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Big Data for Our Smallest Patients

How NCI Is Connecting Kids to Find Cures for Cancer

BY CHRISTOPHER WANJEK, *THE NIH CATALYST*

Every year, roughly 15,000 children and adolescents in the United States are diagnosed with cancer, a diagnosis no parent ever wants to hear. Although treatments have improved over the decades, many pediatric cancers remain stubbornly difficult to manage or poorly understood—and the data to study them are scattered like puzzle pieces under a couch.

That's where the Childhood Cancer Data Initiative, or CCDI, comes in. Launched by the National Cancer Institute in 2019, the CCDI—a 10-year, $500 million effort—aims to do something audacious: Learn from every child diagnosed with cancer in the United States and do so by turning fragments of laboratory, genomic, and patient-reported data into a connected, national research framework.

The goal is deceptively simple: Gather enough high-quality data to better understand rare cancers and ultimately improve treatment and survival. The execution depends on effectively engaging the entire childhood cancer community, including patients and advocates, and an efficient collaboration between NIH extramural and intramural researchers.

Much of the data comes from extramural investigators across the country who enroll patients, collect biospecimens,

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The Science of Why

How Social, Behavioral, and Structural Factors Shape Health

BY MARIE RIENZO AND KARIN HAN, OBSSR

Humans are complicated beings, and the social sciences are even more so. Read about how NIH researchers are tackling what makes us tick and putting together the puzzle pieces of our individual and collective behavioral and social tendencies.

Human behavior shapes health in powerful ways. In NIH's Intramural Research Program (IRP), investigators conducting behavioral and social sciences research dig into the "why" behind the "how" of health—how we think, feel, act, and interact, and how those patterns influence everything from disease risk to recovery.

"Behavioral, social, and structural factors drive many of the leading causes of morbidity and mortality. They point the way to prevention and better health," said **Jane Simoni**, NIH associate director for Behavioral and Social Sciences Research and OBSSR director. "IRP is advancing this work, showing why integrating behavioral and social sciences into biomedical research is essential to NIH's mission."

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FARE THEE WELL

BY NINA F. SCHOR, DDIR

Those of you who regularly read this column in the *NIH Catalyst* already realize that I am not shy and am almost never at a loss for words. I realize that some think that is a good thing and others, not so much! I do not know any way to lead other than to make what I need to say, and what I need those I lead to do, absolutely clear. As many of you know already, my last day as an NIH employee is September 30. So, at this moment when I write my last column for the *NIH Catalyst*, there is something I need to say that relates directly to something I need to urge you to do.

What I need to say is this: Thank you. I know there are those who will think I say this because you have hung in there and kept NIH doing what it does best through difficult times despite unique versions of survivor guilt, through augmented workloads born of denuded org charts, through implementation of plans for cost-cutting that came before elaboration of alternative plans for getting the work of NIH done. I guess that is part of it. But what I really want to thank you for is your support and questioning and partnership in effecting change, and for making NIH a much better place than it was just shy of 10 years ago when I began planning the federal part of my career.

You see, for me (and I know I am not alone in this), the most challenging part of recent days has been the assumption by many that those of us who work at NIH have long thought it perfect and have insisted on maintaining the status quo. It seems to me, it would not take much homework to realize just how much change for the better and for the good, and for the welfare of the people we serve, has taken place in the almost eight years I have been working here. And why would anyone want to be a leader in a place that was perfect? There would be nothing for them to do!

> "We must enhance the diagnostic and therapeutic indices of everything we do by increasing the ratio of good to harm in every discovery and invention. This is best done by engagement, not edict."

Instead, we have been relentless critics of our own recruitments, training, salary structures, interpersonal skills and approaches, and decisions around involvement of animals, humans, and cellular and computer models in research. We have rethought who is empowered to imagine and effect change and what it means to be a good leader or manager or scientist or mentor. We have remade our award and reward systems and created ladders of growth and advancement for people who had been stuck in one career place for a decade.

It is, at best, challenging and, at worst, distracting to know that some people assume that intramural NIH has resisted or been oblivious to the need for change. But you cannot be distracted, and above all, you cannot be diverted from the mission and vision of the NIH. We have been on a path that has elucidated new insights, created new treatments and cures, and mentored the next generation of physicians, scientists, nurses, and administrative leaders. You cannot stop now.

That is not to say that NIH has now reached perfection—it would be truly dangerous for you to even think that. We, both inside and outside NIH, must get better at telling the people we serve our story. We must get better at listening to the stories and answering the questions and needs of those people. We must enhance the diagnostic and therapeutic indices of everything we do by increasing the ratio of good to harm in every discovery and invention. This is best done by engagement, not edict. And that brings me back to my thanks to you. Engagement is not a solitary or self-serving exercise. Engagement requires humility, partnership, and, yes, gratitude.

I am thankful I have not been making this challenging journey alone. I am intensely proud of the legacy I leave at NIH both because of and in all of you. I will be championing NIH from the academic arena as I did for 32 years before I came here, and cheering for all of you from the extramural bleachers!

Godspeed... ●

Cooking Up Health in the NIH Clinical Center

Nicole Farmer's Research Model Focused on Cooking Is Transforming Nutrition Research Into Real-World Health Outcomes

BY JENNIFER HARKER, *THE NIH CATALYST*

When Nicole Farmer's patients told her that her nutrition advice was inspiring but tricky to carry out at home, she listened to them.

"They would say, 'This is great information, but I do not know what I am doing in the kitchen. So, unless I know it will taste good and my family will like it, I am not going to spend the time and money,'" she recounted. That feedback ignited what has become her signature research focus at the NIH Clinical Center: Integrating cooking interventions and behavioral science into a research program and community-engaged protocol called DC COOKS.

Healthy eating is full of flavor, not deprivation

Farmer began by holding small cooking classes for patients in her clinic's break room. With seed funding, those sessions grew into dynamic, interactive medical appointments in which she blended culinary training with preventative medicine. In addition to healthy eating and cooking habits, she spoke with her patients about physical activity and sleep health and their role in obesity and diabetes prevention, as well as about cardiovascular health.

Farmer also dispelled myths about healthy eating. "One of the things that we say in integrative medicine is that health is not the absence of disease; and one of the things I think about in terms of healthy eating is that healthy eating is not the absence of butter," she said.

Instead, healthy eating is the addition of flavors and colors—such as colorful vegetables—and learning good cooking and shopping methods (PMID: 40554551). Patients come in expecting bland meals, but they are surprised when the food is just as tasty—or even tastier—than their usual home-cooked meals. Farmer said her work helped her patients reset taste preferences and create lasting healthy eating habits.

In 2017, Farmer was recruited back to NIH to formally study how cooking behaviors shape health outcomes and now serves as section chief of the Translational Biobehavioral and Health Promotions Branch at the NIH Clinical Center. Farmer's introduction to NIH came through a two-year IRTA fellowship at NIDDK in the early 2000s, which set her on her path to Howard University College of Medicine (Washington, D.C.), and then practicing primary care in Gaithersburg, Maryland.

Implementation science

Scientific evidence supports the health benefits of the DASH and Mediterranean diets (PMID: 33113837) and limiting ultra-processed foods (PMID: 40443924). However, as Farmer noted, if people don't follow those diets, where is the usefulness in preventing chronic disease?

"Implementation science remains underdeveloped. That gap between knowledge and practice is where prevention succeeds or fails," she explained.

Farmer's research reframes cooking as not a barrier but as an implementation vehicle. "Through fostering social support, building self-efficacy, and engaging in the behavior of cooking, we actually see improvements in cardiometabolic health," she said (PMID: 33088581).

Clinical Center collaborations

Farmer almost immediately began to collaborate with the occupational therapy department because cooking is an activity of daily living. Sure enough, cooking groups were being held every Friday.

"I went to observe them because I wanted to get an understanding about how I could start to design group interventions," Farmer recalled.

"What I found fascinating was that the NIMH patients who were coming to the cooking groups were not only engaged in the behavior of cooking, but they also practiced recognizing and responding to social cues, socialization cues, and following intricate recipe directions.

"Their self-regulation to get through the planning phases was similar to what I noticed in my patients in clinic, so I talked to the occupational therapists, and I asked, 'Is this what you routinely see?' And they said, 'Yes, we see this in the kitchen, but it is not present in other settings.'"

"So, part of the work that I have done for the last four years with OT has been on understanding the psychological and neurological mechanisms, and behavioral activation, that occur with cooking that could explain some case studies that have been put out in the rehabilitation medicine literature," Farmer said (PMID: 29121776).

Looking forward

Farmer's research positions cooking not just as a domestic chore but as a bridge between biomedical evidence and daily life.

"NIH has invested millions into nutrition research," she said. "Exploring cooking as a behavior that can drive implementation of higher quality diets is about making sure that investment pays off. The Clinical Center is unique in its ability to integrate research with patient-centered interventions (PMID: 40423611). Understanding the role of cooking on health is about translating science into real-world practice so people can learn the tools, skills, and confidence to bring the science to their own tables." ●

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By uncovering the drivers of healthy habits like good sleep hygiene or of high-risk behaviors like inactivity, poor diet, and tobacco use, IRP scientists are developing smarter, more culturally responsive interventions. The goal is to reduce preventable disease, close health gaps, and turn data into real-world solutions that work for all communities.

At its heart, BSSR at NIH is about connecting discovery to everyday life—transforming science into strategies that help people live longer, healthier lives.

Science in the community

For **Tiffany Powell-Wiley**, senior investigator at NHLBI, tackling cardiovascular disease means looking beyond the clinic and into the neighborhoods where people live. Her lab studies how social determinants—such as access to healthy food, safe spaces for exercise, and exposure to chronic stress—interact with biology to shape obesity risk and heart health.

Tiffany Powell-Wiley

"Obesity is often the first stage toward developing not only heart disease, but also diabetes and even kidney and cerebrovascular diseases," she explains. "Those at highest risk often have the [fewest] resources and the highest environmental stressors."

To unravel these complex connections, Powell-Wiley's team integrates data at multiple scales—from Global Positioning System mapping of where participants spend their time, to wearable devices tracking physical activity, to detailed immune cell measurements. Large epidemiologic datasets reveal patterns, whereas community-based studies test interventions that might work in real-world, under-resourced settings.

At the center of this work is the Hope Center in Northeast Washington, D.C., a research site embedded within a senior housing development. Born from years of relationship-building in local churches, libraries, and community spaces, the Hope Center allows residents to participate in studies, receive health screenings, and connect with educational programs without traveling to the NIH Clinical Center.

Powell-Wiley says this embedded approach is about more than convenience; it's about trust. "It's fragile. You can't take it for granted," she says. "It takes time, presence, and partnerships with trusted community leaders."

The payoff? Interventions that aren't just theoretically sound, but culturally relevant and sustainable. Whether testing digital tools to boost physical activity or measuring how perceptions of safety affect health behaviors, her lab aims for results that improve lives and empower communities.

"I don't see this work as something that's just for my lab," she says. "I hope we're a resource—a bridge between NIH and the communities we serve."

Cracking the brain's code

From making a morning cup of coffee to navigating a complex social interaction, our brains rely on a set of high-level cognitive processes known as executive functions. These "cognitive building blocks" allow us to focus our attention, resist impulsive urges, juggle information in working memory, and make decisions in the face of risks. But when these systems falter—as they often do in disorders such as schizophrenia, obsessive-compulsive disorder, depression, and post-traumatic stress disorder—daily life can become a maze without a map.

Executive dysfunction can make "folks unable to get on with their daily lives and activities," says **Yogita Chudasama**, chief of the Section on Behavioral Neuroscience at NIMH and director of the Rodent Behavioral Core (RBC). "Even when treatments reduce symptoms, they often have little to no impact on executive functioning. These enduring cognitive deficits really impact people's recovery and rehabilitation."

Chudasama's lab focuses on the brain networks that make executive function possible, particularly the prefrontal cortex and its partnerships with other cortical and subcortical regions. Her approach bridges human neuropsychology with animal research, using tasks that allow for cross-species comparisons—from humans to rats to monkeys. "Each animal has its own unique advantages," she explains. For example, rats excel at spatial and odor-based tasks, whereas monkeys are better suited for visual and social-based tasks.

Recently, her team has expanded into studying how executive function intersects with socioemotional regulation—how we process feelings, interpret social cues, and build relationships. The link, she says, is stronger than it might appear. "The circuits involved in high-level cognitions are pretty much exactly the same circuits involved in socioemotional regulation."

To explore these connections, her group observes marmosets, small monkeys that are well-suited for developmental studies. With their rich social lives, cooperative caregiving, and audible vocalizations, marmosets offer a unique window into how early-life experiences shape brain circuits—and, in turn, future cognition and emotional health.

In addition to leading her own research, Chudasama directs the NIMH RBC, a state-of-the-art facility supporting researchers at IRP. The RBC offers tools for assessing rodent behavior across cognitive, emotional, sensory, and motor domains—whether for mental health studies or conditions as far-ranging as cancer, diabetes, and infectious disease.

Two emerging trends are shaping the RBC's future: Recording brain activity during natural social interactions and measuring behavior over long time periods in home-cage environments. Both promise more realistic, reproducible insights into how brains work in the real world.

Looking ahead, Chudasama's priority is to understand how brain development—from before birth through adulthood—sets the stage for lifelong cognitive and emotional health. "By the time a child expresses severe distress, it may already be too late to intervene effectively," she said. "We need to understand the earliest changes in brain development to make a real difference."

Her message to colleagues across NIH is clear: Behavior is essential to understanding disease models, a window into the brain's core functions. "It's the readout of everything the nervous system and body are doing," she says. "Behavior can help us understand treatment responses, patient well-being, and how emotions, cognition, and stress influence disease progression. It may also help improve therapeutic outcomes."

In pursuit of better sleep

Chandra Jackson, a senior investigator at NIEHS, leads groundbreaking research on the environmental and social determinants of sleep health. Her work identifies how factors like light exposure, temperature, and psychosocial stress affect sleep and, in turn, influence cardiometabolic health.

"I am interested in understanding the epidemiology of sleep health—the distribution across the population, determinants, consequences, and approaches to maintain or improve sleep according to our latest recommendations," said Jackson. "Identifying exposure burdens, for instance, provides information needed to develop effective interventions."

Chandra Jackson

A core interest of Jackson's research is the exposome, an initiative strongly supported by NIEHS that examines how environmental exposures affect health over a lifetime. She believes sleep health is an ideal model for exposomic research.

"Sleep is directly affected by many modifiable and non-modifiable exposures in our environment over the life course," she explained. "These exposures also span the entire research spectrum from genetics to job strain to light pollution, and it will be interesting as well as important to investigate which modifiable exposures contribute the most to sleep problems using a more comprehensive approach. This [potential research] could inform personalized prevention and treatment strategies as well as broader environmental changes."

By looking at sleep through an exposomic lens, Jackson aims to identify specific factors that can be modified to improve sleep. Her research seeks to integrate environmental, social, and biological factors, offering a comprehensive approach to studying this important process.

Jackson uses several large-scale epidemiological cohort studies with funding support by NIH, publicly available datasets used to monitor the health of the nation such as the National Health Interview Survey, and a network of community health data centers she has linked to environmental data. These large datasets allow her to look at the broad population in many cases, as well as differential burdens in exposures and health outcomes.

In sleep research, Jackson mentioned that the field is pushing for more accessible diagnostics, such as wearable devices or biological samples such as blood and saliva.

"Identifying objective, reliable, and accessible biomarkers for sleep and sleep-related conditions is a significant research focus with the potential to transform diagnosis, treatment, and monitoring," she said, adding, "While the gold standard remains polysomnography, there's a strong push for more convenient, less costly methods."

Jackson also was senior author on a global call to action. This call, published in *Lancet Public Health*, recommends that organizations with public health priorities include sleep health. The authors note that decades of research across disciplines provide strong evidence that sleep is foundational for human health, just like physical activity and nutrition, and now is the time to begin leveraging sleep health to improve human health and wellbeing worldwide.

For Jackson, sleep is more than just going to bed at night. As she describes it, "Sleep has relevance to nearly all research questions, across disciplines, because it is a biological, psychological, and sociological necessity that intersects with nearly every domain of human function and behavior."

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Intramural Research Briefs

Read About Scientific Advances and Discoveries by NIH Intramural Scientists

NIMH: REWIRING OUR THOUGHTS ON BRAIN PLASTICITY

Visit our online version to watch this video of a participant moving phantom fingers and intact fingers during an observed task.

For more than half a century, neuroscience textbooks have taught a dominant theory of brain plasticity: That when a body part is lost, the brain's map of that part is erased and commandeered by neighboring areas—sort of a conservation of precious brain real estate. This idea, based on decades of cross-sectional studies, has shaped our understanding of how the brain adapts to injury.

Now, an international study published in *Nature Neuroscience*, conducted in part at the NIH, challenges this dogma, revealing a fundamentally different and more resilient picture of the brain's somatosensory system. The research provides compelling evidence that the brain's map of an amputated limb remains remarkably stable, even years after the limb's physical absence.

Instead of a traditional cross-sectional approach comparing a group of amputees with non-amputees, this study followed three adult participants who were scheduled to undergo planned arm amputations. The researchers — based mostly in the United Kingdom and at the NIH—conducted multiple functional MRI brain scans on each participant at different points: Twice before their amputation and then at 3 months, 6 months, and either 1.5 or 5 years post-amputation.

During these scans, participants were asked to perform movements of their fingers, lips, and toes. After the surgery, the participants continued to perform these same movements using their vivid phantom limbs. This unique before-and-after methodology allowed the scientists to directly track and compare the changes in the brain's cortical map over time within the same individuals.

Based on the findings, the research has provided conclusive evidence that the brain's "fingerprint" of the missing limb is not erased but is, in fact, decently preserved. Movements of the phantom hand produced selective and stable activation in the brain's primary sensorimotor regions, with neural patterns for individual phantom fingers remaining highly consistent with their preamputation state. There were no signs of remapping, either, such as by the lips and toes.

These findings have profound implications for future neurotechnologies and therapies. A stable neural representation of a missing limb provides a reliable and persistent blueprint for controlling advanced neuroprosthetics. The study also necessitates a reevaluation of the prevailing model for phantom limb pain, suggesting new therapeutic avenues that do not rely on the premise of cortical reorganization.

This research was co-led by Hunter Schone, who at the outset was a graduate student at University College London (UCL). Through the NIH Graduate Partnership Program (GPP), Schone tapped into the expertise of the NIMH Laboratory of Brain and Cognition, Section on Learning and Plasticity, led by **Christopher Baker**, a senior investigator.

The GPP enabled Schone to work on his doctoral studies on both sides of the Atlantic, combining the amputation expertise at UCL with the neuroimaging expertise at NIH to produce a unique longitudinal study of amputation. Schone is now a postdoctoral associate at the University of Pittsburgh. (NIH authors: H.R. Schone, and C.I. Baker, PMID: 40841477)

NICHD: VAGINAL BLEEDING IN FIRST TRIMESTER MAY AFFECT FETAL LIVER, BRAIN GROWTH

The Fetal 3D Study, a multisite clinical study led by NICHD, performed 2,634 3D ultrasound examinations from 2015 to 2019. NICHD researchers and their collaborators investigated whether first-trimester vaginal bleeding affected fetal growth patterns and organ development. Of about 19% of the singleton pregnancies monitored, the women who self-reported bleeding during the first trimester received up to five 3D ultrasound scans between 15 to 40 weeks of gestation. The examinations assessed fetal body composition (arm, abdomen, thigh, adiposity) and organ volumes (cerebellum, lung, kidney, liver). Linear mixed models incorporating gestational age trajectories were adjusted for maternal age, race, ethnicity, pre-pregnancy body mass index, parity, and infant sex.

Compared to women without bleeding, fetuses of women who had one day or more of first trimester vaginal bleeding exhibited smaller abdominal areas (75.1–264.0 mm^2 reduction) between 30 and 40 weeks, smaller fractional thigh volume (1.1–4.0 cm^3) and fat volume (0.4–2.4 cm^3) from 30 to 40 weeks, but larger cerebellar volumes (0.8–1.6 cm^3) after 35 weeks. Fetuses of women reporting only 1 day of vaginal bleeding showed reduced liver volume (2.6–4.8 cm^3) between 26 and 35 weeks.

These findings suggest that even transient first trimester bleeding may coincide with fetal organ and adipose tissue development implications. Serial 3D ultrasound offers a valuable tool for identifying subtle alterations in fetal growth trajectories that may be linked to early gestational complications. (NIH authors: A. Jean-Louis, J.L. Gleason, Z. Chen, K. Wagner, D. He, J. Grewal, and K.L. Grantz, PMID: 40812363)

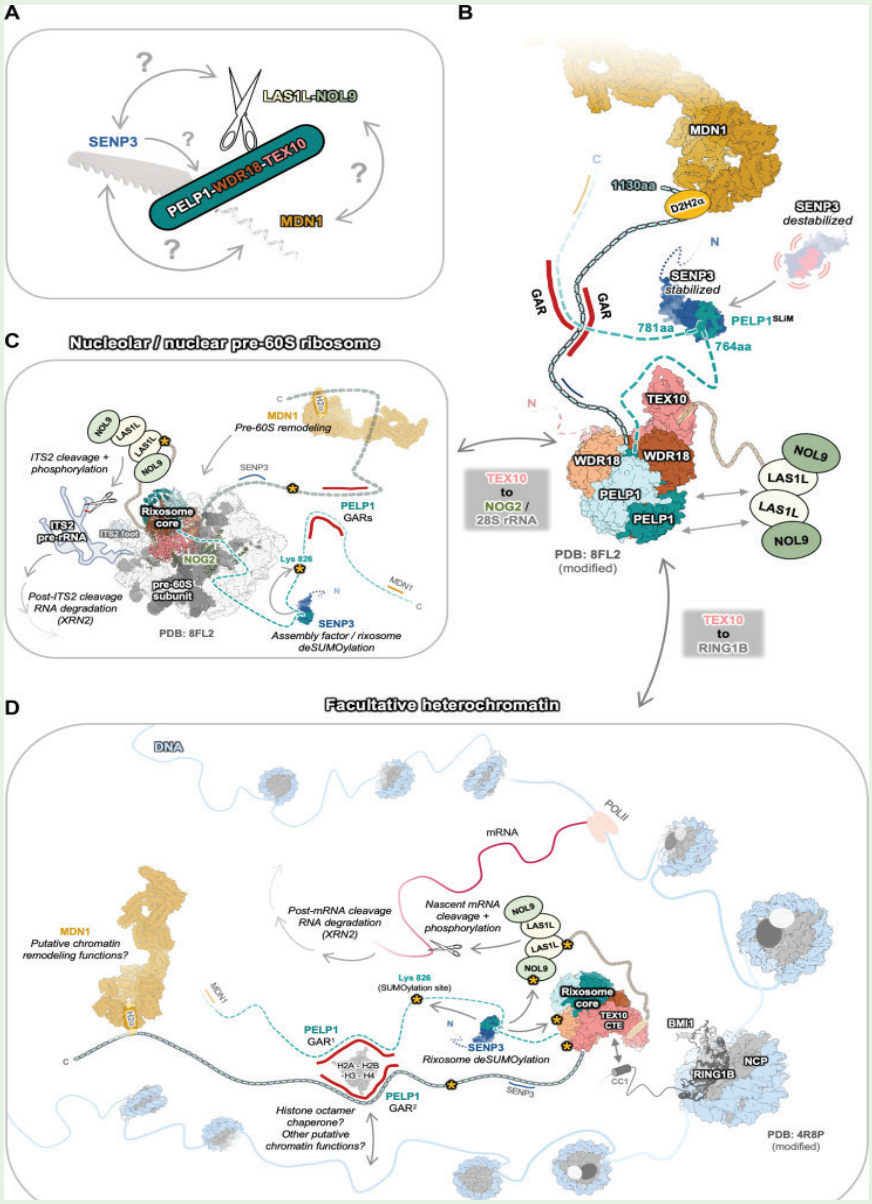
NIEHS: RIXOSOME REVEALED TO CONTAIN A STABLE CORE, FLEXIBLE ENZYMATIC MODULES

NIEHS researchers and their collaborators have mapped the architecture of the rixosome—a large "Swiss army knife-like" protein complex packed with molecular tools that regulate cellular functions.

The rixosome participates in RNA decay during processes such as assembly of the ribosome, a cellular structure that serves as the site of protein synthesis. It also plays an important role in maintaining heterochromatin, a tightly packed form of DNA characterized by its condensed structure. Yet the overall architecture of the rixosome has been hard to visualize because parts of it—called intrinsically disordered regions (IDRs)—lack a fixed 3D structure. Using structural and biochemical techniques, the researchers showed that a protein called PELP1 serves as the central scaffold of the rixosome. Enzymatic subunits assemble on a specific part of PELP1, an IDR that is rich in two types of amino acids called proline and glutamic acid. This flexible section helps PELP1 connect with another protein called SENP3. This protein is a SUMO-specific protease, which means it removes small proteins called SUMOs (small ubiquitin-like modifiers) that act like tags to control how a protein behaves, thereby regulating several key protein functions and gene activity.

Although SENP3 is associated with human diseases such as cancer, heart disease, and neurological disorders, it has not been clear how its protease activity is controlled. According to the authors, this research uncovers an activation mechanism for the SENP3 protease that could lay the groundwork for structural-based design of SENP3-specific protease inhibitors and regulators to treat cancer. (NIH authors: J. Gordon, A.M. Kaminski, S.R. Bommu, R.M. Petrovich, L.C. Pedersen, and R.E. Stanley, PMID: 40712028)

BY JANELLE WEAVER, ORIGINALLY PUBLISHED IN THE NIEHS *ENVIRONMENTAL FACTOR* NEWSLETTER



CREDIT: *SCIENCE ADVANCES*

Swiss army knife model of the rixosome

NIDA: SOCIAL MEDIA ADDICTION

Addiction experts published a recent call to action in the *Journal of Addiction Medicine* calling on experts to engage in rigorous longitudinal and clinical research to develop evidence-based prevention and treatment strategies to mitigate the adverse outcomes of compulsive social media use.

The authors note that problematic social media use exhibits behavioral parallels with substance use disorders, raising concerns about its potential classification within an addictive framework. Neuroimaging studies provide preliminary evidence of structural and functional brain alterations among heavy users that overlap with patterns observed in drug addiction, suggesting shared neurobiological pathways. Emerging data also indicate that excessive or maladaptive reliance on social media is associated with heightened symptoms of depression and anxiety.

Given the widespread prevalence of social media, the public health implications are considerable. Problematic use could exacerbate mental health burdens in vulnerable populations, underscoring the urgency of identifying risk factors and mechanisms underlying this behavior. More research is needed to clarify causality, delineate at-risk populations, and evaluate effective interventions. (NIH authors: R.D. Baler and N.D. Volkow, PMID: 40511818)

Note: The *Journal of Addiction Medicine* has a call for papers on studies funded through the NIH Helping to End Addiction Long-term (HEAL) initiative.

and submit clinical and genomic data to centralized platforms. These investigators include large cooperative groups, pediatric hospitals, and national registries. NCI supports these efforts through contracts, grants, and technical infrastructure.

NIH's intramural research program (IRP), mainly through the NCI Pediatric Oncology Branch, contributes its own clinical trial data. The IRP also helps define the rare cancers included in the CCDI and tests early-stage therapies that may later move into cooperative group trials, some open at the NIH Clinical Center. The broader IRP also helps design the data models and pipelines that ensure information coming into CCDI is usable, searchable, and shareable.

Together, researchers are not merely gathering the missing puzzle pieces of pediatric cancer data but finally fitting them into an accessible and cohesive picture.

The CCDI's progress and current challenges will be on display at its annual symposium, with the theme "Collaborate. Innovate. Transform," October 6–7, at the Natcher Conference Center (Building 45) on the NIH Bethesda campus. This year, CCDI will recognize six years of progress with expert speakers, networking opportunities, and science poster sessions. View the agenda or register to attend at https://events.cancer.gov/nci/ccdisymposium.

What follows below provides a snapshot of the symposium's program with a focus on IRP's role.

A White House call to action

The CCDI was born from a national call to action, publicly announced during the 2019 State of the Union address, when the White House committed to a new federal investment in childhood cancer research. This announcement was the culmination of efforts to address a critical need—the lack of a centralized, accessible system for sharing childhood cancer data (PMID: 37267580).

"Collaborate. Innovate. Transform" is the theme of this year's CCDI annual symposium, slated for October 6–7. The symposium will be held at the Natcher Conference Center (Building 45) on the NIH Bethesda campus. View the agenda or register to attend at https://events.cancer.gov/nci/ccdisymposium.

Then-NCI director Ned Sharpless took the lead in conceiving and developing the initiative. Sharpless recognized that although significant progress had been made in treating many childhood cancers, advancements for others were limited due to data being siloed in individual hospitals and institutions. He believed that by harnessing the power of data from every child, adolescent, and young adult with cancer, researchers could accelerate discoveries and improve outcomes.

With the promise of an annual budget of $50 million for 10 years, the CCDI set off to create a community-centered data ecosystem. This ecosystem would not only collect and harmonize diverse data—from clinical care and research to genomic sequencing—but also provide a platform and the tools to make it accessible to the broader community of researchers, clinicians, and advocates.

The initiative, however straightforward, represents a novel approach to data sharing, according to **Brigitte Widemann**, chief of the NCI Pediatric Oncology Branch and special advisor to the NCI director for Childhood Cancer. Widemann helps to coordinate the intramural component of the CCDI. She said that Sharpless, who left in 2022, believed that if the plan could work at all, it would be in the realm of pediatric cancer, because pediatric oncologists tend to be highly collaborative, and because among cancer patients, a higher proportion of children and young adults are enrolled in cancer clinical trials than older adults. "If you can do this for pediatric cancer, this could be a model for adults," Widemann said.

Enter the conductor

Just before Sharpless left the NIH, he and **James Doroshow**, an NCI senior investigator, recruited **Gregory Reaman** as the CCDI scientific director. Reaman trained as a fellow at NCI in the 1970s. In his own career before NIH, he directed the Center for Cancer and Blood Disorders at Children's National Medical Center; served on the faculty at George Washington University; and worked at the FDA as associate director for Oncology Sciences and later as associate director for Pediatric Oncology in the Oncology Center of Excellence. He also was the founding chair of the Children's Oncology Group (COG), which is the world's largest clinical trials network dedicated to childhood cancer.

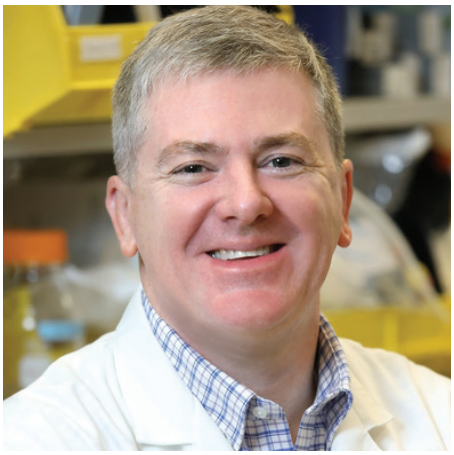
Reaman is now responsible for developing, directing, and coordinating the CCDI programs. Described as the CCDI symphony conductor because of his vast familiarity with all the players, his expertise and scientific oversight have been crucial to driving the CCDI's vision and ensuring that its progress remains aligned with the needs of the childhood cancer community.

He also has been instrumental in the

initiative's core mission of aggregating, harmonizing, and broadly sharing data that would have otherwise remained siloed—which, he said, is still picking up momentum. "There are still plenty of opportunities for people to use data and to contribute data," Reaman said. He noted the need for adding more genomic data, for example, and developing large language models to mine data, particularly unstructured data from medical records, assignments well suited for the IRP.

Molecular characterization initiative

One element of the intramural–extramural CCDI effort is the Molecular Characterization Initiative (MCI), which provides advanced molecular testing to children, adolescents, and young adults newly diagnosed with cancer. One of the co-leaders is **Jack Shern**, a physician-scientist in the Pediatric Oncology Branch, and the project represents a collaboration among the NCI, the COG, and many community partners.



Jack Shern

The goal is to collect and analyze diagnostic tumor samples and germline material to obtain a comprehensive genomic profile of every child's tumor to refine diagnoses, guide treatment, and inform future research. Officially launched in March 2022, the initiative began by offering molecular characterization to patients with newly diagnosed central nervous system tumors. It has since expanded to include soft tissue sarcomas, neuroblastomas, and other rare cancers.

To highlight the initiative's impact on this specific cancer, Widemann said that, since opening, the CCDI has enrolled nearly half of the people who are diagnosed with pediatric soft tissue sarcomas each year in the United States and sequenced their tissue samples.

According to Shern, who studies the genetic and molecular drivers of rhabdomyosarcoma, this effort has, for the first time, allowed researchers to build cohorts of people with these rare tumors that can be studied. "There are groups of patients who due to the rarity of their tumors, we really do not know the best way to treat," he said. "This effort will change that."

One of the initiative's major achievements has been its quick turnaround time. The program aims to return molecular testing results to a patient's physician within 21 days of receiving samples, allowing for timely, informed treatment decisions. Moreover, by performing assays such as whole-exome sequencing, RNA fusion analysis, and DNA methylation profiling, the MCI provides a detailed genetic and molecular blueprint of each patient's tumor, resulting in a more precise classification of tumors and a deeper understanding of the genetic changes that drive these pediatric cancers.

For example, in brain tumors, the MCI has helped to identify over 75 unique tumor categories, allowing for more targeted therapies, according to COG.

The real paradigm shift has been the enhanced data sharing. Data collected through the MCI is de-identified and made available to the broader research community through the CCDI ecosystem in near-real time. This sharing creates an invaluable resource for scientists worldwide to study pediatric cancers and accelerate the development of new treatments.

A critical component of this work has been the close collaboration between NCI and COG (PMID: 40794906). This coordination ensures that high-quality samples are delivered efficiently, vital for the rapid turnaround time the MCI promises, and allows the initiative to receive data from a network of more than 200 institutions.

Key to this collaboration has been Erin Rudzinski, a professor of clinical pathology and laboratory medicine at Indiana University School of Medicine (Indianapolis), lead pathologist for COG's participation in the MCI. Rudzinski oversees the accuracy of pathologic diagnoses of patients enrolled and specimens submitted, which is essential for ongoing analyses of possible associations between gene variants and specific pediatric cancers and their potential relevance to treatment outcomes and the discovery of new actionable targets for drug development.

Patient partners

Widemann, as both a member of the CCDI Steering Committee and co-lead of the CCDI Engagement Committee, has been at the center of the initiative's strategic planning and community outreach. Her background as a pediatric oncologist and her success in developing the first FDA-approved medical therapy for neurofibromatosis type 1-related tumors has informed the CCDI's mission to address the most difficult-to-treat cancers.

Central to the mission, Widemann said, is the CCDI's commitment to integrating the perspectives of patients and patient advocates, which aligns the initiative to the real-world experiences and priorities of the people they aim to help. The CCDI actively seeks input from patients and their families about how rare tumors affect their lives. The CCDI inquires about daily challenges, quality-of-life issues, treatment burdens,

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and other types of information that is not systematically collected.

By participating in workshops and committees, advocates and patients help guide researchers to the questions that are most important to answer and the outcomes that matter most to those living with cancer, Widemann said. For example, patient groups play a fundamental role in communicating the purpose and progress of initiatives, such as MCI, to the wider patient community, encouraging participation in studies and clinical trials.

Such direct involvement helps to ensure that research is not only scientifically sound but also patient-centered, addressing the needs and concerns of the childhood cancer community at every stage of the process, from designing studies to disseminating results.

A registry for the rarest of the rare

The CCDI is attuned to all child and adolescent cancers. "Rare" cancers, by NCI's definition, are those that affect fewer than 15 in 100,000 young individuals. Reaman said that the MCI has enrolled more than 6,000 patients between ages 0 and 25.

However, with community help, the CCDI is about to launch an even rarer "rare cancer registry" for pediatric, adolescent, and young adult populations, defined as between the ages of 0 and 39 years. "Rare" here refers to cancer types thought to be diagnosed in fewer than 2 per 1 million people per year.

Mary Frances Wedekind Malone, an assistant research physician in the Pediatric Oncology Branch, will serve as the principal investigator for this registry. The goal is to gather more clinical data on these very rare cancers, which include chordoma and malignant peripheral nerve sheath tumor, both studied at the NIH Clinical Center.

Wedekind Malone said that the CCDI is building an infrastructure to process clinical data from the medical records, extract important information from those records, add genomic data and molecular profiling attained through sample collection, and place this information in the CCDI database for all researchers to access.

Data collection can be challenging for many reasons, particularly for this population given this time in human life spans many transitions, Wedekind Malone said.

"Teens and those in their 20s are extremely hard to, first off, get a hold of and, second off, have them enroll in clinical studies…especially for clinical trials where they may not feel they are getting a huge benefit." Also hard to reach are individuals in rural areas seen by community physicians and hospitals. In both cases, "we rely heavily on our advocacy organizations," she said.

Scaling for transformation

As the CCDI passes the halfway mark of its 10-year journey, its leaders emphasize that the work ahead may prove even more transformational. The infrastructure is now largely in place, from molecular characterization pipelines to shareable databases, registry frameworks, and patient-engagement platforms.

The next five years are about scaling, Reaman said—enrolling more patients, bringing in harder-to-reach populations, layering in new data types, and ensuring that researchers across the country—and around the world—can give to and take from the CCDI. "It's a resource," said Reaman.

"[The CCDI] has begun to transform how we approach pediatric cancers, I think," Widemann added. "It will be important if we can work toward excellent documentation of the value of CCDI, for example, of the MCI so that health insurances will cover this analysis [after CCDI funding ends]. I also hope we will have created well-characterized cohorts of patients that can serve as control [subjects] for interventional clinical trials."

Gregory Reaman

These ideas and hopes will be on display at the October 6–7 symposium. Beyond highlighting scientific milestones, the CCDI team plans to challenge its stakeholders to press forward on key fronts, including ensuring molecular diagnostics in childhood cancer as part of standard of care; leveraging big data and real-world evidence in childhood cancer research; and engaging industry, regulators, and advocates to drive transformation.

Perhaps most crucially, they aim to foster a shared sense of urgency among investigators, clinicians, and advocates, so that the data ecosystem truly accelerates progress, rather than simply documenting it.

If successful, CCDI may not just change the trajectory of pediatric oncology; it could also fundamentally redefine how we use data to tackle all rare diseases and all cancers. ●

Read our online article at https://irp.nih.gov/catalyst to learn more about the Childhood Cancer Data Initiative and the people behind the effort.

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A team science approach

Diane Putnick is a statistician at NICHD who is helping to shape a more holistic understanding of pregnancy, parenting, and child development by integrating the psychological, social, and biological factors that could improve outcomes for families. She also explores the factors that influence children's mental health and development, from parental behavior and mental health to environmental and social factors.

"I am broadly interested in what makes kids happy and healthy," Putnick said. This broad curiosity has led her to examine a variety of topics, including how neighborhoods, screen time, and parental mental health shape child development.

Putnick describes herself as an "oddball" within the NICHD intramural research program's epidemiology branch, where she is the only psychologist working alongside a team of epidemiologists and other researchers. "Working with experts from different fields really strengthens our research," she said. "For example, in the Study of Pregnancy and Neonatal Health (SPAN), we have a geneticist focused on fetal growth, a physician studying pregnancy health, an epidemiologist focused on paternal contributions to child health, and me, looking at psychological aspects. We are focused on [complementary] but different aspects of pregnancy and wellbeing."

In SPAN, this diverse mix of investigators design studies and decide on data collection methods while ensuring all perspectives are considered. "It really helps when you have people with different expertise explaining why something is important to measure from their perspective," Putnick added.

A complementary study to SPAN that Putnick is involved in is the Upstate KIDS Study. The Upstate KIDS Study is a birth cohort study following over 6,000 children for the first decade of life. This study provides valuable developmental data such as measures of relationship quality, of attachment to the pregnancy, and of in-depth feelings about the experience for both parents, though the study lacks comprehensive biological samples like those being collected in SPAN.

SPAN is focused on a comprehensive view of pregnancy and neonatal health, collecting biological samples such as placental tissue and blood as well as deeper behavioral data from participating families.

Putnick's research is centered on mental health, particularly the role of depression in parents. SPAN will allow a deeper understanding of how paternal mental health affects pregnancy and child well-being.

"People often overlook how men are affected by pregnancy," she said. "They also experience significant life changes, and studying paternal mental health can provide a fuller picture of family dynamics during pregnancy."

Putnick aims for her findings to influence real-world practices. "Progress isn't just about collecting data; it's about making sure our research has a practical application," she said. "The intramural research program spends a lot of time on biology, which is incredibly important. But I feel like we, as the intramural research community, could spend more time on how people think and feel. Psychological factors are tied to biology and disease response and all the things we study here."

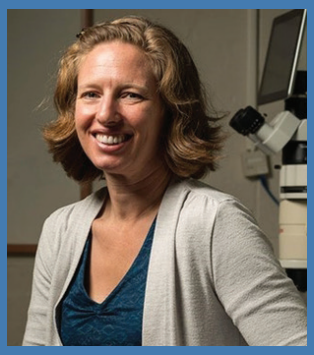
A new coordinating committee

OBSSR is establishing a coordinating committee to identify and advance high-priority, cross-cutting behavioral and social science topics, training opportunities, and common infrastructure needs within and across all ICs to maximize the impact of IRP research. All IRP investigators and trainees interested in behavioral and social sciences are welcome to be part of this new, NIH-wide community. Join the Teams Channel OD-NIH IRP-BSSR-CC (use code cbhy3p1). Send your input, questions, and comments to farheen.akbar@nih.gov. ●

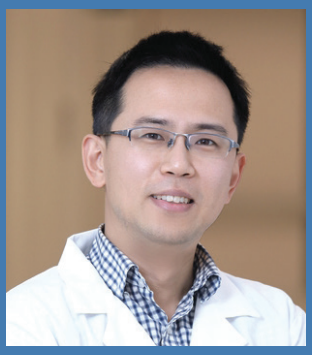
Colleagues: Recently Tenured

Meet your recently tenured colleagues: **Behdad Afzali** (NIDDK), **Farran Briggs** (NEI), **Peng Jiang** (NCI-CCR), and **Melissa Wilson** (NHGRI)

Behdad Afzali, M.D., Ph.D.
NIDDK



Farran Briggs, Ph.D.
NEI



Peng Jiang, Ph.D.
NCI-CCR

Melissa Wilson, Ph.D.
NHGRI

BEHDAD (BEN) AFZALI, M.D., PH.D.

Senior Investigator Immunoregulation Section, Kidney Diseases Branch (NIDDK)

Education: University of London, London (B.S. in immunology), (M.D.); King's College, London, England (Ph.D. in immunology); Royal College of Physicians (UK) (F.R.C.P.)

Training: Postgraduate Diploma in Medical Education (PGDip), Institute of Education, London; Residency Oxford Medical Rotation, Oxford (2001–2003); Nephrology Fellowship, South Thames, London (2004–2012)

Before coming to NIH: Wellcome Trust Intermediate Clinical Research fellow, King's College London, London and John O'Shea's lab at NIAMS (2012–2017)

Came to NIH: In 2018 as a Stadtman tenure track investigator and consultant nephrologist, NIDDK

Outside interests: Reading; photography; cycling

Website: https://irp.nih.gov/pi/behdad-ben-afzali

Research interests: Our research seeks to understand the molecular mechanisms that drive tissue inflammation, a process that underlies a substantial proportion of deaths worldwide from chronic diseases. Despite its enormous impact, tissue inflammation remains poorly understood, and current treatments rely on drugs that are nonspecific and toxic. Our mission is to uncover how microenvironmental cues initiate and sustain tissue inflammation, how networks of transcription factors within immune cells integrate these signals to determine their fate and function, and how tissue inflammation is either resolved, restoring healthy tissue, or progresses to maladaptive scarring. A particular emphasis is placed on understanding how these transcriptional networks operate not only in immune cells but also in tissue-resident cells.

Examples of our work include the identification of transcription factor networks that drive pathogenic versus regulatory states in both immune and non-immune cells during tissue inflammation, including those leading to local production of complement components and receptor signaling (PMID: 30397350; PMID: 32187519; PMID: 33827897; PMID: 34764490).

Future research: The long-term aim is to identify actionable immunoregulatory nodes for therapeutic exploitation to shift the balance between destructive inflammation and protective regulation, or between tissue scarring and healing. Ultimately, our work seeks to move toward more precise therapies that resolve inflammation more effectively, with fewer side effects, and that improve the quality of life for patients living with chronic inflammatory diseases.

COMPILED BY JOHN CARLO COMBISTA, NIMH

FARRAN BRIGGS, PH.D.

Senior Investigator, Thalamocortical Visual Processing Section (NEI)

Education: Dartmouth College, Hanover, New Hampshire (B.S. in biology); University of California at San Diego, California (Ph.D. in biology)

Training: Postdoctoral fellow, University of California at Davis, California, (2003-2010)

Before coming to NIH: Associate professor of Neuroscience, Brain & Cognitive Sciences, University of Rochester, New York; Assistant professor of Physiology & Neurobiology, Geisel School of Medicine, Dartmouth College, Hanover, New Hampshire (2011–2017)

Came to NIH: In 2024 as senior investigator, NEI

Outside interests: I am an outdoorsy person who loves to run and cycle. I just returned from a pretty epic trip around the French Alps, riding the same mountains as the Tour de France, and managed to watch some of the Tour de France—a once in a lifetime experience.

Website: https://irp.nih.gov/pi/farran-briggs

Research interests: I am probably best known for my contributions to our understanding of what feedback from the cortex to thalamus does functionally in the sensory system, specifically in vision. Much progress has been made in restoring retinal tissue and improving visual functions via retinal prosthetics. However, retinal disease does not just affect the eye, it also causes

significant functional remodeling in the brain. My lab's recent paper demonstrates that loss of retinal cells reduces functionality of neurons in the brain center to which they project that are specialized for acuity, while neurons specialized for motion perception in the same center are relatively spared (PMID: 40300832). These results suggest that vision restoration after retinal damage should include therapies that target neuronal pathways specialized for acuity. Our work has been highlighted in NEI Research News. An offshoot of this paper is that some of the downstream effects we see after retinal damage have similar electrophysiological profiles as in patients with schizophrenia. And so, I'm really excited about our work having broad translational implications.

Future research: One of the reasons that I decided to come to NEI is because of the dream experiments, that in academia, wouldn't be feasible. NEI is the kind of place where I can start working on my various interests. I would really like to be able to causally manipulate feedback circuits between cortex and thalamus among different cortical areas using sophisticated molecular (viral) tools.

COMPILED BY ANNELIESE NORRIS, NCI-CCR

PENG JIANG, PH.D.

Senior Investigator, Cancer Data Science Laboratory (NCI-CCR)

Education: Tsinghua University, Beijing, China (B.E. in computer science); Princeton University, Princeton, New Jersey (Ph.D.)

Training: Postdoctoral fellow, Dana Farber Cancer Institute, Harvard University (2013–2019, Xiaole Shirley Liu Laboratory)

Came to NIH: In 2019 as a Stadtman tenure track investigator, NCI

Website: https://irp.nih.gov/pi/peng-jiang

Research interests: My research focuses on developing data-integration and artificial intelligence frameworks (PMID: 36064595) to study intercellular signaling mediated by secreted and extracellular proteins in antitumor immunity. Data-driven analyses estimate that about 2,000 human genes encode secreted proteins. Yet, our literature mining revealed that 61% of these genes lack known roles in cancer. To address this gap, we develop computational methods and apply diverse immunological models to dissect cytokine networks (PMID: 34594031; PMID: 35501486); secreted proteins (PMID: 40730154); and ligand–receptor interactions (PMID: 36732531) in cancer. Ultimately, our goal is to uncover new mechanisms of immune regulation and identify therapeutic opportunities that harness intercellular communication against tumors.

Future research: In the next stage, we aim to identify new secreted proteins regulating antitumor immune response by combining data integration, spatial transcriptomics, and artificial intelligence frameworks. Also, we want to establish long-term collaborations with clinical investigators for translational works.

COMPILED BY JOHN CARLO COMBISTA, NIMH

MELISSA WILSON, PH.D.

Senior Investigator, Center for Genomics and Data Science Research, NHGRI

Education: Creighton University, Omaha, Nebraska, (B.S. in Mathematics); Pennsylvania State University, University Park, Pennsylvania (Ph.D. in bioinformatics and genomics)

Training: Miller Postdoctoral Fellowship, Berkeley University, Berkeley, California (statistics and integrative biology) (2011–2014)

Before coming to NIH: Tenured professor, School of Life Sciences at Arizona State University, Tempe, Arizona (2014–2024)

Came to NIH: December 2024 as a senior investigator, NHGRI

Outside interests: Parenting; science communication; exploring nature; cooking

Research interests: I am a geneticist and computational biologist broadly interested in sex differences in health and disease. Specifically, my lab collaborates with clinicians, physiologists, and computer scientists to understand the cause and consequences of sex differences in human and nonhuman animals.

We take multiple approaches to understanding sex differences, broadly separated into methodology and implementation.

First we develop novel methodology for incorporating the sex chromosomes into genomics analyses. Most genetics methodology was developed for the autosomes (non-sex chromosomes), and often the X and Y break basic assumptions of these approaches.

My lab has developed approaches to improve the detection of DNA variants (PMID: 31289836) and improve the quantification of RNA abundance (PMID: 32693839) on the sex chromosomes. We've further provided best practices for testing genetic models of sex differences in human cohorts (PMID: 37172561).

Second, we are active in assessing the effects of sex as a biological variable on human health and disease. We have shown that sex differences in gene expression early in life persist across adult tissues later in life (PMID: 36550527). We have further identified sex differences in gene expression and mutational processes in liver cancer, suggesting distinct etiologies (PMID: 31615477).

Further, as part of a collaborative project on Alzheimer's disease, we identified, for the first time, a sex-linked transcription factor pair (ZFX/ZFY) associated with more pronounced neuronal loss in females (PMID: 40670382), underscoring the importance of accurately incorporating the X and Y chromosomes into human genetics analyses. ●

COMPILED BY TAYLOR FARLEY, VRC

Your Research Partner: The NIH Library

Chatbot Prompts, 3D Printing, Editing Services, and Bibliometric Tips and Tricks—the NIH Library Can Take Your Next Project to the Next Level

BY YOLANDA JONES, NIH LIBRARY, AND CHRISTOPHER WANJEK, *THE NIH CATALYST*

CREDIT: JASPER SHIDE, NINDS

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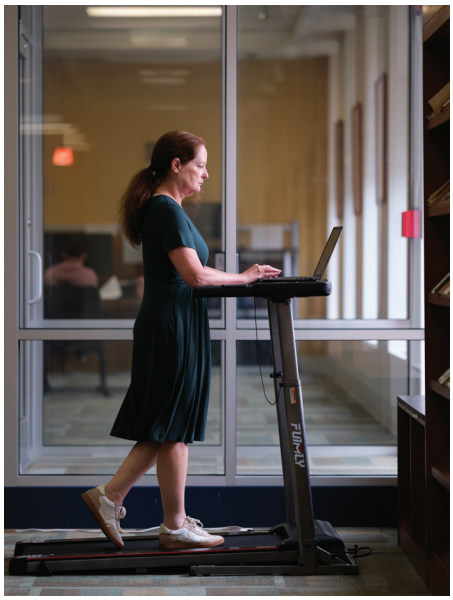

CREDIT: JASPER SHIDE, NINDS

NIHers can still get their 10K steps each day, even when the weather does not allow for a stroll outdoors.

Unlike a simple web search, the NIH Library provides access to powerful specialized tools such as Web of Science, Scopus, and Embase, which allow for in-depth data searching and citation analysis. These resources are essential for comprehensive literature reviews and for demonstrating the impact of your research.

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CREDIT: JASPER SHIDE, NINDS

The NIH Library recording studio can help you with your audio needs.

"I originally took the 3D printing orientation from the library almost 10 years ago," said **John Ball**, a staff scientist in the NEI Retinal Neurophysiology Section. "I started my own journey printing models from 3D-reconstructed neurons and designing my own 3D models. I like to use the library's printers to quickly prototype devices for use in the lab, like custom microscope mounts for samples that use nonstandard plates. I can be more creative with experiment and equipment design than if I'm stuck with off-the-shelf parts or those designed by a company. I can recognize a need, design a component, and have it printed all in two or three days. It's an amazing service to have access to, and the library staff that run that service and maintain the printers have always been phenomenal to work with. I consider it an essential service for my research."

CREDIT: YOLANDA JONES, NIH LIBRARY

If you prefer the outdoors, the NIH Library's spacious patio offers a workspace with sunshine.

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PHOTOGRAPHIC MOMENT

CREDIT: CHIA-CHI CHARLIE CHANG

Music to Our Ears: The National Symphony Orchestra, directed by Gianandrea Noseda, and conducted by Steven Reineke, performed at the NIH Clinical Center on Sept. 3. The performance featured works by Mozart, Beethoven, Copland, Rossini, and other greats. Each level of the atrium filled with music lovers during the afternoon performance. ●

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