuermer.

"A lot of patients have emotions that they don't quite understand yet or are unaware of, and those might come out in art. I help guide them to process those emotions toward healing."

Technologies such as virtual reality and photography apps are making art therapy more accessible and age-appropriate for teenagers, according to Thuermer. Some apps allow those patients to virtually paint graffiti on walls, choosing their color and designs with the added benefit of getting them up and active during their hospital stay.

CREDIT: SARAH THUERMER, CC

Sarah Thuermer

"Nonverbal expression is important," added **Donna Gregory**, chief of the Recreational Therapy Program. "We see pretty much every patient dealing with a rare disease, stressful diagnosis, or stress of being involved in clinical research. Sometimes art therapy is safer and easier than trying to use words." ●

Don't miss our online version of this story to learn more about the art that decks the halls of buildings all over the NIH Bethesda campus. Visit https://irp.nih.gov/catalyst/32/6.

CATALYTIC RESEARCH

CONTINUED FROM PAGE 7

The scientists found a widespread reduction in cortical gray matter volume (GMV) in nearly 80% of brain regions with an average reduction of around 4%, with just a small rebound postpartum. They also found transient increases in white matter microstructural integrity, which is a measure of the health and quality of the connections between brain regions.

"This increase peaked around the second and third trimester and returned to baseline postpartum, so a standard before versus after pregnancy study would have missed this finding," said Chrastil. "This is the first time we have been able to see these types of dynamic changes occurring during pregnancy."

On average, change in cortical GMV was nearly three times that of control samples. **Joshua Faskowitz** and **Daniel Handwerker** in NIMH's Section on Functional Imaging Methods provided expertise in imaging and analysis in the study which was funded in part by NIA.

Although an "N-of-1" study, these findings indicate that during pregnancy the human brain exhibits remarkable changes. Currently, clinicians lack the tools needed for detection and treatment of neurological disorders that co-occur or worsen with pregnancy.

Precision imaging could aid doctors in assessing an individual's risk for certain conditions during pregnancy as well as direct the creation of new therapeutics for neurological disorders. (NIH authors: J. Faskowitz and D.A. Handwerker, PMID: 39284962) ●

[BY MELANIE BARKSDALE, NIAID]

JOIN US!

The NIH Catalyst is seeking volunteer photographers and writers to join our team.

If you are interested in science writing or photography, and would like to learn more about working with the *NIH Catalyst*, please email us at catalyst@nih.gov.

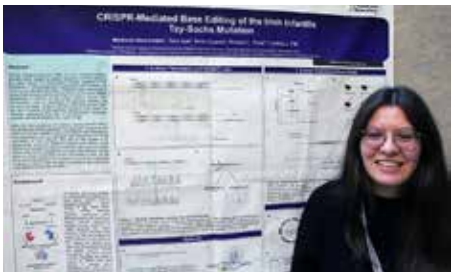
Researchers Display Discoveries at Annual Research Festival

A Showcase of Intramural Science Inspires

BY BRANDON LEVY, IRP

The first day of the 2024 Research Festival kicked off with a series of poster sessions in which scientists from across NIH showcased the innovative science they have been working on, demonstrating research on subjects such as how cooking affects the brain, the impact of vaping on lung health, and 3D models for studying pregnancy complications. Read on to dive deeper into a sampling of the more than 400 research projects presented at this year's celebration of science.

Tackling Tay-Sachs



CREDIT: BRANDON LEVY, IRP

Although **Madison Hernandez** was able to participate in research as an undergraduate at the University of Texas of the Permian Basin (Odessa), she says that she was unable to pursue her niche interests until she landed the opportunity to work as a postbaccalaureate research fellow under the tutelage of NHGRI Senior Clinician **Cynthia Tifft**. With Tifft's help, Hernandez was able to conduct research she finds personally meaningful to her.

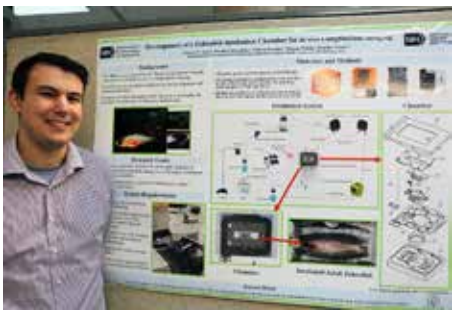
"I was born with a nonprogressive neurological disorder that affects my movement, which ultimately inspired my interest in investigating rare neurodegenerative diseases," Hernandez said. "I grew interested in gene therapy because the idea of correcting a disease at its source fascinated me."

Hernandez has been focused on infantile Tay-Sachs disease, which is caused by mutations in both copies of the *HEXA* gene. Without a functional *HEXA* gene, an enzyme called GM2 ganglioside accumulates in neurons with toxic effects, leading to loss of motor coordination, seizures, and eventually death.

To combat this tragic disease that kills so early in life, Hernandez is trying to figure out how to use the CRISPR-Cas9 gene-editing technique to correct the mutation. However, unlike traditional CRISPR-Cas9 gene editing, which breaks apart both strands of the DNA molecule before stitching them back together, Hernandez is pursuing an alternate approach called "base editing," which can correct a single DNA base pair without causing a double-strand break.

"Our findings would provide a proof of concept on base editing for this mutation, which could later be used to develop a more efficient gene therapy for patients," Hernandez explained.

Designing a device to enable cutting-edge cancer research



CREDIT: BRANDON LEVY, IRP

Tommy Jones designs and builds new contraptions in NIBIB's Instrumentation Development and Engineering Application Solutions (IDEAS) section.

"The IDEAS section provides engineering expertise to NIH researchers, specializing in the development of first-of-a-kind instrumentation design, software development, in-house fabrication of prototypes, and overall collaborative validation in labs and clinical settings," Jones explained.

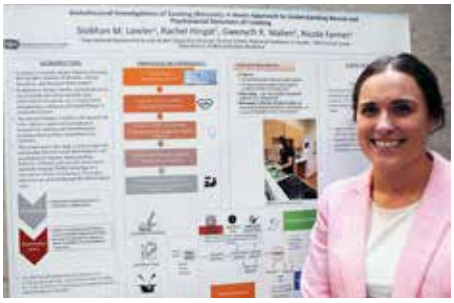
At this year's Research Festival, Jones showed off the design he and his IDEAS colleagues created for a zebrafish (*Danio rerio*) sedation chamber. It will help scientists in the lab of NCI-CCR Senior Investigator **Kandice Tanner** use that model organism to learn about why certain types of cancer spread to specific parts of the body.

The chamber can keep zebrafish sedated for the multiple hours it takes for Tanner's team to take images of the fish's inner workings, and it can work with the multiple types of advanced microscopes Tanner's team uses. The research also requires that the zebrafish remain alive so that the same fish can be examined in the same manner, repeatedly.

"Typically, zebrafish imaging is done in short intervals to ensure the fish's survival," Jones said. "This design enables longer, continuous imaging sessions while preserving the health of the fish. We also designed it to have the ability to look at different developmental stages from younger fish to adults, as all the previous devices were for adults only."

Read more about these accomplished researchers on the "I Am Intramural Blog." Visit https://irp.nih.gov/blog.

Bringing neuroscience into the kitchen



CREDIT: BRANDON LEVY, IRP

Siobhan Lawler landed her first position at NIH through the Graduate Summer Opportunity to Advance Research program, which provides graduate students interested in pursuing a doctorate with the opportunity to spend a summer working in an intramural NIH lab.

Now, after completing her doctorate and a postdoctoral fellowship in another NIH research group, she is in the midst of a second postdoctoral fellowship with **Nicole Farmer**, who studies how cooking might help improve people's mental health and reduce their risks of developing certain illnesses.

The particular study Lawler is working on, called BioCook, aims to determine how cooking affects bodies and minds.

"While cooking has been associated with psychological, social, and dietary benefits, most existing research relies on self-reported data and lacks rigorous scientific investigation with objective measurements," Lawler explained. "Therefore, the BioCook study aims to fill this gap by employing a multimodal approach, including EEG, heart rate variability monitoring, sensory system assessments, repeated salivary stress biomarker analysis, and in-depth video-guided interviews conducted after the cooking task."

Having sampled life in several IRP labs, Lawler says working with her colleagues in Farmer's lab has been particularly rewarding. Lawler says Farmer is deeply invested in her growth and incredibly giving of her time and guidance.

Addressing autism's auditory challenges with brain stimulation

CREDIT: BRANDON LEVY, IRP

It makes perfect sense that an organ as vital as the brain is encased in our thick, hard skulls to shield it from the outside world. Unfortunately, this makes it all the more challenging to treat psychiatric conditions by influencing the brain's electrical firing.

Ethan Greenstein applies a technique called repetitive transcranial magnetic stimulation (rTMS), which uses magnetic fields to alter electrical activity in the brain. Greenstein works with **Sarah Lisanby** at NIMH to investigate whether a particular form of TMS might improve how the brains of people with autism spectrum disorders (ASD) process information about sound and spoken language.

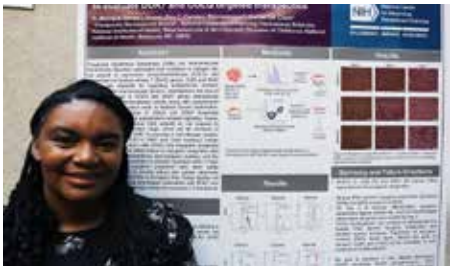
"When I learned about the cutting-edge research being done in Lisanby's lab, especially in the area of noninvasive brain stimulation to more broadly treat mental health conditions, I knew I wanted to be part of the team," he said.

The study, known as DECIBELS, uses rTMS to shift the balance between excitatory signals in the brain that activate neurons and inhibitory signals that make neurons less likely to fire. Scientists think an imbalance between these two types of signals is what underlies the challenges experienced by people with ASD.

Their work has already revealed that rTMS treatment can change the ratios of excitatory and inhibitory chemicals in the brains of cognitively typical individuals, and this change was associated with their responding more quickly to sounds. Now, they hope to see similar results when applying the same approach to individuals with ASD.

"This research is important because social communication challenges are a core feature of ASD, and current interventions do not specifically target the underlying neurochemical imbalances that may contribute to these difficulties," Greenstein explained, adding that exploring noninvasive brain stimulation as a potential intervention could open new pathways for addressing key ASD-associated challenges.

Making muscle cells in a Petri dish



CREDIT: BRANDON LEVY, IRP

Malique Jones is leveraging her experience in the field of muscle biology to develop a sort of "muscle-in-a-dish" model that could help researchers test treatments for a particular set of rare neuromuscular disorders.

Jones is a postdoctoral fellow at NCATS working with **Catherine Chen** in the Therapeutic Development Branch of the Division of Preclinical Innovation. The research team is nurturing induced pluripotent stem cells, which can develop into any other kind of cell found in the body, in a manner that coaxes them to become long cells found in our muscles called myotubes.

"This effort is part of the NCATS Platform Vector Gene Therapy program and establishment of an efficient two-dimensional skeletal myotube model that will provide an excellent resource for advancing preclinical testing and gene therapy development for treatment of rare diseases," Jones explained. ●

A Celebration of NIH Intramural Research

BY *THE NIH CATALYST* STAFF

The 2024 Research Festival did not disappoint! From high-profile lectures to poster sessions, and from vendor events to workshops, these three days of festivities dedicated to highlighting NIH's latest and greatest intramural research had something for every curious mind.

CREDIT: MARLEEN VAN DEN NESTE, NIH

The enthusiasm could hardly be contained at the poster sessions on Monday, September 23.

More than 400 research posters were on display during the three poster sessions held in person on Monday. A virtual research poster event also was held Tuesday, September 24.

CREDIT: MARLEEN VAN DEN NESTE, NIH

Pictured left to right are Giorgio Trinchieri (NCI), DDIR Nina Schor, Kyung Kwon-Chung (NIAID), and Thomas Kunkel (NIEHS). Trinchieri, Kwon-Chung, and Kunkel each offered inspirational lectures about the peaks and valleys of their scientific careers during the National Academy of Sciences (NAS) mini-symposium.

Part two of the NAS mini-symposium will be held November 13, 2–3:30 p.m., in the Masur Auditorium in Building 10, featuring Sandra Wolin (NCI) and Steven Rosenberg (NCI).

CREDIT: MARLEEN VAN DEN NESTE, NIH

Karen Laky (NIAID) offered a workshop for the TGF-beta Scientific Interest Group (SIG) on Monday, September 23. Her talk was titled "TGF-beta Signaling in Development, Homeostasis, and Disease."

CREDIT: MARLEEN VAN DEN NESTE, NIH

Stephen Whitehead, senior investigator and chief at NIAID's Arbovirus Vaccine Research Section, shared his scientific challenges in developing a dengue vaccine at the Philip S. Chen Jr., Ph.D., Distinguished Lecture on Innovation and Technology Transfer on September 25.

Learn more about dengue vaccine development in this "Speaking of Science" podcast: https://irp.nih.gov/podcast/2024/09/defying-dengue.

Save the date for next year's Research Festival, slated for September 8–11, 2025.

The Research Festival resource information fair and biomedical vendor event, held September 23–25 at the Building 10 South Lobby and the FAES Terrace, attracted more than a thousand attendees. Hundreds more came for the Green Labs Fair on September 26.

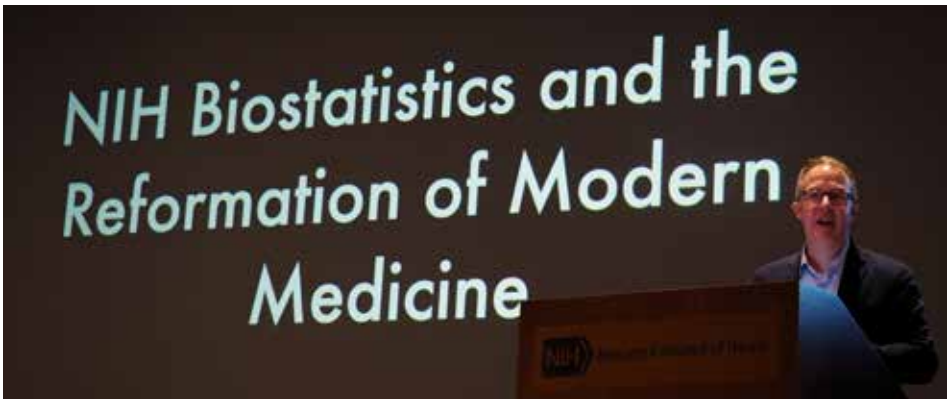
CREDIT: MARLEEN VAN DEN NESTE, NIH

CREDIT: SAINT RIEWESTAHL, ONHM

Namesakes: Victoria Harden and Philip Chen have annual lectures named after them for their extraordinary contributions to the NIH community.

Harden Lecturer Traces NIH's Role in Statistics in the Transformation of Clinical Medicine

BY KRIS HEITMAN, ONHM



CREDIT: SAINT RIEWESTAHL, ONHM

Christopher Phillips delivered the 2024 Victoria A. Harden Lecture in NIH History at the annual Research Festival, held each fall in Bethesda. Save the date for next year's Research Festival, slated for September 8–11, 2025.

In the mid- to late 20th century, clinical medicine underwent a series of major shifts due to innovations in statistical methods and concepts. Christopher Phillips, professor of history at Carnegie Mellon University (Pittsburgh), discussed several of NIH's major contributions in the second annual Victoria A. Harden Lecture in NIH History, titled "NIH Biostatistics and the Reformation of Modern Medicine." Phillips took audience members through a journey of several crucial mathematical innovations at the NIH.

Phillips began by noting that "quantification changes how we think about" both the clinical presentation of disease and potential therapeutic interventions. NIH's early statisticians applied methods from other fields to medical questions, he explained, often to establish rigorous, predictive ways of reasoning about a disease—an area that traditional epidemiology and public-health statistics had not been able to address satisfactorily. By the 1980s, medicine could consider individual patients as "collections of biomarkers" that could be subjected to a purely quantitative risk assessment based on population-level studies.

In the 1940s, Public Health Service leadership asked sociologist Harold Dorn to establish a group of statistical consultants at NCI. Although Dorn's group was small at first and most of its members came from outside of medicine, it rapidly became the best-connected network in cancer research, Phillips said. By the 1960s, the group regularly contributed to studies throughout the United States and played a central role in building scientific consensus. Through intramural fellowships, they also provided well-trained biostatisticians to universities that sought innovative analysis for their NIH extramural grants.

Dorn's consultants began working with the NIH-funded Framingham Heart Study in the late 1940s. Faced with an impressive stream of data, they asked how they could move beyond the initial statistical associations and, in the 1960s, to frame and to answer new, clinically meaningful questions about the progression of heart disease. NHLBI statistician Jerry Cornfield realized that, by thinking of study factors as "doses," he and his colleagues could predict what "dose" of factors would likely result in heart disease. Indeed, by treating individuals as aggregates of numerical data, they could eventually identify effective interventions for that group of variables. This strategy became an important addition to the usual experimental method of trying physical treatments on groups of patients and comparing outcomes.

In the early 1960s, while developing methods for the first Report of the U.S. Surgeon General's Advisory Committee on Smoking and Health (1964), Harvard statistician William Cochran explicitly drew on work by Dorn and Cornfield. Phillips emphasized the similarities between their reasoning about cancer and well-established efforts to prevent industrial harms. Rather than pursuing causal relations in the way epidemiologists traditionally had, he said Dorn, Cornfield, and Cochran asked whether harms observed could be statistically foreseen from the data in hand.

Phillips drew a third example from the work of Nathan Mantel, a colleague of Cornfield's who joined an NCI effort to establish an acceptable level of cancer-causing herbicides in the U.S. food supply. NCI statisticians of the 1940s had worked on a similar problem: After early chemotherapies and radiation therapies presented a mix of benefits and harms, the research challenge was to determine the most effective dose with an acceptable risk of harm. Mantel and his NCI collaborator Ray Bryan recognized that pesticides would also present risks and benefits for human health, so they developed methods to compute a "virtual safe dose" for whatever level of risk the government decided was acceptable.

Phillips closed by noting that statistics, particularly within the U.S. government, has long drawn a much more diverse, inclusive set of workers. Starting with Depression-era work programs, the United States government had become much more open to hiring women, people of Jewish faith or descent, and people of color into statistical and mathematical jobs.

The Harden lecture is held annually by the Office of NIH History and Stetten Museum (ONHM) in honor of its founding director, Victoria Harden. Learn more at https://history.nih.gov. ●

revealing the final unmapped 200 million bases in the 3-billion-base human DNA. Additionally, the international Telomere-to-Telomere Consortium behind the complete assembly used Biowulf's file-sharing service as a centralized location to store and share data within the consortium as they worked together on the downstream analyses of the complete genome, Phillippy said.

"[Biowulf] was one of the draws that helped recruit me to the NIH in 2015," said Phillippy. "Because we were such a compute-intensive group, I could only go somewhere that could support the needs of my group for the genome assembly and sequencing work. When I do my quadrennial reviews, and they have to ask 'Why the NIH Intramural Research Program?' I hold up Biowulf as a resource that's unique to here that I don't have access to elsewhere."

Daniel Pine, chief of the NIMH Section on Development and Affective Neuroscience, is another moderately heavy user who now sees Biowulf as essential to his research, having turned to the system in 2015, some 15 years after joining the NIH.

A clinician-scientist, Pine specializes in brain function and psychopathology, such as stress, anxiety, and emotional problems in children and adolescents. His lab often uses more than a million CPU hours per month on Biowulf to analyze brain magnetic resonance imaging scans. His team can perform a multitude of individual computations on any given image across tens of thousands of microregions in the brain—capturing thickness, surface area, curvature, gyrification (brain folding), and other features—and compare that in parallel with thousands of other brain images.

"To be one of the leading groups in the world [on brain structure and function], you absolutely need access to high-performance computing resources," Pine said. "Ultimately what we want to be able to do is to get information from the brain [scan] that we can't get clinically to understand how we predict what's going to happen to any one child…to better understand treatments."

"For what my group does, which is fairly clinically focused, Biowulf is wonderful," Pine added.

So, what's under the hood?

Biowulf is a cluster of more than 3,000 computer nodes located in the belly of Building 12. Like books on a bookshelf, each node—sort of a computer unto itself, with a motherboard, memory, and processors—sits on a computer rack.

A typical node has between 32 and 192 processors. A CPU hour refers to one hour on one processor. If you do the math and multiply all those processors and nodes (we didn't; they wouldn't grant us access to Biowulf), you'll understand how a single user can use millions of CPU hours over the course of only a few days.

Biowulf comprises 100,000 CPUs and 1,000 GPUs. CPU, one said processor, stands for central processing unit. This has been the mainstay for processors for decades and what is likely supporting your laptop computer. A GPU, short for graphics processing unit, was developed more recently, primarily for computer gaming.

A GPU isn't necessarily better than a CPU, but adding more GPUs to Biowulf is one direction that CIT will pursue to increase speed and capacity, according to **David Hoover**, a computational biologist and chief scientist of Biowulf since 2003.

CPUs are ideal for complex, serial tasks such as protein motion simulations in which each new step in an intricate calculation depends heavily on the previous step, Hoover said. GPUs are ideal for less complex yet parallel tasks, such as identifying variants of gene sequences in very large datasets.

Perhaps more significant for Biowulf's growth, Hoover said, GPUs are needed for the development of AI and ML programs. But there are limitations. First, there's the physical size to consider: a CPU is about

BIOWULF OVER THE YEARS

CREDIT: NIH CIT

Biowulf in its earliest days (circa 2000).

Biowulf in 2017.

Today, more than 6,000 papers have been published by scientists who used Biowulf resources.

CREDIT: NIH CIT

This photo collage of HPC staff was created for the 2017 NIH Director's Award the group received for "doubled computational capacity and storage [that] supported 500+ scientific applications to enable NIH intramural researchers to solve complex biomedical problems." The top photo shows Andy Baxevanis flanked on either side by Susan Chacko and Steve Bailey at the 2017 supercomputing conference, the year Biowulf ranked #66 in the TOP 500 list of most powerful supercomputers in the world.

the size of a tea bag; a GPU is about the size of a tea box. Then there's the cost. GPUs are about 10 to 100 times as expensive as a CPU. And, Hoover said, the highest-quality GPUs are in short supply as the demand has been so high the past two years with the rise of AI that large commercial users are snatching them up.

Another option that CIT is considering to increase Biowulf's capacity is to offload some jobs to the cloud, a lofty term to describe very terrestrial computer servers, some of them as close as northern Virginia. Doing so comes at a high cost for such a commercial service.

Similarly, the CIT has tapped into the Texas Advanced Computing Center at the University of Texas at Austin, funded by the National Science Foundation. Although the cost might be cheaper than commercial cloud services, the queue might be long, Hoover said. And neither are a substitute for the Biowulf team's hands-on service and familiarity with NIH research, including computational biology.

"Hardware is one thing. But people-resource? That's something we have in spades," Hoover said.

Solid infrastructure for exciting, uncertain future

Physical size is not a significant limiting factor for Biowulf; the system is more limited by power and cooling available in the data center, as well as funding for upgrades, according to **Benjamin "Tim" Miller**, the technical lead for NIH HPC responsible for architecture and technical operations—that is, the guy who gets called at 2 a.m. if Biowulf is down.

"We're very fortunate that our data center facilities team at CIT, as well as the Office of Research Facilities, have been very accommodating of our needs," Miller said. "Within the last several years, the chilled water pumps in the data center, which we rely on to cool Biowulf, underwent a major upgrade. Likewise, these groups have been taking good care of the power systems that provide a lot of electricity to the cluster. We just completed a major upgrade of our networking that will allow us to eventually increase our bandwidth to the NIH network backbone."

Miller said he's very excited to incorporate some DPUs, or data processing units, which are ideal for storage, networking, and security operations, essentially offloading these tasks from the CPUs in the system.

To flush out this alphabet soup, what is not in Biowulf's immediate future, Miller said, are TPUs and QPUs. The TPU, a tensor processing unit, is a proprietary processor developed by Google for neural network machine learning and AI; a QPU is a quantum processing unit, still as elusive as quantum stability itself.

One more exciting project for the Biowulf team is "HPC on demand," now in pilot mode. While access to Biowulf is rather simple via a laptop and web interface—you enter your request, and you monitor your job—HPC on demand allows users to work directly on Biowulf in real time for relatively small tasks.

"Users dig it," said Hoover. "It really is just dynamite."

And such is the explosive future for Biowulf as it logs billions of computing hours well into the future. ●

Don't miss the final installment of the Biowulf 25th Anniversary Seminar Series on November 14, 11 a.m. to noon. All four presentations will be available on VideoCast. For more information visit https://hpc.nih.gov/training/biowulf-25th-anniversary-seminars.html.

Meet Deborah Citrin, M.D.

Citrin Named NCI-CCR's New Scientific Director for Clinical Research

BY ANNELIESE NORRIS, NCI

CREDIT: NCI-CCR

Deborah Citrin was named the scientific director for clinical research at NCI-CCR.

Deborah Citrin has been named the new scientific director for clinical research of NCI's Center for Cancer Research (CCR), where she once served as deputy director. Citrin leads the Prostate Radiotherapy Program and is a senior investigator of the Radiation Oncology Branch. She is an internationally recognized expert in prostate cancer, radiation oncology, and normal tissue radiobiology. She received NIH tenure in 2015.

Citrin has held many leadership roles over her career including as an NIH and NCI-CCR Women Scientist Advisor, chair of the NCI-CCR Clinical Promotion Review Panel, and vice chair of the NCI-CCR Clinical Tenure Review Panel. Among her many accomplishments, she has received the NIH Director's Alan S. Rabson Award for Clinical Care (2016), the NCI Director's Emerging Leader Award (2018), and the NIH Director's Ruth L. Kirschstein Mentoring Award (2023).

"I am thrilled that Dr. Citrin has assumed the role of scientific director for clinical research," said **James Gulley**, acting codirector of NCI-CCR. "She brings invaluable institutional knowledge, an extensive clinical background, an unmatched work ethic, and a collaborative team spirit."

From NC to NCI

Citrin grew up in North Carolina, where she earned her medical degree at Duke University School of Medicine (Durham, North Carolina). There, she participated in the Howard Hughes Medical Student Research Fellow Program. She completed an internal medicine internship in 2001 at Washington Hospital Center in D.C., and then a residency in radiation oncology in the then-joint program among NCI, Walter Reed Medical Center, and the Navel Medical Center.

After her residency, Citrin stayed on as a staff clinician at NCI. "At the time there were no tenure-track positions available," she recalled. Her enthusiasm for both laboratory science and clinical research led Lee Helman, NCI-CCR scientific director for clinical research (2007-2016), and Robert Wiltrout, NCI-CCR director (2005-2015), to create the Assistant Clinical Investigator (ACI) program at NCI-CCR. Citrin was one of the first people appointed as an ACI. She later transitioned to a tenure track investigator position.

Targeting prostate cancer

As a radiation oncologist, Citrin treats prostate cancer using various forms of radiation. A portion of Citrin's laboratory is dedicated to developing strategies to enhance the capacity of radiation to kill tumor cells while protecting normal tissue from the side effects of radiation treatment. Although Citrin uses external beam radiation most frequently to treat prostate cancer, she also delivers prostate brachytherapy (PMID: 28576185), which is a widely used treatment that involves placing radioactive sources into the prostate gland to kill the cancer cells while causing less damage to healthy tissue nearby.

She is passionate about developing new strategies to increase the chance of cure and reduce side effects for her patients. To this end, she partnered with a company that developed (nonradioactive) small silicone drug-delivery devices that are preloaded with hormonal medications often delivered systemically to treat prostate cancer during radiation. In collaboration with her colleagues in Urologic Oncology, Interventional Oncology, and Molecular Imaging, Citrin inserts these devices into the prostate tumor using a preloaded needle where the drug elutes over time, and importantly, only targeting the tumor and thus reducing the substantial side effects associated with systemic delivery.

"It's pretty amazing, especially if you only need to deliver the drug to the tumor because the risk of metastasis is small, but the risk of local recurrence is high," Citrin explained.

Whilst only a proof of principle, there are potentially "lots of opportunities for delivering drugs to localized tumors in a way that will minimize systemic side effects," she said, adding the example of using PARP inhibitors or other small molecules to sensitize tumor radiation or

to treat or prevent certain types of cancer when used alone.

In the clinic, Citrin tries to understand whether there are ways to better predict whether a patient's prostate cancer is going to recur after a curative radiation treatment. Citrin and her collaborators, who include **Ismail Baris Turkbey** and **Peter Choyke** of the Molecular Imaging Branch, have conducted several studies to use novel imaging modalities to focally treat prostate cancers that have either recurred after surgery or that have recurred after radiation.

Along with **Adam Sowalsky**, head of the NCI-CCR Prostate Cancer Genetics Section, Citrin is working to integrate imaging, transcriptomics, and tissue biomarkers to predict recurrence with the goal of eventually being able to adapt treatments to personalize prostate cancer treatment (PMID: 37205576).

Raising the bar

Citrin understands the inner workings of NCI, so her vision as the scientific director for clinical research is to foster collaboration between basic and clinical research and to build bridges and develop programs with funding mechanisms that will allow NCI-CCR to capitalize on that relationship. "The ability to rapidly translate laboratory findings into clinical trials to enhance the lives of cancer patients is part of what makes NCI-CCR so unique and special," said Citrin.

Helping CCR leverage NCI's expertise in data science is one of Citrin's priorities. "The possibilities of collectively coming together under one umbrella to learn more from our independent studies through collaboration offers tremendous opportunity," she said.

When she is not working, you might find Citrin in her kitchen baking up a culinary delight or gardening. Citrin has been a science fiction fan since she was a child and is still an avid reader but admits, sadly, these days she does not have much spare time, especially with three children ranging from elementary school to middle school to high school ages—each of whom play sports (soccer and baseball are family favorites). ●

NIH Distinguished Scholars

Congratulations to the 2024 Distinguished Scholars, who gathered October 24 on the Bethesda campus for a kickoff meeting where they were greeted by senior leadership.

CREDIT: CHIA-CHI CHARLIE CHANG

Back row, left to right: Carl Hashimoto, director of Faculty Development, OIR; Roland Owens, principal deputy director, OIR; Ifechukwude Ebenuwa, NIDDK; Farran Briggs, NEI; Carlos Ferreira, NICHD; and Joe Nguyen, NCI-CCR.

Middle row: Risa Isonaka, assistant director of Faculty Development, OIR; Stephanie London, senior mentor, NIEHS; DDIR Nina Schor; NIH Director Monica Bertagnolli; Amreen Mughal, NINDS; Rajula Elango Alleva, NIEHS; Rasika Mathias, NIAID; and Camila Odio, NIAID.

Front row: Pamela Schwartzberg, senior mentor, NIAID; Valerie Darcey, NIDDK; Nicole Farmer, CC; Allison Herman, NIA; Indira Turney, NIA; Victoria Acosta-Rodríguez, NIA; and Philip Adams, NIAID.

NIH ABBREVIATIONS

CARD: Center for Alzheimer's and Related Dementias
CC: NIH Clinical Center
CCR: Center for Cancer Research, NCI
CIT: Center for Information Technology
DCEG: Division of Cancer Epidemiology and Genetics, NCI
FAES: Foundation for Advanced Education in the Sciences
FelCom: Fellows Committee
FNIH: Foundation for the NIH
FNLCR: Frederick National Laboratory for Cancer Research
IRP: Intramural Research Program
HHS: U.S. Department of Health and Human Services
NCATS: National Center for Advancing Translational Sciences
NCBI: National Center for Biotechnology Information
NCCIH: National Center for Complementary and Integrative Health
NCI: National Cancer Institute
NEI: National Eye Institute
NHGRI: National Human Genome Research Institute
NHLBI: National Heart, Lung, and Blood Institute
NIA: National Institute on Aging
NIAAA: National Institute on Alcohol Abuse and Alcoholism
NIAID: National Institute of Allergy and Infectious Diseases
NIAMS: National Institute of Arthritis and Musculoskeletal and Skin Diseases
NIBIB: National Institute of Biomedical Imaging and Bioengineering
NICHD: *Eunice Kennedy Shriver* National Institute of Child Health and Human Development
NIDA: National Institute on Drug Abuse
NIDCD: National Institute on Deafness and Other Communication Disorders
NIDCR: National Institute of Dental and Craniofacial Research
NIDDK: National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS: National Institute of Environmental Health Sciences
NIGMS: National Institute of General Medical Sciences
NIMH: National Institute of Mental Health
NIMHD: National Institute on Minority Health and Health Disparities
NINDS: National Institute of Neurological Disorders and Stroke
NINR: National Institute of Nursing Research
NLM: National Library of Medicine
NSTC: National Smell and Taste Center
OBSSR: Office of Behavioral and Social Sciences Research
OD: Office of the Director
ODP: Office of Disease Prevention
OIR: Office of Intramural Research
ORS: Office of Research Services
ORWH: Office of Research on Women's Health

NIH Hosts Myositis Conference Attendees

Thirty-five Visitors Learned About NIH Clinical Research, Emerging Treatment Options

BY LINDSAY KEY, NIEHS

CREDIT: MARIA MASLENNIKOV, CC

Patients with myositis visited the NIH for a full day of talks, tours, and networking.

People living with myositis learned about research to advance understanding and treatment of the disease during presentations and a tour of the Clinical Center (CC) in Bethesda, Maryland, on September 6. Myositis refers to a set of autoimmune diseases involving chronic inflammation of the muscles. An estimated 75,000 people living in the United States are affected, according to The Myositis Association (TMA).

NIEHS, based in North Carolina, partnered with the CC, NIAMS, and TMA to coordinate this inaugural event. Patients and caregivers attended research-focused talks, toured clinical research facilities, and learned how to enroll in NIH studies. The small group tours, which were led by staff from the NIEHS Environmental Autoimmunity Group and NIAMS research groups studying juvenile myositis and adult myositis, helped attendees get an idea of what it is like to be a patient at the NIH.

Paula Eichenbrenner, TMA executive director, said the visit was an outstanding opening event for TMA's annual international patient conference, which took place in Baltimore September 6–8. "We learned about the latest developments in myositis science and the highly successful, innovative connection between TMA and NIEHS," she said about the conference's off-site excursion offering.

Pinpointing risk factors

NIEHS scientists have researched myositis for more than 40 years. This rare and complex group of illnesses occurs when the immune system attacks muscles in the arms, legs or hips, abdomen, and back.

Types of myositis include dermatomyositis, antisynthetase syndrome, necrotizing myopathy, inclusion body myositis, polymyositis, and juvenile forms of myositis. With no known cure, physicians focus on treating symptoms and the underlying inflammatory processes. These symptoms include muscle pain and weakness, fatigue, photosensitive skin rashes, swelling, and trouble breathing or swallowing.

The incidence of myositis, along with other autoimmune disorders, is rising in the United States, according to **Lisa Rider**, who leads the NIEHS Environmental Autoimmunity Group.

A better understanding of the environmental influences driving the development of the disease, along with genetic risk factors, is needed, she said.

NIEHS scientists have used information from a TMA-led patient registry called MYOVISION to divide patients into subgroups, or phenotypes, to better understand myositis, as well as from environmental risk-factor studies led by NIEHS from the CC. They have identified ultraviolet sun exposure, smoking, stressful events, and exposure to silica and solvents as environmental risk factors, explained Rider.

"Our new approaches and technologies are allowing us to carefully define these myositis phenotypes, to identify these genetic and environmental factors, and to look at their interactions," she said.

A patient-centered approach

In addition to research advances, attendees also learned about new physical therapy techniques for myositis from the CC's rehabilitation medicine team.

Following a lecture led by **Kakali Sarkar**, an NIEHS Environmental Autoimmunity Group biologist, they toured a myositis research laboratory and biorepository, where patient biospecimens are stored. The group also learned about advanced imaging techniques for myositis from **Adam Schiffenbauer**, deputy head and associate research physician in the Environmental Autoimmunity Group.

NIEHS's longstanding partnership with TMA has been crucial to advancing research, according to Schiffenbauer. He noted that patient feedback about the disease has helped his team identify new lines of inquiry.

"We depend on the patients," Schiffenbauer said. "We couldn't do any of the research we do without them."

Martha Arnold, a TMA board member living with inclusion body myositis, said the NIH staff presentations were a highlight of the visit. "Their passion and dedication shone through, and our visit reassured me that excellent work is being done to advance science across myositis diseases," she said. ●

CREDIT: MARIA MASLENNIKOV, CC

Lisa Rider, left, and Rita Volochayev, nurse practitioner in the Environmental Autoimmunity Group, discussed current myositis research and discoveries.

WSA Celebrates Legacy of Anita Roberts

NIAID's Carolina Barillas-Mury to Present the 2024 Anita B. Roberts Lecture

BY MUNA FUYAL, NCI AND CARRIE MAE LONG, NIAID

CREDIT: CAROLINA BARILLAS-MURY

Carolina Barillas-Mury

Join the Women Scientists Advisors (WSA) in celebration of the scientific contributions of **Carolina Barillas-Mury** at the 2024 Anita B. Roberts Lecture, which will take place November 14, 12–2 p.m., live on VideoCast. Barillas-Mury is chief of the Laboratory of Malaria and Vector Research at NIAID and a distinguished investigator and head of the Mosquito Immunity and Vector Competence Section. Her lab investigates the interactions between the mosquito immune system and *Plasmodium* parasites to understand how these interactions affect malaria transmission to disrupt the parasite's life cycle and prevent human disease.

Barillas-Mury's path to studying mosquito immunity began when she joined the laboratory of Michael Wells at the University of Arizona (Tucson, Arizona) for her doctoral research. Born in Guatemala in 1961, Barillas-Mury graduated from medical school at Universidad Francisco Marroquín de Guatemala in 1985 and wanted to explore biology at the molecular level.

Driven by her medical background in human health in tropical regions, her doctoral research on mosquitoes described the enzymatic processes behind mosquito blood-meal digestion.

She continued her training as a postdoctoral scholar with Fotis Kafatos at Harvard University (Cambridge, Massachusetts) and the European Molecular Biology Laboratory (Heidelberg, Germany). She became an assistant professor at Colorado State University (Fort Collins, Colorado) in 1998 and then joined NIH as a tenure track investigator in 2003. She was promoted to senior investigator in 2010 and NIH distinguished investigator in 2016, an honor reserved for NIH's most preeminent senior investigators.

Her continued scientific leadership in understanding the mosquito immune defenses and malaria parasite coping mechanisms has been accoladed by national and international scientific bodies.

She was awarded the 2010 Bailey K. Ashford Medal from the American Society of Tropical Medicine and Hygiene, and the 2013 Sanofi-Institut Pasteur Award in Tropical and Neglected Diseases. She was elected to the National Academy of Sciences in 2014 and National Academy of Medicine in 2021, and was recognized among the 2017 Alumni of the Year of the University of Arizona. Barillas-Mury became a fellow of the American Society of Tropical Medicine and Hygiene in 2017 and of the Entomological Society of America in 2020.

In addition to being a scientific leader in the field, Barillas-Mury also is a passionate advocate for women and underrepresented minorities in biomedical research. She was a member of the National Academy of Science Section 44 Temporary Nominating Group from 2016 to 2023 to promote the nomination of women and other underrepresented groups in NAS.

"It is essential to find joy in your work and inspire the next generation with your enthusiasm for science, ensuring a continuous pursuit of truth as we navigate an ever-growing sea of information and misinformation," said Barillas-Mury, who will deliver a talk titled "Mosquito Immunity and Malaria Transmission."

It comes as no surprise that Barillas-Mury is an admired mentor to her trainees. "Dr. Barillas-Mury is a beacon of scientific integrity and mentorship," said Yeon-Soo Han, who was a postdoctoral fellow in her lab from 1998–2003. "Her commitment to advancing science while nurturing the next generation of scientists including myself is truly inspiring." ●

About Anita Roberts

CREDIT: WSA

The Anita B. Roberts Lecture Series is an annual event sponsored by WSA to highlight the outstanding achievements of NIH women scientists. The lecture's namesake, Anita Roberts, led an illustrious career as a scientist and mentor at NIH. She joined NCI in 1976 and was later promoted to chief of the Laboratory of Cell Regulation and Carcinogenesis. In addition to her scientific success, Roberts was an excellent mentor. The lecture series serves as a testament to her continuing legacy and highlights the importance of fostering a supportive workplace.

Colleagues: Recently Tenured

Meet your recently tenured colleagues: **Rebecca Brown** (NIDDK), **Eric Calvo** (NIAID), **Mitchell Machiela** (NCI), **D. Rebecca Prevots** (NIAID), and **Chengkai Dai** (NCI).

REBECCA J. BROWN, M.D., NIDDK

Senior Investigator, Diabetes, Endocrinology, and Obesity Branch

Education: Rice University, Houston (B.A. in chemistry); Mayo Clinic Alix School of Medicine (formerly Mayo Medical School), Rochester, Minnesota (M.D. in medicine); Duke University, Durham, North Carolina (M.S. in health science)
Training: Pediatric resident, University Hospitals Rainbow Babies and Children's, Cleveland (2002–2005); pediatric endocrinology fellow, NICHD (2005–2008)
Came to NIH: In 2005 as a clinical fellow, NICHD; in 2008 became a senior fellow, NIDDK; in 2012 became an assistant clinical investigator; and in 2015 became a Lasker Clinical Research Scholar, NIDDK
Outside interests: Hiking with my husband and 9-year-old daughter; gardening; reading
Website: https://irp.nih.gov/pi/rebecca-brown

Research interests: The goal of my research program is to understand mechanisms regulating energy metabolism in humans. To accomplish this, I study patients with rare disorders of severe insulin resistance as models to understand perturbations in pathways regulating energy metabolism. I apply what I learn about pathophysiology to develop therapies for these rare and life-threatening diseases and use what I learn from rare diseases to elucidate drug targets for more common disorders of insulin resistance, such as obesity and type 2 diabetes.

I study patients with lipodystrophy, characterized by deficiency of body fat; genetic variants of the insulin receptor gene; and autoantibodies to the insulin receptor. These patients, due to extreme phenotypes and clear etiologies, serve as models to understand pathways causing insulin resistance and metabolic syndrome (PMID: 32191645).

One focus of my lab is understanding clinical effects and mechanisms of action of the adipokine leptin. Patients with lipodystrophy are deficient in leptin because they lack adipocytes. We found that leptin replacement in patients with lipodystrophy dramatically improves metabolic disease, which led to FDA approval of recombinant leptin (PMID: 29644599). We also have elucidated multiple mechanisms by which leptin improves metabolic disease (PMID: 29723161; PMID: 33890058).

Future directions: Going forward, my lab seeks to understand mechanisms leading to inadequate triglyceride storage in adipocytes in both patients with lipodystrophy and those with obesity, and we are exploring therapies to enhance adipocyte function (PMID: 36195542).

We are also engaged in exciting collaborations aimed at understanding how insulin resistance leads to cardiovascular disease in humans.

ERIC CALVO, PH.D., NIAID

Senior Investigator, Molecular Entomology Section, Laboratory of Malaria and Vector Research

Education: University of Havana, Cuba (B.Sc. in biochemistry); Institute of Biomedical Sciences, University of Sao Paulo, Brazil (Ph.D. in parasitology)
Training: IRTA postdoctoral fellow, NIAID (2004-2008)
Before coming to NIH: Staff fellow, Center for Drug Evaluation and Research, FDA, Bethesda, Maryland
Came to NIH: In June 2010 as a staff scientist, NIAID; in 2018 became an Earl Stadtman Investigator and scholar in the NIH Distinguished Scholars Program
Outside interests: Cooking Cuban food; travel
Website: https://irp.nih.gov/pi/eric-calvo

Research interests: I am a vector biologist who is interested in understanding the role of salivary secretions from disease vectors. My laboratory characterizes the functions of salivary proteins from blood-feeding arthropods to understand how they mediate pathogen transmission. This information is synthesized into an integrated model of the vector blood-feeding process and provides new insights into how these processes affect disease transmission and host immunity (PMID: 37469515).

To accomplish these aims, we use a combination of bioinformatic analyses, protein chemistry, vascular and structural biology, assay development, and mosquito gene editing based on the CRISPR-Cas9 system. Our research has significantly enhanced our understanding of biologically active salivary proteins from blood-feeding arthropods, including mosquitoes (*Culicidae* species), sandflies (various genera), and black flies (*Simuliidae* species; PMID: 37909749; PMID: 35417706).

My program has also provided new information on transcriptomics and proteomics of the salivary glands in several major vectors. This work will aid in the identification of salivary proteins that affect virus transmission, in the discovery of immunological markers of vector exposure, and in the identification of pharmacologically active salivary proteins of disease vectors (PMID: 38188518).

Future directions: The functions of most salivary proteins from disease vectors and their effects on blood feeding and disease transmission remain elusive. Approximately 40-50% of these proteins remain to be structurally and functionally characterized. We intend to expand the functional annotation and characterization of salivary proteins for the major insect vectors including mosquitoes, sand flies, and blackflies. Continued technical improvements in the drug discovery field are likely to uncover many new therapeutic leads from salivary secretions.

MITCHELL J. MACHIELA, SC.D., NCI

Senior Investigator, Integrative Tumor Epidemiology Branch, Division of Cancer Epidemiology and Genetics (DCEG)

Education: Calvin University, Grand Rapids, Michigan (B.S. in biology); University of Michigan, Ann Arbor, Michigan (MPH in epidemiology); Harvard T.H. Chan School of Public Health, Boston (Sc.D. in epidemiology)
Training: Cancer Research Training Award Fellowship, NCI, Rockville, Maryland (2012-2017)
Came to NIH: In 2012 as a postdoctoral fellow, NCI
Outside interests: Enjoying the outdoors
Website: https://irp.nih.gov/pi/mitchell-machiela

Research interests: My research is focused on understanding how inherited (germline) variation and acquired (somatic) mutations individually and jointly affect cancer risk. I lead studies of genetic mosaicism to investigate the causes of acquired mosaic chromosomal alterations and their impact on cancer risk. My research uses existing genotype data from DCEG studies and merged international consortia to enable well-powered investigations. I have characterized the frequency and distribution of mosaic chromosomal alterations in existing genotyped populations of blood and buccal DNA (PMID: 25748358), discovered germline contributors to genetic mosaicism (PMID: 27064253; PMID: 38867047), and identified associations between cancer and infectious disease risk, including severe COVID-19 infections (PMID: 38867047). I also perform genome-wide association studies (GWAS) on pediatric and adult malignancies and have developed the GWAS Explorer (https://exploregwas.cancer.gov/plco-atlas) as a platform to examine, visualize, and share GWAS summary statistics across several traits. Pediatric cancers like Ewing sarcoma (ES) provide a unique opportunity to study a homogenous tumor with a potentially larger genetic contribution to risk. I lead GWAS on ES to identify susceptibility regions and elucidate the underlying genetic architecture of ES (PMID: 30093639). Findings from ES GWAS have led to regional sequencing studies detailing germline-somatic interactions with ES fusion oncoproteins (PMID: 36787739). I also develop web-based tools including LDlink (https://ldlink.nih.gov) and AuthorArranger (https://authorarranger.nci.nih.gov).

Future directions: Most current investigations of genetic mosaicism use cross-sectional data. I am currently working with the NCI's Prostate, Lung, Colorectal and Ovarian study to examine the clonal dynamics of genetic mosaicism in a large longitudinal series of blood samples. Additionally, I am expanding genetic mosaicism studies to Sub-Saharan African populations to study potential effects of endemic malarial infections on the frequency and genomic distribution.

D. REBECCA PREVOTS, PH.D., NIAID

Senior Investigator, Epidemiology and Population Studies Section

Education: Barnard College, Columbia University, New York (B.A. in biology); University of Michigan, Ann Arbor, Michigan (Ph.D. and MPH in epidemiology)
Training: Epidemic intelligence service officer, CDC, Atlanta (1991–1993)
Before coming to NIH: Epidemiologist, National Immunization Program (1991–1993 and 1996–2003) and Division of HIV/AIDS Prevention, CDC (1993–1996); Epidemiologist

CONTINUED ON PAGE 23

The SIG Beat: New SIGs

NEWS FROM AND ABOUT THE SCIENTIFIC INTEREST GROUPS

BY *THE NIH CATALYST* STAFF

Six new NIH Scientific Interest Groups (SIGs) were (re)created in 2024.

Artificial Intelligence

In case you missed it, biomedical science is in the midst of a technological revolution driven by artificial intelligence (AI), deep learning (DL) neural network architecture, and a burgeoning availability of computational power. Cutting-edge AI-based techniques are being applied to every subfield of the biological sciences to produce novel, ground-breaking advancements. The Artificial Intelligence Interest Group (AIIG), previously called the Deep Learning and AI in Biomedical Sciences Interest Group, aims to promote the awareness, understanding, and adoption of AI and DL approaches across the NIH. No experience is required to join. The group is intended for experts and novices alike to discuss a wide range of topics in this rapidly expanding field. Login to the weekly AI Journal Club and Seminar Series, where AIIG members from various scientific backgrounds take turns leading a session on a topic of interest. Take part in a new yearly event, the NIH Artificial Intelligence Symposium, at which researchers across NIH can gather to learn and share their AI-related research. For more information, contact **Ryan O'Neill** at ryan.o'neill@nih.gov.

Webpage: https://oir.nih.gov/sigs/artificial-intelligence-interest-group

LISTSERV: artificial-intelligence@list.nih.gov

Malaria

The Malaria Interest Group (MIG) brings together scientists, professionals, and trainees who share an interest in global prevention and control of malaria. The MIG aims to share ideas, expertise, and findings pertinent to malaria research from laboratory and field investigations, and disseminate knowledge of novel detection technologies and strategies, vaccines, and other preventive and therapeutic interventions, including malaria parasite vector control. Expect virtual or hybrid meetings every three months and an annual in-person meeting and mini-symposia. MIG is housed at the NIH, but is open to all government scientists, professionals, and trainees who share an interest in use-inspired research and programmatic approaches relevant to malaria control and prevention. For more information, contact **Patrick Duffy** at patrick.duffy@nih.gov.

Webpage: https://oir.nih.gov/sigs/malaria-interest-group

LISTSERV: malaria-interest-group@list.nih.gov

Small Molecule Therapeutics

Less is more when it comes to targeting disease. The Small Molecule Therapeutics SIG aims to have discussions and seminars and to provide a platform for collaboration on interdisciplinary research that results in the identification of potent, safe, and pharmacokinetically desirable chemical entities as therapeutics against different disease areas. Discovery of small molecule therapeutics, defined as those with a molecular weight less than 750 Daltons, involves collaboration from scientists with expertise in target protein identification and validation, assay development, screening, and lead molecule identification and optimization. Scientists with expertise in biology, medicinal chemistry, structural biology, cheminformatics, and computational chemistry (just to name a few) are invited to engage in this endeavor. For more information, contact **Debananda Das** at dasd@mail.nih.gov.

Webpage: https://oir.nih.gov/sigs/small-molecule-therapeutics-scientific-interest-group

LISTSERV: small-molecule-therapeutics@list.nih.gov

Spatial Biology

The functions of biological systems rely on well-organized, spatially orchestrated cells. Recent advances in spatial molecular profiling offer a unique opportunity to understand the spatial landscape of cells and their interaction dynamics in both health and disease. Cutting-edge imaging and sequencing-based spatial profiling technologies have been implemented at the NIH. The question remains of how to unlock the full potential of the spatial data to understand fundamental biological questions. The Spatial Biology SIG aims to engage researchers in the spatial biology community, ranging from spatial biology, computational method development, and technology advancement, to promote interactions among NIH scientists and facilitate new scientific discoveries. Expect a monthly seminar series presented by both intramural and extramural experts in the field. A scientific symposium will be a potential future event. For more information, contact **Lichun Ma** at lichun.ma@nih.gov.

Webpage: https://oir.nih.gov/sigs/spatial-biology-interest-group

LISTSERV: spatialbiology@list.nih.gov

Read about the Structural Biology Methods and the Adherence Research Network SIGs online at https://irp.nih.gov/catalyst/32/6.

and Technical Advisor, Immunization Program, Pan American Health Organization, Brasilia, Brazil (2000–2002); Public Health Advisor, New York City Department of Health AIDS Surveillance and Epi. Unit (1985–1986)
Came to NIH: In 2003 as epidemiologist, Office of Global Research, NIAID
Outside interests: Biking; dancing (salsa, samba, merengue, contra, and swing)
Website: https://irp.nih.gov/pi/rebecca-prevots

Research interests: I am an infectious disease epidemiologist who joined NIAID with the mission of creating an epidemiology group to enhance the capacity for population-based and clinical research. My lab has focused on the epidemiology of nontuberculous mycobacterial (NTM) pulmonary disease (PD). We seek to integrate data on environmental factors and host factors and apply multivariable and geospatial analytic techniques to further the understanding of risk factors for NTM PD. We are pursuing several avenues of research. First, we have leveraged a range of external data sources to establish the burden and trends for NTM disease in the United States (PMID: 37488500; PMID: 38448840; PMID: 32818422; PMID: 35876462). Second, by associating disease data with climate data, we have identified environmental predictors of disease. As part of this work, we have found that selected trace metals in water increase the risk of NTM PD (PMID: 37840858; PMID: 36249270). These findings have informed clinical and experimental studies that are underway, including a clinical study looking at trace metal concentrations in patients at high risk of NTM PD. Finally, we analyze data from NIH clinical cohorts at risk of NTM to elucidate determinants of disease progression (PMID: 35062891).

Future directions: We are studying the effects of climate change on the increasing incidence of NTM PD and plan to use identified climate factors and trends to forecast future disease burden. Separately, we are conducting a GWAS study using genotyped data from more than 100,000 participants in the Kaiser Permanente Research Biobank to better understand host susceptibility. ●

[COMPILED BY TAYLOR FARLEY, NIAID]

CHENGKAI DAI, PH.D., NCI

Senior Investigator, Proteomic Instability of Cancer Section, Mouse Cancer Genetics Program, Center for Cancer Research

Education: Tianjin Medical University, Tianjin, P.R. China (B.M. in clinical medicine, M.S. in pathophysiology); University of Texas, Graduate School of Biomedical Sciences, Houston (Ph.D. in genes and development)
Training: Postdoctoral fellow, Whitehead Institute for Biomedical Research, Cambridge, Massachusetts (2003–2008)
Before coming to NIH: Associate professor, The Jackson Laboratory, Bar Harbor, Maine
Came to NIH: In 2016 as an Earl Stadtman Investigator, NCI
Outside interests: Traveling; reading
Website: https://irp.nih.gov/pi/chengkai-dai

Research interests: My research focuses on elucidating how proteomic stability enables oncogenesis. We previously revealed that heat shock factor 1 (HSF1), the master regulator of the cytoprotective heat shock or proteotoxic stress response (HSR/PSR), is a powerful pro-oncogenic factor. Subsequently, we discovered that MEK oncoprotein activates HSF1 via Ser326 phosphorylation to repress tumor-suppressive amyloidogenesis (PMID: 25679764). Furthermore, we found that AKT oncoprotein also activates HSF1 via Ser230 phosphorylation (PMID: 33177089). Hyperactive PI3K/AKT signaling drives tissue overgrowth, accompanied by amyloidogenesis. Uncontrolled protein synthesis underlies this amyloidogenesis. However, HSF1 prevents amyloid-induced apoptosis by neutralizing soluble amyloid oligomers to protect the mitochondrial chaperone HSP60. Our findings suggest amyloidogenesis as a checkpoint mechanism to constrain uncontrolled growth and safeguard tissue homeostasis.

Another focus of my research is to delineate the molecular regulations of HSF1. Contrary to numerous activators, we identified that AMP-activated kinase (AMPK) inactivates HSF1 through Ser121 phosphorylation (PMID: 25425574). Accordingly, the antidiabetic drug metformin suppresses HSF1 via AMPK activation, thereby provoking proteomic instability and impeding in vivo tumor growth. We discovered that HSF1, as a substrate, suppresses AMPK reciprocally by inducing conformational switch of AMPK (PMID: 31561952). This transcription-independent action, importantly, controls lipid metabolism and promotes tumor growth. Moreover, we uncovered an unexpected role of HSF1 in protein quantity control. By sequestering JNK, HSF1 enables robust mTORC1 signaling and protein translation, thereby sustaining growth (PMID: 27043084). Our recent studies also elucidated a noncanonical transcriptional action of HSF1. Independent of its DNA binding, HSF1 can potentiate the c-MYC-mediated transcription by physically recruiting the histone acetyltransferase GCN5 (PMID: 37224019).

Future directions: Ongoing research includes the elucidation of how the HSF1-mediated HSR/PSR is initiated by proteotoxic stressors, discovery of novel proteostatic mechanisms, and identification of tumor-associated amyloids. ●

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If you have a photo or graphic that reflects some aspect of life at NIH that would be fit to print in the space to the right, why not send it to us? Email us at catalyst@nih.gov; or mail to: *The NIH Catalyst*, Building 1, Room 160.

We also welcome "Letters to the Editor" and other commentary for publication consideration, as well as your reactions to any content on the *Catalyst* pages.

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https://irp.nih.gov/catalyst/32/6

PHOTOGRAPHIC MOMENT

CREDIT: CHIA-CHI CHARLIE CHANG

On September 19, a commemorative bronze plaque was placed in the NLM herb garden to commemorate the 50th anniversary of the National Research Act, which was created in response to the unethical practices of the U.S. Public Health Service Study of Untreated Syphilis at Tuskegee in Macon County, Alabama (1932–1972). The act established federal protections for human research participants. The plaque honors the 625 Black men in the Tuskegee syphilis study. ●

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