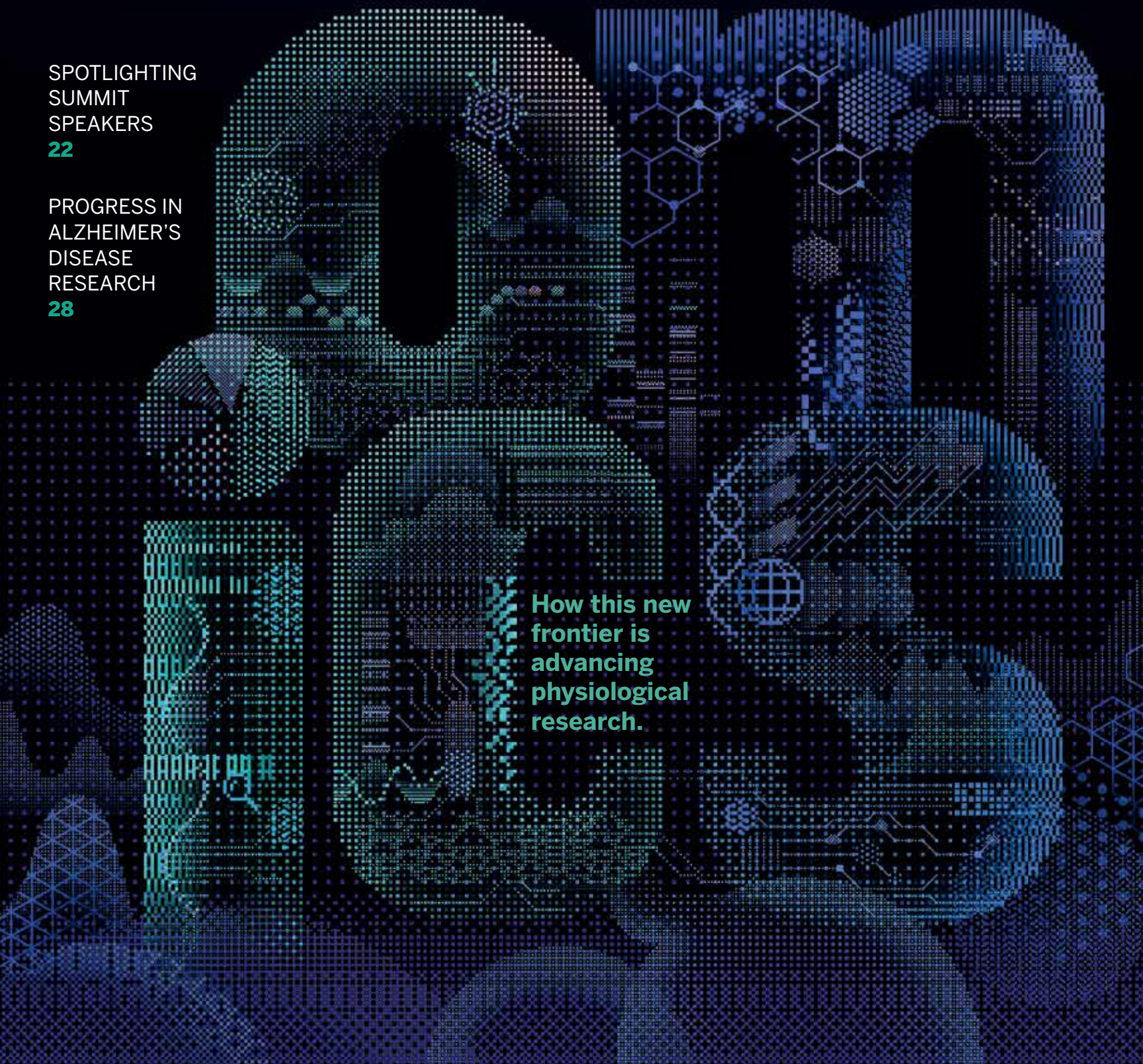
THE Physiologist MAGAZINE

JANUARY 2025



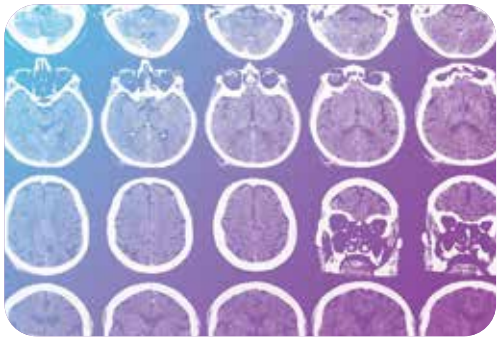
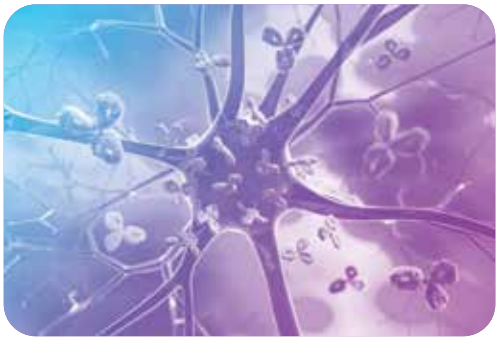
How this new frontier is advancing physiological research.

aps
women's health
research initiative

Raising the Visibility of Women's Health Research

Explore our active cross-journal calls for papers on key women's health research topics.

Alzheimer's Disease • Autoimmune Diseases • Breast Cancer • Cardiovascular Disease
HRT and Menopause • Migraines • Novel Perspectives on Sex as an Investigative Variable
Pregnancy and Postnatal Conditions

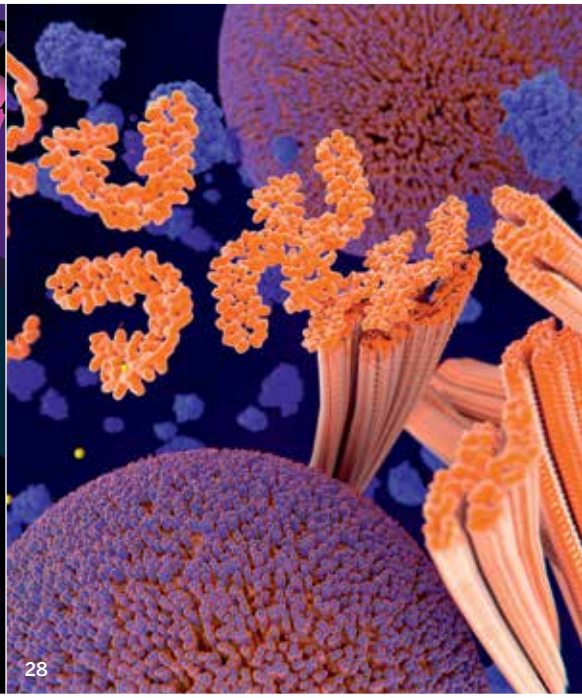




Learn more and submit at journals.physiology.org/womens-health-research-initiative.

CONTENTS

FEATURES

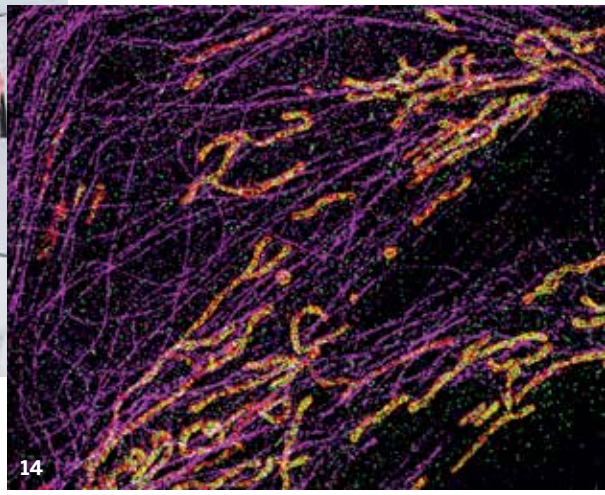


Cover illustration by Phil Wheeler

CONTENTS

DEPARTMENTS

12



14

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40

center for physiology education
AN APS INITIATIVE

Elevate the way you teach.

Connect with inspiring education research experts from around the world.

Learn practical tools to incorporate the core concepts of physiology into your curriculum.

Develop a network of life science educators at the undergraduate through medical school levels.

Join us for From Concept to Classroom, April 23–24 in advance of the American Physiology Summit. Register by March 15.

physiology.org/ConceptToClassroom

Keynote Session: "Homeostasis: The Dynamic Balance of Life"

Keynote speaker Mary Pat Wenderoth, PhD, University of Washington, is a physiology education researcher who has published a wealth of articles on student understanding in physiology and how the use of core concepts can enhance their learning.

A Season of Progress

BY MEEGHAN DE CAGNA, MSC, CAE

As we welcome 2025, this year begins with opportunities to reflect on recent achievements while looking to the year ahead. APS remains steadfast in advancing scientific discovery, advocating for the field of physiology and building a supportive community for researchers, educators and trainees. The Society is driving change across the scientific ecosystem, and we are excited for what the new year holds.

In 2025, the launch of the innovative Subscribe to Open (S2O) publishing model will ensure the APS family of journals continues to serve as trusted hubs for cutting-edge research and discussion. With initiatives like the Editorial Board Fellows program and the newly refocused *Comprehensive Physiology* journal, APS is shaping the future of scientific publishing. These efforts ensure that physiology remains at the forefront of global scientific advancements while providing opportunities for early-career researchers to thrive.

"The Society is driving change across the scientific ecosystem, and we are excited for what the new year holds."

We're equally proud of APS' advocacy for women's health through the Women's Health Research Initiative. This effort, ongoing through 2025, highlights conditions that predominantly affect women or affect them differently than men, addressing longstanding research gaps. Through dedicated calls for papers, events and curriculum development, we are helping to create a more equitable future in research and education. Throughout the year, you'll also see pages of this magazine (including this issue) dedicated to topics on women's health science.

In this issue, our feature article on Alzheimer's disease covers the latest progress in research while exploring the gender gap. Nearly two out of three people with Alzheimer's disease in the U.S. are women, and scientists aren't entirely sure why. But estrogen likely plays a role—learn more on page 28.

Another cutting-edge topic is omics. Our article on page 16 explores how physiologists are learning how to use vast amounts of data to follow their curiosity and advance science.

As we gear up for the American Physiology Summit, April 24–27, in Baltimore, we offer a special look at three primary Summit speakers on page 22. You'll hear more about our keynote speakers and this year's Cannon Award winner, which is the most prestigious honor APS hands out. I can't wait to hear more from these amazing scientists at this year's Summit.

This year also marks a new chapter for *The Physiologist Magazine* as we welcome Amanda Bertholf as our new editor-in-chief. As the Society's director of communications, Amanda brings a wealth of expertise in magazine publishing and a new perspective to our publication. Under her leadership, we aim to continue our coverage of groundbreaking research, amplify our members' voices and continue delivering the high-quality content our readers rely on. Please join me in welcoming Amanda to the helm as we look forward to an exciting year ahead. And as always, you can reach out to me at **tphysmag@physiology.org**.

Meeghan De Cagna, MSc, CAE, is APS chief program officer and associate publisher of *The Physiologist Magazine*.

THE Physiologist MAGAZINE

VOL. 68 | JANUARY 2025

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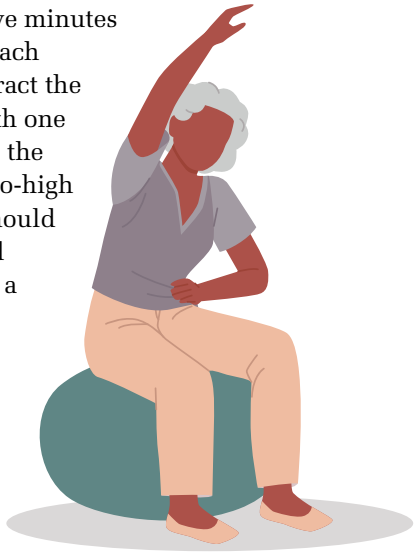
The Physiologist Magazine (ISSN 0031-9376) is published six times a year by the American Physiological Society (APS), 6120 Executive Blvd., Suite 575, Rockville, MD, 20852-4911.

APS EXERCISE CONFERENCE ABSTRACT

Brief Daily Exercise May Offset Dementia

Engaging in just seven to 10 minutes of light-to-moderate exercise—or three to five minutes of moderate-to-high intensity exercise—each day after age 60 may significantly counteract the cognitive decline typically associated with one year of aging. This minimal effort adds to the recommended 150 minutes of moderate-to-high intensity physical activity older adults should aim for weekly. The study was conducted on adults ages 60 to over 80 who lived in a nursing home. The people who were less active had more than triple the risk of cognitive dysfunction than those who participated in some form of exercise daily. The findings stress the importance of regular physical activity—even in the oldest populations—to help preserve cognitive function as we age.



Source: **Mehdi Kushkestani, et al. "Cognitive Function in Nursing Home Residents: A Potential Role of Physiology Activity in Counteracting Age-related Impairment." Integrative Physiology of Exercise, 2024.**

APS EXERCISE CONFERENCE ABSTRACT

Females Heal Faster than Males after Muscle Injuries

More than 65 million people in the U.S. experience muscle injuries each year. Depending on the severity of the injury, not everyone recovers fully. Biological sex can be a factor in healing; inflammation and the development of fibrosis varies by sex.

New research found that female mice recovered 50% to 60% more quickly than male mice from injury to the gastrocnemius muscle in the leg. Sex hormones and other sex-related proteins and genes involved in the inflammatory response may play a role in the time differences in healing.

"By understanding the difference between males and females in the healing process, medical professionals can give personalized treatment plans," says Matthew Kostek, PhD, first author of the study.

Source: **Matthew Kostek, PhD, et al. "Muscle Fibrosis and Regeneration, Females Recover Faster." Integrative Physiology of Exercise, 2024.**

All images: iStockphoto

APS*SELECT* HIGHLIGHTS

The Latest Research from APS Journals

Original research articles chosen for APS*select* have been recently published in one of 10 APS research journals.

Mouse study finds hypertension disrupts normal nighttime blood pressure, dipping in both sexes.

doi.org/10.1152/ajpheart.00131.2024

Research in mice finds the diabetes medication empagliflozin reduces fatty liver. Findings may improve treatment for nonalcoholic fatty liver disease.

doi.org/10.1152/ajpgi.00029.2024

Research suggests older adults with mild cognitive impairment showed greater resistance to brain blood flow than those without cognitive dysfunction.

doi.org/10.1152/japplphysiol.00337.2024

A study shows that people with constipation and hypertension have a higher risk of major cardiac events.

doi.org/10.1152/ajpheart.00519.2024

APS EXERCISE CONFERENCE ABSTRACT

Examining the Emotional Response to Exercise

Less than 30% of people living in the U.S. meet the recommended guidelines for physical activity, even though they know it's good for them. Understanding why people don't meet the guidelines is important to reverse the trend. New research explored how emotional response to exercise correlates with the type of physical activity they prefer.

Adult volunteers participated in exercise activities or watched videos of people exercising at varying intensities. Facial expression recognition software analyzed the participants' positive or negative responses during the activity. The volunteers also ranked their favorite exercise activity and preferred intensity. Among the findings: Women were more positive about lower exercise intensity and tended to choose the treadmill over an exercise bike. Women also were

more positive about physical activity overall. "This [study] could help to tailor exercise prescriptions to exercises that participants 'like' to encourage them to continue," says first author Alexis Jones, PhD.

Source: **Alexis Jones, PhD, et al. "Emotional Response to Varying Exercise Intensity: Impact of Gender and Age Differences." Integrative Physiology of Exercise, 2024.**

APS EXERCISE CONFERENCE ABSTRACT

Older Adults Drink Less, Aren't as Thirsty in the Heat

New research showed clear age differences in when and how much water people drink in a hot environment, with older adults lagging behind younger counterparts. Volunteers stayed in a hot, humid room for four hours and did 10 minutes of light exercise every hour. They could drink as much water as they wanted and were asked to rate how thirsty they were before each drink. The oldest group (ages 66 to 88) didn't drink until around 38 minutes, reported lower thirst levels than the younger group (ages 18 to 39), and drank insufficiently to replace their sweat losses.

Lower thirst and delayed hydration could be physiological, explained first author Thomas Deshayes, PhD, but it could also be due to concerns about frequent bathroom trips. Talking to older adults to learn about their daily activities and habits can help keep them hydrated in the heat, Deshayes says.

Source: **Thomas Deshayes, PhD, et al. "Age-related Differences in Fluid Intake during Heat Exposure." Integrative Physiology of Exercise, 2024.**

A case study of the World's Strongest Man shows that his leg muscles are almost double the size of a typical man's.

doi.org/10.1152/japplphysiol.00342.2024

Research finds blood lactate levels fluctuate after eating and older people have less lactate activity.

doi.org/10.1152/ajpendo.00183.2024

Mouse study finds mom's thirdhand exposure to e-cigarette vapor affects offspring's lung and bone marrow immune cells.

doi.org/10.1152/ajplung.00078.2024

Beetroot juice before exercise may aid aerobic capacity and recovery in late post-menopausal women.

doi.org/10.1152/ajpregu.00150.2024

LAB NOTES

Megan K. Rhoads, PhD

Julie K. Freed, MD, PhD

MENTORING Q&A | TRANSITION TO FACULTY

Setting Yourself Up for Success

Advice on how to create a stimulating, successful lab environment.

Each issue, we ask a student or early-career member to pose their career questions to an established investigator and mentor. Here, **Megan K. Rhoads, PhD**, an instructor in the Division of Nephrology, Department of Medicine, at the University of Alabama at Birmingham, asks **Julie K. Freed, MD, PhD**, how young faculty can set themselves up for success. Freed is executive vice chair, director of clinical research and associate professor of anesthesiology at the Cardiovascular Center at the Medical College of Wisconsin.

Illustrations by Kagan McLeod

Q: What skills do you think young scientists should try to grow as they transition from student to faculty?
A: Aside from the obvious skills, which include scientific writing and experimental design, it's critical that young scientists learn how to mentor and run a research program and laboratory. Up until an individual becomes faculty, their success mainly stems from their own personal effort and quality of work. As a principal investigator, your success now depends on how well others perform. You need to be a good listener, handle issues with professionalism and motivate everyone around you to give you their absolute best.

Q: How can young faculty set themselves up for success in their first job in academia?
A: My best piece of advice is to find a group of peers you can lean on for help and advice when you need it. I belong to a wonderful "research neighborhood" that includes four to five investigators who all study human vascular function. We share equipment and resources, which helps to keep costs down, but more importantly, we mentor each other. It's comforting to know I can pick up the phone or walk down to their office and ask for advice, whether it be scientific or otherwise.

Now I know it's hard to believe, but being an investigator has many challenges, and having people to lean on makes all the difference.

"It takes time to create a strong research program. I often tell people in my lab 'slow is steady and steady is fast.' In other words, just keep inching forward and eventually the results will be there."

Q: What are your most important takeaways for being a great mentor?
A: I find that I learn just as much (maybe more) from the mentee as they learn from me. This is a two-way street, and the mentee and I set expectations for each other right away. I don't think of a trainee as cheap labor but an opportunity for me to help shape someone's career trajectory. My hope is some day when I'm old and gray one of my former trainees will reach out and thank me for having a positive impact on their life!

Q: What do you wish you knew earlier?
A: Sometimes you just need to be patient. Be urgent about making the effort, but be patient about seeing the results. I remember during the first few years of having my lab I wondered why graduate students and postdoctoral fellows weren't knocking down my door wanting to join my lab. It takes time to create a strong research program. I often tell people in my lab "slow is steady and steady is fast." In other words, just keep inching forward and eventually the results will be there.

Q: How do you envision the field of physiology changing in the future? What can we do to retain great minds in our field?
A: The thing about physiology is we will need investigators who study function at all levels (whole organism, organ, tissue, cellular) for as long as humans exist. Technology is advancing faster than we can imagine, and we need to make sure physiologists are able to keep up. As chair of the Translational Physiology Interest Group, I also feel compelled to say we need to make every effort to translate our work to humans. Unfortunately, only roughly 10%–20% of what we discover in preclinical models is found to be true in human beings, which leads to the first "valley of death" in translational research. As for retaining great minds, we need to do everything possible to create a stimulating, supportive, inclusive and fun environment for all. I can't imagine doing anything else, and my wish is for others to feel the same.

Got a career question you'd like to submit? Email it to tphysmag@physiology.org. We may use it in an upcoming Mentoring Q&A.

STATS & FACTS

7 million

The number of Americans living with Alzheimer's disease in 2024.

Alzheimer's Association

The genomic sequencing of one tumor creates two terabytes of data, the same as 1,000 hours of video.

Center for Connected Medicine

31

The number of new genes researchers identified in 2022 that appear to affect biological processes known to be at play in Alzheimer's disease.

Nature Genetics

Between 2000 and 2021, deaths from heart disease decreased 2.1%. Deaths from Alzheimer's disease increased 141%.

Alzheimer's Association

FROM EXPERIENCE | SHARING SCIENCE

Talk to Strangers

When it comes to science, making yourself a little uncomfortable can lead to growth. This might include things such as presenting at a conference or talking to a group of undergraduate students or visiting professors. "That's helpful because it teaches you how to explain science in a non-scientific manner," says Brian Shariffi, a graduate assistant and PhD candidate in the Department of Nutrition and Exercise Physiology at the University of Missouri in Columbia. "It's important for scientists to expose themselves to all these different areas because wherever they go, whether it's academia, industry or wherever, they're going to be interacting with people. And it's crucial to not only know how to do the science but also how to translate the science—a lot of people don't understand the language we speak." And the best way to do that is to get out there and start talking.

Share your best advice, leadership tip or productivity hack with us at tphysmag@physiology.org.

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POLICY IQ | ANIMAL RESEARCH

Communicating about Animal Research

Workshop provides tools to improve conversations about the importance of animal research.

Communication on research involving animals has long been a fraught topic. The dialogue among opponents of animal research, researchers and the public has oscillated between openly hostile to ineffective or nonexistent. In recent years, public polling has shown that the scientific community has an opportunity to improve public perception on animal research by providing more context. This requires the research community to participate in an open dialogue with the public regarding research that involves the care and use of animals.

The National Academies of Sciences, Engineering and Medicine (NASEM), capitalized on this opportunity by convening a workshop called "Effective Communication with the General Public about Scientific Research that Requires the Care and Use of Animals" in December 2023. APS members, as well as the former chair of the APS Animal Care and Experimentation Committee, Jeff Henegar, PhD, and APS Science Policy Manager Alissa Hatfield, participated on the planning committee for the workshop. APS member Bill J. Yates, PhD, FAPS, spoke at the event.

"The workshop highlighted the problems we face to effectively communicate about animal research," Henegar says. "It provided excellent tools for understanding and overcoming those problems."

The workshop convened 27 presenters and over 530 participants, including academic and industry researchers, veterinarians, educators and communications specialists. The large number and diversity of participants indicates a broad interest in improving communications on this topic.

The workshop addressed public opinion regarding animals involved in research; interactions with the media, science writers, nonscientists and institutional leadership; challenges and opportunities in communicating about research activities involving animals; and openness in communication. The workshop proceedings can be read at **bit.ly/NASEMWorkshop**.

While most researchers may not do media interviews about animal research, many will talk with friends and family. The workshop emphasized that all these interactions benefit from the researcher being open to a two-way dialogue and can improve public understanding.

"The event reiterated the complex communication skills needed to communicate about animal research to avoid a message being lost or misconstrued," Yates says.

Send questions or comments to tphysmag@physiology.org.

Animal Research Talking Tips

- Be proactive
- Be open
- Start with your goals
- Provide context
- Be authentic
- Listen, empathize and be respectful
- Prepare ahead of time
- Be direct
- Be concise
- Exit gracefully

STATS & FACTS

1994

The year a team of researchers coined the term "proteome," although initial studies that could be considered proteomics were published nearly 50 years ago.

Chemistry of Life Processes Institute

The lifetime risk for Alzheimer's at age 45 is 1 in 5 for women and 1 in 10 for men.

Alzheimer's Association

8

The number of drugs available for treatment of Alzheimer's disease.

Alzheimer's Association

"Identical twins often develop different characteristics, even though they carry the same sequence of DNA nucleotides. How can this be? The answer lies in epigenomics."

Laura Bonetta, PhD, in *Nature*

UNDER THE MICROSCOPE | HUMAN PERFORMANCE

Flying High

A developing love for science led to a career studying human performance in extreme environments.

Christopher M. Hearon Jr., PhD, is an assistant professor at the University of Texas Southwestern Medical Center and the Institute for Exercise and Environmental Medicine. His research investigates the mechanisms of vascular and autonomic dysfunction in patients with heart failure, obesity and hypertension.

"My most memorable findings have come from 'wait … what?!' moments when you observe the opposite of what you hypothesized."

Hearon's research relates to human health and performance in extreme environments, including altitude and simulated spaceflight. Here's what he shared with us:

INSPIRED YOUNG. One of my earliest childhood memories was creating a homemade science fair experiment with my father to test whether acceleration due to gravity was dependent upon the mass of an object. Remarkably, we found little variation in acceleration due to gravity for objects of different masses (unpublished observations, San Antonio Science Fair, 1995).

FINDING A CAREER. I didn't seriously consider a career as a scientist until very late in my undergraduate education. There wasn't a single moment of inspiration, but rather the gradual realization that I genuinely enjoyed learning about biology and the basic sciences. The people who stirred my passion for learning and science were all professors and scientists. Their example inspired me to continue to graduate school and eventually to pursue a career as a scientist.

EVERY DAY IS DIFFERENT. My favorite part of my job is the diversity of projects I contribute to. I've been to the Andes mountains, the summit of Mount Everest (simulated) and experienced the weightlessness of microgravity during parabolic flight. I've had the privilege of working with some of the most amazing people, ranging from elite athletes to patients with rare conditions. Some days are spent running on the treadmill testing pilot protocols, tinkering in the lab or working at the bench, while others are spent reading, writing, teaching and traveling.

Hearon floats in simulated microgravity during parabolic flight.

FEELING FAINT. For one of my investigations, we wanted to provide volunteers with short video demonstrations of how to execute various stressor protocols to help standardize instruction and provide reassurance that the stressors were nothing to be feared. Since it was my study, I volunteered to be filmed performing the protocols. One of the protocols involved a cold pressor test—submerging my hand in ice water—which can be quite uncomfortable. Pushing through a long day, I skipped lunch to keep filming. The scene was set, the camera was rolling and as I placed my hand in the ice water, I felt all the classic symptoms of a vasovagal response wash over me. Luckily, my lab mates sprang into action to rescue me, while the camera kept rolling. The video of me passing out during the cold pressor test did not make the final cut, as it wouldn't have been too reassuring for our prospective volunteers!

UNEXPECTED FINDINGS. The biggest misconception, not only of physiology but science broadly, is that most progress comes from a steady stream of "aha!" moments where your hypothesis was proven correct. My most memorable findings have come from "wait … what?!" moments when you observe the opposite of what you hypothesized.

Do you know someone we should meet? Email us at tphysmag@physiology.org and tell us more.

Courtesy of Christopher M. Hearon Jr., PhD

PUBLISH WITH POLISH | METADATA

3 Types of Metadata You Should Know About

Persistent identifiers give research a unique label.

Publishing experimental results in a journal article drives researchers forward. Dissemination of those data is just as, if not more, important. How do we guarantee that the information is getting where it needs to go? How do we ensure proper credit is given? Metadata, or data about data, gives publishers and authors the leverage to do those things and more. This may take the form of persistent identifiers (PIDs). Metadata and PIDs are like clothing labels that tell you where your favorite shirt was made and how to care for it. Here are three types of PIDs you should know about:

1. ORCID

What: Most authors are familiar with ORCID, or Open Researcher and Contributor ID. ORCID provides a means of attributing research outputs to a unique identity, distinguishing people with similar names.

How: An author's ORCID record allows them to keep track of all publications and prevents name changes from splitting up a publishing record into subgroups of name variants. ORCID identifiers also facilitate broad-reaching linkage of an author's works across multiple databases, such as PubMed, Scopus, Web of Science and others.

Need to know: APS journals require corresponding authors enter an ORCID at the time of submission. Obtaining an ORCID is easy and free of charge, and all authors are encouraged to obtain one.

iStockphoto

2. Research Organization Registry (ROR)

What: ROR is like an ORCID but for institutions. We ask authors to carefully select their affiliation details, so we have accurate data on where they performed the research.

How: Many universities want to know where their scientists are publishing and whether they are publishing open access. The ROR ID becomes even more important for APS authors in 2025 under our Subscribe to Open (S2O) business model.

Need to know: APS is providing an open access publishing guarantee to all 10 primary research journals for corresponding authors from institutions that subscribe to the APS Digital Library or to all seven *American Journals of Physiology* (AJP) journals for corresponding authors from institutions that subscribe to AJP Consolidated. We will use ROR to identify those authors who will receive automatic CC BY licensing. Authors should make sure to apply the correct ROR ID at the time of submission.

3. Open Funder Registry (OFR, formerly FundRef)

What: OFR is managed by Crossref, the nonprofit behind digital object identifiers. (DOIs are the GOAT of PIDs.)

How: Just like universities want to know where their researchers are publishing, so do funders. Funders use these metadata to catalog where their award recipients are publishing and to confirm compliance with funding mandates. For example, National Institutes of Health (NIH) funding requires adherence to the NIH Public Access Policy, and NIH does check for compliance.

Need to know: Recently, APS deployed an automation that will flag content for delivery to the NIH Manuscript Submission system or the European counterpart, Europe PMC plus, aiding authors with the power of metadata.

Send questions or comments to tphysmag@physiology.org.

STATS & FACTS

1907

The year Alois Alzheimer described the first patient with a presenium dementia. His pupil, the Italian neurologist Perusini, provided the first autoptic description of an Alzheimer's brain, reporting the presence of abnormal fibrous inclusions within the perikaryal cytoplasm of neurons and miliary foci, subsequently known as neurofibrillary tangles and amyloid plaques, respectively.

Physiological Reviews

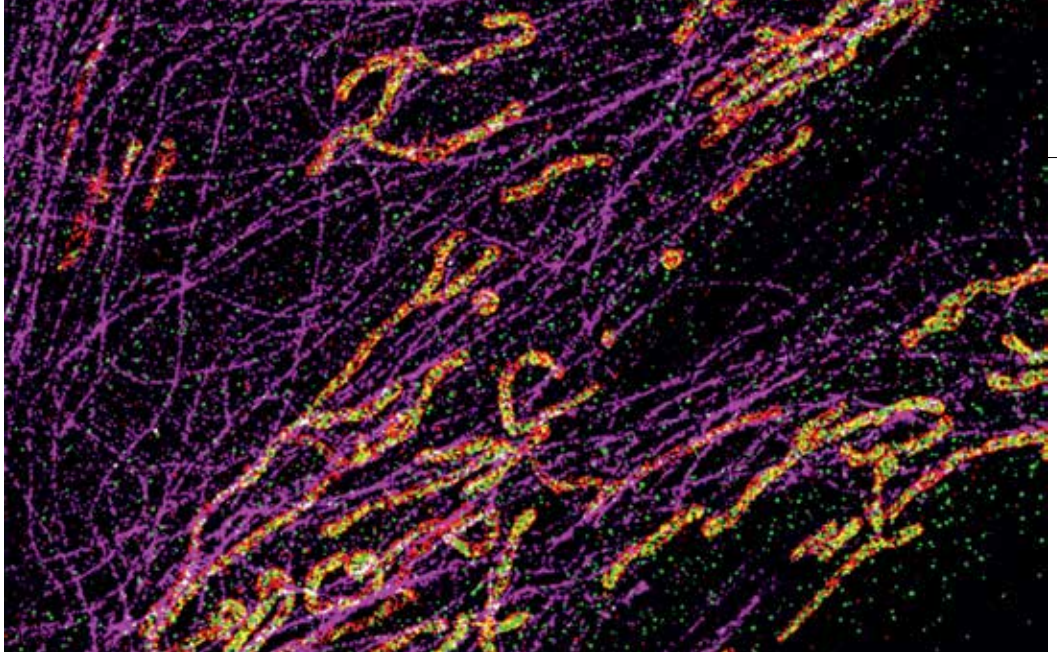
"The complexity in proteomics makes it a challenge. That's why it takes so long to get the complete proteomes for every organism, because proteins change a lot depending on conditions."

Aleksandra Nita-Lazar, PhD, co-chair of the National Institutes of Health's Proteomics Scientific Interest Group, in an interview with *JAMA*.

93%

The percentage of the human proteome that has been identified—with 18,407 proteins identified, from an estimated 19,750 proteins that the human genome encodes.

Human Proteome Organization



Multi-color STORM imaging using a single fluorophore.

Unveiling the Invisible

Revolutionary imaging methods expose cellular secrets.

Xiaowei Zhuang, PhD, is an investigator at Howard Hughes Medical Institute and the David B. Arnold Professor of Science at Harvard University. Her groundbreaking imaging methods—including stochastic optical reconstruction microscopy (STORM) and multiplexed error robust fluorescence in situ hybridization (MERFISH)—have facilitated unprecedented nanoscale insights into cellular structures and previously unknown organization of cells in tissues.

How did you become interested in developing new imaging methods?
I am a physicist by training and first encountered advanced imaging during my postdoctoral training. I remember the first time I saw an image of single molecules. Each molecule produced light that looked like a twinkling star; it was mesmerizing.

After establishing my own lab at Harvard University, I became very interested in studying biomolecules in their native context—in living cells. I wanted to do things like observe how virus particles enter cells by interacting with cellular machinery. However, because a virus is smaller than the diffraction limited resolution of light microscopy, which is a few hundred nanometers, it appears like a blob under the microscope. Many cellular structures are likewise blurred by this diffraction limit. This motivated me to develop imaging methods that could overcome this resolution limit, and we went on to develop STORM.

How does STORM work, and what discoveries has it made possible?
STORM is a super-resolution microscopy method that uses the time dimension to separate images of molecules that are otherwise inseparable in space. Our group and others have used it to study a variety of subcellular structures both in cultured cells and in brain tissues. For example, we identified a previously unknown structure in neurons, which we named membrane-associated periodic skeleton. This structure, which is made of ring-like actin filaments connected by the protein spectrin, had not been seen before because these filaments were not resolvable with a traditional diffraction-limited light microscope.

We were stunned by this beautiful structure when we first observed it. Through a series of subsequent studies, we discovered many molecular components and crucial functions of this structure, information that has made a significant impact on our understanding of the cell biology of neurons.

What is MERFISH, and how does it achieve genome-scale imaging?
MERFISH achieves genome-scale imaging by error-robust barcoding, combinatorial labeling and sequential imaging. We assign error-robust barcodes to individual genes, physically imprint the barcodes onto RNAs of these genes using a library of DNA probes, and then read out these barcodes bit by bit with sequential imaging. This method can identify and quantify thousands of RNA transcripts simultaneously within individual cells, providing a comprehensive view of gene expression patterns.

Previously, to image multiple genes, you could label them with different color probes, but doing this at a genome scale would require labeling thousands of genes with thousands of different colored probes,

PLoS ONE. doi:10.1371/journal.pone.0101772

which obviously is not possible. Alternatively, one could use multiple imaging rounds, one gene per round, to image multiple different genes, but imaging thousands of genes with thousands of imaging rounds is also very challenging.

"I remember a period of time when I thought about this problem every night. Then one night, it just clicked, and I figured out how to do it."
—Xiaowei Zhuang, PhD

I remember a period of time when I thought about this problem every night. Then one night, it just clicked and I figured out how to do it. Using the combinatorial strategy I described allows the number of genes imaged to grow exponentially with the number of imaging rounds. It then took us a few years to overcome practical challenges in the implementation of this idea and produce genome-scale images of individual cells with high accuracy.

What insights have been made possible with MERFISH?
Among the fundamental questions are: How many different types of cells are there in our body? And, how are these cell types organized, and how do they interact to give rise to tissue and organ functions?

The spatial organization of various cell types is critical to how they function together, and one of the major applications that we've used MERFISH for is to construct the cell-type atlas for complex tissues, in particular the brain. MERFISH can be used to image individual RNA molecules, determine their identities, and hence determine the gene expression profiles in individual cells within intact tissue. This can be used to determine the cell-type identity of each cell and map their spatial organization.

Soon after we developed MERFISH, we applied it to the preoptic region of the hypothalamus in collaboration with Catherine Dulac's lab at Harvard. We created a molecularly defined and spatially resolved cell atlas of this brain region, uncovering dozens of different cell types and their functional roles in controlling social interactions such as parenting, mating and aggression.

Recently, we reported the cell atlas of the whole mouse brain, which revealed thousands of transcriptionally distinct cell populations and their spatial organization and predicted cell-type-specific interactions between cells, providing a tremendously useful resource for neurobiology.

MERFISH not only provides genome-scale information for understanding cell type organization within organs, but also offers insights into subcellular organization, including the 3D organization of genomic DNA, which is crucial for gene expression regulation.

How do you collaborate across fields to advance this work?
The nature of our work is inherently interdisciplinary. For example, physics and chemistry are crucial for our development of imaging instrumentation and the design of molecule-specific labeling methods. The immense amount of data generated in genome-scale images requires computational innovation. Biological knowledge is fundamental for identifying important problems to study, extracting the knowledge from the data and developing methods that are important for understanding biological systems.

As someone with experience in physics, chemistry, biology and computation, I find all these aspects important and serve as a cohesive force within our lab. Drawing from my own multidisciplinary knowledge, I connect team members with different backgrounds to foster collaboration and learning, and I also encourage each one of them to become multidisciplinary themselves.

Interview conducted by science writer Nancy D. Lamontagne. Send questions or comments to tphysmag@physiology.org.

STATS & FACTS

220,945

The number of metabolite entries contained in The Human Metabolome Database, including both water-soluble and lipid soluble metabolites.

The Human Metabolome Database

"To me, the ability to determine the transcription profiles of individual cells within complex tissues like the mammalian brain and others is very exciting. It allows the comprehensive identification of all cell types in the respective tissue and ultimately the entire human organism. It also allows detailed analyses of how cellular transcription and cell state get derailed in disease."

Alexander Stark, PhD, senior group leader at the Research Institute of Molecular Pathology, Vienna, on the advancements in transcriptomics technology.

66

Total number of Alzheimer's drug trials.

National Institutes of Health

How this new frontier is advancing physiological research.

BY DARA CHADWICK

If you've ever stood at the ocean's shore, experiencing awe at its vastness while feeling the sand shift beneath your feet, you understand how physiologists working in omics sometimes feel. During the past two decades, new technologies have opened ever-changing pathways to vast quantities of molecular measurements and spawned a new era in physiological research.

"Omics" is the suffix used to describe scientific approaches that incorporate technologies like high-throughput sequencing and mass spectrometry to amass huge, searchable pools of data. Using omics, researchers can explore precise hypotheses by zeroing in on specific biological systems and cells. They can also follow their curiosity by querying and analyzing volumes of data to see where patterns and trends emerge.

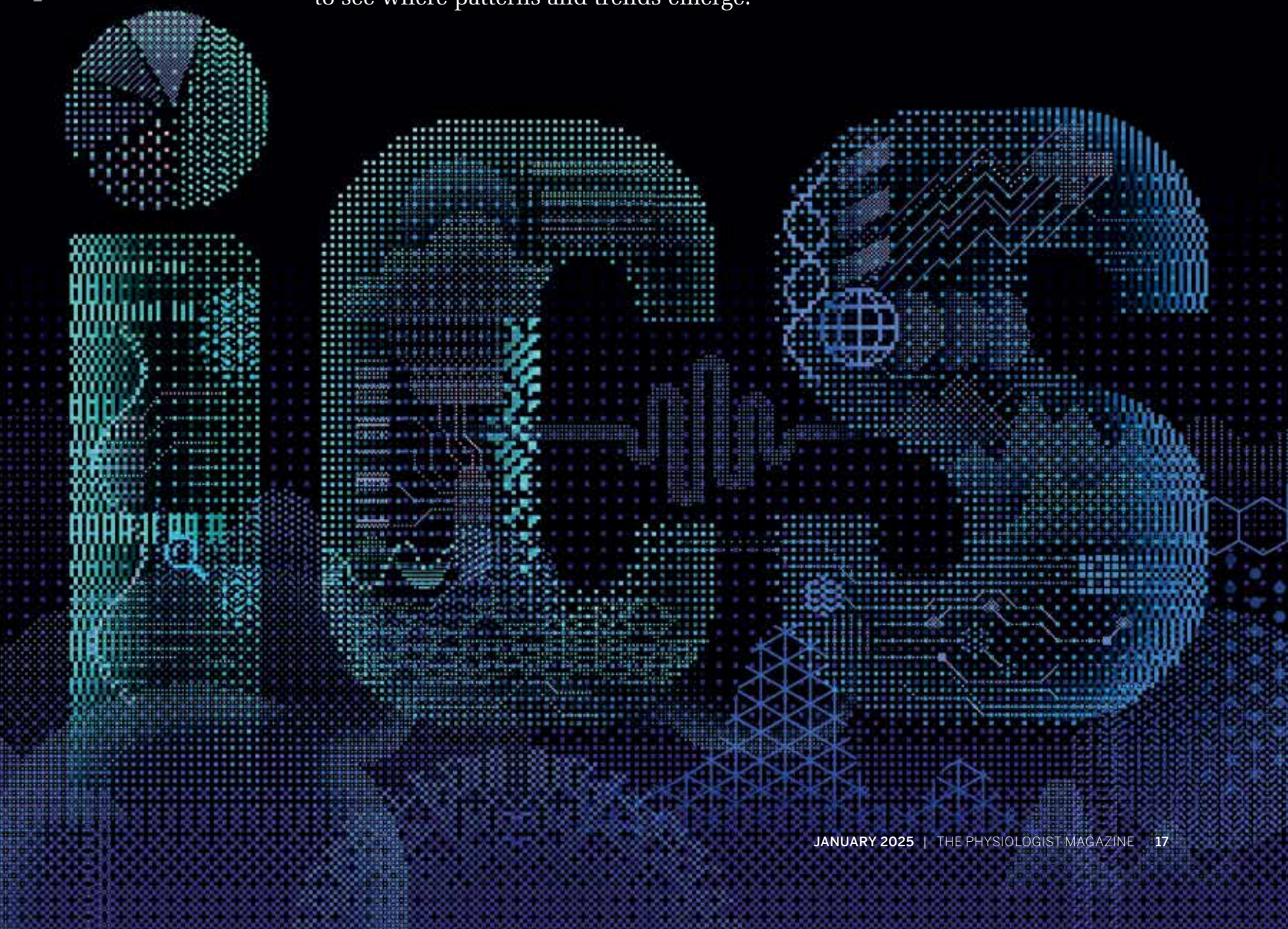
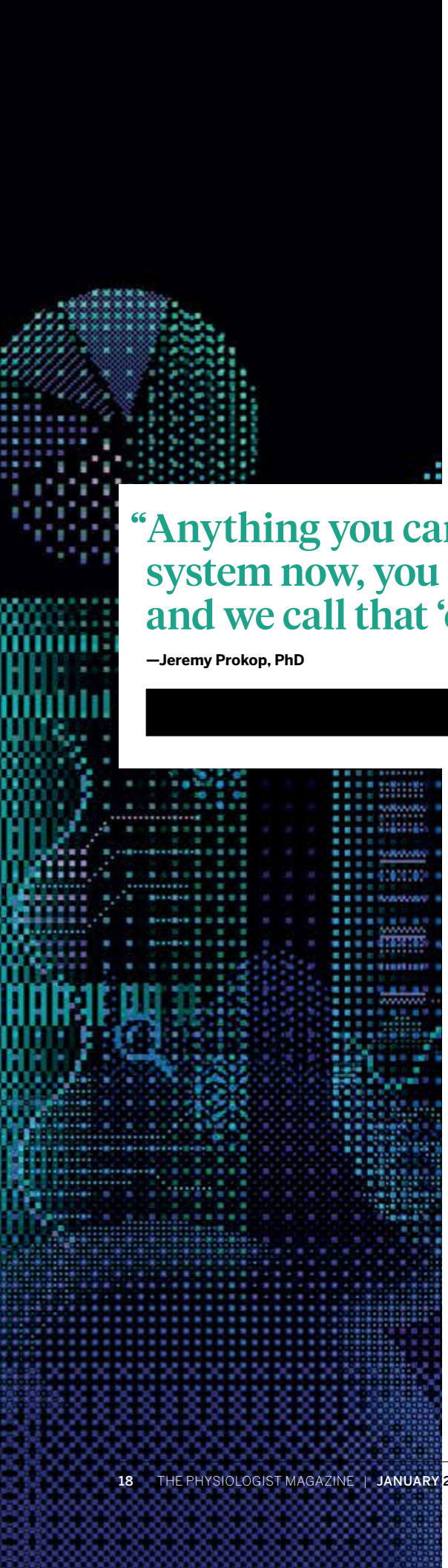


Illustration by Phil Wheeler



"Omics can be an incredible amount of information about one person, or it can be a whole bunch of information about many people," says Jeremy Prokop, PhD, data science adviser at Corewell Health in Grand Rapids, Michigan, and associate professor at Michigan State University College of Human Medicine. "Anything you can measure in a system now, you can look at in bulk and we call that 'omic.'"

> **"Anything you can measure in a system now, you can look at in bulk and we call that 'omic.'"**
>
> **—Jeremy Prokop, PhD**

But incorporating omics isn't as simple as opening a laptop and accessing a database for most physiologists, says Dennis Brown, PhD, FAPS, professor of medicine at Harvard Medical School and APS chief science adviser. "These giant datasets use sophisticated techniques, algorithms and artificial intelligence," he says. "You need experts in the field to guide you."

Where can physiologists find the data science expertise needed to embark on an omics approach? Start by exploring data science resources close to home. "You don't have to start from scratch," says Jasmine Plummer, PhD, director of the Center for Spatial Omics at St. Jude Children's Research Hospital in Memphis, Tennessee. "Dig into what's available in your community and apply physiology to it. Lean heavily on fields where you can find collaborators, but also work within your own university or academic environment."

HARNESSING BIG DATA'S PROMISE

There's no denying the potential of omics. As an example, Prokop cites the whole genome's role in exploring rare diseases. "We have 2 million individuals who have had their genome sequenced to date. I can look through all the genomes to see where variants occur commonly," he says. "Then, I can take your individual genome, scan it and see a change you have that we don't see commonly in the others, which might be the explanation of a rare disease."

These data are transforming personalized medicine. "As physiologists, we embrace phenotypic measurements like blood pressure, temperature and cytokine levels," he says. "Now, we're talking about incredible scale of medical record integrations. I've got a genome, a transcriptome, knowledge of your viruses and your clinical records for 20 years. As we look at these omic datasets, we start to find signals that converge, such as inflammatory states or certain gene signals."

These convergent signals tell a story, Prokop says. "AI and big data give us the ability to see how signals converge. Think of it like sonar: One ping doesn't really inform me about something, but multiple pings let me track movement. With omics, we have the potential to see all these incredible signals and how they merge."

Omics can also offer new cellular views. Gina Yosten, PhD, professor of pharmacology and physiology at Saint Louis University School of Medicine, uses spatial transcriptomics and spatial proteomics to study G-protein coupled receptors (GPCRs). Using spatial omics, which has emerged during the past five years, she and her team can understand how a cell's transcriptotype translates to its function in three-dimensional space.

"Often in anatomical studies, such as when we're staining with antibodies, we're looking at two dimensions. We're looking at just one slice of tissue and losing a lot of information," she says. "When we apply these large datasets to anatomy, we get all these rich data about where messenger RNA molecules are within a cell, which is important because location dictates function. We have access to techniques that tell us which cell contains each transcript and where it's located within the cell."

Ultimately, spatial omics could allow researchers to generate precise hypotheses about how the body may respond to different stressors. "It could tell us how cells might respond to different drugs, depending on their genetics and their transcriptotype," Yosten says.

Plummer uses single cell spatial omics to examine why cells move from a normal state to a disease state. She began her career in bulk genomics before moving into using technologies like RNA sequencing and ChIP-Seq—a combination of chromatin immunoprecipitation (ChIP) assays with sequencing—to perform epigenomic profiling.

"What we realized is that when you mush up an entire piece of tissue, what you get is a mixed signal," she says. "I was an early adopter of single cell omic biology. We took the same genomic techniques—bar coding and using a sequencer—and added new molecular tools to isolate the cells."

At St. Jude, Plummer and her team use spatial omics to examine isolated cells in situ to determine their function within a spatial context, as well as interactions between cells. "Maybe cells that are in the right place at the right time move along a normal trajectory," she says. "But if a cell is in the wrong place at the wrong time, maybe that moves you into a path of disease. Most diseases are within a tissue. I think a lot about how we're good at diagnosing cancer, but we can't link it to outcomes. You can diagnose a certain type of cancer and put a child on a certain type of treatment. One child might do amazing on that treatment and another child might not."

Differences in treatment response may occur because one cell has escaped treatment, she says. Identifying that rogue cell is where she sees the potential of spatial omics. "What was the surrounding environment that allowed that cell to escape?" she says. "What was it encased by?" Understanding the spatial context of cells may hold a critical key, she says.

Hilary Coller, PhD, professor of molecular, cell and developmental biology at the University of California, Los Angeles, and editor-in-chief of *Physiological Genomics*, uses next-generation and high-throughput approaches to understand how cells transition between proliferation and quiescence. "This transition is a critical aspect of normal physiology, and we

Omics in Space

Odette Laneuville, PhD, associate professor and director of the Biomedical Sciences Program at the University of Ottawa in Canada, studies the transcriptome. Her team explores how the composition of white blood cells in space travelers compares to white blood cells in deconditioned bed-ridden hospital patients.

She began studying the effects of microgravity through a head-down tilt bed-rest model study. Twenty healthy individuals stayed in bed for 60 days with their heads tilted down minus six degrees. "That's a model for microgravity because blood flows from the legs to the upper part of the body, which is what happens to astronauts in space," she says.

Laneuville used transcriptomics to analyze study participants and compare them to pre-flight, in-flight and post-flight blood samples from astronauts who spent six months at the International Space Station. Her goal was to find molecular mechanisms that may lead to deconditioning, both in space and on Earth.

She hopes to find predictors of physiological change, such as genes that may affect bone remodeling. "Bones in microgravity lose density. If I know the genes involved, I can find the predictors," she says.

These answers could help bed-ridden hospital patients by allowing clinicians to identify people with predictors of deconditioning, she says. They might also identify patients who are more susceptible to infection. Medical teams could act early to prevent progression of these conditions, Laneuville says.

Among the unanswered questions about space travel's effects on the human body is the full impact of gravitational force. It's a mystery, Laneuville says.

With omics, these answers may become available. A study published in the June 2024 issue of *Nature* highlighted a new database and sample repository from several SpaceX and NASA space missions. The Space Omics and Medical Atlas (SOMA) will include biomarkers that offer new insights into potential health impacts of spaceflight. Laneuville and her colleagues at the University of Ottawa are among an international team of researchers who contributed their expertise to the design of SOMA.

"These technologies are superb, but that's only half the story. ... People are realizing that you need creative, independent physiologists to interpret these data at the cellular, organ and whole-body levels."

—Dennis Brown, PhD, FAPS

think it's involved in pathophysiology," she says. She and her team have used mass spectrometry metabolomics to understand changes in cells' metabolism as they become quiescent. They've also used proteomics to examine what happens to chromatin when fibroblasts transition from proliferating to quiescent states.

Understanding this transition could help improve our clinical knowledge of how to treat cancer and chronic wounds. Coller credits omics with advancing this work. "There's been so much we've discovered that we just weren't going to figure out with hypothesis-based testing," she says. "There was no way I was going to be able to guess which genes went up with quiescence. It's a small fraction of the whole genome. Only when you see them in aggregate can you start to tease out patterns and consistencies."

MANAGING THE CHALLENGES

For all their research promise, omics aren't without challenges. One such challenge is data standardization. "If you're going to try to merge data generated by different people, there are some potential problems," Coller says. "There are stories about people thinking they saw something or that they had a great effect."

Coller shares an anecdote she heard about a research project in which the controls were run on one day and the experimental samples were run on a different day. While the differences between the experimental samples and the controls were found to be a result of day-to-day variability in technical procedures rather than differences between the experimental and control samples, hearing that story was an important reminder of the importance of rigor in experimental design, Coller says—especially when data are included in a common dataset.

In large datasets, methodological standardization across experiments isn't possible, according to Yosten.

"An animal in my lab is not the same as an animal in someone else's lab, even if it's the same species, age and sex," she says. "It's a living body of work and as we expand our datasets, we can capture the remarkable genetic diversity present within the human species."

What's more important to think about is standardizing *how* researchers share information—for example, by providing rich annotation. Yosten says that rather than simply sharing raw RNA transcript counts, for example, researchers should also share detailed information about the source of tissue samples, how cells were collected and which platform was used.

Another challenge of omics is the at-times overwhelming volume of available data. "These technologies are superb, but that's only half the story," Brown says. "Physiologists need to use these big datasets, even if we don't generate them ourselves, to interrogate physiological processes. That can be a daunting task because there are now hundreds of variations in identified genes. What is biologically significant? People are realizing that you need creative, independent physiologists to interpret these data at the cellular, organ and whole-body levels."

Yosten encourages physiologists to use omics data for both directed and undirected discovery. "You can test a hypothesis based on data you already have, and you can use it to confirm what you think is happening," she says. "You can also let the data determine the direction. You can use an unbiased analysis and see what emerges."

WHAT'S NEXT?

As new technologies and artificial intelligence change physiological research, it's natural to wonder how the physiologist's role may change. Prokop says physiologists are more important than ever in the omics era.

"Two hundred years ago, physiology was observational science," he says. "It was a lot of cadaver studies to learn how the body works. What omics is teaching us right now is the many ways we get disease states. It comes back to this idea of hypothesis design and observational science. Omics allow us to embrace a new age of observational science and apply it to clinical domains. We're back to the origins of physiology, and that's why I think physiologists are the greatest minds to think about this."

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PROFILES BY MIKE DE SOCIO

OPENING KEYNOTE

A Biologist Is Born

James Rothman, PhD, found himself questioning everything.

Nobel laureate James Rothman, PhD, grew up in a time so brimming with scientific inspiration, it almost felt like a foregone conclusion that he and his peers would aspire to be physicists. That is until an intervention from Rothman's father shifted his course slightly.

It was the 1950s, "a time in which the public was extraordinarily aware of science and technology," Rothman says. The Soviet Union shocked the world in 1957 when Sputnik launched as the first artificial satellite to orbit Earth. The space race that followed captured the imagination of Rothman and his young peers, who spent their adolescence building rockets and running to Radio Shack to grab the latest transistors. Some of the most admired people in society at the time—the likes of J. Robert Oppenheimer and Albert Einstein—were, not surprisingly, physicists.

"I can't really remember not being interested in science or not somehow knowing that I was going to be a scientist," Rothman says. "I always wanted to be a physicist, and the only thing that changed is I ended up being a biologist."

Rothman, who is now a Nobel Prize winner and the Sterling professor of cell biology and professor of chemistry at Yale University, followed his childhood interest in physics well into college. But his dad, a small-town pediatrician, insisted that his son take at least one biology course. Rothman resisted: He wanted to be a physicist—a category of scientist he held in high regard—not a biologist. But Rothman, whose dad was paying the tuition, didn't have much of a choice. He obliged and enrolled in a biology course. "I completely fell in love with it, and that was the end of physics," Rothman says.

There was something alluring about biology that hooked Rothman immediately. Whereas in physics you needed a high level of understanding to pose a meaningful research question, in biology "the questions just jump out of even the most elementary facts," Rothman says.

He found himself questioning everything, seduced by the inquisitive and accessible nature of this new field. "You could find your way into a lab and understand what they were doing in a matter of weeks, not a matter of years," he says.

Rothman loved it so much that he convinced the university to put him in a special program his senior year, where he could forgo traditional coursework and instead do research on biological membranes.

That work eventually led him to the research that would occupy his academic life through the 1980s and '90s. But first, Rothman would take a detour to Harvard Medical School—again at his father's insistence—before landing at Stanford in 1978 to start his own lab. It was there that he zeroed in on vesicles and conducted the work that earned him the 2013 Nobel Prize in Physiology or Medicine.

Rothman's award recognized his insights on vesicles, which transport molecules within and between cells. He showed that "vesicles fuse with specific surfaces in the cell so that transports arrive at the correct destination," as his Nobel Prize biography puts it.

But making such a discovery was no sure thing. From the very beginning of his inquiry, Rothman faced intense resistance from other scientists. He remembers approaching some of the top figures in his field to gather

After taking a biology course, "I completely fell in love with it, and that was the end of physics."

At left: iStockphoto; at right: © Nobel Media AB. Photo: A. Mahmoud

advice, with many of them responding with some version of, "Really? You really want to do that?"

Their skepticism was rooted in a prevailing view at the time that reconstituting transport processes in a test tube system, as Rothman was trying to do, was simply impossible. It would take many years, but Rothman proved those doubters wrong. His team was indeed able to reconstitute the vesicular transport process, providing important insights for large swaths of genetics and physiology.

The discovery is extremely valuable as a way of understanding a crucial process that takes place throughout the body. Rothman's research has illuminated how vesicles, and the neurotransmitters they carry, are involved in controlling functions as varied as "movement, perception, cognition, memory and mood," according to *Yale Medicine Magazine*.

Today in his lab, Rothman is continuing his focus on neurotransmitter release and the transport of molecules through vesicles.

But while the "fundamental machinery" is shared throughout the body, Rothman is fascinated by some key differences in the brain. For example, neurotransmitter release occurs in under one-one thousandth of a second, whereas in other parts of the body, that release is often measured in seconds or minutes. His lab is working to understand the mechanics of that "turbo charge" in the brain, as he calls it.

Physiologists will hear more about Rothman's current research when he delivers the opening keynote during the 2025 American Physiology Summit. He will give a deeper look into this neurotransmitter research, which he says will provide "a novel way of looking at the regulation of neurotransmitter release, and therefore, the regulation of synaptic physiology."

Beyond his own lab, Rothman is intrigued by other developments in the field of neurophysiology. In particular, he has his eye on biological condensates, also known as protein phase separation.

"It represents another biological level of organization of genetically encoded material," he says. Rothman is interested in how these condensates underlie immunological synapses—something the field is only just beginning to wrap its arms around, but which could provide a new platform for studying regulation and disease processes.

"There's a whole realm of physiology that's on the edge of being understood biochemically," he says.

CLOSING KEYNOTE

Focusing on Female Physiology

Holly Ingraham, PhD, had an early passion for science.

Holly Ingraham, PhD, was just a child the first time she peered down the eyepiece of a microscope and let her mind fill with wonder.

She had collected some water samples at a swampy pond in California's Bay Area suburb of Walnut Creek, then an uncrowded locale populated with pear orchards. When she slid the samples under the lens of an 1890 Bausch and Lomb microscope—a family heirloom from her great-grandfather—she was amazed to discover that all sorts of tiny things were moving around in a single droplet of water.

"I thought, 'This is really cool,'" Ingraham says. "I got intrigued."

She took that early passion for science through her years in high school,

where she was fascinated by the structure of DNA, and thrived in chemistry class, each experiment serving as a fun puzzle for Ingraham to solve.

In the decades since, Ingraham hasn't strayed very far from those interests. Today she is a professor of cellular molecular pharmacology at the University of California, San Francisco, where her research focuses on unlocking the secrets of female physiology.

"Most of what we think about in terms of female physiology is all centered around just reproductive issues … and in health, it all has been focused primarily on breast cancer," Ingraham says. "But we are missing many more dimensions in women's health, resulting from the dynamic and adaptive responses in female physiology across the lifespan."

Through her research, Ingraham is trying to broaden the focus and understand how hormone fluctuations throughout a female's life impact physiological systems, such as neuronal circuits in the brain.

She's especially proud of a July 2024 *Nature* article she co-authored, "A maternal brain hormone that builds bone." It outlines a newly discovered hormone that plays a role in strengthening bones for women who are losing calcium to produce breast milk.

She described the discovery as "one of those unusual moments in one's career," where things come together and "the science is beautiful and exquisite." But she got there almost by accident.

Ingraham and her lab started out trying to understand what estrogen signaling was doing in one region of the brain. They planned to use an EchoMRI machine to conduct experiments, but on this particular day the machine was broken, forcing them to pivot to use a DXA machine instead, which yields detailed information about bone density.

The bone density results were surprising to Ingraham, motivating her group to investigate why a sex-specific increase in bone density was observed. Following up on this tangent led to the discoveries published in the *Nature* article and has opened up a new research interest in her lab.

Ingraham, who is the recipient of the 2024 Federation of American Societies for Experimental Biology Excellence in Science Lifetime Achievement Award, will be sharing more about her work during a keynote address at the American Physiology Summit. She plans to walk through her brain-bone study and also talk about emerging research on how estrogen may increase gut sensitivity in females.

"Most of what we think about in terms of female physiology is all centered around just reproductive issues. … We are missing many more dimensions in women's health."

What excites her most is the way her current work is forcing her to look at multiple body systems at once—from the brain to the gut and the bones. This broader approach counters the tendency some physiologists have to focus only on their "favorite organ," she says.

"Afterall, physiology is the integration and control of multiple systems and there is much more to be discovered," she says.

CLOSING KEYNOTE

Neverending Discoveries

George A. Brooks, PhD, FAPS, has a full-circle moment.

When George A. Brooks, PhD, FAPS, received a call from APS recently, there were two pleasant surprises. First, he learned he was being honored as the recipient of the APS Physiology in Perspective Walter B. Cannon Award Lectureship, APS' highest honor.

The second surprise was more serendipitous: The person delivering the news was Timothy Musch, PhD, FAPS, who is not only the current APS president but was a student in Brooks' 1971 exercise physiology course.

It was a full-circle moment for Brooks—now a professor in the Department of Integrative Biology at the University of California, Berkeley—who has spent his academic career conducting research that would eventually "turn the whole field on its ear," he says.

Brooks came to physiology as a good, but not spectacular, college runner interested in learning more about how the body worked. "I tried very hard, and I guess I was OK, but I wasn't near as well as I wanted to be," he says of his athletic prospects. Instead, he turned his focus onto the science behind running and exercise.

His research quickly landed on lactate, something even the casual runner often hears about as a source of soreness and muscle fatigue. Brooks studied the molecule in rats and humans, and his discoveries soon began to cut against the traditional understanding of lactate, which had long been referred to as "lactic acid" and was generally seen as a waste product in the body. But Brooks' research indicated something different, a theory he would term "lactate shuttling" that saw the substance as a fuel crucial to many organs.

He also learned that lactate shuttling was occurring not just during exercise but during rest periods too. And he realized that the shuttles were traveling farther afield than previously imagined: from cell to cell, but also between organs in the body.

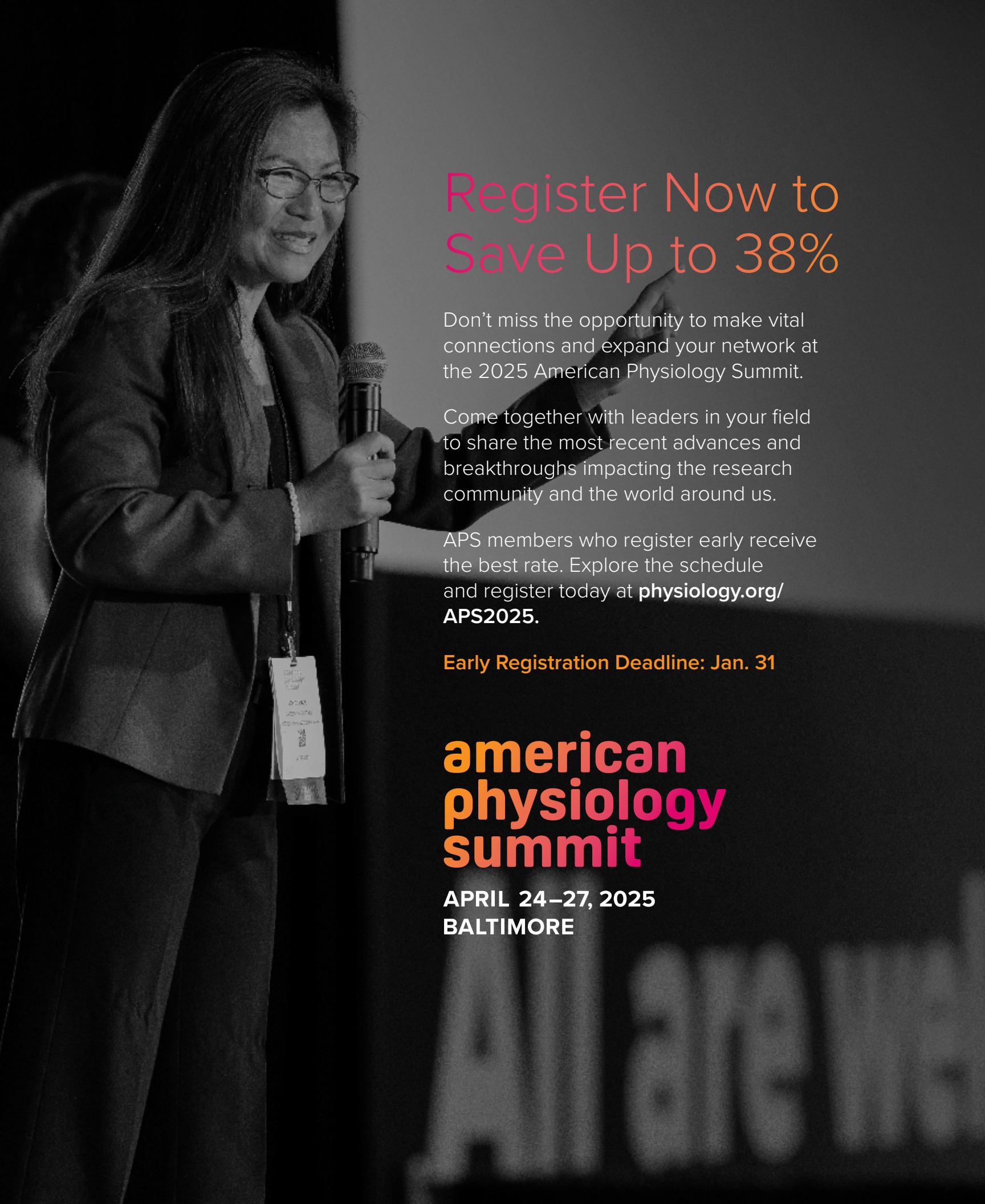
Other work by Brooks has focused on carbohydrate carbon flow, which occurs when humans eat carbs or especially when they exercise. He has studied how the mitochondrial network—a muscular system he calls the "energy highway"—allows that carbon to flow through the body.

Those discoveries continue to have big implications. Brooks collaborated with a neurosurgery team at UCLA to see how lactate shuttling could be used to aid recovery of traumatic brain injuries. Scientists are also investigating the potential use of lactate as resuscitation during heart failure. And early evidence suggests exercise may have a role in preventing or minimizing age-related dementia, which ties back to Brooks' research. "It might be that lactate is the fuel, but it's also a signaling molecule," he says.

Brooks will present his Physiology in Perspective lecture at the 2025 American Physiology Summit. He plans to share a history of his research, tracing the course of discovery of the lactate shuttle and mitochondrial biogenesis.

Reflecting on his career and the Cannon Award, Brooks is thankful for his many collaborators, which include students, colleagues, mentors and administrators. "I need to especially acknowledge all the people that helped me along the way," he says. "Nobody does anything [alone] anymore—it's not like Einstein's thought experiments."

George A. Brooks, PhD, FAPS, will present a closing keynote, the **Physiology in Perspective Walter B. Cannon Award lecture**. He will share a history of his research, tracing the course of discovery of the lactate shuttle and mitochondrial biogenesis. Learn more at **physiology.org/Brooks**.



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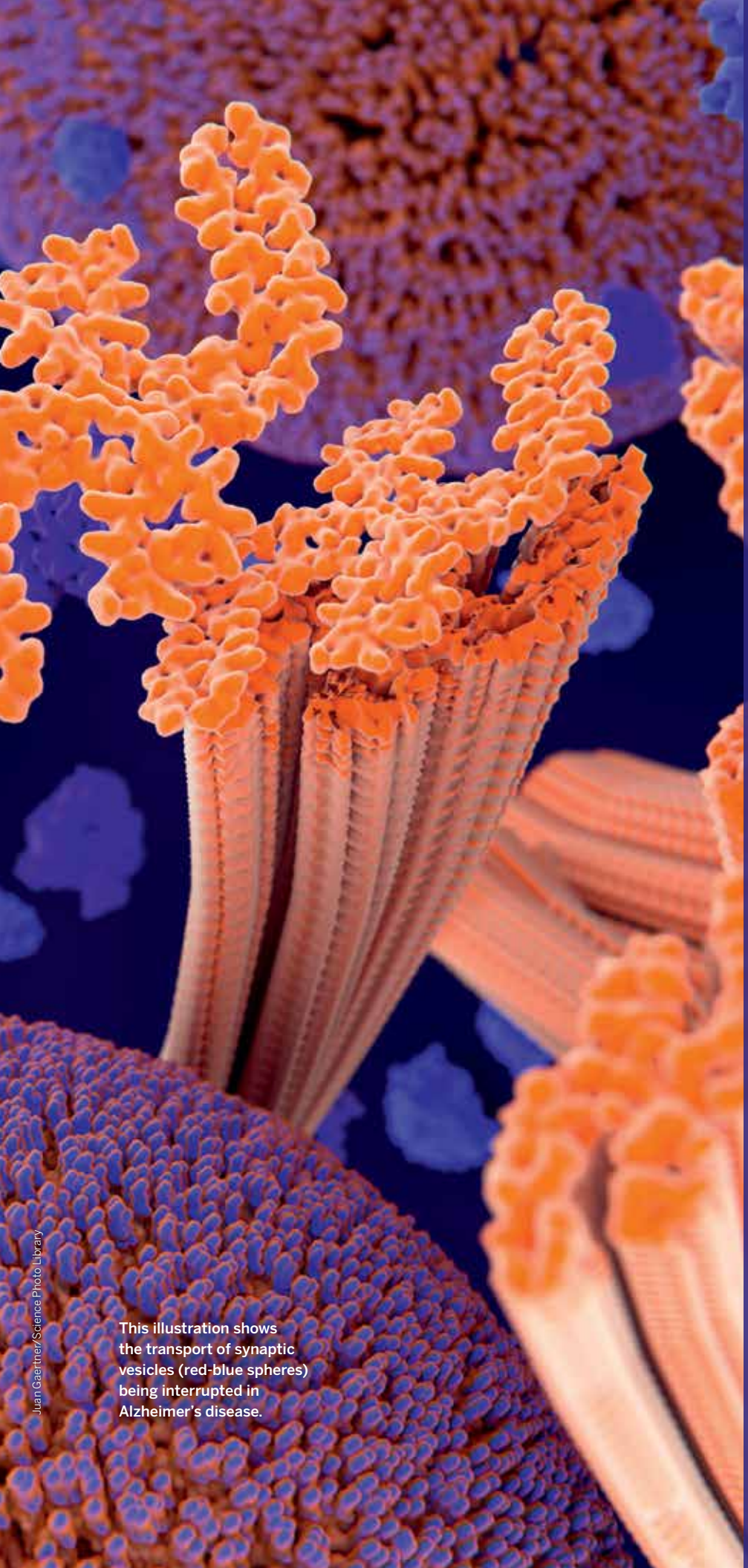


Juan Gaertner/Science Photo Library

This illustration shows the transport of synaptic vesicles (red-blue spheres) being interrupted in Alzheimer's disease.

Researchers are making great strides to diagnose, treat and understand Alzheimer's disease.

BY TYLER SANTORA

Just five years ago, there was very little you could do if you were diagnosed with Alzheimer's disease. You could try physical or cognitive therapy or a medication to manage symptoms. But you couldn't stop the disease from progressing. Now, monoclonal antibody treatments offer the first hope at slowing the development of Alzheimer's disease, a brain disorder in nearly 7 million Americans that causes memory loss and eventually the inability to carry out simple tasks.

"Patients can confidently feel that they're doing something about a disease that previously all they could do was try to manage symptoms as best as possible," says Gregory Jicha, MD, PhD, a professor of neurology at the University of Kentucky College of Medicine. "That's a fundamental game-changer."

> "It's going to be an incredibly different place, where Alzheimer's remains a problem, but a chronic disease problem that is fully manageable with appropriate diagnosis and treatment."
>
> —Gregory Jicha, MD, PhD

Researchers have also made enormous progress in diagnosis. Before the early 2000s, Alzheimer's disease could only be confirmed after death with autopsy. In the past couple of decades, however, scientists have developed ways to diagnose the disease by analyzing positron emission tomography (PET) scans and cerebrospinal fluid. But these tests are costly and resource-intensive—and most people would rather not have a spinal tap.

Simple blood tests for Alzheimer's disease have revolutionized diagnosis since becoming clinically available in 2023. In addition to making it possible to screen large swaths of people, blood tests can also identify those with preclinical Alzheimer's, meaning they're in the very early, pre-symptomatic stages of the disease. Once these people are identified, clinicians can target them for lifestyle interventions. Clinical trials are even investigating whether the new monoclonal antibody treatments could delay or even prevent disease development in people with preclinical Alzheimer's. And that's just the beginning.

"I'm so excited about where we're going to be 10 years from now," Jicha says. "It's going to be an incredibly different place, where Alzheimer's remains a problem, but a chronic disease problem that is fully manageable with appropriate diagnosis and treatment."

BLOOD BIOMARKERS

There are two major proteins that Alzheimer's experts are concerned with: beta-amyloid and tau. In people with Alzheimer's disease, beta-amyloid proteins clump together to form plaques that damage neurons and disrupt their communication. Levels of tau are often also increased in the Alzheimer's brain, where they form tangles inside neurons and block communication.

New tests can accurately detect high levels of beta-amyloid and tau in the blood, years before a person develops Alzheimer's symptoms. Because the tests are new, however, they may not be widely available, and not all insurance companies cover them. Experts expect that blood biomarker tests will become more accessible soon.

For now, positive blood test results require a cerebrospinal fluid test or PET scan to confirm diagnosis. More data over the near future will confirm the validity of the blood tests, determine which of the available tests is the most accurate, and assess how they're being used clinically.

"In the next year or two, these will be much better understood," Jicha says. "Our confidence in the ability to use them as less invasive and less costly biomarkers for the disease is going to become commonplace in medical practice."

For now, clinicians are mostly using blood tests to determine whether an older person's cognition issues are due to Alzheimer's so that they can receive treatment. Soon, though, they could be used to detect people with preclinical Alzheimer's so they can be offered preventive interventions.

"It's a lot easier to preserve brain function than recover it after you've lost neurons, so that's why people are really interested in using blood tests to look early," says Jill Morris, PhD, an associate professor of neurology at the University of Kansas Medical Center and director of the University of Kansas Alzheimer's Disease Research Center Developmental Projects Program.

Experts are also excited about the possibility of using blood tests to detect less infamous proteins that contribute to Alzheimer's and related diseases. "There are so many other proteins circulating, and we're getting more of a sense of what's existing in the blood at certain times during disease processes," says Rachel Buckley, PhD, an associate professor of neurology at Massachusetts General Hospital and Harvard Medical School.

ANTI-AMYLOID TREATMENTS

Although experts don't know what causes Alzheimer's disease, there is a predominant theory: the amyloid hypothesis, which states that the

disease is caused by accumulation of beta-amyloid in the brain. Because of this theory, researchers have been trying for the past 30 years to develop a therapy that targets beta-amyloid.

In 2021, they succeeded, with the first anti-amyloid therapy, aducanumab (Aduhelm), being introduced in the U.S. Although Aduhelm has since been discontinued by its manufacturer, two more anti-amyloid therapies have been added: donanemab (Kisunla) and lecanemab (Leqembi). These intravenous therapies work by removing beta-amyloid from the brain at different stages of plaque formation. They are monoclonal antibody therapies, or lab-made antibodies that bind to a specific disease-causing target, then recruit the immune system to destroy it.

These therapies aren't perfect, however. For one, they only help people in the early stages of Alzheimer's because they can't reverse damage. Second, only a small percentage of people in the early stages are eligible for the treatments, largely due to chronic health conditions. Third, the treatments only slow progression by 30%.

"The next step will be, can we make them any better?" says Irina Skylar-Scott, MD, a clinical assistant professor of neurology and neurological sciences at Stanford University. One way to improve the treatments' efficacy could be to give them to Alzheimer's patients sooner, including in the preclinical stage—which has only become possible recently thanks to blood biomarker tests. Researchers are also investigating whether it could help to shuttle monoclonal antibodies past the blood-brain barrier directly into the brain itself.

Another important area of investigation is in decreasing the side effects of anti-amyloid treatments, namely amyloid-related imaging abnormalities, known as ARIA, which can cause brain bleeds and swelling. "Once we understand the basic physiology of the system, we can use adjuvant therapies that … reduce the incidence of this potentially lethal adverse effect," Jicha says.

Experts like Jicha and Buckley are also excited about the possibility of combining anti-amyloid treatments with other therapies being developed and tested, including some promising anti-tau therapies.

Alternative treatments under development could help people who are ineligible for anti-amyloids. Jicha is looking forward to research on RNA silencers that could slow the production of beta-amyloid and tau to a level that the brain can naturally clear out on its own. This is currently being researched in people with Down syndrome who develop Alzheimer's in midlife, but if successful it could be expanded to all people in the early stages of Alzheimer's.

Researchers are also looking into whether anti-inflammatory therapies and GLP-1 drugs such as Ozempic could protect the brain against Alzheimer's disease by altering the immune system and metabolism, respectively. However, there's no real evidence in these areas yet, Buckley says.

MIND THE GENDER GAP

Nearly two out of three Americans with Alzheimer's disease are women. Why is not entirely clear. One potential reason is that women live longer on average, so they have more time for Alzheimer's to develop. Another is that women—and racial minorities, many of which have an increased Alzheimer's risk—may be less likely to have modifiable risk factors such as high blood pressure addressed during midlife, Jicha explains.

The most important factors, however, are estrogen and menopause. Estrogen is a powerful sex hormone that protects the brain, so losing it through menopause is a shock to the system and puts women at risk. This is supported by the fact that women who start hormone therapy during perimenopause tend to decrease their risk of Alzheimer's disease.

However, women who begin hormone therapy years after menopause increase their risk of Alzheimer's, along with other diseases such as cancer, stroke and osteoporosis. This is particularly true in women who

"It's a lot easier to preserve brain function than recover it after you've lost neurons, so that's why people are really interested in using blood tests to look early."

—Jill Morris, PhD

are already not at their healthiest. "Reintroducing a superpower like estrogen back into the body when it hasn't had it for a while causes a whole bunch of things to go haywire," Buckley explains. The body has already learned to compensate for the lack of estrogen, and adding it back could throw the body into chaos.

There are many other sex differences that affect Alzheimer's disease: Women, even healthy women, have more tau than men. And women's extra X chromosome may provide some risks and some protection against Alzheimer's pathology. Also, APOE4, which is the strongest risk factor gene for Alzheimer's disease, puts women at higher risk than men who have the gene. In addition, anti-amyloid treatments may be less effective in women.

None of these phenomena are well-understood. "There is just not enough data out there," Buckley says. Studies on how sex differences, menopause and reproductive health affect women's Alzheimer's risk are few in number and small in size. "We have a lot more work to do."

PREVENTION AND PROGRESSION

Classic Alzheimer's prevention advice remains the best: Follow an all-around healthy lifestyle. Keep your brain engaged, get enough sleep, stay social, exercise and eat a healthy diet. Vaccines that target tau, beta-amyloid and inflammation to prevent Alzheimer's are in development too. "There are some promising candidates out there," Jicha says. "But, of course, large-scale studies will need to be done, and there are always issues with balancing safety and immune responses and efficacy."

For people who have already developed Alzheimer's, lifestyle changes could slow progression, but more research is needed. "Once the disease develops, you have a lot of changes in the body and changes in the ability to function that might further affect disease progression," Morris explains. For example, people with Alzheimer's may be less likely to exercise, but it's possible that physical activity could slow progression.

Therapeutic interventions coming down the pipeline could also slow Alzheimer's progression, including anti-amyloid and RNA silencing therapies.

ZOOMING OUT OF THE NEURON

"The field is shifting focus from just studying what's happening in the neurons and [is now] looking broader inside the brain at what is happening to other cell types that could be contributing to the onset and acceleration of Alzheimer's disease," says Paulo Pires, PhD, an assistant professor of physiology at the University of Arizona College of Medicine-Tucson.

Pires is interested in how three other aspects of brain physiology contribute to Alzheimer's. The first two are microglia and astrocytes. These are immune cells in the brain that can cause damage via multiple pathways, including by increasing inflammation, which can kill neurons and play a key role in Alzheimer's pathology.

The third is the brain's vascular system. Research is revealing how impairments in neurovascular coupling—changes to the vasculature in response to brain activity—may impair the delivery of nutrients to the brain and removal of its waste. This opens up the opportunity for therapeutics, as improving waste clearance could slow Alzheimer's progression, although this hasn't yet been well-studied, Pires says.

Morris is zooming out even further to look at the entire metabolic system. "We're starting to realize that there's bioenergetic changes throughout the body, specifically in non-brain tissues like muscle and liver, that might be important in the context of Alzheimer's disease," she says.

For instance, highly metabolic areas of the brain are among the first to accumulate amyloids, which signals to Morris that metabolic dysfunction may contribute to Alzheimer's neuropathology. And research has shown that people with Alzheimer's disease have impaired function of the energy-producing organelle mitochondria, so it could be a therapeutic target.

Between these emerging areas of research and the recent developments in diagnostics and therapeutics, the landscape of Alzheimer's disease is fundamentally changing, for the better. "We all hope that this is the beginning and not the end of a new era for Alzheimer's disease," Skylar-Scott says.

On-Demand Webinar on Sex Differences in Dementia

Learn more about the sex differences in dementia, focusing on diagnosis, tauopathy and implications for clinical trials. Watch the on-demand recording of "Genetic and Hormonal Components of Sex Differences in Alzheimer's Disease," a webinar featuring Rachel Buckley, PhD, an associate professor of neurology at Massachusetts General Hospital and Harvard Medical School. The webinar highlights the state of the literature about sex differences in prevalence and incidence rates of dementia and the gaps that remain. Learn more and watch the recording at **physiology.org/sex-differences**.

aps
women's health
research initiative

Women's Health: A Physiological Analysis Webinar Series

Watch On Demand

Genetic and Hormonal Components of Sex Differences in Alzheimer's Disease

Rachel Buckley, PhD, Massachusetts General Hospital

Metabolic Mechanisms Contributing to Reversible Pregnancy-induced Cardiac Growth

Helen Collins, PhD, University of Louisville

Effects of Ovarian Failure on Muscle Form and Function

Parastoo Mashouri, PhD candidate, University of Guelph

Sympathetic Regulation in Human Pregnancy

Qi Fu, MD, PhD, University of Texas Southwestern Medical Center

Preeclampsia Research from Hippocrates to Present Day

Stella Goulopoulou, PhD, Lawrence Longo Center for Perinatal Biology, Loma Linda University

Cardiovascular Disease in Polycystic Ovarian Syndrome

Licy Yanes Cardozo, MD, University of Mississippi Medical Center

Learn more and register at physiology.org/WHRIwebinars.

Upcoming Sessions

Hormonal and Chromosomal Influences on Autoimmunity and Lupus
Wednesday, Jan. 29, 11 a.m.
Betty Diamond, MD, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell; Melissa Cunningham, MD, PhD, Medical University of South Carolina

Challenges and Opportunities for Treatment of Metastatic Breast Cancer
Wednesday, Feb. 5, 11 a.m.
Marsha Rosner, PhD, University of Chicago

Controversies in Menopause: A Public Health Mandate
Wednesday, Feb. 19, 11 a.m.
Wen Shen, MD, Johns Hopkins School of Medicine

All times listed are EST.

AWARDS

Heddwen Brooks, PhD, professor and chair of the Tulane University School of Medicine Department of Physiology, has been named a **2024 Health Care Hero**. The award, coordinated by New Orleans CityBusiness, honors health care professionals in the New Orleans area in the categories of animal care, first responders, nursing, physicians, professionals and volunteers. Honorees are selected based on industry achievement and community involvement. Brooks is editor-in-chief of the *American Journal of Physiology-Renal Physiology* and researches sex differences in hypertension, diabetes and the immune system.

Naveen Sharma, PhD, professor in Central Michigan University's Herbert H. & Grace A. Dow College of Health Professions, is a 2024 recipient of the college's **Faculty Excellence Award**. Sharma is recognized for his user-friendly approach, effective teaching methods and going above and beyond to make sure his students grasp complex concepts with clarity. His research interests include the molecular mechanisms that lead to age-associated insulin resistance.

Bina Joe, PhD, FAPS, the Frederick-Hiss Endowed Professor and chair of the University of Toledo College of Medicine and Life Sciences' Department of Physiology and Pharmacology, received the **American Heart Association Excellence in Hypertension Research Award**. Joe is also director of the university's Center for Hypertension and Precision Medicine. Her lab was the first to use CRISPR-Cas9 gene editing to positionally clone genes that cause hypertension.

Jennifer Sullivan, PhD, dean of the graduate school at Augusta University, received the **American Heart Association Harriet Dustan Award**. Sullivan works to provide a rich intellectual environment for students. Her research focuses on sex differences in cardiovascular physiology and pathophysiology.

The following APS members also received awards from the American Heart Association:

- **HTN Mid-career Award for Research Excellence**
  Meena Madhur, MD, PhD
- **Lewis K. Dahl Memorial Lecture**
  Pablo A. Ortiz, PhD
- **Stephanie Watts Career Development Award**
  Cristina Espinosa-Diez, PhD
- **Award for Support of Underrepresented Minorities**
  Beryl Khakina
- **Donald Seldin Lecture**
  Tianxin Yang, MD, PhD

PROMOTIONS

Joseph Brozinick, PhD, was named an **associate vice president** at Eli Lilly and Company. Brozinick was previously director of a preclinical pharmacology lab in the Endocrine Division and an executive director in the Cardiorenal Group at Eli Lilly.

Loren Wold, PhD, FAPS, was named interim **senior associate vice president** for the Ohio State University (OSU) Enterprise for Research, Innovation and Knowledge. A former associate dean for research operations and compliance in the OSU College of Medicine, Wold is editor-in-chief of *The FASEB Journal* and researches the environmental triggers of heart disease, with a focus on air pollution and e-cigarette exposure.

Tell us about your news, awards, promotions or career moves, and we'll consider it for inclusion in an upcoming issue. Email tphysmag@physiology.org.

Amplify the message. Advocate for science.

Raise your voice in support of scientific research with just a few clicks. Sign up to receive APS Action Alerts, and hear about strategic opportunities for members like you to speak out collectively on the issues that matter most to physiologists and the broader scientific community.

physiology.org/advocacy

american physiological society®

AWARDS

Porter Fellows Announced

The Porter Physiology Development Fellowship encourages diversity among students pursuing full-time studies toward a PhD in the physiological sciences and encourages their participation in APS. As one of the largest awards APS gives, the Porter Fellowship has a more than 50-year history of recognizing and celebrating underrepresented researchers for their work and potential. Congratulations to the 2025 fellows:

Mason McIntosh
Auburn University

Jessica Atencio
University of Oregon

Nani Kaluhiokalani
Brigham Young University

Travis Brady
Johns Hopkins University

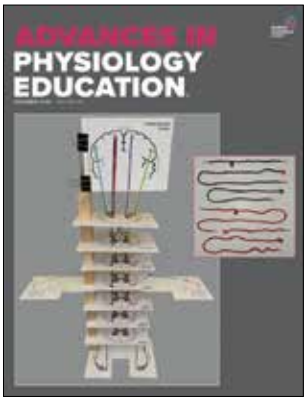
Alyssa Tipler
University of Florida

Adam Weiner Aponte
University of California, Davis

Jonathan López-Carrasquillo
Ponce Health Sciences University

PUBLICATIONS

Call for Editor-in-Chief Nominations



The Society invites nominations for the next editor-in-chief of *Advances in Physiology Education*. The current editor's term ends on Dec. 31, 2025. Candidate interviews will take place in spring 2025. *Advances in Physiology Education* promotes and disseminates educational scholarship to enhance teaching and learning of physiology, neuroscience and pathophysiology. The journal publishes peer-reviewed descriptions of innovations that improve teaching in the classroom and laboratory, essays on education, and review articles based on the current understanding of physiological mechanisms.

Submissions that evaluate new technologies for teaching and research and for educational pedagogy are especially welcome. The audience for the journal includes educators at all levels: K–12, undergraduate, graduate and professional programs. Nominations are due Jan. 15, and applications are due Jan. 31. Learn more and submit a nomination at **journals.physiology.org/call-for-nominations-advances**.

HONORS

APS 2025 Class of Fellows Announced

The Fellow of the American Physiological Society (FAPS), the highest honor APS bestows upon a member, recognizes distinguished leaders who have made significant contributions to the physiological sciences and who have served the Society. Please join us in congratulating the 2025 FAPS inductees:

Erika I. Boesen, PhD, FAPS
University of Nebraska Medical Center

Gregory Funk, PhD, FAPS
University of Alberta

Eric Schmidt, MD, FAPS
Massachusetts General Hospital

Michael Sturek, PhD, FAPS
Corvus Biomedical LLC and Corvis Foundation Inc.

Clintoria Williams, PhD, FAPS
Wright State University

Learn more about the FAPS award at **physiology.org/faps**.

ELECTIONS

Your Voice, Your Vote

Voting for the next slate of APS leaders—president-elect and members of the Board of Directors—begins in January. Meet the candidates and see what they could bring to these roles at the virtual town hall in late January. After the town hall, ballots and a recording of the event will be emailed to all members. Watch your email for more details.

PRESIDENT-ELECT CANDIDATES

Curt D. Sigmund, PhD, FAPS
James J. Smith & Catherine Welsch Smith Chair of Physiology, Department of Physiology Medical College of Wisconsin

Sue C. Bodine, PhD, FAPS
Professor, Aging and Metabolism Research Program Oklahoma Medical Research Foundation

BOARD OF DIRECTORS CANDIDATES

Robert A. Fenton, PhD
Professor of Cell Biology, Department of Biomedicine
Aarhus University, Denmark

Scott D. Kirkton, PhD, FAPS
Professor, Department of Biological Sciences
Union College

Sadis Matalon, PhD, ScD (h.c.), FAPS
Distinguished Professor and Alice McNeal Endowed Chair, Department of Anesthesiology and Perioperative Medicine, and Director, Pulmonary Injury and Repair Center
University of Alabama at Birmingham

Damian G. Romero, PhD, FAPS
Professor, Department of Pharmacology and Toxicology
University of Mississippi Medical Center

Farah Sheikh, PhD
Professor, Department of Medicine
University of California San Diego

Michael Sturek, PhD
Chief Scientific Officer
CorVus Biomedical LLC and CorVus Foundation Inc.

2025 SUMMIT

Last Chance to Register Early for Summit Savings

Don't miss the premier event for researchers exploring the science behind some of the most important questions affecting life and health. Registration for the 2025 American Physiology Summit is now open, and early registration ends Jan. 31.

Come together with your colleagues and leaders in your field April 24–27 in Baltimore to share the most recent advances and breakthroughs in the research community. The Summit meeting is designed and programmed by working scientists to share discoveries on the cutting edge of bioscience and connect you with your vibrant, diverse community. All career levels are welcome, including established scientists, principal investigators, experienced educators and trainees. Learn more and register today at **physiology.org/APS2025**.

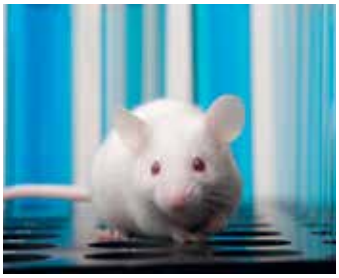
american physiology summit

APRIL 24–27, 2025
BALTIMORE

Improve Communication about Animal Research

2025 American Physiology Summit
Thursday, April 24, 12–1:30 p.m. ET

Join the APS Animal Care and Experimentation Committee for a pre-conference session at this year's American Physiology Summit. The session is designed to help researchers learn how to engage with their Institutional Animal Care and Use Committee (IACUC) members, veterinary staff and other institutional resources to get the most out of their animal research. Talks from experts on animal research will be followed by a panel discussion. The IACUC at each institution plays an important role in overseeing ethical research with animals. Beyond that, it can serve as a valuable resource to help researchers navigate study design and create protocols that maximize scientific value while protecting animal welfare. Learn more at **physiology.org/preconference**.



DATES & DEADLINES

AWARDS

Award deadlines vary and may be subject to change. For the latest information, including award descriptions, amounts, eligibility requirements and to apply, visit ***physiology.org/awards****.*

JAN. 6

WATER & ELECTROLYTE HOMEOSTASIS

Jane Reckelhoff Mid-career Achievement Award

Leonard Share Award

New Investigator Award

JAN. 15

Porter Physiology Development Fellowship

TEACHING SECTION

Labfront Mid-career Educator Award

GASTROINTESTINAL & LIVER SECTION

Horace W. Davenport Distinguished Lectureship

John S. Fordtran Distinguished Research Award

New Investigator Award

Raj and Prem Goyal Lectureship in Pathophysiology of the Gastrointestinal & Liver Disease

JAN. 20

Graduate Student Ambassador

FEB. 15

COMPARATIVE & EVOLUTIONARY SECTION

August Krogh Distinguished Lectureship

FEB. 26

CARDIOVASCULAR SECTION

Carl J. Wiggers Award

Gabor Kaley Lectureship Award

Robert M. Berne Distinguished Lectureship

FEB. 28

RENAL SECTION

Carl W. Gottschalk Distinguished Lectureship

Mid-career Achievement Award

MARCH 15

CELL & MOLECULAR PHYSIOLOGY SECTION

Hugh Davson Distinguished Lectureship

MARCH 21

ENVIRONMENTAL & EXERCISE PHYSIOLOGY SECTION

Edward F. Adolph Distinguished Lectureship

Impact Award

More details: physiology.org/awards

CALLS FOR PAPERS

New! **Explore our ongoing cross-journal calls for papers on key women's health research topics:**

- Alzheimer's disease
- Autoimmune diseases
- Breast cancer
- Cardiovascular disease
- Hormone replacement therapy and menopause
- Migraines
- Novel perspectives on sex as an investigative variable
- Pregnancy and postnatal conditions:
  - Endometriosis
  - Gestational diabetes
  - Preeclampsia
  - Polycystic ovary syndrome

Join APS in advancing our mission to improve health care outcomes and promote greater scientific understanding of women's health. Learn more about this special call for papers at **journals.physiology.org/womens-health-research-initiative**.

American Journal of Physiology-Cell Physiology

- Refining Inflammatory Disease Entities by Insights into Endotypes (ongoing)

American Journal of Physiology-Endocrinology and Metabolism

- Immunometabolism (March 1)

American Journal of Physiology-Regulatory, Integrative and Comparative Physiology

- Exploring the Inflammatory Theory of Disease: Mechanisms Underlying Chronic Inflammatory Diseases (Jan. 31)

American Journal of Physiology-Renal Physiology

- Renal Tubular Function in Health and Disease, Honoring Prof. Gerhard Malnic (Jan. 31)
- The Pathophysiology and Therapy of Polycystic Kidney Disease (March 31)

Function

- Neuroscience (ongoing)

Journal of Applied Physiology

- Context-dependent Mechanisms of Striated Muscle Dysfunction (March 1)

More details: journals.physiology.org/calls

MEETINGS & EVENTS

American Physiology Summit
April 24–27
Baltimore

- Late-breaking abstract submission deadline: Jan. 31
- Early registration deadline: Jan. 31
- Housing deadline: March 31
- Regular registration deadline: March 31

More details: physiology.org/APS2025

WEBINARS

WOMEN'S HEALTH RESEARCH: A PHYSIOLOGICAL ANALYSIS

Hormonal and Chromosomal Influences on Autoimmunity and Lupus
Jan. 29, 11 a.m. EST

Challenges and Opportunities for Treatment of Metastatic Breast Cancer
Feb. 5, 11 a.m. EST

Controversies in Menopause: A Public Health Mandate
Feb. 19, 11 a.m. EST

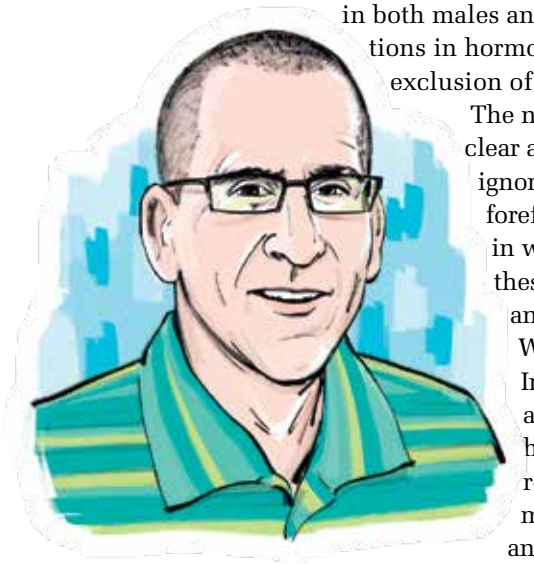
More details: physiology.org/webinars

Keep Pushing Women's Health Research Forward

BY PAUL J. FADEL, PHD

Women's health research has gained a lot of well-deserved attention in recent years, and while important advances have been made, we have much more work to do to make up for a long history in which women were regularly overlooked in research.

Researchers excluded women from studies due to concerns about their menstrual cycles and hormonal fluctuations. There was also the notion that there was more inherent variability in females compared to males. The latter has definitively been shown to not be the case; there is plenty of biological variability in both males and females. Plus, fluctuations in hormones does not justify the exclusion of women.



The need to study both sexes is clear and should no longer be ignored. APS has been at the forefront of promoting research in women, and to further these efforts the Society has announced the 2024–2025 Women's Health Research Initiative. This initiative aims to elevate women's health and highlight the research conducted by APS members to address health and disease in women. We should applaud these efforts because while progress has been made, more work is needed.

A recent study found that women only accounted for 41% of participants in clinical trials from 2016 to 2019. While this may sound good, for many of the diseases being studied, women make up over 60% of the population affected. Another major issue is the exclusion of women from minority groups. For example, non-Hispanic Black women are at equal or even greater risk than non-Hispanic Black men for hypertension and cardiovascular disease—rates much higher than any other racial group. But in many clinical trials, race is not being fully considered and non-Hispanic Black women remain underrepresented.

The National Institutes of Health policy on sex as a biological variable has maintained the expectation that all studies in vertebrate animals and humans will factor sex into research design, analysis and reporting. This policy has undoubtedly facilitated the inclusion of women in research studies, and we now also see many vertebrate animal studies including female animals. While this is needed and encouraging, care needs to be taken to make sure comparisons between males and females are statistically powered when drawing conclusions.

Many studies that now include males and females will have low numbers of each because the intention is not to investigate sex differences per se. This is fine. However, sometimes reviewers will ask about sex differences and authors will be obliged to say there are no differences. The problem is that statistical power is not being fully considered, and now a false finding of "no" sex differences is in the literature. All of us—from editors to reviewers and authors—need to make sure this does not happen! Let's not take a positive of including both sexes and turn it into a negative because it's not statistically powered.

Despite tremendous progress, we still have a way to go in advancing women's health research to continue to close the gap and make sure health-related decisions for treatment are well-founded for women.

Paul J. Fadel, PhD, is a professor in the Department of Kinesiology, associate dean for research, director of clinical translational science and the Moritz Chair in Geriatrics, College of Nursing and Health Innovation at the University of Texas at Arlington. His research focuses on the investigation of neural control of the circulation at rest and during exercise in human health and disease, with a specific emphasis on the sympathetic branch of the autonomic nervous system.

Illustration by Brett Affrunti

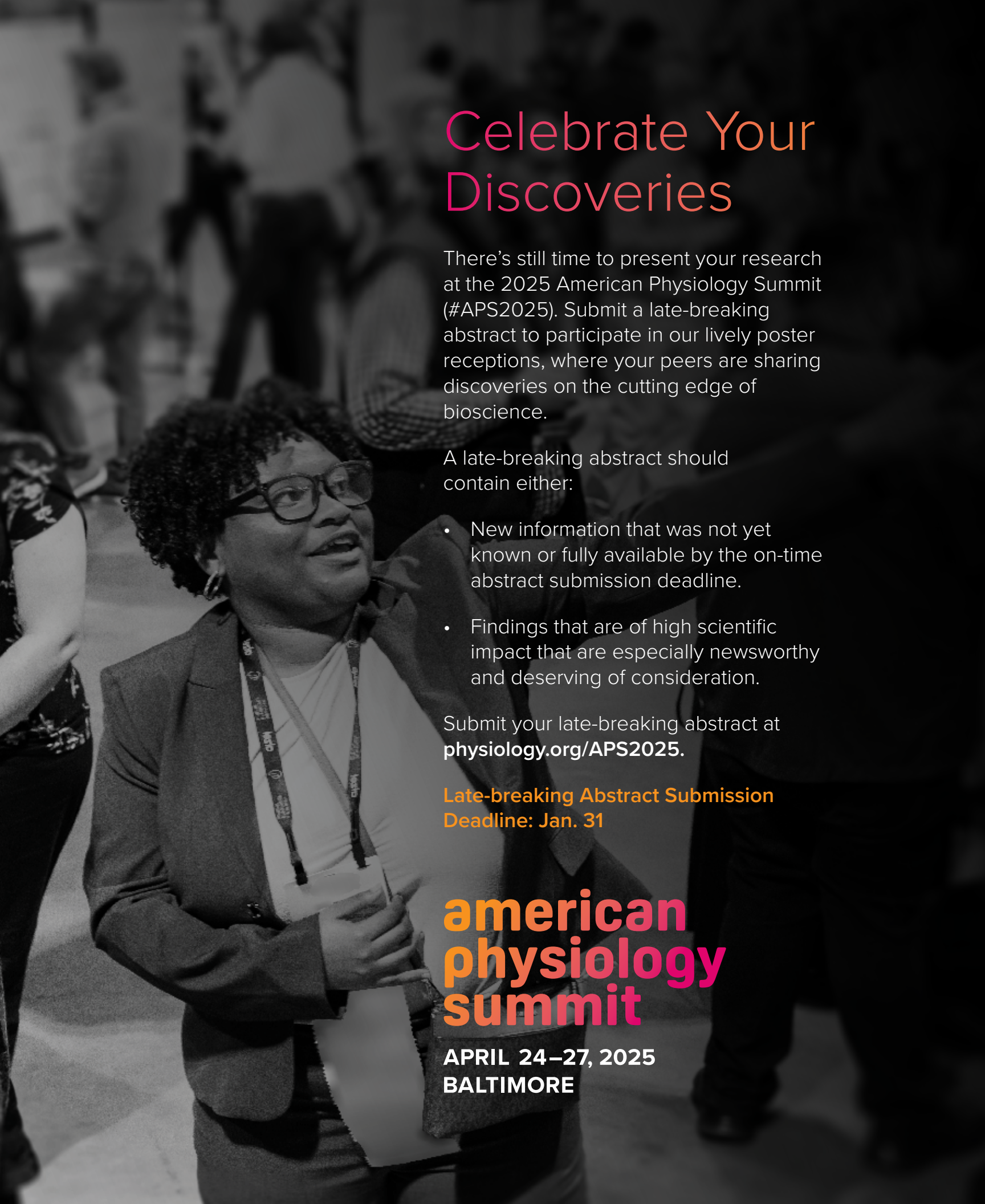
Advocate for Women's Health Research Funding

Conditions that are specific to women, predominantly affect women or affect women differently than men have long been under-resourced, resulting in **critical gaps that affect women's health**. Your perspective and experience as a scientist uniquely qualify you to explain the current research inequities and the societal importance of funding basic, translational and clinical studies related to women's health.

Raise your voice in support of women's health research at our in-person Hill Day in Washington, D.C., on Wednesday, April 23, in advance of the American Physiology Summit. Add the Hill Day event to your Summit registration by Feb. 15.

physiology.org/HillDay

aps
women's health
research initiative



Celebrate Your Discoveries

There's still time to present your research at the 2025 American Physiology Summit (#APS2025). Submit a late-breaking abstract to participate in our lively poster receptions, where your peers are sharing discoveries on the cutting edge of bioscience.

A late-breaking abstract should contain either:

- New information that was not yet known or fully available by the on-time abstract submission deadline.
- Findings that are of high scientific impact that are especially newsworthy and deserving of consideration.

Submit your late-breaking abstract at **physiology.org/APS2025.**

Late-breaking Abstract Submission Deadline: Jan. 31

american physiology summit

APRIL 24–27, 2025
BALTIMORE