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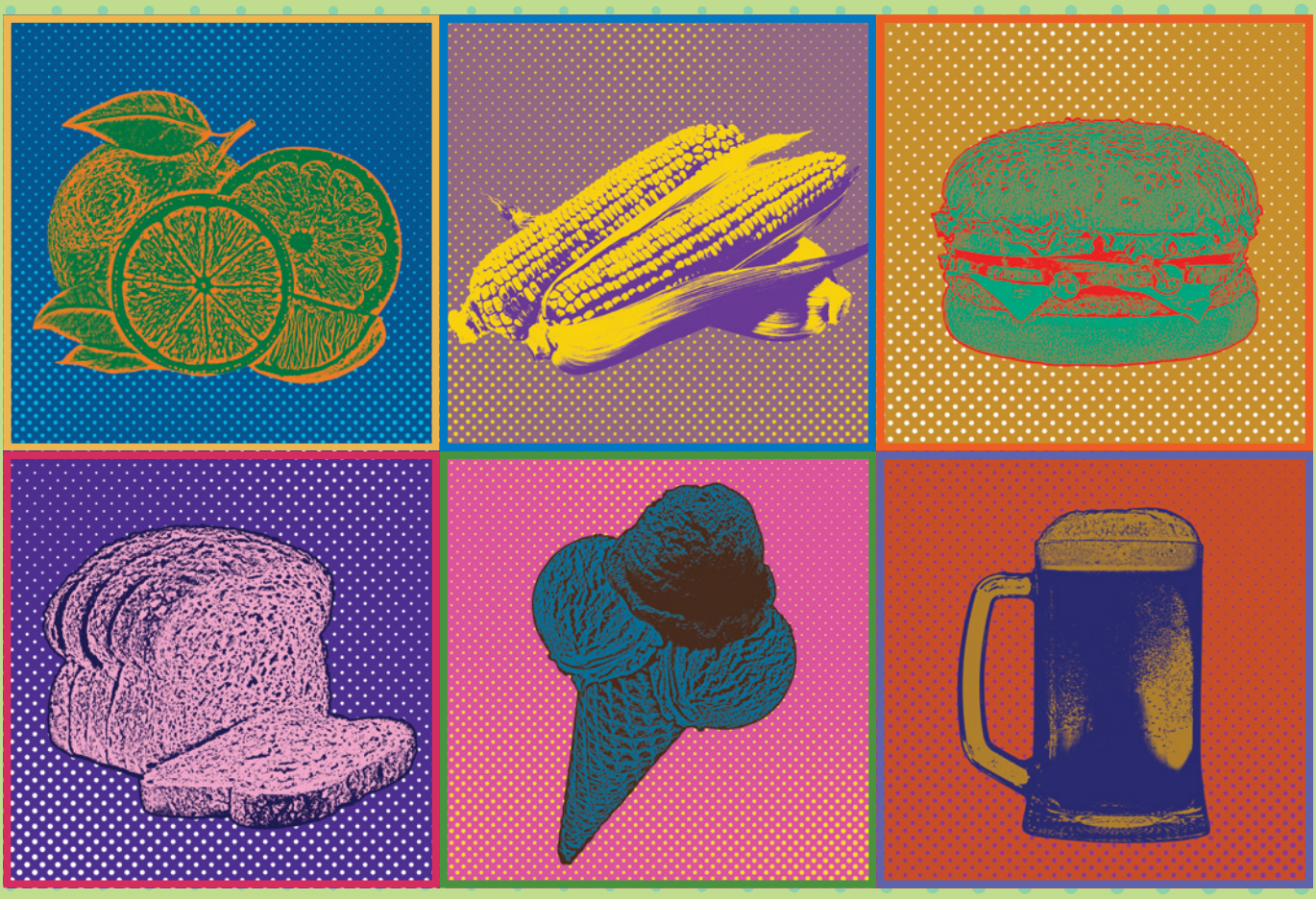
ASBMB TODAY

THE MEMBER MAGAZINE OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

Adapting FOOD WITH biochemistry



| SPECIAL SECTION INSIDE |

Join an ASBMB interest group.

ASBMB interest groups provide an opportunity for members to connect with other members interested in similar areas of research virtually and in person.

Learn more at asbmb.org/interest-groups.

- BMB education
- Cancer biology
- Cell and developmental biology
- Chemical biology
- Computational biology, predictive technology and AI
- DNA structure and function
- Enzyme chemistry and catalysis
- Epigenetics and gene regulation
- Glycobiology
- Immunology
- Lipid Research Division
- Metabolism
- Microbiology
- Neurobiology
- Pharmacology and drug discovery
- Plant biology and natural products
- Protein structure, function and engineering
- Proteomics and mass spectrometry
- RNA
- Signal transduction

Benefits

- Propose, organize and participate in an interest group session at the ASBMB Annual Meeting
- Gather at meetups at the ASBMB Annual Meeting
- Connect virtually with one another on the society's online forum, the ASBMB Active Site

asbmb.org/interest-groups

ASBMB
American Society for Biochemistry and Molecular Biology

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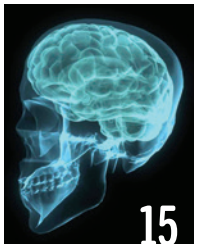

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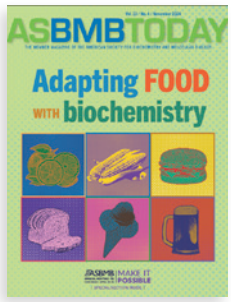

PERSPECTIVES

ASBMB TODAY
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Redefining 'what's possible' at the annual meeting

By Joan Conaway

I am so looking forward to the 2025 ASBMB Annual Meeting, April 12–15 in Chicago, and to seeing you there. This year's theme is "Make It Possible." How fitting for an event that drives discovery, changes the trajectories of research projects and careers, and helps determine what's on the horizon in biochemistry and molecular biology. We will visit the vibrant city of Chicago and have a lot of fun along the way.

I have attended the annual meeting for decades, and it is a highlight of my professional year. Since I first started attending, the meeting's content has evolved with the field, organizers have experimented with new formats, and we've embraced new ideas and directions. All the while, the meeting has maintained its core commitment to scientific excellence and community building. Those are what keep bringing me back — and I hope will bring you.

It's a high-impact event — a worthwhile investment for all who are dedicated to advancing the field of biochemistry and molecular biology and their careers.

Scientific programming

There's a lot to be excited about in 2025. Foremost, the scientific program features groundbreaking research and visionary talks that will ignite new ideas and propel innovation.

JOAN CONAWAY

Thematic symposia: A dozen scientific symposia with more than 100 invited speakers will highlight new findings and approaches that are redefining what we will do next and how we will do it. These events also offer important opportunities to present your science and interact with colleagues across the diversity of biochemistry and molecular biology — including chemical, structural and synthetic biology; rapidly developing areas in metabolism, molecular transport and pseudoenzyme function; and exciting new directions in cancer biology, RNA and the metals of life. As 2025 co-chairs Donita Brady and Dave Pagliarini wrote: "Creativity and innovation emerge from intersections — of perspectives, approaches and experiences." I urge you to submit an abstract for consideration for a spotlight talk or lightning talk!

Featured speakers: The 2025 program is packed with great speakers — from

pioneers to people whose work is upending what we thought we knew.

Two special lectures will highlight how fundamental science transforms the future of health.

The first will feature Melissa J. Moore, a pioneering RNA researcher and Howard Hughes Medical Institute investigator who served as the chief scientific officer of Moderna when it was developing its COVID-19 vaccine that helped rein in the pandemic. She received the ASBMB William C. Rose Award for distinguished mentorship in 2011.

The second special session will feature Richard Silverman of Northwestern University, a pioneering basic scientist working on the molecular mechanisms of potential medicines. His work led to the blockbuster drug pregabalin, more commonly known as Lyrica, used to relieve pain in patients with fibromyalgia and other conditions.

In addition, we will have 10 plenary lectures by ASBMB award-winning scientists covering scientific topics and career journeys that will connect you across our broad field — such as cancer therapeutics, genome stability, phase separation, the kinome, liver cancer, lipid-binding proteins and antimalarial drug resistance.

Emerging investigator seminars: This brand new, daylong event will feature seminars from outstanding postdoctoral and graduate student researchers. Speakers will be selected from volunteered abstracts, so please indicate your interest in presenting when you submit yours. And if you're a hiring manager scouting for talent, you will want to be at this event.

Poster sessions: The poster sessions are always a high point. More than a thousand researchers will present their very latest findings, making this exhibit floor a hub of groundbreaking science and fresh ideas that will spark new collaborations and propel the next big breakthroughs.

Special interest groups: Finally, we are enhancing our special interest groups to help you connect with others who are as excited as you are about your work, discuss shared challenges and formulate solutions together. Or maybe you want to explore a new area for development — these interest groups offer a great way to introduce yourself and engage with a new, welcoming community. The interest groups will hold scientific sessions that include time for networking, and, to extend these discussions, they will also hold meetups in the exhibit hall.

Education, careers, diversity and networking

ASBMB values its vibrant community of scientist–educators who are developing the next generation of scientists. These members teach, mentor and coach undergraduate and graduate students, and the meeting will offer a range of content geared to improve all of our teaching and learning strategies. We will also have networking opportunities and dedicated programming to celebrate women in BMB and support diversity in the research workforce.

And there is still more — the annual meeting also offers an array of professional-development workshops and sessions as well as one-on-one mentoring to meet the needs of scientists at all stages of their careers, including technical skills, publishing, grant writing and leadership. And a new career fair will welcome employers and graduate programs eager to connect with ASBMB members. ASBMB's federal advocacy, such an important part of our year-round work, will also be visible with sessions that engage federal funders and explore advocacy strategies in the new year.

Join us!

ASBMB's annual meeting has something for everyone — you and your science belong here. It's a gathering where the future of biochemistry and molecular biology takes shape: driving scientific advances, connecting across subspecialties and getting a glimpse into the exciting possibilities ahead. All as part of a welcoming and engaged professional community.

Join us! Together, we'll determine what's possible for our field, build careers and new connections, and enjoy a wonderful time in an exciting and culturally rich city.

Look for details about this year's ASBMB Annual Meeting programming on pages 28–36 of this issue of ASBMB Today. I look forward to seeing you in Chicago in April!

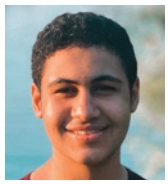
Joan Conaway (Joan.Conaway@UTSouthwestern.edu) is a professor of molecular biology and the vice provost and dean of basic research at the University of Texas Southwestern Medical Center. She is ASBMB's president.

Sewer scholarship recipients announced

By Sian Puckerin

The American Society for Biochemistry and Molecular Biology recently announced the 2024 recipients of the Marion B. Sewer Distinguished Scholarship. This award, created by the ASBMB's Maximizing Access Committee, gives 10 undergraduate students interested in biochemistry and molecular biology $2,000 each toward their tuition and related educational costs.

Mohamed Salem, junior, Penn State University



Salem's focus is on treatment for high-grade gliomas using drugs developed for other purposes. He aspires to university teaching and providing direct patient care and business development.

Danielle Amaegbo, junior, Austin College

Amebego is interested in the biochemistry of drug research, specifically drug delivery and infection development processes. She aims to earn a biochemistry Ph.D. and hopes to join the drug industry.

Jonathan Martin, sophomore, University of San Diego

Now in his second year majoring in biochemistry, Martin aims to attend medical school and complete a residency in orthopedic surgery with the training to treat musculoskeletal conditions.

Sara Beth Bouchard, senior, Wesleyan University

Bouchard wants to develop biopharmaceutical candidates, and she has enrolled in the chemistry Ph.D. program at the University of Connecticut. She wants to work in industry and inspire young scientists.

Mya Soto, junior, Rochester Institute of Technology

Soto would like to pursue a biochemistry major in mechanisms in infectious disease, and continue her studies in graduate school. Her long-term goal is to carry out research and teach.

Adam Chernoff, sophomore, Tufts University

Chernoff is focused on combating diseases that disproportionately affect rural and underserved populations. He aims to pursue a M.D./M.P.H. degree and work in the U.S. Army Medical Corps.

Anita Nguyen, senior, University of South Alabama

Nguyen aspires to be a dentist who can both treat patients and advance dental technology through research. She has connected with orthodontists in Mobile and gained respect for researchers during her time in a lab at the university.

Soliana Yohannes, senior, University of California, Berkeley

Yohannes is a research assistant in a neuroscience lab focusing on autism. Her goal is to blend research with clinical practice as a physician–scientist to contribute to society, satisfy intellectual curiosity and grow in her field.

Pamela Green, junior, University of Virginia

Green's goal is to become a physician and scientist. She'd like to work in a lab that specializes in diabetes research and prevention, and become a primary care doctor who helps patients manage the disease.

Dymuhn Williams, junior, Georgia Southern University

Williams is interested in cancer biology research; she plans to apply to M.D./Ph.D. programs with the hope of becoming a pediatric oncologist with her own research lab.

Read more about these scholarship recipients:

Sian Puckerin (spuckerin@asbmb.org) is the ASBMB's education and professional development assistant. She has a B.S. in family and human services from Towson University.

Shu-ou Shan has been awarded the National Academy of Sciences Award in Molecular Biology. Shan is an endowed professor of chemistry and the executive officer for biochemistry and molecular biophysics at the California Institute of Technology. Her lab deciphers the molecular basis of diverse protein biogenesis pathways.


SHAN

Adriana Bankston has been named a Congressional Policy Fellow by the American Society of Gene & Cell Therapy. Bankston is a policy advisor for the Universities Research Association's Science Policy and Advocacy for Research Competition program and a biomedical workforce and policy research investigator at the Sai Resident Collective.


BANKSTON

Robert Landick won the Hilldale Award from the University of Wisconsin–Madison. Landick is a professor of biochemistry at UW–Madison. His work focuses on the biochemical processes behind the form and function of DNA and RNA.


LANDICK

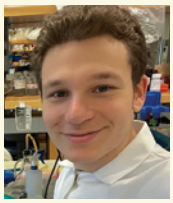
Russell DeBose–Boyd won the Hill Prize from the Texas Academy of Medicine, Engineering, Science and Technology. DeBose–Boyd is a distinguished chair in biomedical science and a professor of molecular genetics at the University of Texas Southwestern Medical Center. His research investigates the feedback mechanisms that control cholesterol synthesis.


DEBOSE-BOYD

Lea V. Michel has been awarded the Faculty Beacon Award by the Rochester Institute of Technology's division of diversity and inclusion. Michel is a professor of chemistry and materials science and the director of diversity, equity and inclusion in the College of Science at RIT. Her research focuses on finding diagnostic biomarkers for Gram-negative sepsis.


MICHEL

Theodore Nelson was named a 2024 Churchill Scholar in science, math and engineering. Nelson is an undergraduate at Columbia University studying computer science. His research focuses on long noncoding RNA biology and epitranscriptomics.


NELSON

Pau Castel was awarded the Early Career Research Award by the Biochemical Society. Castel is an assistant professor of biochemistry and

The following American Society for Biochemistry and Molecular Biology members were named Goldwater Scholars:

Hannah Barsouk, mentored by Ronald Breaker, is an undergraduate at Yale University.

Taylor Bias, mentored by Mary Konkle, is an undergraduate at Ball State University.

Sarah Boyer, mentored by Garland Crawford, is an undergraduate at Mercer University.

Grace DeCostanza is an undergraduate at Ursinus College.

Marion Duval, mentored by Sarah Smith, is an undergraduate at Bucknell University.

Satvik Elayavalli, mentored by Anita Corbett and Jennifer Spangle, is an undergraduate at Emory University.

Aidan Miller, mentored by Lea V. Michel, is an undergraduate at the Rochester Institute of Technology.

Dylan Moran, mentored by Lydia Contreras, is an undergraduate at the University of Texas at San Antonio.

Paul Nguyen is an undergraduate at the University of South Alabama.

Emma Rudisel, mentored by Kristin Dittenhafer–Reed, is an undergraduate at Hope College.

Shelby Sliger, mentored by Mark Hall, is an undergraduate at Purdue University.

Sebastian Velez, mentored by Karen Lewis, is an undergraduate at Texas State University.

Natalie Walsh is an undergraduate at Saint Louis University.


CASTEL

molecular pharmacology at the New York University Grossman School of Medicine. His research focuses on oncoprotein transformation in cancer and congenital disorders.

Kasey Parks has been awarded the Daniel E. Atkinson and Charles A. West undergraduate research fellowship in metabolic research from the University of California, Los Angeles. Parks is an undergraduate in chemistry at UCLA. She performs research on the role of 5′ adenosine monophosphate–activated protein kinases in redox homeostasis.


PARKS

Brian Kelch won the University of Massachusetts Chan Medical School's Educational Service Award. Kelch is an associate professor of biochemistry and molecular biotechnology at UMass. His research investigates the macromolecular machines that aid in virus assembly and DNA replication and repair.


KELCH

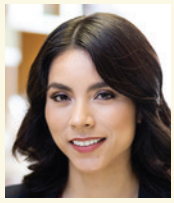
Adnan Alrubaye received the University of Arkansas Bumpers College International Education Award. Alrubaye is an assistant professor of poultry science and associate director of the cell and molecular biology graduate program at the U of A. His lab investigates bacterial chondronecrosis in broiler chickens.


ALRUBAYE

Michael Marletta was named a fellow of the American Institute for Medical and Biological Engineering. Marletta is a professor of chemistry and molecular and cell biology as well as the chair of molecular biology of diseases at the University of California, Berkeley. He researches nitric oxide signaling, gas sensing and polysaccharide monooxygenases.


MARLETTA

Heankel Lyons received the 2024 Nominata Award. Lyons is a graduate student in the genetics, development and disease Ph.D. program at UT Southwestern. She researches disordered regions of proteins and how they organize and regulate gene expression.


LYONS

Peter Kennelly was conferred the title of professor emeritus by the Virginia Tech Board of Visitors. Kennelly is a professor of


KENNELLY

CONTINUED ON PAGE 8

Neil Kelleher, Alexandra Newton, David Craik, David Cortez and Jeffery W. Kelly were honored by the Protein Society.

Kelleher is a professor of molecular biology and the director of the Chemistry of Life Processes Institute and Northwestern Proteomics at Northwestern University and received the Christian B. Anfinsen Award.

Newton is a professor of pharmacology at the University of California, San Diego, and received the Marie Maynard Daly Award.

Craik is a professor of chemistry and structural biology at the University of Queensland and director of the Australian Research Council Centre of Excellence for Innovations in Peptide and Protein Science and received the Emil Thomas Kaiser Award.

Cortez is the chair and a professor of biochemistry at Vanderbilt University and received the Hans Neurath Award.

Kelly is a professor of chemistry at the Scripps Research Institute and received the Stein & Moore Award.


KELLEHER


NEWTON


CRAIK


CORTEZ


KELLY

The following ASBMB members were named fellows of the American Association for the Advancement of Science:

Lizabeth Allison is a chancellor professor at the College of William & Mary. Her lab focuses on thyroid hormone receptor intracellular trafficking.


ALLISON

Kevin Campbell is a professor of molecular physiology and biophysics at the University of Iowa. The Campbell lab researches muscular dystrophy development and therapeutic strategies.


CAMPBELL

Colin Duckett is a professor of pathology and the vice dean for basic science at Duke University. He researches cellular transformation during Hodgkin's disease and anaplastic large cell lymphoma.


DUCKETT

Katrina Forest is a professor of bacteriology at the University of Wisconsin–Madison. She investigates bacterial proteins using primarily X-ray crystallography.


FOREST

Ross Hardison is a professor of biochemistry and molecular biology at Pennsylvania State University. His lab uses epigenetic marks and comparative genomics to predict gene regulatory modules.


HARDISON

Takanari Inoue is a professor of cell biology and the director of the Center for Cell Dynamics at Johns Hopkins University School of Medicine. His lab develops molecular machines that can assay actions in live cells.


INOUE

James Keck is a professor of biomolecular chemistry at the University of Wisconsin–Madison. His research focuses on structural mechanisms behind DNA replication, recombination and repair reactions.


KECK

Liwu Li a professor of biological sciences at Virginia Tech and director of the genetics, bioinformatics and computational biology program. Li's lab examines the systems dynamics of innate immune memory.


LI

Daniel Leahy is a professor of molecular biology at the University of Texas at Austin. His lab studies epidermal growth factor receptor and Hedgehog signaling pathways.


LEAHY

Mary Munson is a professor of biochemistry and molecular biotechnology at the University of Massachusetts Chan Medical School. Her lab studies membrane trafficking, the flow of materials between the plasma membrane the cell's inner compartments.


MUNSON

Tanya Paull is a professor of molecular biosciences at the University of Texas at Austin. Her research examines the DNA damage response and, specifically the DNA end processing and signaling events that follow chromosomal double-strand breaks.


PAULL

David Rockcliffe is a program director in the division of chemistry in the Directorate for Biological Sciences at the National Science Foundation.


ROCKCLIFFE

Gisela Storz is an investigator in the section on environmental gene regulation at the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Storz's research centers on small, noncoding RNAs and the proteins encoded by small open reading frames.


STORZ

CONTINUED ON PAGE 8

The following ASBMB members were named fellows of the American Association for the Advancement of Science:

CONTINUED FROM PAGE 7

David Muddiman is a professor of chemistry at North Carolina State University. His lab focuses on developing mass spectrometry measurements, including an ambient ionization method to analyze a diverse range of materials.


MUDDIMAN

Bradford Schwartz is a professor of medicine and biomolecular chemistry at the University of Wisconsin–Madison and CEO of the Morgridge Institute for Research. His research focuses on the initiation and regulation of protease cascades.


SCHWARTZ

Jürgen Wess is chief of the Molecular Signaling Section, Laboratory of Biological Chemistry at the National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases. His research investigates G protein–coupled receptors to identify therapeutics for Type 2 diabetes and related disorders.


WESS

CONTINUED FROM PAGE 6

biochemistry in the College of Agriculture and Life Sciences at Virginia Tech. His lab uses archaea to dissect the development and evolution of protein phosphorylation and dephosphorylation.

F. William Studier won the Richard N. Merkin Prize in Biomedical Technology. Studier is a senior biophysicist emeritus at the U.S. Department of Energy's Brookhaven National Laboratory. He pioneered the development of the T7 expression system, which utilizes the T7 bacteriophage RNA polymerase to induce high-level gene expression in E. coli.


STUDIER

Ryan Arvidson has been awarded the Carl F. Wittke Award for Excellence in Undergraduate Teaching by Case Western Reserve University. Arvidson is an assistant professor of biochemistry at the CWRU School of Medicine. His research combines bioinformatics, molecular modeling and cell biology techniques to understand the structure–function relationships of G protein–coupled receptors.


ARVIDSON

Pedro Beltrao, Mikhail M. Savitski and **Aviv Regev** were elected to the European Molecular Biology Organization.

Beltrao is a professor of molecular systems biology at the Swiss Institute of Bioinformatics. His lab develops comprehensive models to study how DNA changes alter biomolecular structure and function and ultimately phenotypic traits or disease.


BELTRAO

Savitski is a team leader and head of the Proteomics Core Facility at the European Molecular Biology Laboratory. His lab uses and develops stability proteomics methods to understand protein aggregation and disaggregation, cell phenotyping and protein interactions with drugs, metabolites, DNA and RNA.


SAVITSKI

Regev is the executive vice president and head of Genentech Research and Early Development. Her lab develops and applies experimental methods and computational algorithms to study cells, their intracellular circuits and their interactions in tissues, in both health and disease.


REGEV

Look for more member news details here:

Igor Dawid, a pioneer in biology and genetics who worked on the molecular mechanisms of development, died Feb. 13. Dawid was a member of the American Society for Biochemistry and Molecular Biology for 56 years. He discovered that extrachromosomal nucleoli have copies of genes for ribosomal RNA in frog oocytes.

Herbert Cheung, a biochemist who specialized in the use of fluorescence technology, died March 28 in his Birmingham, Alabama, home. He had been a member of the American Society for Biochemistry and Molecular Biology since 1972. Cheung's research focused on the function regulatory proteins in skeletal and cardiac muscle, using fluorescence resonance energy transfer microscopy.

Andrew Wright, a biochemist who studied cell cycles and spent almost five decades at Tufts University, died Oct. 9, 2023. He had been a member of the American Society for Biochemistry and Molecular Biology since 1971. He revealed the long-term stability of growth in E. coli where the mother and daughter cells exhibit weak correlation between consecutive cell cycles.

Maxine Singer, a revolutionary molecular biologist, National Medal of Science recipient, federal health official and inclusion advocate, died July 9 in Washington, D.C. She had been a member of the American Society for Biochemistry and Molecular Biology for over 60 years. Singer found that specific amino acids correspond to coding regions in RNA. Her discovery was foundational to deciphering the genetic code and laid the groundwork for future discoveries in genetic engineering.

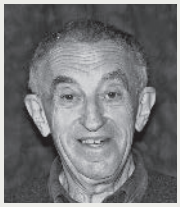
Lubert Stryer, a researcher and author whose work has shaped biochemistry for decades, died April 8 from cancer. Stryer was a member of the American Society for Biochemistry and Molecular Biology for 40 years and was known for his pioneering discoveries in fluorescence spectroscopy, human vision and high-speed genetic analysis, and for writing an influential textbook used worldwide.

Thomas M. Devlin, professor emeritus at Drexel University College of Medicine and a member of the American Society for Biochemistry and Molecular Biology for more than 60 years, died March 24. Devlin's research focused on mitochondrial energy transduction, metabolic enzymes and the biochemical changes that occur in tissues as the result of ischemia.

Gary Felsenfeld, a longtime researcher at the National Institutes of Health and member of the American Society for Biochemistry and Molecular Biology since 1962, died May 1, at the age of 94. Felsenfeld identified insulator proteins capable of blocking the crossfire of gene activation. His research revealed the dynamic nature of chromatin and its role in gene expression and epigenetic regulation.

Karl A. Schellenberg, a professor and the founding chair of biochemistry at Eastern Virginia Medical School, died April 10 at his home in Virginia Beach. He had been a member of the American Society for Biochemistry and Molecular Biology for 56 years. Schellenberg studied a variety of biochemical reactions, including radiation damage to DNA molecules and tryptophan's role in yeast metabolism, and he held six patents.

Julius Adler, renowned for his work in chemotaxis, died April 2 at the age of 93. Adler was a member of the American Society for Biochemistry and Molecular Biology and received the society's William C. Rose Award in 1996. His research advanced the understanding of how bacteria and other organisms sense and respond to chemical stimuli in their environment.



Read news obituaries and personal retrospectives of ASBMB members here:

Cholesterol synthesis and cancer

By Jessica Desamero

Too much cholesterol can cause disease. Therefore, controlling how cells acquire and store cholesterol helps keep the body healthy.

Cholesterol can be acquired by synthesis where multiple enzymes influence the rate of reactions in the synthesis pathway. In a recent study in the **Journal of Biological Chemistry**, researchers at the University of New South Wales found that the active form of one key cholesterol synthesis enzyme, squalene monooxygenase, or SM, is upregulated in endometrial cancer tissues.

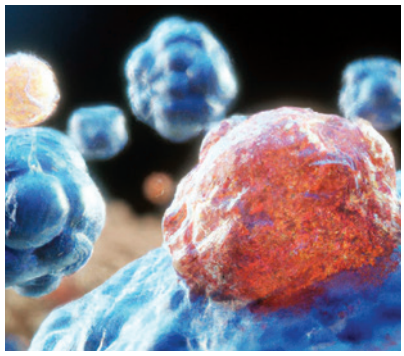
Andrew J. Brown, Hudson W. Coates and their team investigate how cholesterol synthesis is controlled. "Very little was known about the control of the cholesterol synthesis pathway, apart from this early rate-limiting step HMG CoA-reductase," Brown said.

Then the researchers found SM.

"SM is involved in one of the slowest reactions in the pathway, meaning that it's a key bottleneck in the entire pathway," Coates said.

The amount of SM protein influences how much cholesterol can be produced. At high cholesterol levels, SM recognizes it must be degraded and sends itself to the cell's garbage disposal, the proteosome, to be fully destroyed. But sometimes, the proteosome machinery gets jammed and only truncates SM's N-terminal regulatory domain.

"You then have this unleashed protein. Because it is lacking its N-terminus needed for inhibitory control, it becomes constitutively active," Brown said. "We like to think of this as the enzyme going rogue."



VILLALOBOS/OPACKWIKIMEDIA COMMONS

Abnormal growth of a cancer cell.

"This fragment of SM can no longer be sent to the garbage disposal," Coates said, and with nothing to stop it, "It can essentially produce as much cholesterol as it wants to."

Cancer biologists are interested in SM as a proto-oncogene, as it is needed for normal cell growth but promotes cancer cell growth when overactivated, and as a potential target for chemotherapy. Since SM is involved later in the pathway, targeting SM may block cholesterol synthesis without affecting production of other important molecules.

However, past studies have shown that inhibiting full-length SM enzyme does not turn it off but instead truncates and activates it.

"Knowing the biology of this truncation may give us an insight into how to better target SM," Brown said.

Previously, the team saw that a lack of oxygen, which is common in solid tumors, also truncates SM. To investigate whether truncated SM, or trunSM, and endometrial cancer are connected, the team analyzed trunSM levels in samples of endometrial cancer tissue versus adjacent noncancerous tissue. They found that levels of both trunSM and the biomarker for hypoxia, HIF1alpha, increase in the cancerous tissues.

The team studied the relationship between trunSM and lipid droplets, or LDs, which bud off the membrane of the endoplasmic reticulum, or ER. LD accumulation is broadly linked to cancer progression. SM is normally embedded in the ER membrane, so the researchers wondered if truncation would let the enzyme move more freely and to LDs.

They found that full-length SM does not associate with LDs, but trunSM does.

"We're really showing that this fragmented form of SM has very different properties to the full-length normal version," Coates said.

These studies suggest that upregulated truncation may contribute to SM-related oncogenesis, so SM may be a viable chemotherapeutic target.

"If we could selectively target the rogue version in tumors, it might be the best way forward," Brown said.

"If we can stop cells from producing this overactive fragment of SM, we might be able to reduce the amount of cholesterol that cancer cells produce and bring it back to a normal level," Coates said. "That might help suppress their growth."

DOI: 10.1016/j.jbc.2024.107232

ASBMB Today contributing writer Jay Thakkar contributed to this article.

Jessica Desamero (jdesamero@gradcenter.cuny.edu) is a graduate of the City University of New York's biochemistry Ph.D. program and volunteers with science outreach organizations. She is an ASBMB Today volunteer contributor.

New gene, new strides in gangliosidosis

By Farah Aziz Annesha

Imagine a factory built to produce potato chips. A conveyor belt takes the chips to be packaged and sent to warehouses. But the belt machinery is faulty, so when the factory begins production, chips are prepared but nothing is packaged or sent out. The chips pile up in one place. Over time, the piles of chips interfere with the machinery, causing the whole factory to shut down.

Something similar happens in the brain of Jojo, a little girl born with the neurodegenerative disorder GM1 gangliosidosis. Lipids accumulate in her brain cells because the machinery that breaks down those lipids is faulty.

GM1 gangliosidosis is caused by mutations in the GLB1 gene that codes for the enzyme lysosomal β-galactosidase, which breaks down the lipid GM1 ganglioside. Deficiency of this enzyme causes GM1 ganglioside to accumulate, which results in symptoms including delayed growth and development, enlarged liver and spleen, poor muscle tone, skeletal abnormalities and impaired vision.

When Jojo arrived at the National Institutes of Health in 2016 at the age of 7, she was able to walk, talk and write. Within three years, she needed help standing, walking, speaking and doing almost every activity. In 2019, 10-year-old Jojo became the first person to receive an experimental gene therapy treatment for GM1 gangliosidosis.

In 2023, Laura Allende and her colleagues at the NIH were working on a disorder similar to GM1 gangliosidosis: Tay-Sachs disease. Tay-Sachs is caused by a mutation in the HEXA gene, which codes for an enzyme responsible for degrading GM2 ganglioside. When Allende genetically altered mice to mirror the mutation in humans, the mice had less severe symptoms than humans, leading her team to think another gene was creating a bypass pathway to break down the accumulated lipids in the mice.

The researchers postulated that the gene sialidase NEU3 was helping to degrade the lipids. So, even when the HEXA gene malfunctioned, NEU3 created a bypass pathway causing less severe Tay-Sachs.

The team then hypothesized that NEU3 could also mitigate symptoms in GM1 gangliosidosis. In a recent article published at the **Journal of Lipid Research**, they confirmed that NEU3 provided an alternate route for GM1 ganglioside degradation, leading to a less severe form of the disorder.

The researchers genetically altered one group of mice to lack mutations of the GLB1 gene and a second group to lack both GLB1 and NEU3 genes. They compared the symptoms of both groups and compared their GM1 lipid levels. The mice with NEU3 had less severe symptoms while those lacking both genes showed symptoms similar to those in human patients.

So, why can't humans, who also have the NEU3 gene, use the bypass pathway to degrade the lipids?

"We tested human cells for the NEU3 gene and its associated enzyme activity," Allende said. "We found that the gene is not so active in humans, due to having a different genetic sequence than the one found in mice."

But Allende thinks this discovery can still help people with the disease.

ERNESTO DEL AGUILA III/NATIONAL HUMAN GENOME RESEARCH INSTITUTE

Jojo, the first recipient of a new GM1 gangliosidosis gene therapy treatment, and Cynthia Tifft, an author on the JLR study, celebrate with a tea party.

"Knowing about NEU3 will help open up new potential therapeutics for GM1 gangliosidosis in humans," she said. "Our next step will be to observe how NEU3 operates. If we can turn on this alternative pathway in humans or make the NEU3 enzyme more active towards lipid degradation, then we can help alleviate the symptoms and progression of this disease in patients."

GM1 gangliosidosis affects infants and can progress quickly, sometimes resulting in death during childhood; the earlier the disease is diagnosed the greater the chances are for a longer and better life.

DOI: 10.1016/j.jlr.2023.100463

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Seeking the sweet spot to beat a pig parasite

By Senegal Carty

Outbreaks of the nematode Trichuris suis, or porcine whipworm, can be costly for pig farmers and inflict suffering on animals with severe infections. This worm reproduces in pigs' digestive tracts, causing dehydration, malnourishment and sometimes death. Understanding how a pig's immune system reacts to T. suis is a step toward developing better strategies to clear it.

Iain B.H. Wilson's lab at the Universität für Bodenkultur in Vienna, in collaboration with Richard Cummings' lab at Harvard Medical School, tackled the question of how the pig immune system recognizes sugar molecules, or glycans, found on T. suis proteins. The group recently reported their findings in the journal **Molecular & Cellular Proteomics**. Lead author Barbara Eckmair, along with co-author Katharina Paschinger and Wilson walked us through their process, their findings and the importance of this study.

The group extracted glycans from worms and then separated different types of glycans using high-performance liquid chromatography, a technique that isolates compounds within a mixture based on how easily they separate due to their size and structure. They then created arrays of spots made up of the separated glycans. Using these arrays, they tested several innate immune system proteins, as well as immunoglobulin G and M, or IgG and IgM, antibodies from T. suis–infected pigs, to see how well they bound to each glycan spot.

"Some large molecular-weight glycans seemed to have the bulk of the response to the antisera," Wilson said. "So that left the question as to what the exact structures were."

They found that many fucose residues and up to eight phosphorylcholine residues could decorate some of the glycans.

"Lots of other nematodes have phosphorylcholine on their N-glycans," he said, "and these are very often associated with immune system downregulation."

However, this was the first time such large structures had been found in T. suis.

Wilson said this research is especially impactful for organic farming because animals raised this way receive fewer antiparasitic drugs and are at higher risk of worm infections. Earlier studies suggest that vaccination against these parasites is an attractive potential strategy.

"There are indications from Haemonchus, which is a sheep parasite, that the glycans would be important for making the vaccine," Wilson said.

Asked about the next steps for this research, co-author Paschinger said that determining which glycans are bound by IgE, an antibody that plays a key role in the immune response to parasites, is an important question to answer.

Eckmair, the paper's lead author, explained that IgE binding could not be addressed in this study because the reagents needed to test pig IgE binding are difficult to procure, but she said future experiments could tackle this and many other questions.

PASCAL DEBRUNNER

Organically farmed pigs are at especially high risk of whipworm infection. Research into their immune responses to sugars made by this parasite could help scientists develop vaccines.

"Of course, there is more immunological work that we could do, because we still have some of the arrays left," Eckmair said. "This was really a lucky case because we have so much material that we could test."

This research is not only a step toward understanding the pig immune response to T. suis; by helping researchers understand the immune response to glycans found in Trichuris trichiura, the human whipworm, it might lead to medical advances for humans as well.

DOI: 10.1016/j.mcpro.2024.100711

Senegal Carty (senegalc@bu.edu) recently graduated from Boston University Chobanian and Avedisian School of Medicine with a Ph.D. in molecular and translational medicine. She is an ASBMB Today volunteer contributor.

Cristea takes the reins at MCP

New EIC plans to enhance visibility, reach of the proteomics journal across fields

By Marissa Locke Rottinghaus

Ileana Cristea began her five-year term as editor-in-chief of the American Society for Biochemistry and Molecular Biology's journal Molecular & Cellular Proteomics, one of the society's three open-access, peer-reviewed journals, in August.

Cristea, a professor of molecular biology and director of graduate studies at Princeton University, has been a member of the editorial board since 2011 and served as the editor for an MCP special issue in 2017.

Her research lies at the intersection of virology and proteomics. Cristea's lab uses molecular virology, microscopy, mass spectrometry–based proteomics and bioinformatics to study the battle between virus and host during infection.

"Ileana appreciates the importance of maintaining rigorous standards in the reporting of mass (spectrometry) data that has been a hallmark of MCP since its inception," Ann Stock, ASBMB past president, said. "At the same time, she recognizes the increasing capabilities and accessibility of the technology and desires to decrease barriers for participation of authors who might not identify themselves as experts in mass spectrometry but utilize proteomics in their research."

Cristea has published many manuscripts, over twenty of which appeared in MCP, including work on how DNA sensors distinguish between host and viral DNA to induce immune signaling during viral infection.

"The Molecular & Cellular Proteomics journal captures the versatility of proteomics and the breadth of its impact on multiple fields of research," Cristea said. "It does this by providing a hub, at the highest level, for papers describing both technological developments and applications of proteomics to biological and medical studies. Having gained a reputation for representing excellence in proteomics research and for setting standards for the field, the MCP journal also has an important educational component for our scientific community."

Ileana Cristea's research focuses on the proteomics of virus–host interactions.

Cristea is excited to bring her leadership and multidisciplinary expertise to the journal and plans to implement programs to enhance the visibility and reach of MCP across fields.

She earned her master's degree in medicinal chemistry and a Ph.D. from the University of Manchester Institute of Science and Technology. Then, she pursued a postdoctoral fellowship in the Laboratory of Mass Spectrometry and Gaseous Ion Chemistry at Rockefeller University.

Cristea has also earned many awards including the National Institutes of Health Avant Garde Award, the Human Frontiers Science Program Young Investigator Award, the Early Career Award in Mass Spectrometry, the American Society for Mass Spectrometry Research Award, the Mallinckrodt Scholar Award, the Human Proteome Organization Discovery Award in Proteomic Sciences and the Princeton University Graduate Mentoring Award.

"We are fortunate to work in an exciting field of research that grows at a fast pace, in conjunction with rapid changes to diverse fields of biology," Cristea said. "The communication between scientific fields is more extensive, and we are watching the development of a remarkable wave of multidisciplinary scientists who will revolutionize the paths to scientific discoveries. I am enthusiastic to help bring MCP a forward-looking vision for this fast-moving field of research."

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for ASBMB.

From the journals

We offer summaries of papers recently published in the **Journal of Biological Chemistry**, the **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.

A faster way to detect peroxisomal disorders

Peroxisomal disorders, or PDs, such as X-linked adrenoleukodystrophy, or ALD, and Zellweger syndrome, or ZS, are genetically diverse metabolic conditions characterized by malfunctioning peroxisomes. Peroxisomes are organelles that aid in the β-oxidation of very long-chain fatty acids, or VLCFAs which contain more than 22 carbons, and hydrogen peroxide detoxification. PDs require distinct treatments, so accurate diagnosis is critical.

Genetic defects in peroxisomal β-oxidation lead to VLCFA accumulation, triggering health problems, including nervous tissue demyelination. To diagnose PDs, physicians often measure plasma levels of VLCFAs. Quantifying VLCFAs through direct transesterification followed by gas chromatography analysis is the gold standard for diagnosis; however, it is time-consuming and labor-intensive. In a recent study published in the **Journal of Lipid Research**, Blai Morales–Romero and his team at the Center for Biomedical Research Network on Rare Diseases in Spain, report that very long-chain lysophosphatidylcholine, or LPC, levels, measured by liquid chromatography with tandem mass spectrometry, may

Read more news from ASBMB journals here:

Maternal metabolite promotes offspring survival

Recent studies have shown that not only genetic information but also information from RNA, proteins and metabolites, can be transferred across generations and influence offspring phenotype. Of these molecules, parental metabolites can affect the lifespan and metabolism of fruit fly offspring. However, scientists know little about how the maternal metabolic environment affects progeny. In a recent study, published in the **Journal of Biological Chemistry**, Naoto Hikawa and colleagues at the University of Tokyo used targeted liquid chromatography–mass spectrometry analyses of the fly ovary, transcriptome analyses of oocytes and other biochemical techniques to fill this gap.

The metabolite kynurenine, or Kyn, is produced upon tryptophan metabolism. The authors' previous studies revealed that the fat body, a fruit fly organ similar to the mammalian liver and fat tissues, regulates Kyn levels in fly larvae. Using liquid chromatography–mass spectrometry analyses of ovaries of different mating-aged flies, the authors revealed that Kyn production significantly increased after mating. They also established, using genetic knockdown studies, that Kyn levels mediate communication between the fat body and ovary. Furthermore, elevated

Kyn levels increased offspring starvation resistance and maintained lipid homeostasis.

This study underscores the importance of a single maternal metabolite, Kyn, which can affect offspring survival. Furthermore, these results suggest that parental dietary routine affects the lifespan and metabolism of the next generation. As maternal metabolites have been found to affect disease outcomes in humans with autism and other neurodevelopmental disorders, modulating parental diets could be a key factor to alleviate similar conditions.

DOI: 10.1016/j.jbc.2024.105663

—Seema Nath

be a faster approach.

The team found they could detect LPCs more accurately than traditional plasma VLCFAs, especially in girls. The authors suggest using analysis of VLCFA to LPC ratios to differentiate ALD from ZS and call for more studies with diverse patient groups.

DOI: 10.1016/j.jlr.2024.100516

— Aswathy Rai

Novel genetic variants in thyroid cancer

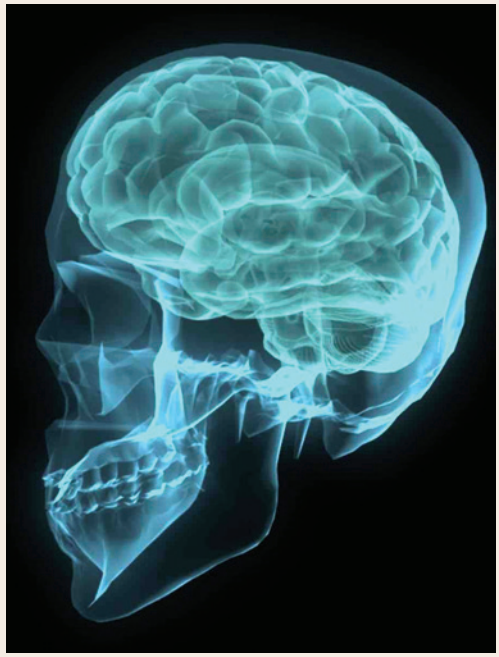
Familial nonmedullary thyroid cancer, or FNMTC, comprises 5% to 15% of nonmedullary thyroid cancer cases. The genetic basis of syndromic FNMTC, which affects first-degree relatives, is well-defined, but scientists have not found a genetic cause for nonsyndromic FNMTC.

In an article published in the **Journal of Biological Chemistry**, Carolina Pires of the Portuguese Oncology Institute and a team of researchers identified CHEK2, a tumor suppressor gene, which is overexpressed in FNMTC cells. The authors sequenced 94 genes associated with cancer predisposition in two unrelated FNMTC families and found two novel germline variants in CHEK2. A kinase assay on the two variants showed that both CHK2 protein variants had lower enzymatic activity compared to the wild-type protein. The authors performed molecular dynamics simulations and circular dichroism and found no distinct structural changes in the CHK2 protein variants. However, immunohistochemical analysis showed that the CHEK2 mutations cause CHK2 protein overexpression in patient tumors.

These preliminary results require follow-up studies on additional

Binge drinking and bacterial lipoprotein regret

Alcohol binge drinking, or ABD, is defined by the number of alcoholic drinks consumed in a period of time, usually four to five or more. Most common among women and young adults, ABD is associated with serious injury to the brain, gut and liver as well as risks due to cognitive decline in memory and thinking.



ABD also affects the gut microbiome; it allows bacterial lipopolysaccharides, or LPS, a major structural component of the outer membrane of Gram-negative bacterial cells, to move from the gut to the bloodstream. Lipid A is the most bioactive component of LPS and a potent endotoxin. During ABD, lipid A aggregates and binds to apolipoproteins, or Apo proteins, in the prefrontal cortex, or PFC. Brain lipid A–Apo protein aggregates activate the immune system and can induce inflammation in the brain.

In a recent study published in the **Journal of Lipid Research**, Leticia López–Valencia of the University of Madrid and collaborators explored the effects of alcohol on the PFC and cerebellum of rats.

Upon oral delivery of ethanol, the rats showed elevated LPS-binding protein in the blood plasma equally in both males and females. Unlike in males, the female plasma ApoAI levels were elevated, and female brains contained aggregates of Lipid A with ApoAI in the PFC. In addition, males, but not females, showed Toll-like receptor 4, the immune cell receptor for LPS, upregulation in the brain.

These results suggest that alcohol introduces small bacterial components into the brain where they form aggregates with different apolipoproteins, which can drive intoxication. The study suggests males and females have distinct signaling pathways that lead to neuroinflammation after ABD.

DOI: 10.1016/j.jlr.2024.100509

— Sephra Rampersad

patients. Concurrently, researching mutant CHK2 inhibitors could also be valuable for FNMTC treatment.
DOI: 10.1016/j.jbc.2024.105767

— Jay Thakkar

Untangling complex proteomics mass spec data

Researchers use data-independent acquisition, or DIA, to analyze proteomes by mass spectrometry, or MS. In DIA, all detectable ions from a proteomics sample are analyzed, much like observing a crowded street one angle at a time. Despite its broad coverage and sensitivity, DIA has difficulty discerning similar molecules with overlapping signals in a complex sample.

In a recent study published in the journal **Molecular & Cellular Proteomics**, Sophia Steigerwald at the Max Planck Institute of Biochemistry and colleagues combined DIA with an advanced signal processing method, the phase–constrained spectrum deconvolution method, or ΦSDM, to tackle the challenge of complex spectra. This method imposes mathematical constraints based on the phase information of peptide ions to untangle overlapping signals within a mass spectrum. The authors tested the approach using HeLa cells.

By implementing ΦSDM signal processing on additional graphics processing units, the researchers quickly achieved a higher signal-to-noise ratio and 15% more peptide coverage than conventional methods, particularly in samples with short gradient times.
DOI: 10.1016/j.mcpro.2024.100713

— Indu Sridharan

Using an old drug to treat a new skin disease

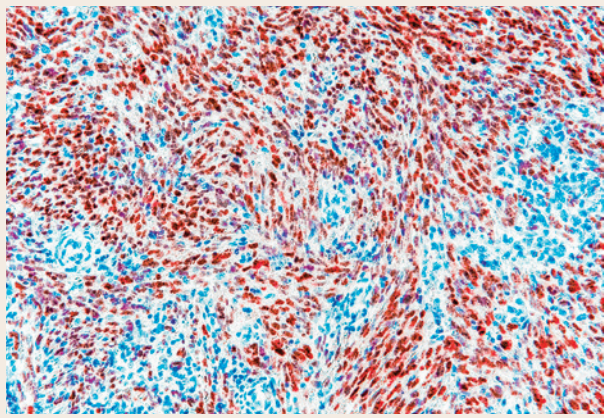
Ion channels in skin cells sense tactile stimuli, including heat and pain. The TRPV3 ion channel is expressed in keratinocytes, the primary cell type in the outer layer of skin, where it opens and closes to regulate calcium conductance in response to temperature changes. Gain-of-function mutations in the gene encoding this channel have been implicated in skin disorders such as hyperkeratosis, dermatitis and abnormal hair growth, suggesting that inhibition of TRPV3 signaling holds potential for treating skin diseases.

In recent work published in the **Journal of Biological Chemistry**, Yimei Xu and colleagues from Qingdao University in China screened a library of FDA-approved drugs

Beyond microscopy: Mass spec's role in biopsies

Microscopy is a standard method to assess biopsied tissue and look for abnormalities. This approach focuses largely on immunohistochemistry, or IHC, to identify and label cell lineage markers and therapeutic targets to provide insights for cancer diagnosis and treatment options. IHC has revolutionized cancer diagnosis and treatment, but it has faced significant obstacles in terms of standardization and consistency. While progress is being made to enhance IHC, its limited multiplexing capability and dependence on monospecific reagents may make it unsuitable for certain applications.

A recent perspective in the journal **Molecular & Cellular Proteomics** by William Phipps and colleagues at the University of Washington and Fred Hutchinson Cancer Research Center discusses the challenges of using IHC for cancer diagnostics. It suggests that liquid chromatography-tandem mass spectrometry, or LC-MS/MS, might supplement biopsy testing methods. As laboratories use many different antibodies for IHC, antibody-based protein detection technologies may become less useful long-term; it may be hard to repeat results both within and between testing sites. Mass spectrometry could address conflicting results and supplement IHC.



The authors suggest that solutions using LC-MS/MS have several advantages, including increased specificity and sensitivity, decreased interference and turnaround time and the ability to multiplex. The authors stress that these methods would need to be appropriately calibrated, validated and consistently evaluated when used in the clinic.
DOI: 10.1016/j.mcpro.2023.100648

— Naushin Raheema

against TRPV3 using molecular docking simulations. They found that the drug flopropione, developed from a small molecule derived from a medicinal plant and used to treat spasms in nervous system disorders, reduced the probability of the TRPV3 channel being in the open conformation without altering its conductance when open. They also showed that topical application of flopropione alleviated skin lesions and ear skin swelling in mice genetically altered to have skin inflammation.

DOI: 10.1016/j.jbc.2023.105595

— Ken Farabaugh

The many roles of lactate

The central metabolic pathway, glycolysis, converts glucose in food to provide fuel. One critical product of glycolysis is lactate, which serves as a carbon source for making raw materials in the cell, a signaling molecule, and an immune response regulator. With new technology and high-throughput omics, researchers have found that lactate also participates in metabolic reprogramming to adjust for changes in the cellular environment and protein lactylation, an epigenetic modification.

In a review published in the journal **Molecular & Cellular Proteomics**, Zhimin Wang and a multinational team dive deep into the metabolic fate of lactate-derived carbon, the cross talk between glycolysis and mitochondrial energy production, and lactylation. The team discusses the role of excess lactate in inducing an acidic microenvironment in the cell, leading to differences in immune cell activation.

The authors discuss protein lactylation's role in diseases and disorders such as infections, cancer, fibrosis and heart failure. They argue that combining the study of histone acetylation sites and the metabolomics of lactates might open doors for future research and potential therapeutic targets.

DOI: 10.1016/j.mcpro.2023.100641

— Ankita Arora

Protein deletion improves metabolic disorders

The gut microbiome plays an important role in the human metabolism. Altered gut bacterial composition can lead to gastrointestinal diseases, cancer and other disorders. Small heterodimer partner, or Shp, is an atypical orphan nuclear receptor that regulates processes in the liver including bile acid, lipid and glucose homeostasis as well as immune responses. The synergistic effects of dysregulated bile acids and gut microbiota contribute to metabolic disorders such as obesity and nonalcoholic steatohepatitis, or NASH.

In a recent **Journal of Lipid Research** study, Ryan Mifflin, Jung Eun Park and Mikang Lee from Northeast Ohio Medical University and a group of researchers showed that Shp deletion improves symptoms in mice genetically altered for obesity and NASH. They studied the metabolic and gut microbial profiles of wild-type and Shp knockout mice using cohousing experiments. Shp knockout mice reared separately from wild-type mice showed decreased triglycerides and elevated levels of deoxycholic acid, a secondary bile acid. The Shp knockout mice had elevated levels of Bacteroidales and Clostridiales bacteria compared to the wild-type mice. Cohousing of Shp knockout and wild-type mice disrupted this enrichment and returned levels to baseline. On a Western diet, the Shp knockout mice absorbed less fat and had lower microbial-derived serum lipopolysaccharide and phenylacetic acid levels than controls.

This suggests Shp ablation may modulate the microbiome and provide a viable therapeutic strategy to improve obesity and NASH outcomes.

DOI: 10.1016/j.jlr.2023.100469

— Swarnali Roy

More journal news online

Look for these articles about papers in ASBMB journals in the Science section at asbmb.org/asbmb-today.

JOURNAL OF BIOLOGICAL CHEMISTRY

Harnessing a natural plant insecticide for commercial use
By Elisabeth Adkins Marnik
Researchers in Australia have identified circular peptides, called cyclotides, that affect the formation of cell membranes, causing death or restricted growth.

Cardiolipin helps fruit flies take flight
By Naushin Raheema
Researchers at New York University have found that this long-lived phospholipid may underlie the insect's extraordinary wing strength.

JOURNAL OF LIPID RESEARCH

Breaking fat: How exercise boosts your metabolism
By Carmen Morcelle
Researchers at the University of South Carolina help decipher the mechanisms by which exercise impacts lipid metabolism.

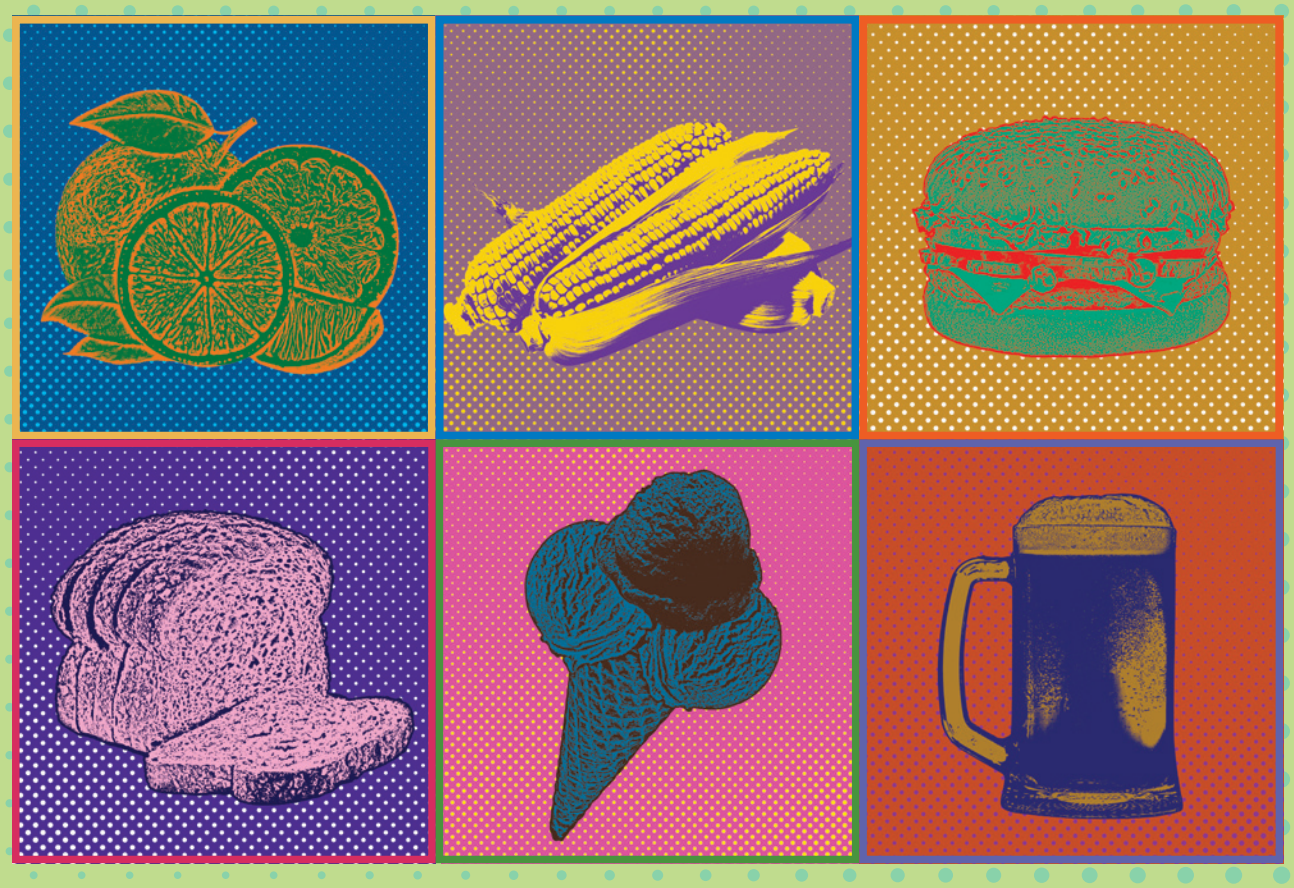
MOLECULAR & CELLULAR PROTEOMICS

Mapping out the protein path to hearing
By Briana James
To determine the profile of inner hair cell proteins, a team of researchers develops a technique that optimizes proteomics for limited sample sizes.

Adapting FOOD WITH biochemistry

Biochemists, molecular biologists and geneticists can redefine how we think about food — whether by helping crops adapt to a changing climate, enhancing nutritional value in sustainable ways or simply making food easier to eat or more delicious. This collection explores how scientists use the building blocks of life to innovate what we eat and ensure our food meets the needs of the future.

Marissa Locke Rottinghaus



From lab to land:

Modifying crops to tackle tomorrow's climate

Scientists use genetics, biochemistry and engineering to preserve a changing world's food supply chain

By Marissa Locke Rottinghaus

Imagine sitting on a shady porch on a perfect summer day, a glass of ice-cold lemonade in your hand. The citrusy tang dances on your tongue as you take a sip. But this simple pleasure is under threat. Rampant citrus disease, extreme weather and intense air pollution jeopardize the lemon trees that provides your refreshment.

Citrus greening, caused by the bacterium Candidatus Liberibacter, or CLas, spreads via the invasive Asian citrus psyllid insect, whose habitat has expanded to Florida, California and Texas as a result of global warming. Infected trees produce misshapen, bitter fruits and eventually die off. Just one of these pests can decimate an entire grove. The disease appeared in the U.S. only two decades ago and could wipe out fresh citrus within the next 15 years.

Kranthi Mandadi, a professor of plant pathology and microbiology at Texas A&M University, wants to ensure that generations after him can enjoy a glass of fresh-squeezed orange juice with breakfast.

"Here in Texas, and around the world, we love our oranges and grapefruits," Mandadi said. "But the citrus farmers are facing devastating challenges, such as unpredictable weather and water deficit, and I am surrounded by citrus greening, so I wanted to find a way to solve it."

Thousands of years ago, this bug likely would have appeared gradually over time, Mandadi said. Climate change accelerated that timeline. So scientists like Mandadi and Hiroshi Maeda, a professor of botany at the University of Wisconsin–Madison, have turned to more rapid solutions: genetically and biochemically modified crops.

COURTESY OF KRANTHI MANDADI

Kranthi Mandadi, a professor of plant pathology and microbiology at Texas A&M AgriLife Research, Texas A&M University, harvesting grapefruits from a grove during a field trial of their therapies to combat citrus greening.

"Climate change is happening so fast that classical breeding approaches are not enough to overcome the challenges we are facing," Maeda said. "It took 10,000 years for us to domesticate the crops, and we do not have that kind of time. We must accelerate the process. Using biotechnology, gene editing and transgenic approaches, combined with breeding technology, is critical."

The spread of citrus greening isn't the only climate change–induced phenomenon that threatens the food supply. Farmers and scientists face increasing temperatures, rising greenhouse gas levels and mounting climate instability. To overcome these obstacles, researchers like Rebecca Roston, an associate professor of plant sciences at the University of Nebraska, are studying how cold-tolerant plants adapt to temperature swings to create new staple crops, such as corn, that are ready for tomorrow's climate.

Public skepticism and regulatory hurdles

Since the advent of modern genetically modified organisms, or GMOs, in the 1990s, food and crop scientists have faced public backlash and struggled to receive funding. According to a recent study of mentions on social media, 32% expressed negative sentiments toward GMOs.

"Scientists and engineers want to be ready when new crops are needed," Maeda said. "Of course, we shouldn't push the technology if society isn't ready, but knowing a drastic change in climate is here, it may be now that we need these solutions."

Developing a strategy to combat disease in plants is the first step.

The Asian citrus psyllid is the insect vector that spreads citrus greening, which is caused by the bacterium Candidatus Liberibacter spp.

However, like most pharmaceuticals, less than 10% of crop solutions make it out of the lab.

"The biggest challenge to transgenic crop releases is the regulatory process," Mandadi said.

Getting a biopesticide approved by the Environmental Protection Agency can take one to 12 years and usually costs between $5 million and $10 million. Whereas, approval for a GMO seed typically takes over 13 years and costs up to 40 times more.

"As a scientist, I could just say that GMO or CRISPR citrus is a long-term solution," Mandadi said, adding that approval is at least 10 years away and costs hundreds of millions of dollars. "Hence, even though, scientifically, we know that transgenic crops can work, we took a different approach of biopesticide that is more acceptable to the consumer to get the product faster to the growers."

Therefore, Mandadi said he prefers to focus on chemical-based or transiently expressed biopesticides for now.

Combatting citrus greening with BMB

Short-term efforts to mitigate citrus greening, such as training dogs to sniff out diseased trees, screening antimicrobial compounds and analyzing the chemical fingerprint of diseased leaves, focus on limiting spread rather than prevention.

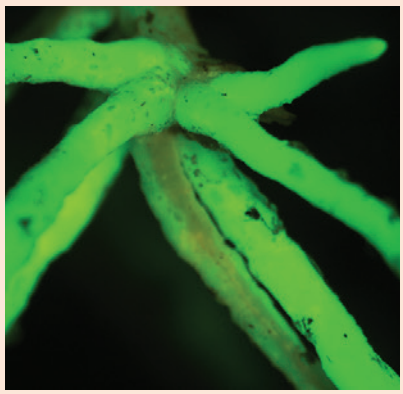
On top of that, CLas is almost impossible to study in the lab.

"(The bacteria) is hard to work with because you can't remove the pathogen from the plant itself," Mandadi said. "It's an obligate intracellular pathogen so it's unculturable, or what we call fastidious. … It can take up to two years to test one antimicrobial."

Mandadi's group generated a system to screen chemical and genetic antimicrobials against the bacteria. CLas requires a plant vascular system to grow, so they created biological vessels in the form of hairy roots from CLas-infected citrus plants using Agrobacterium rhizogenes. The team used this system to grow CLas in the lab on demand and test various therapies.

"This system is about four times faster than a traditional test that you would do in a greenhouse or in a field trial," Mandadi said in a Citrus Industry article. "It is not going to replace those trials, but it will step up the speed of preliminary screening."

Mandadi then developed a solution that could fight infection altogether. His team screened several antimicrobial peptides, originally isolated from spinach, against CLas infection. When they expressed the spinach defensins into the CLas-hairy roots or transiently in citrus trees using a viral vector, they greatly reduced CLas infection and improved fruit yield.



COURTESY OF KRANTHI MANDADI

Kranthi Mandadi developed the citrus hairy root system to speed the screening of various antimicrobials against the bacterium that causes citrus greening.

"One of our biggest challenges is to move the discoveries from the lab to the field as (commercial) products," Mandadi said.

He and his group couldn't do it alone, so they joined forces with Southern Garden Citrus and Silvec Biologics. The team can deliver the defensins into the trees using a self-replicating virus vector, via grafting without the need for engineering the citrus tree itself. In orange groves, they've seen that this treatment improves yields by up to 40%. Now, Southern Garden Citrus, Silvec, and Mandadi are seeking EPA approval for this new biopesticide.

Adapting to changing temperatures

Many people think of higher temperatures and heat waves when they think of climate change, but cool seasons are also affected.

According to the U.S. Climate Program Office, the expanding Arctic polar vortex — a strong band of winds in the stratosphere around the North Pole — is bringing extreme winters to parts of the U.S. Colder temperatures stunt the growth and productivity of essential crops such as sorghum, a close relative of corn found in some cereals and pastas.

To combat food insecurity caused by extreme temperatures, Rebecca Roston, the Nebraska plant sciences professor, and Sunil Kenchanmane Raju, Roston's collaborator and an assistant professor of plant resilience

CRAIG CHANDLER, UNIVERSITY OF NEBRASKA, UNIVERSITY COMMUNICATION

Rebecca Roston, an associate professor and chair of plant sciences at the University of Nebraska, studies plants, such as sorghum seen here, to make them more cold-resistant.

at the University of California Riverside, use omics to make crops like sorghum resistant to chilling stress.

"The reality is that the cold has driven human habitation and agriculture for millennia, and it is a problem that is so big that we don't see it, because it's opportunity loss, not direct crop loss," Roston said. "If we could choose to grow plants year-round, we would have much more gain from the same land."

To fortify crops so they can survive cold spells, Roston's team turned to sorghum's cold-tolerant cousin, foxtail millet.

After exposing sorghum and foxtail millet to cold temperatures, the team used whole genomic and lipidomic sequencing to analyze their responses. They found that both grains' defenses are governed by the circadian clock. However, foxtail millet's lipid profile showed a few key alterations.

"Circadian rhythms exist across all walks of biology," Roston said. "Plants have a strong dial rhythm that happens over 24 hours like other animals. … But they also have an additional layer of really strong metabolic influences in response to stresses."

After a few hours of cold exposure, foxtail millet upregulated the membrane lipid monogalactosyldiacylglycerol, or MGDG, and eliminated many of its rigid membrane double bonds. MGDG and other unsaturated fatty acids promote fluidity at low temperatures, which may allow foxtail millet to resist membrane sheering when facing cold stress.

The team identified multiple gene candidates for improving membrane tolerance to cold. In their future experiments, Kenchanmane Raju will modulate cold-responsive genes and lipids in sorghum to take advantage of its natural heat tolerance in regions with colder springs.

Playing with gene and lipid expression is a double-edged sword, according to Kenchanmane Raju.

"It's always a challenge to think about engineering any plants by utilizing these stress-responsive or stress-tolerant genes," he said. "There's always an energy cost. So, if you overexpress a particular gene throughout the plant body, there's always some negative consequences to its growth or other biological processes."

To propel genetically altered crops to the field, Kenchanmane Raju and Roston will need to fine-tune their approach. Few resources exist for single-cell sequencing in plants, meaning that nonspecifically genetically engineering an entire plant can lead to off-target effects.

COURTESY OF SUNIL KENCHANMANE RAJU

Sunil Kenchanmane Raju, an assistant professor of plant resilience, recently opened his own lab at the University of California Riverside and will develop single-cell sequencing technologies in plants.

"There are many ways to mitigate these effects," Kenchanmane Raju said. "One of them is to try to find out where and when the plant needs the stress-responsive genes. Once we understand this, we precisely engineer the targeted genes to be expressed in the optimal conditions and cell types."

Roston said incorporating these alterations could be a game changer for farmers, allowing them to move up their growing season without worrying about the risk of early or late freezes.

"To mitigate the effects of high temperatures during reproductive stages, when the plants are much more susceptible, we must think about changing some of the agronomic practices," Kenchanmane Raju said. "Farmers can try to plant early (when soil is cooler) so the peak reproductive stage does not coincide with the highest temperatures. … I think our chilling stress–tolerant plants are indirectly helping mitigate the effects of high temperatures late in the season."

Conquering greenhouse gases

Perhaps the best-known consequence of climate change is the disappearing ozone, caused by accumulating greenhouse gases and smog, about a third of which are linked to food production and agriculture. According to Joseph Jez, a Howard Hughes Medical Institute professor of biology at Washington University in St. Louis, a 1% decrease in the ozone layer leads to a 1% drop in soybean yield. Since 1979, the ozone threshold has plummeted by more than 47%.

"One percent may not seem like

SEAN GRACIA, WASHINGTON UNIVERSITY IN ST. LOUIS ARTS & SCIENCES

Joseph Jez, a professor of biology at Washington University in St. Louis, and Ashley Sherp, a former Ph.D. student in the Jez lab, work together on understanding metabolic regulatory networks and environmental responses in plants.

much," Jez said. "But each percent leads to a few billion dollars lost each year by farmers in the American Midwest."

This decline in atmospheric air quality can exacerbate respiratory and cardiovascular conditions and put pressure on global health systems. With the global population rising, society needs food solutions that don't exacerbate the greenhouse gas problem.

Hiroshi Maeda, the UW–Madison botany professor, has dedicated his research career to unlocking the mysteries of plant metabolism and developing innovative solutions to combat climate change.

"I've always been fascinated with how plants regulate different metabolic processes and control the competition of their growth and chemical production," Maeda said. "At the beginning of my career, I thought there would be big potential impacts for society in this area, but plant biotech was lagging behind."

When Maeda and Jez serendipitously found a mutation in the model plant Arabidopsis that increased CO_2 fixation by up to 30%, they immediately capitalized on it.

"Nature is always mixing and matching solutions to different molecular, cellular, developmental and environmental problems," Jez said. "If we understand how plants respond to environmental changes, stresses or challenges, can we engineer them or use pathways from other plants or microbes to give them an advantage?"

Jez and Maeda found that a mutation in the gene suppressor of tyra2, or sota, eliminated a negative feedback loop in the shikimate pathway, a key gateway in aromatic amino acid synthesis in plants. This mutation decouples the plant's internal regulation, allowing the cells to pump more CO_2 molecules into the synthesis pathway. From a structural perspective, Jez said the gene acts like a dimmer switch.

This mutation boosts the capturing of carbon dioxide from the atmosphere. On top of that, the mutant pathway could be utilized to make valuable aromatic compounds, such as woods, pigments, beneficial nutrients, medicine, and even industrial bio-based materials.

"I think our technology provides a very exciting dual benefit," Maeda said.

Now, Maeda and Jez are tweaking this pathway in crops such as soybeans and corn. However, Jez said this is a difficult task because, even though all plants use the amino acid synthesis pathway, each plant species evolved its own regulatory checks and balances.

SARAH FRIEDRICH, UNIVERSITY OF WISCONSIN–MADISON

Hiroshi Maeda is a professor of botany at the University of Wisconsin–Madison, who studies the evolution of complex plant metabolic pathways across different species to mitigate the effects of climate change.

"When you learn about the amino acid (synthesis) pathway in class, you think, 'Oh, that's already known. This is boring; it's old fashioned,'" Jez said. "But then you realize nature has evolved all of these other little alternative routes and minutiae to do what it needs to do."

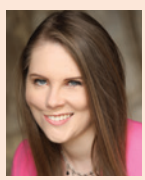
Researchers like Jez, Maeda, Kenchanmane Raju, Roston and Mandadi are racing against time to create cold-resistant crops, novel biopesticides and alternative farming methods to combat climate change's assault on citrus, sorghum and other crops.

"The plants we have now are not going to be the plants we have in 2050," Jez said. "The big unknown is whether we can either breed or edit the path forward to make plants survive the climate of 2050 or 2100. Can we do it fast enough while also trying to figure out how to do it with less water and less soil? There are a lot of big systems biology challenges here, but I think that's where biochemistry, genetics and developmental biology can make a difference."

These innovations could help ensure enough crops to meet demand — But is society ready to accept GMO foods?

"One way to change consumer sentiments is by gaining their trust. We can each reach out to our friends and family and connect with them to share the benefits of the new technologies and encourage them to share the same with their friends," Mandadi said. "It's in our hands to improve foods and save our changing world."

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for ASBMB.



Pea-yond mainstream meat alternatives

Scientists use enzymes to create a beef-like texture

By Marissa Locke Rottinghaus

Have you ever bitten into a plant-based burger expecting the texture of meat and gotten an astringent, chewy alternative? You can probably blame your disappointment on the pea proteins that make up ground beef alternatives from brands such as Beyond Meat.

Meat analogs such as the Impossible burger are made with wheat proteins, which produce a more realistic beef-like texture. And Impossible products, compared with Beyond, are sold by almost twice as many fast-food retailers.

But your Impossible Whopper might be in for competition. B. Pam Ismail, founder and director of the Plant Protein Innovation Center, and colleagues at the University of Minnesota are working to modify pea and other legume proteins so their texture more closely resembles beef.

Why? Wheat gluten is one of the nine leading causes of food allergies in the U.S. And legumes such as peas are easy to grow and have several environmental benefits.

COURTESY OF THE UNIVERSITY OF MINNESOTA PLANT PROTEIN INNOVATION CENTER

Fan Bu, a Ph.D. student at the University of Minnesota, uses cold plasma jet technology on pea protein isolate to eliminate contamination and improve solubility.

Greener alternatives

According to some experts, the beef industry is one of the driving causes of climate change. A single cow produces about 220 pounds of methane and requires a whopping 15,400 liters of water per year.

"Consumers are becoming more aware of the impact of the meat industry on the use of the current available land and the impact on the environment, such as greenhouse gas emissions, water use and soil health," Ismail said.

Alice H. Lichtenstein, a senior scientist and leader of the Cardiovascular Nutrition Team at the Jean Mayer U.S. Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, encourages people to cut down on the amount of meat they consume and shift to more plant foods for health as well as environmental benefits.

"The biggest differences between beef and plant-based meat alterna-

COURTESY OF THE UNIVERSITY OF MINNESOTA PLANT PROTEIN INNOVATION CENTER

Pam Ismail, a professor of food science, started the Plant Protein Innovation Center to seek sustainable and environmentally friendly sources of plant-based proteins.

tives are that the latter contain more unsaturated and less saturated fat and is better for the environment," Lichtenstein said. "However, it is important to keep in mind that plant-based meat alternatives are an ultraprocessed food and tend to be high in sodium."

Replacing beef with plant-based alternatives could slow the effects of climate change. However, the U.S. is also entrenched in a water crisis. According to a recent study, nearly half of the country's freshwater basins may not be able to meet national water demands by 2071.

According to Lichtenstein, people can modify their food choices in other ways to make them better for the environment, for instance, by choosing plant-based sources of protein in their unmodified state such as legumes, peas or beans, and nuts, as well as dairy products and eggs in moderate amounts.

This is where pea crops come in. Compared with pea plants, wheat crops require about seven times more water per year. So, farmers prefer to grow peas over wheat.

Meat analog molecular mechanisms

Before Ismail founded the Plant Protein Innovation Center in 2018, she saw a disconnect between academic and industry food science.

"In industry, I noticed that there is a big lag in the knowledge and research on proteins," Ismail said. "And I thought, if I don't start the center, somebody else will."

Ismail works with companies such as Bayer, Cargill, General Mills and other corporations to bring academic discoveries to the market. Driven by consumer demand for more healthful meat alternatives with realistic textures, these companies are investing resources in protein research.

Ismail and her team decided to see if they could modify the molecular structure of pea protein to impart a firm, gel-like texture.

Unlike wheat gluten and soy proteins, pea and chickpea proteins have low molecular weight polymers and form fewer disulfide bonds within and between protein molecules. Accordingly, pea and chickpea proteins form a relatively weak gel, making the end product loose and stodgy.

"We try to look at and adapt the furthest upstream steps during protein ingredient production," Ismail said. "Can we protect the protein integrity during processing so it's not damaged or make it more soluble or stable while forming a gel?"

Ismail and colleagues hypothesized that modifying pea and chickpea proteins with an enzyme might make them more likely to link up. They treated the proteins with transglutaminase, what Ismail calls a "meat glue" that promotes covalent bonds between glutamine and lysine, both of which are abundant in these proteins. This enzyme naturally occurs in the human body and promotes wound healing.

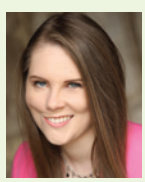
Compared with unmodified and commercially available pea and chickpea proteins, their transglutaminase-treated counterparts formed larger molecular-weight polymers and stronger gels.

"When you add transglutaminase, it promotes a certain linkage between protein molecules to make them form a longer polymer so that they can form a gel and hold water," Ismail said.

After downstream processing, transglutaminase-treated proteins could create a firm, beef-like texture in a product like a burger, she said. Ismail and her team will work with company partners to figure out how these results could be efficiently translated into a marketable product.

"We need to develop more sustainable processes to get the protein out of the plant," Ismail said. "There's a lot of work involved when scaling something from bench to the industry scale. That's why we partner with companies: to ensure these processes are scalable and sustainable."

Marissa Locke Rottinghaus (mlocke@asbmb.org) is the science writer for ASBMB.



Fortifying food to fight malnutrition

Microparticles increase shelf life of vitamins

By Marissa Locke Rottinghaus

What if you could create a meal for Bill Gates? But as a scientist, not a chef.

Ana Jaklenec did just that when she was a research scientist working with Robert Langer, a professor at the Massachusetts Institute of Technology.

Jaklenec and Langer teamed up with the Bill & Melinda Gates Foundation on a strategy to fight malnutrition. They developed a microparticle to encapsulate micronutrients in staple foods such as flour, preventing nutrient decay during storage.

In developing nations, lack of proper food storage can prevent people from getting the nutrients they need. Micronutrients are unstable and have short shelf lives, so they're difficult to incorporate into food staples.

"We know that for many (nutrients), absorption is better via food rather than pills or supplements," Jaklenec said. "So that was the motivation behind this project."

Jaklenec and colleagues created a heat- and water-stable microparticle slightly larger than the diameter of a human hair made of basic methacrylate copolymer, or BMC. The team added iron-containing BMC to flour and fed volunteers, including Gates, bread baked with the fortified flour. The recipients absorbed iron encapsulated in BMCs at similar percentages to free iron.

Both Langer and Gates tried the fortified flour–containing bread. "And we're all doing fine," Langer said in a press release.

A nutrient boost

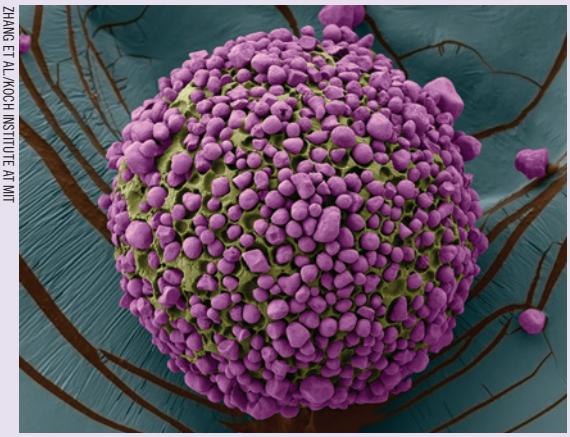
In her own lab, Jaklenec, now a principal investigator at MIT, and grad student Linzixuan (Rhoda) Zhang have taken BMC a step further, loading it with vitamin A. In regions of sub-Saharan Africa and South Asia, more than 45% of children are vitamin A deficient, which can cause blindness.

Vitamin A is commonly found in enriched flour but, according to a UNICEF study, in high-heat conditions, such as those in some developing African nations, stored flour loses more than 85% of its vitamin A content within three months.

Compared with free and commercially available encapsulated vitamin A, the researchers found that vitamin A–BMC microparticles remained stable two and six hours longer, respectively, in boiling water. The microparticles became even more stable when added to bouillon cubes.

The team next used rats to examine how well cooked vitamin A was absorbed, either free or encapsulated in BMC. Absorption was nine times greater in rats fed vitamin A–BMC microparticles than free vitamin A.

When tested in humans, their vitamin A–BMCs were absorbed in the stomach and gut much like free vitamin A.



ZHANG ET AL/KOCH INSTITUTE AT MIT

A polymer coating (green) stabilizes micronutrients and protects them from heat degradation caused by cooking. The starch (purple) on the outside makes it easier for the particle to incorporate into foodstuffs such as flour or bouillon cubes. When digested, the particles break down, and the body absorbs the nutrients.

The team is now working on another microparticle. BMC is only soluble once it reaches the acidic stomach and is a nonbiodegradable polymer. Jaklenec said this generates some concern that BMC polymers harm the environment, so Zhang created a novel microparticle that is broken down to sugar and amino acid–based derivatives by hydrolysis during the cooking process. The lab has done preliminary testing, and Zhang is working to get U.S. Food and Drug Administration approval.

"We hope this polymer will be on the shelf one day," Zhang said.

The scoop on no-melt ice cream

By Marissa Locke Rottinghaus

MICHAEL KING, UNIVERSITY OF WISCONSIN–MADISON

Cameron Wicks, then a Ph.D. student at the University of Wisconsin–Madison, prepares samples of her "no-melt" ice creams for melting tests.

Nothing beats a frozen treat on a scorching summer day — until you face the race to finish before it all melts away. But now biochemists at the University of Wisconsin–Madison are working on creating ice cream that stays in the cone instead of dripping onto your hands — or the sidewalk.

Cameron Wicks, a recent Ph.D. graduate at UW–Madison, spent time in the lab perfecting her "no-melt" ice cream recipe. The secret? Polyphenols.

Also known as tannins, polyphenols are naturally occurring compounds in fruits and vegetables that boast antioxidant properties and health benefits. However, Wicks had a different purpose for these molecules in mind.

She was inspired by a Japanese no-melt popsicle that went viral on social media.

At UW–Madison, she applied the same principles used in the Japanese popsicle by adding polyphenols to cream and found that some of these molecules slowed its melting rate.

Brad Bolling, an associate professor of food science and Wicks' mentor, provided his expertise in creating sustainable foods to the project. "This is another ingredient we can add to our food science toolkit," he said.

However, polyphenols are a large family of molecules, so finding the right ingredients and concentration required extensive optimization.

By performing melting tests, Wicks narrowed down the choice of molecules and landed on tannic acid as the polyphenol with the greatest "no-melt" effect.

When she examined the ice cream supplemented with tannic acid closely using a microscope, Wicks found that tannic acid links up with the water, fat and protein molecules to create a lattice network, which holds the water molecules in place, she explained, and doesn't allow them to accumulate.

"It's more of a no-drip ice cream," she said. "The fat aggregates caused by the polyphenols are the reason why the system is able to hold water and the matrix for extended periods of time."

Commercial ice cream contains chemical stabilizers designed to combat freezer burn. However, Wicks said, replacing these with polyphenols, such as blueberry powder, could eliminate unfamiliar ingredients and enhance the health benefits of sweet treats.

"In our typical diets, we are not getting enough fruits, vegetables and whole grains, which are the major sources of polyphenols," Bolling said. "So, if we can create a meal that includes polyphenols in the appetizer, main course and dessert, why not look for those applications? … This research project demonstrates the feasibility of that."

Future work at UW–Madison will focus on optimizing the taste and texture of ice cream that contains polyphenols. In addition, Wicks said she looks forward to introducing polyphenols into dairy-free ice creams, which have a faster melting rate than cream-based treats due to their high water content.

"When you think about nondairy ice creams, there are a lot of challenges to overcome when creating a system that delivers a similar experience to its dairy counterpart," Wicks said. "I'm definitely excited to see how this research might be able to help make nondairy ice cream better quality and more palatable."

Biochemistry lightens up beer brewing

Geneticists study what produces a refreshing sip

By Marissa Locke Rottinghaus

While beers such as ales, stouts and sours have their own fanbases, America has long favored a crisp, refreshing lager. But what makes a yeast variety suitable for light, lager beer rather than ales?

According to Chris Todd Hittinger, a professor of genetics at the University of Wisconsin–Madison, Saccharomyces cerevisiae, or baker's yeast, requires a warm environment for optimal fermentation. This works well for brewing heavier beers, such as ales. However, to produce a lager, brewers need yeast that ferments best at cool temperatures.

Industrial lager brewers favor S. pastorianus, a hybrid of S. cerevisiae and a wild ancestor. Scientists did not understand how S. cerevisiae evolved to give rise to a cold-dwelling species until they discovered the wild ancestor of lager yeast, S. eubayanus, in 2011.

To understand this evolution, Hittinger's lab compared the genomes of S. cerevisiae and S. eubayanus and found that S. eubayanus acquired cold tolerance in part through its mitochondrial genome.

"When we do experiments where we take a strain of industrial lager yeast, all of which have the S. eubayanus mitochondrial genome, and swap in the S. cerevisiae mitochondrial genome, the temperature preference of the yeast shifts upwards," Hittinger said. "We think this is one of the big smoking guns, and it explains why all industrial lager strains have an S. eubayanus mitochondrial genome."

Sugar, sugar, sugar

Beer starts with three main components: hops, yeast and wort — a sugary grain water that contains maltose and maltotriose.

"Unless you like cloyingly sweet beers ... you need to ferment all of the fermentable sugars into carbon dioxide and ethanol to create a nice, crisp, dry lager you'd enjoy on a hot summer day," Hittinger said.

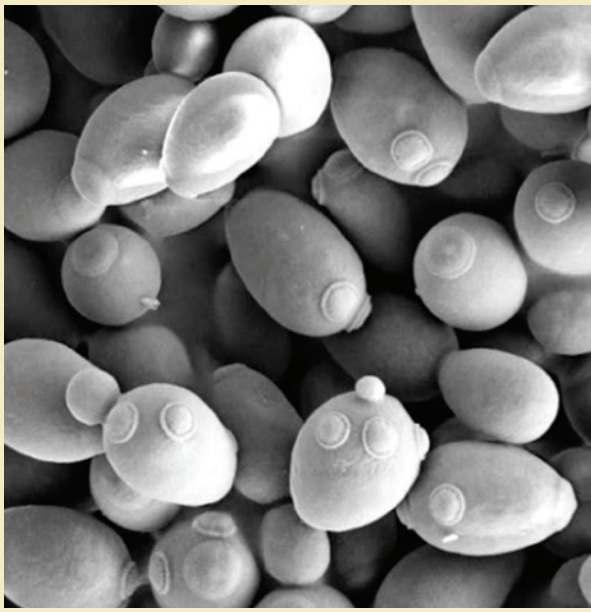
Domesticated lager yeasts can ferment maltotriose, but S. eubayanus cannot. Hittinger, John Crandall, a Ph.D. student in the Hittinger lab, and collaborators performed adaptive evolution experiments to find out how S. eubayanus could have acquired this trait. They found two distinct mechanisms.

"Both of our studies show that it takes pretty dramatic mutations to evolve this key trait," Crandall said.

When selecting for maltotriose use, they found S. eubayanus acquired a novel, chimeric maltotriose transporter via genetic recombination of two MALT genes, which alone drive maltose metabolism.

Conversely, when they performed experiments selecting for maltose use, they found that the mutant S. eubayanus changed from diploid to haploid. This change activated an alternative metabolism in the yeast cells, allowing a haploid-specific gene to activate a previously dormant sugar transporter.

"Most of the advantage that haploids have comes from the fact that they express a small set of haploid-specific genes, which defines their cell type," Crandall said. "None of these (haploid) genes were known to have any regulatory crosstalk with metabolic pathways in Saccharomyces cerevisiae, where that cell type–specification circuit has been extensively studied."



COURTESY OF MOGANA DAS MURTEY AND PATCHAMUTHU RAMASAMY VIA WIKIMEDIA COMMONS

Shown is a scanning electron microscope image of Saccharomyces cerevisiae budding.

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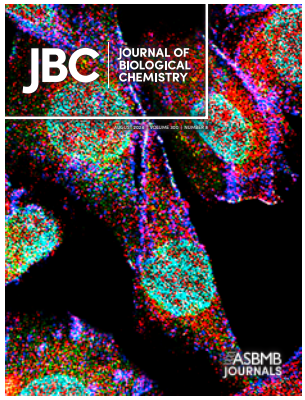

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Melissa J. Moore

Professor, University of Massachusetts Chan Medical School
Chief scientific officer emerita, Moderna

Richard Silverman

Professor, Northwestern University

KEYNOTE LECTURES

- **David A. Fidock:** Molecular insights into antimalarial drug resistance, *winner of the Alice & C.C. Wang Award in Molecular Parasitology*
- **Benjamin A. Garcia:** An unlikely career in science and academia, *winner of the ASBMB Ruth Kirschstein Diversity in Science Award*
- **Neena Grover:** Embracing collaborations: Loving what we do and doing what we love, *winner of the ASBMB William C. Rose Award for Exemplary Contributions to Education*
- **Robert N. Helsley:** The contribution of fatty acid oxidation to diet-induced hepatocellular carcinoma, *winner of the Walter A. Shaw Young Investigator Award in Lipid Research*
- **Andre Nussenzweig:** Maintaining genome stability, *winner of the Bert and Natalie Vallee Award in Biomedical Science*
- **Rohit V. Pappu:** Phase separation in cells: Insights from biophysical computations, *winner of the ASBMB DeLano Award for Computational Biosciences*
- **Joseph Schlessinger:** Cell signaling by receptor tyrosine kinases: From basic principles to cancer and other therapies, *winner of the Herbert Tabor Research Award*
- **Judith Storch:** Functional analysis of intracellular lipid-binding proteins, *winner of the Avanti Award in Lipids*
- **Vincent Tagliabracci:** Expanding the kinome, *winner of the Earl and Thressa Stadtman Young Scholar Award*
- **Nicole C. Woitowich:** Special remarks at the Women's Networking Dinner, *winner of the ASBMB Emerging Leadership Award*

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The program planning committee, chaired by **Donita Brady** of the University of Pennsylvania Perelman School of Medicine and **Dave Pagliarini** of Washington University School of Medicine in St. Louis, has assembled a slate of inspiring symposia, described on the following pages.

Chemical tools to reveal new biology


Organizers: George Burslem, University of Pennsylvania, and Yael David, Memorial Sloan Kettering Cancer Center

Chemical biology is a powerful interdisciplinary bridge linking basic and translational research. This symposium will focus on cutting-edge chemical technologies developed and applied to understand, modulate and control various biological systems. Stay up to date on the latest methodologies and scientific approaches that you can take back to your lab.

Metabolism and biosynthesis


Organizers: Lydia Finley, Memorial Sloan Kettering Cancer Center, and Gerta Hoxhaj, University of Texas Southwestern Medical Center

Dive into how metabolic pathways are regulated, how they support growth and how cells balance competing metabolic demands with field leaders in this symposium. We will cover recent research in the basic architecture of metabolic networks, emerging approaches to monitoring metabolism and insight into how these pathways contribute to disease.

Synthetic biology


Organizers: Vatsan Raman, University of Wisconsin–Madison, and Danielle Tullman–Ercek, Northwestern University

Synthetic biology tools and approaches allow us to interrogate and engineer microbial and mammalian systems across scales: from molecular (nucleic acids, proteins, lipids) to network (regulation, metabolic pathways) to multicellular systems (tissues, biofilms, microbiomes). This symposium will highlight the latest synthetic biology applications from human health to sustainability. Discover emerging ideas and techniques that you can apply to your own research program.

Host–pathogen interactions

Organizer: Tamara O'Connor, Johns Hopkins University School of Medicine

The interplay between pathogens and their hosts is a critical determinant of infectious disease. In this symposium, we will examine the chemical cross talk between pathogens, microbiota and immune cells that enable host colonization. We will also delve into pathogen macromolecular machines, host cell takeover and pathogen dissemination. Come share your insights to make the next generation of antimicrobial drugs possible.

Empowering futures: The transformative power of mentorship in science

Organizers: Nisha Cavanaugh, Sanford Burnham Prebys Medical Discovery Institute; Orla Hart, Purdue University; and Reinhart Reithmeier, University of Toronto

Dive into a world where mentorship meets innovation, growth and community building. This symposium will examine mentorship at different stages. We will spark conversations about what it means to have successful mentoring relationships and creative approaches for engaging trainees. Reconnect with colleagues and meet new ones to inspire, educate and explore the transformative power of mentorship.

Interorganellar signaling and communication

Organizers: Navdeep Chandel, Northwestern University and Isha Jain, Gladstone Institutes–University of California, San Francisco

Organelle cross talk is essential for coordinating compartment-specific metabolism within the cell. In this symposium, we will explore how organelles exchange materials and communicate during homeostasis and how this breakdown could lead to disease. Join us as we explore the latest research on the intricate cellular dialogues.

Metals of life: From microbes to medicine

Organizers: Sabeeha Merchant, University of California, Berkeley, and Amit Reddi, Georgia Tech

Transition metals play important roles as cofactors and signaling molecules. We will highlight and explore how cells sense metals to balance their essential functionality and toxicity in this session. Join us and contribute your expertise to this discussion of metallobiology.

Lipids and membranes


Organizers: Gerry Hammond, University of Pittsburgh, and Judith Simcox, University of Wisconsin–Madison

Dysregulated lipid levels and signaling are hallmarks of metabolic diseases including Type 2 diabetes, cardiovascular disease, cancer and neurodegenerative diseases. This symposium will cover the basic and disease-driving functions of lipids in cellular regulation and disease etiology. Discover the latest insights that will make the next generation of lipid-modifying drugs possible.

Oncogenic hubs: Chromatin regulatory and transcriptional complexes in cancer


Organizers: Cigall Kadoch, Harvard Medical School, and G. Greg Wang, Duke University School of Medicine

Oncogenesis can be initiated or maintained by altered biomolecular condensates, or "hubs," involving proteins such as transcription factors and RNA-binding proteins as well as chromatin–regulatory and ATP-dependent chromatin remodeling complexes. This symposium will advance our understanding of perturbed chromatin structure and aberrant gene expression in cancer and other diseases. Stay up to date and kickstart your next breakthrough in oncogenic hubs.

Molecular movement and compartmentalization


Organizers: Nora Kory, Harvard T.H. Chan School of Public Health, and Tim Levine, University College London

This symposium will explore the establishment, maintenance and regulation of spatial compartment heterogeneity and the dynamics of molecular transfer. We will highlight the impacts of disrupted metabolic compartmentalization in human disease, emphasizing the roles of solute carriers and molecular transfer across organelle contact sites. Join us as we discuss the latest in molecular movement and compartmentalization.

Structural biology of proteins and subcellular structures


Organizers: Christopher Barnes, Stanford University, and Breann Brown, Vanderbilt University

For decades, determining macromolecular structures has been pivotal in deciphering the complexities of biology and cell signaling. This symposium will spotlight the evolution of computational and imaging methods, which has transformed our study of elusive macromolecules and cellular architectures. Learn about the latest methods in structural biology that can kickstart your next structural discovery.

Maximizing access through diversity, equity, inclusion and accessibility


Organizers: Carlos Lopez, Altos Labs, and Teresita (Tere) Padilla–Benavides, Wesleyan University

This symposium will amplify the interests of underrepresented scientists. Speakers will share their personal narratives of navigated barriers and transformed scientific culture through their contributions to science. It will highlight scientists' innovative ideas and initiatives on mentorship, skills development, community-building and strategies for improving recruitment, retention and sense of belonging.

New frontiers in enzyme and pseudoenzyme research


Organizers: Shantá D. Hinton, College of William and Mary, and Vincent Tagliabracci, University of Texas Southwestern Medical Center

Some proteins act as moonlighting enzymes, performing the canonical enzymatic function of the superfamily as well as alternate functions, while pseudoenzymes have no catalytic function but play important roles in human health and disease. Join us and explore the expanding roles of these unique proteins across diverse areas of biology.

RNA biology


Organizers: Sergej Djuranovic, Washington University in St. Louis, and Olivia S. Rissland, University of Colorado School of Medicine

This symposium will showcase how coding and noncoding RNAs throughout the cell are central players in a wide spectrum of biological processes. See how we are making the next generation of technologies and RNA-based therapies possible together.

Network and discover new findings, approaches and connections.

This is your chance to learn, grow, contribute and make more amazing discoveries possible.

g investigator seminar: A daylong event for graduate students and locs, featuring an interactive career panel and oral presentations. For a ance to share your research in an oral presentation, indicate your interest when you submit your abstract.

Poster sessions: A forum for scientists and educators at all career stages to present their latest research and gain valuable feedback.

Workshops: Learn technical skills and shape the future of science via education, professional development or diversity, equity, access and inclusion. Designed and presented by scientists and science educators.

One-on-one mentoring: Personal mentoring on a variety of career-related topics to elevate your professional profile, such as: CV, résumé and cover letter writing, career exploration advice and much more.

erest group sessions: Share the latest in the field, exchange s and learn about new areas of interest.

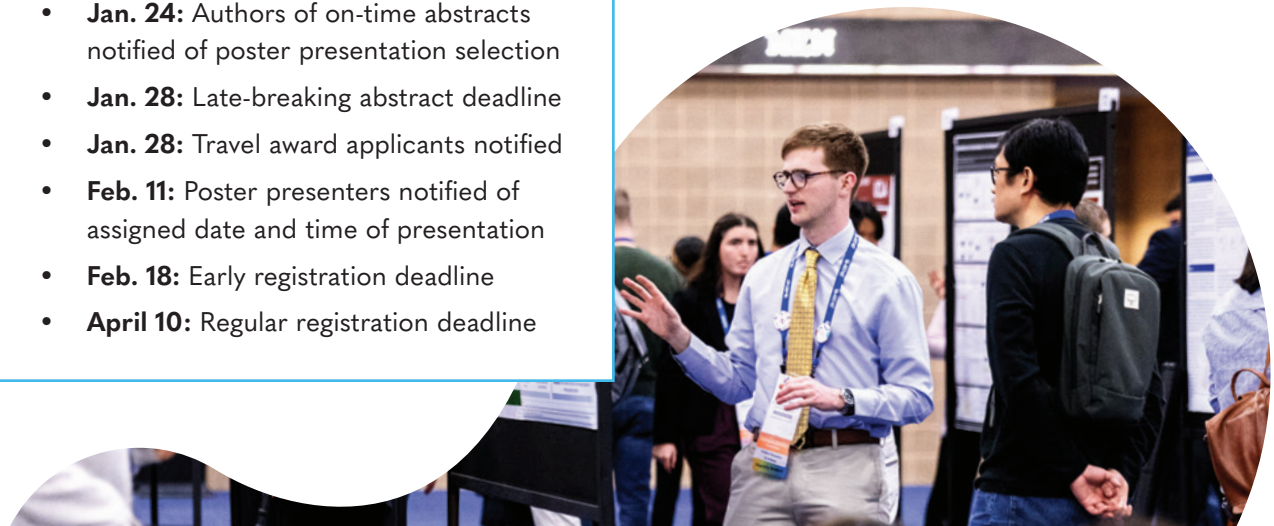
Meetups: A casual venue to share experiences, brainstorm solutions and forge new connections.

Professional development: Career coaching, sessions and networking to help you chart your next career move.

Exhibitions: The latest products and services that make your research possible. Engage with company representatives in the exhibit hall.

Important deadlines

- **Dec. 9:** On-time abstract deadline
- **Dec. 9:** Travel award application deadline
- **Jan. 6:** Late-breaking abstract submission opens
- **Jan. 17:** Authors of on-time abstracts notified of talk selection
- **Jan. 24:** Authors of on-time abstracts notified of poster presentation selection
- **Jan. 28:** Late-breaking abstract deadline
- **Jan. 28:** Travel award applicants notified
- **Feb. 11:** Poster presenters notified of assigned date and time of presentation
- **Feb. 18:** Early registration deadline
- **April 10:** Regular registration deadline



The 2.5 points of no return in my scientific career

By Gertrude-Emilia Costin

"Once you leave academia for industry, you will never return — or want to return."

I am an academic and biochemist and have worked the last 17 years as a toxicologist in industry. I've faced many inflexion points during my career, but I considered none of those transitions among similar fields to be of no return.

Several crossroads, however, are worth sharing.

Point 1: The pace

I interview many young academic scientists who say, "Yes, I've heard of this fast pace in industry, but academia is no different."

I smile and say to myself, "Oh, you better believe it — it is very much different."

There's no point in debating. Some love how addictive it is, and some run away at the first opportunity.

Working in industry was a new language for me to learn. For some time, I listened and understood nothing. Gradually, colleagues translated the industry terms, and I learned about advertising, marketing, sales, competition and intellectual property. Then the marathon started. The infectious rhythm in industry cannot be paralleled.

The politics of academia and the writing of grants seemed to exist in a distant past, and my desire to return to them waned.

Point 2: The rules

In labs that are not governed by good laboratory practices, or GLPs, researchers have some flexibility in how they document, check and keep experimental records. However, GLPs require that every entry is initialed and dated, every error is addressed following set rules, and every change to an experimental protocol is made by amendment.

Once this GLP microbe got into my system, it never went away. I know some scientists who have left a GLP environment for one with looser regulations, and they could not stand it. They preferred dealing with regulated records and audits.

I would find it difficult now to function in a laboratory without the strictness of GLPs, and I'd try to implement them where they don't exist.

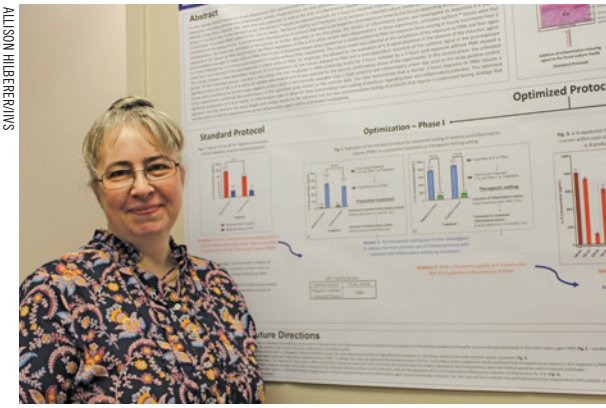
Point 0.5: The promotion

Another point of no return can be the moment a scientist leaves the trenches of the operations side and steps into management.

This one, however, is like riding a bicycle: If asked to step back into the lab, a scientist will find their way to a pipette and quickly remember how to follow a protocol.

I recently had to do just that when I provided training on a method I had not performed in the lab in nearly two years. I had to execute it without error. It didn't take much effort — the memories rushed back, connecting neurons, eyes and hands until it seemed I had done it yesterday.

ALLISON HILBERER/IIVS



Gertrude-Emilia Costin shares a poster at the 2023 Institute for In Vitro Sciences "Share Your Science Day," an internal event for researchers. IIVS is a nonprofit that works to advance alternative testing methods.

I now spend more time at my desk and in meetings, but I don't lose any opportunity to step into the lab. As study director, I remain connected to the thrill of lab work.

I find it nearly impossible to lead anyone in operations if I don't know what they go through every day. So this point is only 0.5 of no return for me. My journey continues, for I am a traveler between both worlds.

What about you? What are the points of no return in your scientific world?

This is an edited excerpt.
Read the complete essay here:

Gertrude-Emilia Costin (ecostin@iivs.org) is the director of laboratory services and study director at the Institute for In Vitro Sciences, Inc. in Gaithersburg, Maryland.

At a career crossroads

Exploring postdoc, faculty and industry paths

By Thiago Pasin

Am I ready for a faculty position? Do I need more training? Will I be able to get funding? Am I prepared to teach?

These are some of the innumerable questions that fly through my mind as I complete my postdoc.

While my current principal investigator suggests I am not yet ready for an independent career, the PIs who have interviewed me for new postdoc roles say I am more than ready to apply for a faculty position. Who should I listen to? Who is right about my career? I am not feeling ready. But will I ever feel ready?

On the one hand, another postdoc offers the allure of continued research in a supportive environment without the need to make big decisions, apply for grants or manage people. I can delve deeper into my research interests, collaborate with experts in my field, learn new and cool techniques and potentially publish more papers. Another postdoc could enhance my credentials, increase my skills and make me more competitive for a faculty position in the future.

On the other hand, applying for a faculty position represents a significant shift in my career. It means taking on new responsibilities, such as teaching and mentoring students, and navigating the complexities of academia as an independent researcher. People in academia say this would make me a "grown-up scientist with a real job." This exciting prospect comes with its own challenges and uncertainties. Will I be able to secure funding? Can I balance the demands of research, teaching and administrative duties?

Oh, wait. What about industry jobs? Is it too late now? This option remains open, and it is tempting if I want to use my skills and expertise in a more applied setting. I could work on real-world problems and collaborate to develop applied solutions. Industry jobs often come with higher salaries and better benefits than academic positions.

However, in an industry role, I would need to develop new skills and adapt to a different work culture. The environment may not offer the same level of intellectual freedom, publication interest or opportunity for academic recognition. How much do I value these aspects of my work?

My decision is complicated by the current job market, visa timing issues and the availability of positions in my field. The academic landscape evolves constantly, and competition for faculty positions can be fierce. Industry jobs are also competitive.

I need to weigh not just what will propel my career, but also what resonates with my values and long-term objectives. I aspire to make a lasting impact on my field and nurture future scholars. This goal transcends specific roles.

Given this, I've decided to take on a new postdoc position and tweak my research focus to pick up some new skills. I hope this will refresh my project ideas, make them more relevant to science and society, and boost my chances of securing funding as a faculty member.

This is an edited excerpt.
Read the complete essay here:

Thiago Pasin (tmachadopasin@dental.ufl.edu) is a postdoctoral associate in Department of Oral Biology at the University of Florida College of Dentistry. He is an ASBMB Today volunteer contributor.

The fourth third of my career

Reliving the postdoc dream

By Jonathan Monroe

I enjoyed being a postdoc, except for the constant worry about getting a permanent job. I could focus on research without having to teach or serve on committees. After a few decades as a professor, I thought it would be fun to return to that type of position. This is the story of how I made that happen in the chemistry and biochemistry department at James Madison University.

My first three thirds

In the first third of my career at JMU, I did enough research and service to get tenure, but my passion was teaching. I honed my lecture style to be as inspirational as I could, developed several course-based undergraduate research experiences, and co-led a change in our curriculum.

Over the second third, I developed my leadership skills serving on committees and as an interim department head. That cured me of any further administrative aspirations.

During the third third, my research blossomed. I spent more time doing experiments with my students at the bench, and I discovered several interesting things about plant starch metabolism.

I was able to focus on research because I learned how to say "no" more often, and I developed a collaboration with Chris Berndsen, whose protein structure and biochemistry skills complemented my plant physiology and molecular biology skills. Together, we developed a research program describing the structure and cellular function of beta-amylases.

Retiring as a postdoc

This leads me to the fourth third of my career. I wanted to be a postdoc again, without all the pressures and responsibilities of being a professor. I'd been telling friends and colleagues of this postretirement desire for decades.

In the fall of 2023, I retired at 63, became an emeritus professor and moved into Chris' lab in the neighboring building. There, I get to help mentor research students, and faculty meetings are history.

I faced some challenges making this arrangement work. Research faculty don't exist at JMU, so I had to use broad communication to define my role to the institution. And we had to merge two research programs into a single unit. We had to find space for my Arabidopsis plants in the Physics and Chemistry Building and places in Chris' lab to store the residual supplies from my career. Thirty-one years of experiments leads to the accumulation of a lot of stuff.

What is my place in the lab from the perspective of the undergraduates? A few of them knew me in my previous role, and we had to define early on where I fit into the existing team. Fortunately, they quickly adapted to calling me Jon, and I slid into my role as something like a postdoc. Chris and I have adjusted to the new working relationship where he is the boss through clear communication and knowing that this is a process.

COURTESY OF JONATHAN MONROE

Jonathan Monroe in the lab at James Madison University with some of his Arabidopsis plants.

Wouldn't it be nice if universities had a program that allowed a retired faculty member to pair up with a junior or mid-career faculty member to assist with their research program and help mentor students and trainees?

We all hope for rewarding experiences after retirement, and that can happen in a wide variety of ways. For me, using my skills and creativity in a less pressured way was in the back of my mind for a long time. Now I can truly claim that I am living the dream.

This is an edited excerpt.
Read the complete essay here:

Jonathan Monroe (monroejd@jmu.edu) is a professor emeritus in the biology department and a research associate in the chemistry and biochemistry department at James Madison University, Harrisonburg, Virginia.

With curiosity, a career is both a journey and a circle

A conversation with John Peters

By Jennifer DuBois

John Peters' career trajectory has had its share of twists and turns. In a professional climate where linearity is less and less the norm, up-and-coming scientists might take comfort. A career punctuated by change and a more-than-occasional shot of risk can lead you someplace where you might enjoy the view.

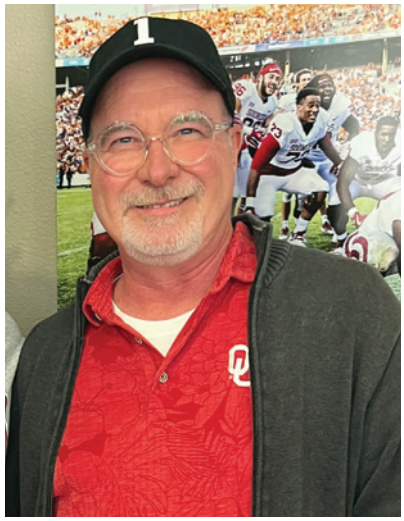
Peters has been a faculty member at four institutions and is a department chair at his undergraduate alma mater, the University of Oklahoma.

I recently asked Peters about the journey that took him from his college days in Oklahoma and back there again.

"I was really unfocused as a student and just interested in everything," he said. "As an undergraduate, I had majors like geology, then changed to engineering. … I think I was just really curious, so I just kept changing my major … and then I took a couple of microbiology classes."

The biochemistry department at Oklahoma had some of the few U.S.-based faculty investigating anaerobic metabolism. The subject seemed to Peters both on the fringes and utterly fundamental. They were asking deep questions about life and the boundary conditions for survival: How, in principle, could an organism get the necessary building materials and energy to function, especially without the powerful driving force provided by the reduction of oxygen?

This line of questioning led Peters



COURTESY JOHN PETERS

John Peters has served on the faculty at four institutions and is now a department chair at his undergraduate alma mater, the University of Oklahoma.

to other strongholds of anaerobic microbiology: Virginia Tech and then CalTech.

"When I finished my Ph.D. at Virginia Tech, structure was the thing that was going to solve all the problems," he said. "So I wanted to go to a structure lab that was open to the type of problems that I was interested in, like anaerobic metabolism."

A huge feat

When it came time to begin his own research program, Peters aimed high, looking for a challenging problem where structural work would be impactful. In the so-called iron-only hydrogenase, he found a perfect match. The iron-containing hydrogenase was the subject of much speculation but no structural data.

"It was an interesting time to do structures where we didn't really have everything figured out," Peters said.

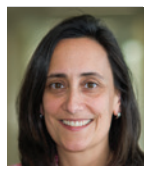
He set up and carried out a complex data collection experiment. The beam line didn't even have a simple detector.

"I measured the whole thing on film at that time," Peters recalled, "and then when I saw I had gotten really good data, I was just amazed. …I was thinking when I was looking at it that. … I'm the first person to ever see this thing."

The structural biology of hydrogenases opened a series of questions. How do these oversized enzymes bring together two tiny electrons and two protons, catalyzing their combination to make hydrogen gas? Why are some hydrogenases more and some less oxygen-sensitive? How did these catalysts evolve and diversify? What controls the biological interplay between hydrogen gas and reactions that make or consume methane? And what can humanity learn from some of nature's tiniest creatures about making and using hydrogen gas as a fuel?

This is an edited excerpt. Read the complete essay here:

Jennifer DuBois (jennifer.dubois1@montana.edu) is an associate professor at Montana State University and a member of the ASBMB Today editorial advisory board.



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