

Homegrown AI

NIH Researchers Are Creating AI Tools Benefiting the Broader Biomedical Community

BY CHRISTOPHER WANJEK, *THE NIH CATALYST*

ARTIFICIAL INTELLIGENCE (AI) is reshaping research across the NIH, with scientists creating tailored tools to meet the demands of their own complex datasets and questions.

Tapping into the power of neural networks, large language models (LLMs), and other AI architectures, NIH researchers are teasing apart single-cell gene expression patterns and denoising fragile microscopy images, to name just a few emerging AI applications.

These tools don't simply automate what was previously manual; they enable entirely new modes of analysis previously impossible. And in many cases, these homegrown AI solutions—created to solve a local problem—are proving to be useful for the broader biomedical research community.

Such ideas will be on display at the NIH Artificial Intelligence Symposium 2025 on May 16 at Masur Auditorium and on the FAES Terrace. This full-day event will explore a broad range of AI approaches in biomedical science and will feature two external keynote speakers and a smattering of intramural research posters.

Read on for a sample of four homegrown AI tools among the dozens pouring out of today's NIH labs.

CONTINUED ON PAGE 4 ➡

18th NIH Director: Jayanta Bhattacharya

New Director Shares Priorities for Replication Studies, Autism Research, and Five Aims for the Future of Biomedical Research

BY *THE NIH CATALYST* STAFF



CREDIT: CHIA-CHI CHARLIE CHANG

NIH's new leadership team toured the Clinical Center in April and learned about the life-saving treatments delivered to patients enrolled in clinical research. Jayanta Bhattacharya (pictured right, center) became the 18th NIH director on April 1 after 38 years at Stanford University.

JAYANTA BHATTACHARYA BEGAN HIS TENURE AS THE 18TH NIH DIRECTOR ON April 1. Bhattacharya, a Stanford University (Stanford, California) graduate, professor of health policy, and director of the NIH-funded Center on the Demography and Economics of Health and Aging, presented his priorities for the future of biomedical research to the NIH Council of Councils on April 21.

"I want to talk about my love for the NIH, for the mission of the NIH, and my absolute commitment to the NIH to make sure that the NIH continues to be the crown jewel of biomedical research in the whole world," Bhattacharya said at the event.

CONTINUED ON PAGE 14 ➡

CONTENTS

FEATURES • [\[1, 4\]](#) Homegrown AI [\[1, 14\]](#) 18th NIH Director [\[3\]](#) NIMHD's New SD [\[10\]](#) Medical Simulation Program: The Power of Practice [\[12\]](#) NIH Helps Children Live Longer, Healthier Lives

DEPARTMENTS • [\[2\]](#) DDIR: Bold and Robust Science [\[8\]](#) Catalytic Research [\[13\]](#) What We're Reading [\[16\]](#) Meet 17 Stadtman Investigators [\[20\]](#) Photographic Moment



Bold and Robust Science

The NIH continues to prevent the transition from health to unhealth

BY NINA F. SCHOR, DDIR

WE OFTEN SAY THAT, IN THE NIH Intramural Research Program (IRP), we can do a kind of research that would be challenging at best to do anywhere else. Are we deluding ourselves, or is this statement actually true? If true, do we leverage this capability to create and share something unique? In the answers to these questions lie the *raison d'être* and marketing strategy for the IRP, the promise of the research conducted on our campuses for the populations we serve, and the potential for collaboration and synergy between NIH IRP research and that done in universities and industries around the United States and the world.

Thinking about this is insomnia-worthy, and many of you have noticed I have looked more tired than usual recently! Since the founding of what is now the NIH, the scientific community and environment around it have changed vastly. Universities now have sizable endowments and physical structures devoted to research. Industry has forged partnerships with universities and government to derisk the research it does by collaborating with university colleagues, funding university-based developmental research, or purchasing licensing rights to promising basic and developmental findings and assets. Research institutes sit within and side by side with patient care facilities and hospital systems with enormous patient numbers that combine in mega-consortia in ways that the Clinical Center could never hope to do. No longer is NIH the only bastion of research in the generic or the only home of research excellence and innovation.

What makes the research that can be done only at NIH unique is largely the way in which NIH IRP researchers and research are evaluated and resourced. Whereas extramural researchers write grant applications based on individual projects and need to demonstrate the worthiness and feasibility of performance of those future projects to obtain funding, intramural researchers present their entire portfolio every four years and are largely funded for the future based on their accomplishments in the past. In other words, instead of funding projects, the IRP funds people and teams.

What this means is that IRP investigators can pursue projects that are not a “sure shot.” They can pursue longitudinal projects that might take longer than the 4- or 5-year duration of an R01 grant. This difference enables IRP investigators to do such things as first-in-human studies or studies that require invention of novel instrumentation or methods that might not work at first, or studies that phenotype a cohort of patients from conception to late adulthood.

What of the Make America Healthy Again (MAHA) agenda? Is NIH uniquely positioned to contribute to this national enterprise? From the standpoint of the study of chronic disease and its basic mechanistic underpinnings, we are already leveraging our unique evaluation system and resources to do this. At last count, with of course some overlap, 86 intramural investigators are working on diabetes; 64 working on obesity; 31 working on renal failure; and 25 working on stroke. Similarly, I counted

205 investigators working on aging; 121 working on chronic infection; 112 working on inflammation; 72 investigators working on autoimmunity; 67 investigators working on environmental exposures; and 70 working on oxidative stress.

The real crux, however, of ensuring the health of the people we serve is preventing the transition from health to unhealth. What better environment is there in which to detect, characterize, and work toward preventing that transition than one in which the study of life-course cohorts is not only possible, but facilitated and rewarded?

What better environment is there in which to take chances, be audacious, and juxtapose ideas, tools, and mechanisms from different fields than one in which people and teams—and innovation and creativity—are the currency in which value is judged? Only through such studies that engage the communities around us; follow and deeply phenotype their biological, psychological, social, and environmental characteristics; and determine the turning point from health to unhealth and its mechanistically verified precipitants will we be able to keep America and the world healthy.

We must ensure the robustness and boldness of the NIH IRP; refuel the robustness and boldness of the complementary research communities in academia and industry; and restore the robustness and boldness of the teams we enlist to critique and hold accountable all components of the research enterprise.

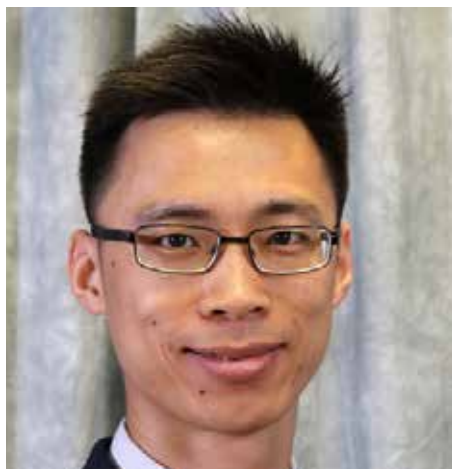
Our nation and the world are depending on us. ●

Kelvin Choi Named NIMHD's New Scientific Director

Choi Will Lead Scientific Efforts at NIMHD to Advance Health Disparities Research

BY JOHN CARLO J. COMBISTA, NIMH

CREDIT: NIMHD



Kelvin Choi, Ph.D.

Choi serves on the *NIH Catalyst* Editorial Advisory Board.

KELVIN CHOI WAS NAMED SCIENTIFIC director (SD) of NIMHD in November 2024 after serving as acting scientific director since March 2023. His appointment follows the retirement of former scientific director Anna Nápoles.

Choi leads an intramural research program comprising three branches: the Social and Behavioral Sciences Branch, the Population and Community Health Sciences Branch, and the Epidemiology and Genetics Branch. He also oversees the mentoring and training of trainees and fellows, reflecting NIMHD's commitment to supporting the next generation of researchers. Choi has been with NIMHD since it was established as an institute in 2010 through legislation. He is grateful for the opportunity to lead NIMHD with institutional knowledge.

"I have been here [since] shortly after the establishment of the NIMHD Division of Intramural Research, and I hold the institutional knowledge of NIMHD, so I want to provide continuity with the programs and projects started by the previous scientific directors and guide NIMHD with its future research directions," Choi said.

Colleagues across the NIH celebrated Choi's appointment. "I was thrilled to learn that Dr. Choi was selected as the NIMHD scientific director," said **Laura Koehly**, senior investigator in NHGRI's Social and Behavioral Research Branch. "He has demonstrated his ability to build relationships, mentor and develop members of his team and early career scientists, and inspire innovative science. The future of the NIMHD intramural research program looks bright with Kelvin at the helm."

The NIMHD Division of Intramural Research examines disparities in individual, clinical, behavioral, and contextual factors that affect health outcomes in populations experiencing health disparities. One project that NIMHD is focusing on is the U.S. Health Disparities Project (PMID: 37544309).

"It's really an important project because this helps us understand how the interactions of sociodemographic factors and geography potentially influence the difference in health outcomes, and we are able to observe that across the country," Choi said.

Choi is best known for his research on understanding tobacco use disparities in the United States. He also aims to develop and evaluate the impact of tobacco control interventions on reducing tobacco use disparities.

His journey to the NIH began when he moved from Minnesota to join NIMHD as the first Stadtman tenure-track investigator of the institute. Since, he had been promoted to senior investigator and received the NIH Director's Ruth L. Kirschstein Mentoring Award for his exceptional leadership and mentoring skills.

Choi leads the Tobacco-Related Disparities and Control Lab, which has pioneered research on how cumulative

cigarette discount coupon exposure influences the trajectories of cigarette smoking behavior of U.S. adults through a longitudinal analysis, suggesting that prohibiting these coupons could be an important tobacco control strategy (PMID: 37015744). His lab also seeks to understand how people respond to higher prices of tobacco products and found that low socioeconomic status people who smoke were most likely to find ways to reduce the financial cost of smoking—such as switching to cheaper brands or rolling their own cigarettes—after a cigarette tax increase (PMID: 28219975). He also studied how the interaction of different sociodemographic factors, including education, relates to tobacco product use among U.S. adults (PMID: 36239224).

Choi is grateful to his doctoral mentor, Jean Forster, who introduced him to the field of tobacco health disparities research, and the members of his dissertation committee who influenced the trajectory of his research at NIMHD. He is also grateful to his mentors, Bruce Simons-Morton, scientific emeritus and former chief of the NICHD Social and Behavioral Sciences Branch, and Laura Koehly, who helped him navigate the scientific and administrative side of doing research at the NIH.

"Our goal is to really provide everyone in the United States the opportunity to achieve optimal health outcomes, and our research will help us get there. By working with researchers and the community members, someday we'll get there," Choi said.

Outside of work, he spends most of his time attending his daughter's synchronized ice-skating competitions. He also loves riding his bicycle and recently did a 42-mile bike ride in Maryland. His goal this year is to go 50 miles. ●

I can see clearly now, the noise is gone

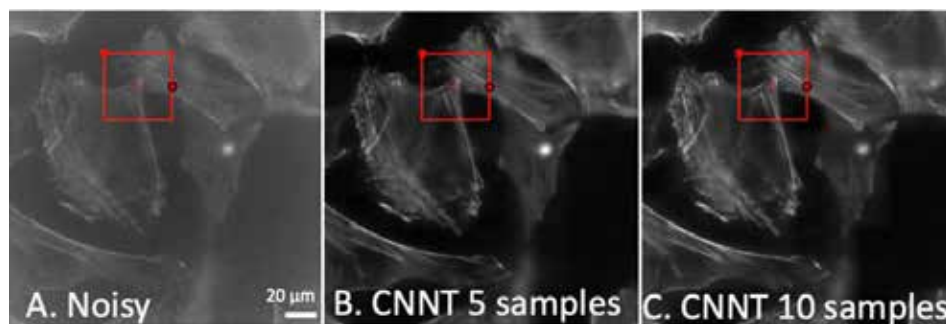
Scientists and engineers have made incredible strides in microscopy, with biological imaging close to the molecular level. They have probed not only more deeply but also more gently, with techniques such as fluorescent labeling and light-sheet microscopy that impart less photon damage to the objects imaged, enabling the study of live cells in unprecedented detail.

Nevertheless, fluorescent signals can restrict both spatial and temporal resolution, and researchers often rely on low light levels during imaging to minimize photobleaching and reduce cellular stress, which is critical when working with live, moving samples. This results in “noisy” or fuzzy images.

One common AI technique to denoise microscopy images, called convolutional neural networks (CNNs), a type of deep learning model, has had limited effectiveness because it can be time-consuming, tedious, and, in the end, rather image-specific. Hoping to develop a tool that would be faster and more broadly applicable, researchers at the NIH and their external colleagues created what has become known as convolutional neural-network transformer (CNNT).

As the name implies, this deep-learning model added a “transformer” tool to the CNNs. The transformer tool has been famously used in ChatGPT to help computers understand language, such as figuring out what a sentence means or predicting the next word. But the tool also is ideal to help decode complex patterns in images.

With the CNNT, this team—comprising researchers at NHLBI, NIBIB, FDA, HHMI, Janelia, and Microsoft—devised a denoising system based on a single, strong “backbone” model using many examples from one microscope. From this backbone—analogue to a human skill, such as piano playing, which can be adapted to play classical or jazz or pop—other



Coming into focus. Seen here are mouse embryonic fibroblast cells in increasingly clear resolution. The first (A) is a low-quality noisy image as an input for the model. Images B and C show the improved clarity from the convolutional neural network transformer after it was trained for 30 cycles using five and ten training images, respectively.

CREDIT: SCIENTIFIC REPORTS

microscopes can be trained with just a few new images. “This saves enormous effort in training time and resources for each new experiment,” said **Chris Combs**, director of the NHLBI Light Microscopy Core, who co-led the development of the tool.

The team demonstrated CNNT’s performance on three types of microscopy: Wide-field imaging of mouse cells, two-photon imaging of zebrafish (*Danio rerio*) embryos, and confocal imaging of mouse lung tissue. Perhaps the most exciting application lies in large-scale imaging tasks. In one experiment, CNNT enabled a sevenfold increase in imaging speed while maintaining image fidelity, a breakthrough for working with fragile live samples or time-lapse recordings.

A paper describing the CNNT tool was published in August 2024 in *Scientific Reports* (PMID: 39107416) and features, among many, first author Azaan Rehman, a former postbac with NHLBI, and senior author Hui Xu, former director of the NHLBI AI Core, now at Microsoft.

Combs said his team hopes to improve their CNNT model by scaling it up with larger and more diverse training datasets, which could eventually lead to a light microscopy foundation model with broader applicability.

Help is on the way for single-cell analysis

Members of NEI Laboratory of Immunology, led by **Rachel Caspi**, have developed a tool called SCassist, an AI-powered workflow assistant for single-cell analysis. Its first application has been to

probe the immune function of Müller cells in the retina, the results of which will be published in the coming months. But the tool itself will be broadly useful to anyone drowning in single-cell RNA sequencing (scRNA-seq) data, the team said.

First, the science. Müller cells are the principal glial cells in the retina. They help to maintain retinal structure and physiological homeostasis and support neuronal function. During retinal injury or disease, these cells can shift to a state called reactive gliosis and perform immune-like functions such as inflammatory signaling. Their varying activation states coupled with the unique retinal environment—comprising disparate layers of retinal cells, a blood–retina barrier, and numerous immune cells interacting in space and time—make it difficult to discern their precise role in immunity.

Caspi and her collaborators had discovered that Müller cells can profoundly inhibit inflammatory lymphocytes, capable of attacking the retina, through cell–cell contact. However, the inhibitory molecules remained unidentified, largely because the technology to reveal them in a comprehensive fashion had not yet been developed.

To tackle this problem, Caspi’s group turned to scRNA-seq to determine gene expression profiles of individual Müller cells, initially by re-analyzing a publicly available scRNA-Seq dataset of Müller cells from eyes with autoimmune inflammation. This analysis could reveal the potential of these cells to express immune-related genes and functions and help demonstrate how Müller cells use them

to inhibit inflammatory lymphocytes.

The problem with scRNA-seq, however, is that the investigators are blessed with an abundance of data—thousands of genes in thousands of cells—that is difficult to analyze. Caspi's team started analyzing the scRNA-seq data several years ago using the standard tools available, which was cumbersome and laborious and not ideal to make system-level interpretations.

With the rise of AI, **Vijay Nagarajan**, a staff scientist in Caspi's lab specializing in bioinformatics, had an idea: Apply the power of LLMs to create an assistant that would help analyze the complex scRNA-seq data and provide humanlike interpretations, connecting dots.

The AI tool that Nagarajan created and has now patented, SCassist, is built on Google's Gemini and Meta's Llama3. He worked with fellow NEI staff scientist **Guangpu Shi**, who had spent years studying ocular cells involved in immune responses. Shi used SCassist to create a comparison matrix for a detailed functional analysis of Müller cell subpopulations.

Among their findings, the team identified nine distinct Müller cell subgroups; found that three of them are activated in an inflamed retina; found two distinct activated Müller cell phenotypes with macrophage-like properties, governed by *Neurod1* and *Irf* family transcription factors; and learned about key interactions with helper T lymphocytes. "The ability to combine the power of scRNA-seq with AI is a complete game changer," Caspi said.

Nagarajan and Shi have since teamed up to create IAN, which they describe as an "R package designed to perform contextually integrated 'omics data analysis and reasoning," building on SCassist and leveraging the power of LLMs to unravel complex biological systems.

Are you being served?

Zhiyong Lu, a senior investigator who leads the NLM Biomedical Text Mining

Research Group, has been creating AI tools since his arrival at the NIH in 2007. The "Best Match" button for PubMed searches is one of the tools his team created.

This tool, introduced in a 2018 *PLoS Biology* paper (PMID: 30153250), uses natural language processing (NLP) and other AI-based algorithms to better understand the intent behind a user's search query and match it with relevant articles.

But Lu said much bigger plans are on the horizon. "In my 20 years of research with AI and NLP, we have never seen any AI algorithm so powerful and so amazing [than what's out now] in terms of its capability for text understanding and generation. Period."

Tapping into this power of recent LLMs such as ChatGPT, Lu's group created TrialGPT to streamline the process of matching patients to clinical trials. There have been attempts to accomplish this important and seemingly straightforward task using AI, but none have resulted in an accurate product that warrants its use in practical applications.



This group photo features members of Rachel Caspi's (front row, center) lab, including Vijay Nagarajan (front row, far left) and Guangpu Shi (front row, far right).

CREDIT: DUSTIN HAYS, NEI

Qiao Jin, a postdoctoral fellow in Lu's group, approached the task by having the AI tool analyze patient notes against each single inclusion and exclusion criterion of a trial protocol and then forcing AI to not only determine who would be eligible for a match—that is, yes or no—but also state why the decision was made for improved explainability and transparency.

The "asking why" part prompted the AI tool to better assess its output, resulting

in a matching accuracy of more than 80%, comparable to human experts, but in a fraction of the time.

A paper describing this tool was featured in *Nature Communications* and ranked among the top 25 most downloaded health science papers last year (PMID: 39557832). See the NIH Director's Blog from last December for a rewarding summary.

Lu said this unique tool will assist, not replace, doctors and nurses by saving time and making patient connections that otherwise could have been missed.

Another AI tool that Lu's group is working on—and they have many, in collaborations across the NIH and beyond—is for gene-set analysis, a routine task for interpreting high-throughput data to understand the collective function for a set of genes, not just one. The go-to method has been a statistical enrichment analysis based on databases of known gene-set functions. However, when the database does not contain a significant subset of the genes in question, the statistical analysis is on shaky ground.

Standard LLMs can already predict function as effectively as the aforementioned statistical analysis rather quickly and even explain its reasoning. "While impressive, these results are not always reliable, as they remain vulnerable to hallucinations," Lu said. That is, even the "why" could be a fabricated answer.

In response, **Zhizheng Wang**, another postdoctoral fellow in Lu's group, proposed GeneAgent, an LLM-based tool featuring a built-in AI agent that automatically retrieves relevant gene-centric knowledge from expert-curated databases to verify initial predictions and make corrections when necessary. By doing so, GeneAgent effectively minimizes hallucinations and enhances performance. Lu's group has a preprint describing GeneAgent (PMID: 38903746), which is expected to be published in *Nature Methods*.

CONTINUED ON PAGE 6

Lu's group addresses the challenges of implementing LLMs in health care in an April article in the journal *Annual Review of Biomedical Data Science* (PMID: 40198845). Said Lu, simply, "I want our AI tools to be used."

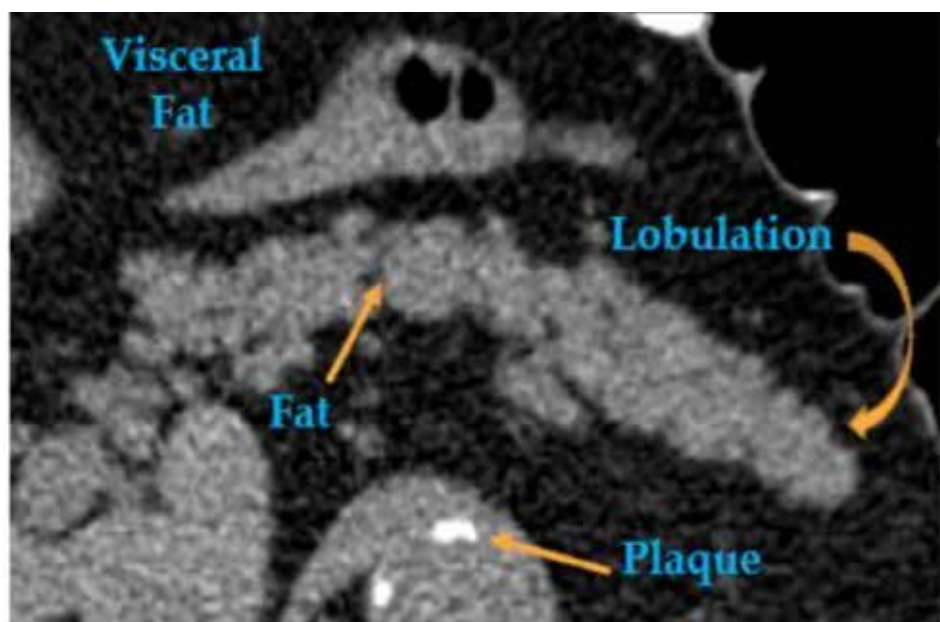
Predicting diabetes on CT scans

The letters "CT" are not in "diabetes," and you may be surprised to learn of a connection. A team of NIH Clinical Center researchers and their colleagues have used AI to predict type 2 diabetes in patient computed tomography (CT) scans with an accuracy of upward of 90%.

While there are other more accurate ways to diagnose diabetes, the novelty of this method is that it reveals the promise of predicting chronic disease from CT scans originally performed for unrelated reasons. Also, diabetes is a disease often diagnosed late, when organ damage has already begun, but this AI approach can reveal biomarkers from abdominal CT scans that are strongly predictive of disease status even years in advance.

The work, led by **Ronald Summers**, a senior investigator in the Clinical Center's Imaging Biomarkers and Computer-Aided Diagnosis Laboratory, in collaboration with Perry Pickhardt at the University of Wisconsin at Madison, builds upon incremental advances first in automating the detection of CT biomarkers in and around the pancreas that point to type 2 diabetes (PMID: 35380492), then developing AI models to trace the pancreas in CT images, a task called segmentation, which is complicated by the pancreas' small and irregular, wrinkled shape (PMID: 38944630).

For this latter part, Summers and his team tested five segmentation models on more than 350 scans from a database of Clinical Center patients. Three models—TotalSegmentator, AAUNet, and AASwin—consistently performed the best, producing pancreas outlines that closely matched those drawn by radiologists.



CREDIT: RADIOLOGY

Pancreatic computed tomography scans can help predict type 2 diabetes: Images in a 67-year-old man with type 2 diabetes who was diagnosed 595 days after CT. This pancreas is relatively inhomogeneous due to fatty atrophy, lobulated, and irregular in contour.

With very accurate outlines, the AI tool could measure fat, tissue density, and the presence of nodules on the organ surface, all potential indicators of diabetes.

With models in hand, the team put the method to the test in a retrospective study of more than 9,700 patients at two medical centers, the Clinical Center and the University of Wisconsin School of Medicine and Public Health. They compared biomarkers derived from three segmentation algorithms and trained machine learning models to predict whether patients had diabetes at the time of the scan or developed it within four years.

Despite variations in segmentation, the key attenuation-based biomarkers—particularly average pancreas density and intrapancreatic fat fraction—showed high agreement across models and a strong predictive performance, with positive predictive values up to 84% and negative predictive values as high as 94%.

There is no standard clinical practice for visually diagnosing or predicting diabetes from pancreas morphology on CT. Therefore, this AI approach isn't outperforming radiologists per se; it's enabling a type of analysis that would otherwise be impractical or unavailable in routine clinical care. Manual segmentation

of the pancreas is extremely labor-intensive and rarely done outside of research.

The findings, which will appear in *Academic Radiology* (PMID: 40121118), underscore the potential for using routine CT scans opportunistically to screen for chronic disease. The approach could be integrated into clinical workflows without needing scan protocols tailored to diabetes detection.

This team—which includes **Pritam Mukherjee**, an associate scientist in Summers' lab, and now extramural collaborators in NIDDK's T1DAPC/DREAM study and in the Consortium for the Study of Chronic Pancreatitis, Diabetes, and Pancreatic Cancer (PMID: 30325859)—are now investigating the use of their algorithms for patients with acute or chronic pancreatitis.

Summers noted that as segmentation algorithms become more accurate and generalizable, CT-based biomarker extraction could be applied to detect or predict a wide range of conditions—from metabolic syndromes to malignancies—all without additional patient burden.

These studies mark a key advance in using AI to transform existing radiological data into predictive tools for preventive medicine. ●



NINDS

1950
2025

JOIN US AND SPREAD THE WORD

Since 1950, the National Institute of Neurological Disorders and Stroke has played a pivotal role in unraveling the complexities of the brain and nervous system.

Through groundbreaking research, training the next generation of scientists, working closely with people with lived experience, and improving diagnosis, treatments, and prevention strategies, NINDS continues to lead the way in neuroscience discoveries.

Learn more about NINDS's *lasting impact on neuroscience* and check out upcoming events:

ninds.nih.gov/75years | [#NINDS75](https://twitter.com/NINDS75)



National Institute of
Neurological Disorders
and Stroke



Intramural Research Briefs

Read About Scientific Advances and Discoveries by NIH Intramural Scientists

NIAAA, NIDCD: BRAIN NETWORKS ASSOCIATED WITH TASTE AND SMELL CAN PREDICT ALCOHOL INTAKE

There may be something to that whole swirl, sniff, sip process when ordering a bottle of wine, according to a recent NIH study.

Taste and smell—the senses that are key to detecting chemical cues in our environment—are also key triggers of alcohol craving, activating reward pathways in the brain that can lead to increased consumption. In fact, patterns in the connectivity between taste- and smell-related brain regions can help predict alcohol consumption, according to a new study by researchers at the NIAAA, NIDCD, and the National Smell and Taste Center.

Based on this knowledge, NIH researchers believed the strength of connectivity between taste and smell networks in the brain could serve as a predictor of alcohol consumption. To test their theory, the researchers analyzed brain scans from young adults, a population at high risk for developing alcohol use disorder. Three different brain connectivity patterns associated with smell and taste were observed to be consistently correlated with alcohol intake behaviors.

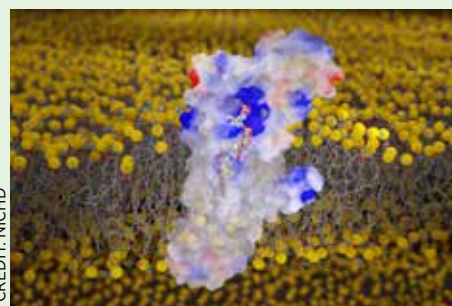
Using these connectivity patterns and self-reported alcohol intake, the researchers then trained a machine learning model to predict drinking behavior. The trained model successfully predicted specific alcohol intake behaviors from new brain scans, based on the strength of connectivity between the identified regions. For example, connectivity within odor-related networks accurately predicted wine intake, while taste-related connectivity predicted total alcohol use and the number of drinks consumed per day.

These findings highlight the potential use of brain-based biomarkers in identifying individuals at risk for alcohol use disorder. They also underscore the role of sensory networks

in the brain in shaping behaviors related to alcohol craving and consumption. (NIH authors: K. Agarwal, D. Tomasi, N.D. Volkow, and P.V. Joseph, PMID: 39962224)

[BY ABIGAIL HOLDER & MEAGAN MARKS, NIAAA]

NICHD: NIH-DEVELOPED METHOD BOLSTERS UNDERSTANDING OF A KEY PROTEIN MODIFICATION PROCESS



CREDIT: NICHD

NICHD: The Pep-PAT assay

NICHD researchers have developed a cell-free system to study a key protein modification called S-acylation, in which fatty acids are attached to certain sites on the protein to help regulate its action. S-acylation has been implicated in diseases ranging from cancer to neurodegenerative disorders, and developing ways to block the process could help treat these conditions.

The new system, called the Pep-PAT assay, allows researchers to evaluate interactions between the enzymes that carry out S-acylation and their substrates (the proteins upon which they act). A detailed understanding of these interactions is crucial for developing ways to inhibit S-acylation. In the future, Pep-PAT assay also could be used to evaluate potential new drugs for diseases such as breast cancer.

NICHD's Section on Structural and Chemical Biology, led by Anirban Banerjee, developed Pep-PAT as a reconstitution assay, an experiment in which a complex process is recreated in a controlled environment. This setup allows precise assessment of interactions

between purified zDHHC enzymes and fragments of their likely substrates.

Using the Pep-PAT assay, the researchers investigated the ability of three zDHHC enzymes to S-acylate seven potential substrates. The substrates included EGFR, other human proteins, a viral protein, and a bacterial protein.

The Pep-PAT assay offers a new tool to help researchers better understand how zDHHC enzymes recognize their substrates, knowledge that will help guide development of strategies to treat diseases by blocking S-acylation of certain proteins.

"We are particularly intrigued by the possibility to apply Pep-PAT to the discovery of new drugs against breast cancer, as EGFR is among the zDHHC substrates we established in our assay," said lead author Banerjee. (NIH authors: T. Mondal, J. Song, and A. Banerjee, PMID: 40090582).

[BY HILLARY HOFFMAN, NICHD]

CRC, NIAID: OVER A DECADE OF NOROVIRUS SURVEILLANCE AT THE NIH CLINICAL CENTER

A 12-year study tracked the presence and persistence of different genotypes of norovirus in the stool of immunocompromised patients at the NIH Clinical Research Center (CRC).

This NIH study reported that diverse noroviruses could establish chronic infection in immunocompromised patients, with some exhibiting viral shedding for many months to even years. This chronic infection contrasts with norovirus infection in immunocompetent individuals in whom, typically, shedding ceases only weeks after initial infection.

These results raised the question of whether persistent viral shedding in immunocompromised individuals might contribute to hospital-acquired infections with norovirus, although no evidence of this occurring at the CRC has been found.

Further, researchers established that the dominant genotypes infecting CRC patients at the NIH over the 12 years of surveillance mirrored the dominant genotypes in global circulation at the time. Taken together, it is likely that patients with persistent norovirus infections with globally circulating variants were infected outside of enrollment in NIH studies.

Norovirus is a dominant cause of infectious enterocolitis worldwide, affecting up to 1 in 15 people in the United States annually. There currently are no vaccines or treatments. Research like this aims to aid in the development of effective strategies to combat chronic and severe norovirus infection in vulnerable patient populations. (NIH authors: N. Chaimongkol, D.Y. Kim, Y. Matsushima, J. Durkee-Shock, K. Barton, C.N. Ahorrio, G.A. Fahle, K. Bok, A. Behrle-Yardley, J.A. Johnson, D.A. de Jesus-Diaz, G.I. Parra, E.A. Levenson, F.Y. Maeda, S.V. Sosnovtsev, and K.Y. Green, PMID: 39207021).

[BY TAYLOR FARLEY, NIAID]

NLM: KEY HURDLES TO REAL-WORLD INTEGRATION OF LARGE LANGUAGE MODELS IN HEALTH CARE

Large language models (LLMs) in health care applications have the potential to enhance data management, support decision-making, and improve operational workflow. However, their implementation in health care is deterred by obstacles highlighted in a recently published review by researchers at NLM.

The article highlights four areas of concern: Performance and assessment difficulties, operational vulnerabilities, ethical considerations, and legal and regulatory compliance. Although many models are reported to achieve expert-level performance on standardized benchmarks such as multiple choice exams, such tests do not typically reflect the open ended nature of clinical decision making. Models can arrive at correct answers via flawed or hallucinated reasoning, undermining trust in their outputs.

These issues can be alleviated through comprehensive evaluation and verification mechanisms, such as human-based self-reflection and quality checks. Beyond that, technical reliability, ethical considerations around privacy, and security are equally critical when implementing AI systems in health care. Training data imbalances may perpetuate disparities in care recommendations, while malicious manipulations can threaten patient confidentiality or promote third-party interest.

Encryption, authentication, and continuous auditing are essential to safeguard sensitive health information and to deter manipulation of model outputs. Finally, compliance with regulations on intellectual property and device standards is crucial to defining physician liability and malpractice risks with the use of medical LLMs. Clarifying liability frameworks and establishing clear safety and efficacy standards will be necessary to define physician responsibilities and to integrate LLMs as trusted aids rather than opaque black boxes.

By tackling these concerns, the health care field can responsibly harness the full potential of LLMs and unlock new insights from the ever-growing body of medical data. (NIH authors: Y. Yang, Q. Jin, Q. Zhu, Z. Wang, F. Erramuspe Álvarez, N. Wan, B. Hou, and Z. Lu, PMID: 40198845)

[BY CASEY CARGILL, NEI]

NIDDK: THE IMPACT OF PSYCHOLOGICAL DISTRESS ON MALADAPTIVE EATING



NIDDK: The path model from psychological distress to weight gain through maladaptive eating behaviors.

When stress and fear become chronic or excessive, they can lead to an increase in anxiety, psychological distress, and unhealthy coping mechanisms. During 2020 to 2021,

there was a 25% increase in anxiety and depression worldwide.

A team of researchers at NIDDK’s Phoenix Epidemiology and Clinical Research Branch and their collaborators focused on understanding how a rise in fear regarding environmental stress, or times of psychological distress, contributed to maladaptive eating behaviors.

From February 2022 to February 2024, researchers recruited 4,390 participants to complete surveys determining their eating behaviors and perceived environmental and general psychological distress.

Participants completed a questionnaire measuring their current environment-related stress and three additional questionnaires that assessed their general perceived psychological distress. They also completed three questionnaires that determined the extent to which they were engaging in maladaptive eating behaviors, such as binge eating or excessive nighttime eating.

Researchers found that both perceived environmental and general psychological distress led to an increase in maladaptive eating behaviors. Psychological distress was associated with higher emotional and uncontrolled eating, increased odds of binge eating, and a higher body weight and body mass index.

This research suggests that when faced with increased fear and stress, participants may turn to maladaptive eating behaviors as a coping mechanism. These findings provide insight into the long-term impact of societal and environmental stressors and how even after experiencing psychological distress, they can continue to have a long-term effect on human behavior. (NIH authors: M. Willig, T. Cabeza de Baca, E.J. Stinson, T. Rodzevik, S.B. Votruba, J. Krakoff, and M.E. Gluck, PMID: 40217216) ●

[BY MELANIE BARKSDALE, NIAID]

The Power of Practice

The NIH Clinical Center Medical Simulation Program Delivers Real-World Training

BY SEPPIDEH SAMI, NIH CLINICAL CENTER AND *THE NIH CATALYST* STAFF; PHOTOS BY DONA JONES, NINR

POOR SCOTT WATKINS. HE SEEMS TO suffer one medical catastrophe after another. Today it was an anaphylactic event during an outpatient visit right here in the NIH Clinical Center (CC). He was exhibiting the classic symptoms: Shortness of breath, generalized rash, and gastrointestinal stress. But his treatment was—how shall we say this delicately—subpar.

The medical provider didn't recognize the symptoms at first. Then they fumbled with the EpiPen, applying it incorrectly. Scott remained in full cyanosis with eyes partially open. Call the Code Blue team!

Fortunately for this medical provider—admittedly, a new trainee at the CC, still wet behind the ears in treating patients—Scott is not human and not even alive. Scott is a manikin, a sophisticated medical simulation tool used by the CC to teach trainees about proper medical care.

The CC has five such manikins that staff—with the help of clothing, wigs, and a touch of makeup—personify as adult and child, male and female patients. There's 10-year-old Camille Jenkins with sepsis, 7-year-old Riley Morgan with a neurological emergency, 7-year-old Gabriel Romero with respiratory failure, 8-year-old Bianca Visconti with an adrenal crisis...collectively known as Pediatric HAL S2225. The adults, SimMan 3G and SimMan 3G Plus, take on similarly diverse personalities.

And the entire crew—including SimBaby and PediHAL S3005—is part of the NIH Clinical Center Simulation Program, a joint program of the Office of Clinical Research Training and Medical Education and the Nursing Department's Office of Nursing Professional

Development. Since 2020, the program has been coordinated by **Mabel Gómez**, a medical doctor who serves as the simulation facilitator and educator.

Building a coordinated program

Clinical simulation has long played a role in health care education, offering a safe space to practice clinical skills, build confidence, and refine decision-making in high-pressure scenarios.

The Critical Care Medicine Department began its simulation program in the 1990s under the leadership of **Nitin Seam**, then director of the Critical Care Fellowship. The goal was to provide interprofessional simulation exercises using clinical scenarios of rare but high-risk occurrences seen at the CC, in which critical decisions needed to be made in seconds.

In 2019, then CC CEO **James Gilman** envisioned an expanded simulation program. "As an institution focused on rare and especially stubborn medical issues committed to preventing lapses and error whenever possible, improving our simulation capabilities is of high importance," as noted in the 2019 Strategic Plan, "People, Places, Capabilities: The Clinical Center at 65."

Gilman assigned David Henderson, deputy director for clinical care (now retired); **Tom Burklow**, director of the CC Office of Clinical Research Training and Medical Education; and Gómez to build a strategy to advance and expand the Simulation Program.

The program has steadily grown since 2020, when it started with three projects and 98 participants; by the end of 2024, it had 317 participants and 15 projects. Gómez, having received training from the Center for Medical Simulation at Harvard Medical



Michael Shoykhet, a pediatric intensivist and simulation champion, guides a participant in providing adequate bag valve mask ventilation to Emma Felton, a simulated pediatric patient (PediHAL S3005) with a medical history of infantile cystinosis and respiratory failure due to anaphylaxis, during the "Pediatric Bridge to Practice" course in February.

School, was a natural pick for the team.

"Health care simulation allows me to combine my passion for medicine and education," she said. "I can explore and apply different simulation modalities to support our experienced clinicians in sustaining performance as well as the new trainees completing the learning curve, with the patient's well-being as the ultimate goal."

Ron Gillis is the program's health care simulator technician. He had served as a simulation operations specialist at Walter Reed National Military Medical Center's Simulation Center (Bethesda, Maryland) and as a simulation technician at Inova Fairfax Hospital in Fairfax, Virginia. He ensures that every element from scenario setup to technology management creates a realistic and immersive learning environment. "You need a blend of meticulous planning, technical expertise, and adaptability," said Gillis.

Meet the nonhuman staff

The CC manikins are rather dynamic for lifeless creatures. Costing tens of thousands of dollars apiece, they offer realistic tactile feedback for clinical training scenarios, including injections, hands-on procedures, and emergency interventions. They look and feel like humans to the touch.

The manikins and the health scenarios they are placed in are so real that Gómez said “they don’t die”—that is, no health scenario ends in a death, because that would be too traumatic for the trainees.

The program offers four work streams designed with different objectives in mind:

- Clinical simulation: To improve and sustain performance in interprofessional and non-interprofessional teams with varying levels of training
- Translational simulation: To process improvement, system testing, and safety analysis
- Innovation: To help teams build task trainers, enhance fidelity of simulation sessions using electronic health records, and apply concepts of moulage
- Simulation-based research: To be the priority for the next five years

The simulation team tailors every case scenario to meet the learners’ needs and reflect the patient population and clinical practice at the CC.

The medical simulation team makes much use out of the model called Pediatric HAL S2225, an advanced child-sized medical simulator designed for realistic pediatric emergencies. It can simulate lifelike facial expressions, speech, emotional responses, and physiological reactions such as breathing, pulse, and airway obstruction. It can support training procedures such as cardiopulmonary resuscitation (CPR), intubation, IV access, trauma care, and



Mabel Gómez (left), simulation facilitator and educator, monitors IV fluids during a simulation training.

patient interaction.

Pediatric HAL S2225 is but one machine that can take on a multitude of personalities. And its realistic responses help health care providers and students practice both technical skills and compassionate care for young patients, Gómez said.

The models SimMan 3G and SimMan 3G Plus have similar capabilities but are adult size. Both support advanced airway management, drug recognition, and real-time vital signs, and both can be equipped

with female or male genitalia. The SimMan 3G Plus, the overachiever in this family, adds enhanced physical realism with modular limbs and improved joint articulation.

Broad training opportunity

As the program has grown, so has the spectrum of its learners and faculty. In addition to CC-based staff who are already licensed and credentialed, such as intensivists, bedside nurses, anesthesiologists, hospitalists, respiratory therapists, and others, the program welcomes medical students and interns who join an interprofessional training environment to develop new skills and to learn the importance of interprofessional communication and collaboration.

Post-simulation debriefings are the most essential part of simulation-based training, Gómez said. During the debriefings, they apply the concept of collective intelligence, where every participant is key to the program’s success. Every team member brings value to the discussion, facilitating reflections on actions to improve future performance.



Julie Hogan, a simulation champion, guides participants in conducting a comprehensive neuro-assessment on Diana Tobin, a simulated pediatric patient (PediHAL S2225) with a medical history of Batten disease in status epilepticus.

CONTINUED ON PAGE 19 ➡

NIH Physicians, Researchers Help Children Live Longer, Healthier Lives

Research on Rare Disease of Infancy Provides Insights into Skeletal Disorders

BY ELIZABETH MCMAHON, NICHD

CREDIT: NICHD



Ferreira and Natalie in 2014

LIKE MANY FIFTH GRADERS, NATALIE keeps busy after school with sports, clubs, piano lessons, and playdates with friends. But unlike her peers, Natalie has a social network that extends far beyond her north Texas hometown.

The 12-year-old has friends in Ireland, the United Kingdom, and Hungary whom she can talk to about living with complications of a rare disease known as generalized arterial calcification of infancy (GACI). Caused by mutations in the *ENPP1* or *ABCC6* genes, GACI is a progressive condition that starts before birth with extensive buildup of calcium in the blood vessels—blockages that can ultimately cause heart attack, stroke, and death. At least 20 babies in the United States are born each year with GACI, a diagnosis that can be fatal for half within the first six months of life.

It's a tragedy that Natalie's parents, Jerry and Anne Van Wyk, know too well. Though they have three other living children—Drew, 20, and twins Julia and Graham, 15—Natalie's older brothers, Reid Christopher and Ian James, were born with GACI and died within weeks. Determined that Natalie wouldn't share the same fate, the Van Wyks started a journey in 2013 that would save their daughter's life and lead them to Carlos Ferreira, a skeletal genomicist and head of the Unit on Skeletal Genomics at NICHD.

Ferreira, a trainee when he first met

Natalie just months after her birth, now leads research on rare genetic skeletal disorders from his lab in the NIH Clinical Center. By identifying the molecular mechanisms underpinning these conditions, he and his colleagues hope to understand skeletal growth and metabolism more broadly.

"There's a lot that excites me about this field," Ferreira said. "First, there are new technologies we can use to answer questions about the diagnosis or the mechanism of the rare disease we are studying. Also, we can provide better medical care to patients because we can offer more targeted therapies."

Of those born with GACI, up to 20% who survive infancy develop hypophosphatemic rickets by age two, and the vast majority develop the disease by adolescence (PMID: 33005041). The condition causes bone pain, deformities, and short stature, among other complications. Additionally, those who have *ENPP1* deficiency may experience early hearing loss as well as skin changes, retinal damage, and other musculoskeletal complications later in life.

When she came to NIH, Natalie was one of the first patients Ferreira and William Gahl, senior investigator at NHGRI, had seen with GACI. Building from previous studies and working with collaborators in Germany, they gradually amassed a cohort of more than 200 GACI patients in 19 countries, yielding the first natural history study of *ENPP1* and *ABCC6* deficiencies, which advanced the understanding of the disorder's progression, prognosis, and symptoms (PMID: 34355424).

For Natalie's family, the NIH researchers' focus on their daughter's disease, progression, and treatments felt like a major step forward after years of

struggle. "In our journey to have a family, we felt we were climbing uphill, and it was an insurmountable climb," Jerry Van Wyk said. "So, for us to be invited to come to NIH to participate in any research, the answer was, 'Absolutely, immediately, and what can we do?'"

While scientists understand the molecular basis for why *ENPP1* deficiency causes widespread arterial calcification and cardiovascular complications, they have not established why the deficiency later causes abnormal phosphate concentrations in GACI survivors, leading almost universally to rickets. Among other research, Ferreira's lab conducts studies to understand the origins of rickets and the skeletal complications in patients with *ENPP1* and *ABCC6* mutations.

The Ferreira Lab monitors Natalie's rickets, which started around age three and is managed closely with daily medications, such as phosphorus. They also collaborate with researchers at the Yale School of Medicine (New Haven, Connecticut) who developed an enzyme replacement therapy (ERT) that prevented arterial calcification and later complications in preclinical trials (PMID: 26624227).

Though Natalie is not currently participating in ERT trials, GACI Global, a nonprofit organization founded by her parents and others, has been an essential resource for clinical trials and research. Founded in 2018, the group has connected



X-ray of genu valgum, or "knock knees," in a child with rickets.

CREDIT: GENETICS IN MEDICINE

families around the world who have children born with *ENPP1* and *ABCC6* mutations with information, clinical trials, and community support.

“For years we thought we were all alone, so to see all that’s happened, and to have ERT trials happening, is mind-blowing to us,” Anne Van Wyk said.

As his team’s research on GACI and other skeletal diseases continues, Ferreira is hopeful that the growing body of knowledge about *ENPP1* and *ABCC6* deficiencies will yield uniform standards of care for better identifying and managing people with the condition. GACI continues to be under diagnosed—only half of those born with the condition are accurately diagnosed—so early detection is critical.



Natalie and Kingston enjoy many playful days together.

“One great way to improve the diagnostic accuracy would be newborn screening for GACI. Every baby born in the United States gets some screening. Can we do a heel prick and analyze that blood? This is a dream right now,” Ferreira said.

Though she has had a long medical journey, Natalie says her frequent visits to Dr. Ferreira and her contributions to research have had an unexpected upside: She is considering being a nurse when she grows up. For her parents, working with Ferreira and doing what they can to advance rare disease research after heavy loss is invaluable.

“Participating in research at NIH has been an absolute privilege for us. Having NIH be on our side in fighting, combatting, and learning about this was like wind in our sails,” Jerry Van Wyk said. ●

A NEW SPIN ON AN OLD SECTION, “WHAT WE’RE READING” IS NOW A PEEK INSIDE THE MINDS OF THE NIH SCIENTIFIC COMMUNITY. HERE, WE HIGHLIGHT COMMENTARIES RECENTLY PUBLISHED THAT CHALLENGE THE SCIENTIFIC STATUS QUO.

NIA: THE INTERNEURON HYPOTHESIS OF AMYOTROPHIC LATERAL SCLEROSIS, *BRAIN*

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder that affects the motor neurons—so, unsurprisingly, much of the research in the field has focused on these neurons. However, motor neurons might not tell the whole story. Interneurons, which connect sensory and motor neurons, have been shown to be damaged in people with ALS, particularly in their primary motor cortexes. Neurophysiological data also show that impaired functioning of inhibitory cortical interneurons may be responsible for cortical hyperexcitability—a common feature of ALS. It’s not entirely clear why these interneurons are being damaged in people with ALS. One theory is that the overfiring of excitatory neurons has the downstream effect of exhausting the inhibitory capabilities of the interneurons. Another potential explanation is that there’s a genetic component to more directly leading to interneuron death. Mechanisms aside, it’s become clear that interneurons play a significant role in ALS pathogenesis. (NIH author: B.J. Traynor, PMID: 40179249)

[BY AMELIA MARVIT, NIAID]

OIR: EQUIPPING AI FOR UNBIASED AND INCLUSIVE NEUROLOGY, *JAMA NEUROLOGY*

As artificial intelligence (AI) becomes increasingly integrated into medicine, it is essential that the data used to train these systems reflect the full diversity of the population. To advance personalized medicine and achieve truly individualized outcomes, AI must include outlier populations such as children, elderly adults, racial and ethnic minorities, and individuals facing economic or social disadvantages. Neurologists and other clinicians are essential partners in this effort.

Without their direct involvement in developing and validating AI tools, machine learning models, and large language models,

there is a real risk that these underrepresented groups will be excluded from the knowledge base these technologies rely on. This can lead to care shaped by technologies that fail to recognize their own limitations and may generate inaccurate or biased outputs to fill informational gaps. By involving medical experts and ensuring inclusive, representative data, AI can move toward more equitable, informed, and effective health care for all. (NIH author: N.F. Schor, PMID: 39585712)

[BY KAMRYN CREGGER, NIAID]

ONR: THIS IS THE MOMENT: ADVANCING FOOD IS MEDICINE THROUGH RESEARCH, *AMERICAN JOURNAL OF CLINICAL NUTRITION*

Food insecurity is a driver of obesity, diabetes, and cardiovascular disease. As a cornerstone of health, nutrition plays a critical role in preventing disease and promoting wellness. ONR is addressing these challenges through coordinated, cross-agency efforts.

For example, one project is evaluating the impact of medically tailored food pantries for patients with cancer; others look at prescriptions for produce and videoconference-based cooking classes. Many of these projects assess cost-effectiveness and the majority are randomized clinical trials. The NIH, in partnership with the *All of Us* Research Program, is also supporting the largest national investment in nutrition research, Nutrition for Precision Health.

Given the complex factors influencing nutrition-related conditions, a multidisciplinary, cross-sectoral research approach is vital—an effort in which the NIH plays a central role. The goal is to generate publicly accessible data that can inform targeted, affordable, and accessible nutrition strategies to prevent disease, reduce metabolic risk, improve overall health, and enhance quality of life at both individual and population levels. (NIH authors: N.J. Jury, E.G. Guillen, and A.A. Bremer, PMID: 39900117)

[BY KAMRYN CREGGER AND AMELIA MARVIT, NIAID]

ASD and a real-world data platform

Bhattacharya said he, at the request of the president and HHS Secretary Robert F. Kennedy Jr., will create a research program to gain a better understanding of the etiology of the autism spectrum disorders (ASD).

Bhattacharya said NIH will launch a real-world data platform. The NIH and CMS have since publicly announced a partnership to use electronic health records (EHRs) and claims data from Medicare and Medicaid recipients. HHS also plans to use Veterans Administration EHRs, private sector EHRs, and government and private industry genetics data, pharmacy records, and environmental exposures data.

“The idea would be that somewhere between 10 to 20 groups of researchers from across the country would be able to ask questions using methods ranging from basic science to epidemiological approaches to other more applied approaches to ask what causes autism and how best we can treat and manage autism so that so many millions of families have an easier time dealing with the problems caused by having an autistic child,” he said.

5 Major Aims: Building Blocks to Improving Health

Bhattacharya presented his blueprint for the future of biomedical research. Following is a short review of the five major aims discussed at the meeting.

1) **Improve population health:** Chronic diseases such as obesity, diabetes, and heart disease will be addressed through the Make America Healthy Again (MAHA) initiative. “We have to find better ways to prevent, treat, and cure chronic diseases,” he said.

2) **Ensure reliable results:** The NIH will restore replication and reproducibility of research by rewarding scientists who participate in replication efforts at the R01 funding level, by launching a replication studies journal, and by instilling replication as a core activity of the NIH.

3) **Make big advances:** “We have seen the graying of the scientific workforce with the age of the first large grant moving from mid-30s to the mid-40s.” He said it is time to ask big questions to realize the possibility of giant advances and cures for diseases, and he noted that it is “time to swing for the fences with bold ideas.”

4) **Maintain safety and transparency:** Noting the COVID-19 pandemic and gain of function research, Bhattacharya said, “I am going to make sure that with congressional efforts and efforts by the administration to regulate the research that we do, that we meet the highest ethical standards and do not endanger human populations in the conduct of research itself.” NIH and HHS have since launched the Generation Gold Standard universal vaccine platform.

5) **Encourage academic freedom:** NIH must foster a culture in which scientists can express disagreement respectfully, he noted, adding that “scientific progress depends on the right for researchers to dissent against scientific dogmas and the NIH will work to make sure that intramural researchers have this kind of academic freedom and that we encourage the same kind of academic freedom with the external scientific community.”

New approach methods for preclinical safety testing, changes in grant funding, and the restructuring of the NIH and HHS were among the topics discussed during the Q&A session that followed his presentation.

“The NIH absolutely must address the key health needs of the country,” Bhattacharya concluded. “Every inch of the federal government is under scrutiny and of course the NIH is not exempt. The mission of the NIH will continue as we navigate these challenges. At the end of all of this, the NIH will be a stronger institution that fosters scientific discussion and debate and advances new technologies and new ways of thinking that will meet the mission better than we currently are.” ●



CREDIT: CHIA-CHI CHARLIE CHANG

READ LONGER ARTICLES AND
VIEW MULTIMEDIA ONLINE AT
<https://irp.nih.gov/catalyst/33/3>



Bhattacharya and his newly appointed leadership team toured the NIH campus in April to learn about our mammoth biomedical enterprise.

The group toured the Clinical Center and Building 10, the Roy Blunt Center for Alzheimer's Disease and Related Dementias Research (CARD), the Children's Inn, and visited labs and scientists.

All photos by Chia-Chi Charlie Chang



Stadtman Investigators

Meet 17 New Stadtman Investigators

BY THE NIH CATALYST STAFF

SLOWING BLINDNESS PROGRESSION, UNDERSTANDING THE MOLECULAR, cellular, and genetic drivers of cancer development, applying decision science in clinical settings, and preventing hearing loss and balance disorders are just a few examples of the exciting research being conducted by the latest cohort of scientists selected for the Earl Stadtman Tenure-Track Investigators Program.

The Stadtman program, which began in 2009, is named for renowned biochemist, senior investigator, and mentor Earl Stadtman (1919–2008), who devoted his 57-year NIH career to identifying the mechanisms of cellular energy expenditure and metabolism.

The program crosses all areas of biomedical and behavioral research, designed to attract a diverse group of talented early-career scientists who might not typically apply to NIH via general searches conducted by individual institutes and centers (ICs).

Here, the NIH Catalyst introduces the 17 Stadtman Investigators who joined various NIH ICs in 2022 and in 2023.



MUSTAPHA ABUBAKAR, M.D., PH.D.

ICO: NCI-DCEG Integrative Tumor Epidemiology Branch

Website: <https://irp.nih.gov/pi/mustapha-abubakar>

Research interests: Applies computational pathoepidemiology to explore how tissue ecosystem disruption drives the etiology, natural history, tumor heterogeneity, and clinical outcomes of screening-detectable cancers.

Learn more: PMID: 40210131;
PMID: 33952648

Became Stadtman Investigator in 2022.



STANLEY ADORO, PH.D.

ICO: NCI-CCR Experimental Immunology Branch

Website: <https://irp.nih.gov/pi/stanley-adoro>

Research: Researches the mechanisms of immune cell dysfunction and blood cancers with a focus on the role of proteome stress sensing and resolution in blood cell development, immunity, and leukemogenesis.

Learn more: PMID: 39789376;
PMID: 38352301

Became Stadtman Investigator in 2022.



ANGELA BALLESTEROS MORCILLO, PH.D.

ICO: NIDCD Section on Sensory Physiology and Biophysics

Website: <https://irp.nih.gov/pi/angela-ballesteros>

Research: Explores how mechanoelectrical transduction channel complex and sensory inner ear hair cell physiology effect hearing loss and balance disorders.

Learn more: PMID: 35921424;
PMID: 30063209

Became Stadtman Investigator in 2022.



ERIC DANG, PH.D.

ICO: NIAID Molecular Mycology and Immunity Unit

Website: <https://www.niaid.nih.gov/research/eric-van-dang-phd>

Research: Researches the microbiology and immunology of host colonization by fungi, in particular, exposure to the skin, gut, and lung tissue barriers.

Became Stadtman Investigator in 2022.

**JINANI JAYASEKERA DEVADOSS, PH.D.**

ICO: NIMHD Health Disparities and Decision Sciences Laboratory

Website: <https://irp.nih.gov/pi/jinani-jayasekera>

Research: Applies mathematical modeling and decision sciences to develop individualized interventions that could help reduce disparities and improve breast cancer care.

Learn more: PMID: 36455167; PMID: 34251881
Became Stadtman Investigator in 2022.

**DIPTAVO DUTTA, PH.D.**

ICO: NCI-DCEG Integrative Tumor Epidemiology Branch

Website: <https://irp.nih.gov/pi/diptavo-dutta>
Research: An 'omics researcher who explores the genetic etiology of cancers, primarily focusing on genome-wide association studies and the downstream analysis to identify molecular and 'omic targets.

Learn more: PMID: 35501419;
PMID: 38671320

Became Stadtman Investigator in 2022.

**AMIRAN DZUTSEV, M.D., PH.D.**

ICO: NCI-CCR Laboratory of Integrative Cancer Immunology

Website: <https://irp.nih.gov/pi/amiran-dzutsev>

Research: Explores the role of the gut microbiome in cancer susceptibility and outcomes, especially as it relates to immune function.

Became Stadtman Investigator in 2022.

**TIARNÁN KEENAN, BM BCH, PH.D.**

ICO: NEI Division of Epidemiology and Clinical Applications

Website: <https://irp.nih.gov/pi/tiarnan-keenan>

Research: An expert in age-related macular degeneration (AMD) who has noted AMD consists of multiple partially distinct diseases and is working toward better diagnoses and treatments to slow progression to blindness.

Learn more: PMID: 39025435;
PMID: 38657840

Became Stadtman Investigator in 2023.

**MARDO KÕIVOMÄGI, PH.D.**

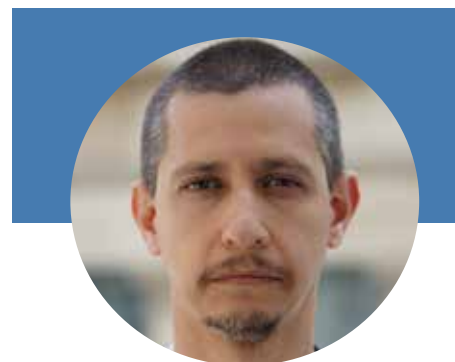
ICO: NCI-CCR Laboratory of Biochemistry and Molecular Biology

Website: <https://irp.nih.gov/pi/mardo-koivomagi>

Research: Takes a multidisciplinary approach to build quantitative models of the cell cycle and develop cancer-specific therapeutic strategies that target key interactions during cell division.

Learn more: PMID: 40174666;
PMID: 30982746

Became Stadtman Investigator in 2022.

**AUGUSTIN LUNA, PH.D.**

ICO: NLM Computational Biology Branch

Website: <https://www.nlm.nih.gov/research/researchstaff/LunaAugustin.html>

Research: Conducts pan-cancer, specific cancers, and rare cancer analyses via mechanistic and statistical computational models that involve gene regulation, genomic alterations, proteomics, and metabolism to varying degrees to better understand the network properties of human disease.

Became Stadtman Investigator in 2022.

STADTMAN INVESTIGATORS

CONTINUED FROM PAGE 17



LICHUN MA, PH.D.

ICO: NCI-CCR Cancer Data Science Laboratory

Website: <https://irp.nih.gov/pi/lichun-ma>

Research: Seeks to understand the intrinsic biology of liver cancer by integrating cutting-edge single-cell spatial 'omics assays with machine learning approaches to identify therapeutic vulnerabilities for effective cancer interventions.

Learn more: PMID: 31588021; PMID: 37725716
Became Stadtman Investigator in 2022.



FRANCIS O'REILLY, PH.D.

ICO: NCI-CCR Center for Structural Biology

Website: <https://irp.nih.gov/pi/francis-oreilly>

Research: Visualizes and describes how proteins are organized by using cross-linking mass spectrometry and other proteomics-based technologies combined with cryo-electron microscopy to functionally characterize protein interactions to understand their molecular relevance to human health and cancer.

Became Stadtman Investigator in 2022.



MARGARET RODGERS, PH.D.

ICO: NIDDK Ribonucleoprotein Assembly Section

Website: <https://www.niddk.nih.gov/about-niddk/staff-directory/biography/rodders-margaret>

Research: Uses single-molecule methods to understand the molecular mechanisms guiding assembly of essential RNA-protein complexes, or ribonucleoproteins, and how disruptions contribute to disease.

Learn more: PMID 37116495; PMID: 31761536
Became Stadtman Investigator in 2022.



VASSILIKI SALOURA, M.D., PH.D.

ICO: NCI-CCR Thoracic and GI Malignancies Branch

Website: <https://irp.nih.gov/pi/vassiliki-saloura>

Research: Explores the mechanisms through which protein methylation mediated by protein methyltransferases and demethylases drives oncogenesis, therapy resistance, and immune evasion in squamous cell carcinoma of the aerodigestive tract, with a special focus on human papilloma virus-negative head and neck squamous cell carcinoma.

Learn more: PMID: 37463106; PMID: 39310755
Became Stadtman Investigator in 2022.



BLAKE WARNER, D.D.S., PH.D.

ICO: NIDCR Salivary Disorders Unit

Website: <https://irp.nih.gov/pi/blake-warner>

Research: Combines genomics, spatial biology, and clinical research to understand pathogenic immune-epithelial interactions, uncover novel mechanisms, and develop targeted therapies for diseases associated with salivary gland dysfunction, including Sjögren's disease and immune checkpoint inhibitor-associated sicca.

Learn more: PMID: 38527764; PMID: 38016469
Became Stadtman Investigator in 2022.



URBAIN WEYEMI, PH.D.

ICO: NCI-CCR Developmental Therapeutics Branch

Website: <https://irp.nih.gov/pi/urbain-weyemi>

Research: Explores cancer biology by mapping redox and metabolic changes associated with genomic instability in tumor cells.

Learn more: PMID: 40208791; PMID: 36724254
Became Stadtman Investigator in 2022.



HAOYU ZHANG, PH.D.

ICO: NCI-DCEG Biostatistics Branch

Website: <https://irp.nih.gov/pi/haoyu-zhang>

Research: Explores the genetic architecture of breast cancer subtypes by creating or applying Mendelian randomization and polygenic risk score methods.

Learn more: PMID: 32424353;

PMID: 37749244

Became Stadtman Investigator in 2022. ●

The Stadtman Tenure-Track Investigators Program application cycle typically runs from August 1 through September 30.

Learn more online at <https://irp.nih.gov/careers/trans-nih-scientific-recruitments/stadtman-tenure-track-investigators>.

JOIN US!

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

Interested?
Email us at
catalyst@nih.gov.



CREDIT: DONA JONES, NINR

Jennifer Jabara, a nurse educator, has supported the simulation program for more than six years through the use of innovative nursing education, interprofessional simulation, and evidence-based, multimodal teaching strategies.

An example of such collaboration is a two-day nursing training course, “Essentials in Pediatric Nursing: Care of the Acute/Critically Ill Child,” which brings together skilled critical care nurses in adult medicine, who have no pediatric experience, with skilled pediatric nurses so that they can learn from one another.

One of the outcomes Jabara is proud of in interprofessional simulation is the meaningful debriefing sessions that follow each clinical simulation.

“When we are able to simulate high-risk, low-volume scenarios that allow providers to walk away from the debrief with new insight into the way their interprofessional colleagues think, [with] policies that drive practice, and with a reminder that we are all coming to the table to do the best we can for our patients every day—that is truly powerful,” Jabara said. “Our participants go forth in their clinical care even more prepared and confident, something our patients deserve every time they step foot inside Building 10 [where the Clinical Center is located].”

The simulation team has enhanced pediatric acute and critical care nursing education and training by creating four pediatric simulations, according to Patricia Todd, a pediatric clinical nurse specialist

in the CC Nursing Department. This approach provides a learning experience in which learners from different nursing areas share their knowledge and experiences to gain confidence in caring for the clinically deteriorating child in a supportive and collaborative environment.

The 1-NW Pediatric Unit and the CC Simulation Program have had several successful collaborations. Helen Mayberry, program director of the Nursing Professional Practice in the NIH CC Nursing Department, highlighted one such case. She said that the simulation program enhanced neuroscience nursing training for staff by integrating high-fidelity simulation with an innovative training methodology for a Neurological Clinical Decision Aid Tool.

“Since 2020, we have focused on Dr. Gilman’s vision, developing and expanding a coordinated program that serves all ICs,” said Gómez. “The next goal is to create opportunities for simulation-based research, taking advantage of being in the best place in the world to accomplish this goal.” ●

The NIH CC Simulation Program is available to all NIHers. If interested, access the Simulation Program website through the Clinical Center intranet, under Resources for Patient Care and Clinical Care Resources, look for the Request to Partner in Simulation link, which will take you to a brief survey, and the Simulation Team will reply.

U.S. DEPARTMENT OF HEALTH AND
HUMAN SERVICES
National Institutes of Health
Building 1, Room 160
MSC 0140
Bethesda, Maryland 20892

FIRST-CLASS MAIL
POSTAGE & FEES PAID
DHHS/NIH
Permit No. G-802
Publication No. 25-6250

Official Business
Penalty for Private Use \$300

 Printed on at least 20% recycled content paper
and can be recycled as office white paper.

CATALYTIC REACTIONS?

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.

**READ LONGER ARTICLES AND
VIEW MULTIMEDIA ONLINE AT**
<https://irp.nih.gov/catalyst/33/3>

PHOTOGRAPHIC MOMENT



CREDIT: THE NIH CATALYST

SPRING HAS SPRUNG! SEASONS CHANGE AND WITH THAT COMES NEW BEGINNINGS. The NIEHS North Carolina campus is bustling with new life all around Lake Discovery, the little-known gem nestled between NIEHS and its Environmental Protection Agency neighbor. From baby geese to sprouting shrubs, April showers really did bring May flowers...and four new furry little friends. ●

The NIH Catalyst is published
bimonthly for and by the NIH
Office of Intramural Research.

Address correspondence to:
Building 1, Room 160, NIH
1 Center Drive
Bethesda, MD 20892

phone: 301-201-1106
email: catalyst@nih.gov

Read the *NIH Catalyst* online:
<https://irp.nih.gov/catalyst>

PUBLISHER
NINA F. SCHOR
Deputy Director for Intramural Research, OD

EDITORS
JANICE LEE
Clinical Director, NIDCR
Deputy Director for Intramural Clinical
Research
RICHARD S. CHADWICK
Scientist Emeritus, NIDCD
CHRISTOPHER WANJEK
Director of Communications, OIR

MANAGING EDITOR
JENNIFER L. HARKER

COPY EDITOR
SHAUNA ROBERTS

CONTRIBUTING WRITERS
JOHN CARLO J. COMBISTA,
KAMRYN CREGGER, AMELIA
MARVIT, ELIZABETH MCMAHON,
SEPPIDEH SAMI

RESEARCH BRIEFS
MELANIE BARKSDALE, CASEY CARGILL,
TAYLOR FARLEY, HILLARY HOFFMAN,
ABIGAIL HOLDER, MEAGAN MARKS

PHOTOGRAPHERS/ILLUSTRATORS
DONA JONES

EDITORIAL ADVISORY BOARD
DAN APPELLA, NIDDK
TREVOR ARCHER, NIEHS
TOM BURKLOW, CC
JEAN LUD CADET, NIDA
KELVIN CHOI, NIMHD
MICHAEL ESPEY, NCI
MICHAEL GOTTESMAN, NCI
AUDRAY HARRIS, NIAID
BRADLEY MOSS, OD-ORS
ROLAND OWENS, OD
HYUN PARK, NCI
JULIE SEGRE, NHGRI
GISELA STORZ, NICH
WEI YANG, NIDDK