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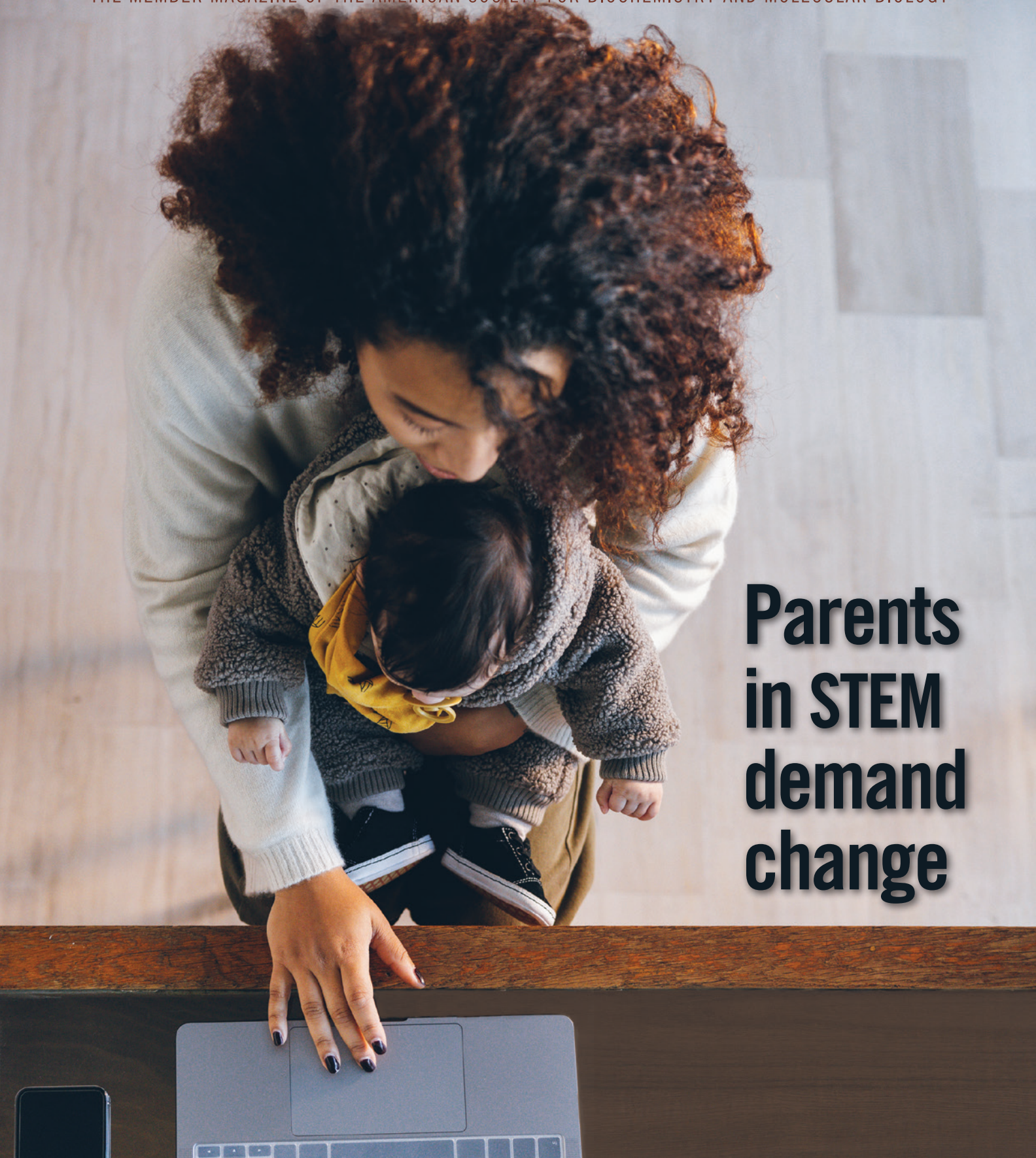
ASBMB TODAY

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



Parents in STEM demand change

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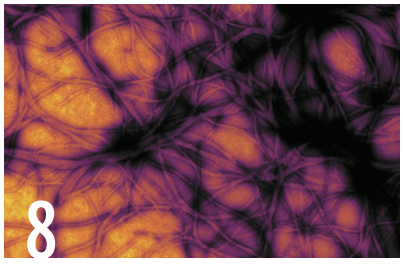

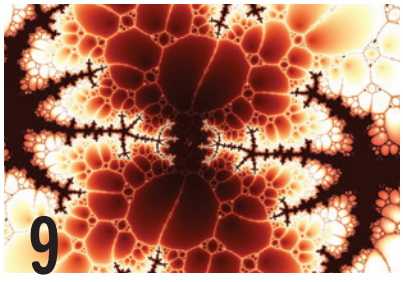

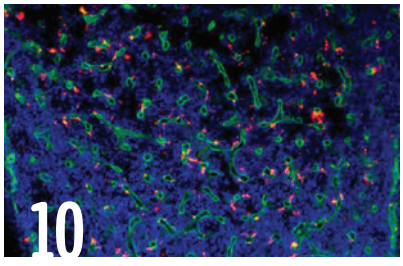

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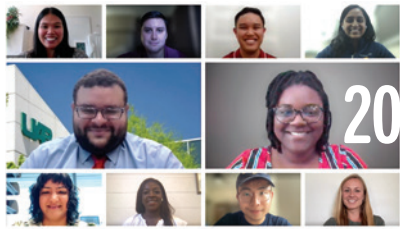

Discover BMB | 2023

PERSPECTIVES

ASBMBTODAY
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How far we've come

By Ann Stock

As president of the American Society for Biochemistry and Molecular Biology, I often think about the society leaders who came before me and how they influenced our organization and the science that we do today.

University of Washington colleagues Ed Krebs and Eddy Fischer are two of them. Krebs was president of the ASBMB when I was in graduate school. Fischer served as an editorial board member of our flagship Journal of Biological Chemistry.

Krebs and Fischer trained many future ASBMB members who have continued to make seminal contributions to the field. Indeed, Krebs' and Fischer's impacts were legion long before they won the 1992 Nobel Prize in physiology or medicine for describing reversible protein phosphorylation.

In March, I will have the great privilege of presiding over our annual meeting — Discover BMB — in Seattle.

It pleases me to share with you that John Scott, who today chairs the UW department that Krebs once led, and Alexandra Newton of the University of California, San Diego, who is president of the International Union of Biochemistry and Molecular Biology, will host a special event for us.

"ASBMB–IUBMB tribute to Eddy Fischer: Reversible phosphorylation" will be held on Sunday, March 26, and will feature a great lineup of speakers:

- Rachel Klevit, University of Washington.
- Dario Alessi, University of Dundee.
- Smita Yadav, University of Washington.

It will look back briefly on the remarkable discoveries Krebs and Fischer made, and, given that we now understand phosphorylation affects all aspects of cellular behavior and that aberrant modification underlies disease, it will look ahead to what's on the horizon of phosphorylation research, including discovery-based design of kinase inhibitors.

It should be of great interest to students, trainees and researchers from academia and industry, particularly those who are investigating phosphorylation-based signaling mechanisms in disease.

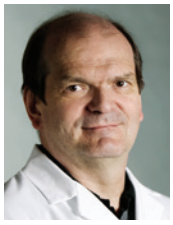
I hope to see you in Seattle and at this event.

Ann Stock (stock@cabm.rutgers.edu) is a professor of biochemistry and molecular biology at the Robert Wood Johnson Medical School at Rutgers and resident faculty member at the Center for Advanced Biotechnology and Medicine. She became the ASBMB's president in July.

Biophysical Society honors Palczewski, Fleming, Gardner

Three members of the American Society for Biochemistry and Molecular Biology have been named 2023 award winners by the Biophysical Society. **Krzysztof Palczewski** will receive the 2023 Anatrace Membrane Protein Award. **Karen G. Fleming** will receive the 2023 Avanti Award in Lipids. **Kevin H. Gardner** will receive the 2023 BPS Award in the Biophysics of Health and Disease. They will be honored, along with other award winners, at the Biophysical Society's 67th annual meeting in February.

Palczewski, a professor and director of the Center for Translational Research at the University of California, Irvine, is recognized for his foundational work on the G protein–coupled receptor rhodopsin and disease mechanisms and treatments and for his impact on structural biology, notably lipid interactions and conformational changes exhibited on ligand binding and isomerization. Funded by Anatrace Inc., this award recognizes an outstanding investigator who has made a significant contribution to the field of membrane protein research.



PALCZEWSKI

Fleming, a professor of biophysics at Johns Hopkins University and an associate editor of the Journal of Biological Chemistry, is recognized for her groundbreaking contributions to fundamental understanding of membrane protein stability, folding, biogenesis and insertion through development and application of novel experimental tools that quantify membrane protein folding kinetics and thermodynamics. Avanti Polar Lipids Inc. established this award to recognize an investigator for outstanding contributions to our understanding of lipid biophysics.

FLEMING

Gardner, a professor at the City College of New York and director of the CUNY Advanced Science Research Center's Structural Biology Initiative, is recognized for his development and application of magnetic resonance methodology to elucidate the regulation mechanism of molecular switches, leading to the development of PAS domain inhibitors for cancer therapies and the exceptional translation of this understanding to the development of an effective cancer drug. The Biophysics of Health and Disease Award, established by the Biophysical Society, honors significant contributions to understanding the fundamental cause or pathogenesis of disease or to enabling treatment or prevention.

GARDNER

EMBO names new members

Three members of the American Society for Biochemistry and Molecular Biology have been recognized by the European Molecular Biology Organization, an organization of researchers that promotes excellence in the life sciences in Europe and around the world. **Ralf Erdmann** and **Michiel Vermeulen** were named EMBO members this year, and **Jamie Rossjohn** was named an associate member.

Erdmann is a professor of biochemistry and pathobiology at Ruhr-Universität in Bochum, Germany.

ERDMANN

His lab investigates the biogenesis of peroxisomes with emphasis on the transport of folded proteins into the peroxisomal matrix and screening of corresponding inhibitors as new drugs against parasite diseases. The lab's contributions include the discovery of peroxins, the AAA family of ATPases, the peroxisomal exportomer, transient peroxisomal protein translocation pores, alternative peroxisomal import pathways and novel drugs against parasitic diseases. Erdmann served from 2010 to 2016 on the editorial board of the Journal of Biological Chemistry.

Vermeulen is a professor of molecular biology and director of the Radboud Institute for Molecular Life Sciences at Radboud Universiteit. His lab uses quantitative mass spectrometry–based interaction proteomics and next-generation DNA sequencing technology to decipher genetic and epigenetic regulation of gene expression in stem cells and to study deregulation of gene expression in cancer. Vermeulen is a member of the editorial board of Molecular & Cellular Proteomics.

VERMEULEN

Rossjohn is a professor of biochemistry and molecular biology at the Biomedicine Discovery Institute at Monash

ROSSJOHN

University in Melbourne, Australia. His lab investigates the molecular bases underpinning protective and aberrant immunity. This includes studying how T-cell receptors and natural killer cells recognize peptides presented by molecules encoded by the major histocompatibility complex and how T-cell receptors recognize lipids and metabolites presented by the CD1 family and MR1, respectively. Rossjohn recently was elected a fellow of the Royal Society.

Miller named distinguished professor

The University of Kentucky has named **Anne-Frances Miller** its 2022–23 College of Arts and Sciences Distinguished Professor. Miller, a chemistry professor, is being honored for her outstanding research, effective teaching and professional service. She will deliver the annual "Distinguished Professor Lecture" in the spring.

MILLER

The Miller lab studies enzymatic redox catalysis, working to understand energy efficiency in biological systems as well as mechanisms for optimizing the storage of intermittent energy and deploying it with maximum versatility.

For her research, Miller has received the Biophysical Society Young Investigator Award and the 2021 Herty Medal from the Georgia Section of the American Chemical Society. She was invited to chair the Gordon Research Conference in her field, and she recently completed a term as chair of the American Chemical Society's Division of Biological Chemistry.

Miller's academic leadership includes reinventing a molecular biophysics course to enhance student quantitative thinking. She has sought to make science more accessible to artists through the development of courses such as Plant Pigments, Fragrances and Fibers.

Miller recently was elected to the American Society for Biochemistry and Molecular Biology Publications Committee, on which she previously served from 2013 to 2016. She was a member of the Journal of Biological Chemistry editorial board from 2007 to 2012.

Garcia–Blanco appointed chair

Mariano A. Garcia–Blanco, an expert in virology and RNA biology, has been named chair of the Department of Microbiology, Immunology and Cancer Biology at the University of Virginia School of Medicine. He comes to UVA from the University of Texas Medical Branch at Galveston, where he served as chair of the biochemistry and molecular biology department since 2014.

GARCIA–BLANCO

Garcia–Blanco's lab is known for its research on RNA-binding proteins in infection and immunity. His work has identified numerous RNA-binding proteins that affect the replication of flaviviruses such as dengue, yellow fever and Zika. They also have studied the role of RNA helicase DDX39B in alternative splicing of the interleukin 7 receptor, which affects autoimmune disorders such as multiple sclerosis.

A member of the United Nations' Council of Scientific Advisers for the International Centre for Genetic Engineering and Biotechnology, Garcia–Blanco previously served on the National Institutes of Health's National Advisory General Medical Sciences Council. He is a member of the Association of American Physicians and a fellow of the American Association for the Advancement of Science; the American Academy of Microbiology; and, most recently, the American Academy of Arts and Sciences.

Garcia–Blanco has taught undergraduate, graduate and medical students such topics as gene regulation, nucleic acids, cancer biology and autoimmunity. Along with his research and teaching at the UT Medical Branch, he has been an adjunct professor of emerging infectious diseases at Duke–NUS Medical School in Singapore. He was a faculty member at Duke University from 1990 to 2014.

Austin Newton

Austin Newton, a longtime professor at Princeton University and a pioneer in molecular biology, died May 13 at age 85. He was a member of the American Society for Biochemistry and Molecular Biology for 40 years.

Born in Richmond, Texas, Newton graduated from the University of Texas at Austin in 1959 with a degree in chemistry and then in 1964 headed to the University of California, Berkeley, where he earned a Ph.D. in biochemistry. As a postdoctoral fellow, he joined the lab of Nobel laureate Jacques Monod at the Pasteur Institute in Paris, where he studied the effect of genetic mutation in E. coli.

Newton started his independent research career in 1966 as an assistant professor at Princeton, where he continued his work on E. coli. He later developed an interest in asymmetric cell division, and he did extensive work in this field with his longtime collaborator and wife, Noriko Ohta. As a model system, they exploited the Gram-negative alphaproteobacterium Caulobacter crescentus, which is widely present in freshwater lakes and streams. Their research group focused on understanding the progression of the cell division cycle throughout successive developmental events and how multiple histidine protein kinases regulate the signal transduction pathways of C. crescentus in cell division. Newton's work was recognized as "pioneering" and a "completely new field (that) requires vision, scientific creativity, guts, and fortitude," in a 2009 biographical sketch published by Princeton.

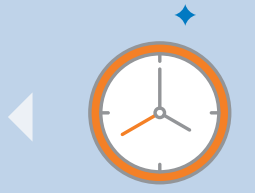
Newton was promoted to associate professor at Princeton in 1972 and became a full professor in 1978. His research was funded by grants from the National Science Foundation and National Institutes of Health. He served on the editorial board of the Journal of Bacteriology and as an associate editor of Developmental Genetics. In 1998, he was elected as a fellow of the American Academy of Microbiology. He served as a director of graduate studies in the biology department and biochemical sciences program from 1977 to 1984 and later as a founding member of the Princeton Department of Molecular Biology until 1989. He retired in 2009.

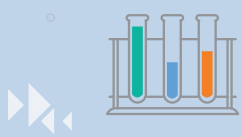
In a Princeton obituary, Newton's colleagues and students remembered him fondly for his "scientific imagination" and "wry sense of humor." He was passionate about sub-Saharan and West African sculpture and textiles and also loved music and art.

Newton is survived by his wife, Noriko Ohta, and his sister Margueritte Dell Austin.

— Swarnali Roy

Upcoming ASBMB events and deadlines





MARCH

7–10	**ASBMB Deuel Conference on Lipids**
23	Discover BMB regular registration deadline
24	Discover BMB on-site registration
25–28	**Discover BMB**

APRIL

15	IMAGE workshop application deadline
21	Advocacy training program application deadline

MAY

10	Motifs, modules, networks conference early registration deadline
10	Motifs, modules, networks conference abstract submission deadline
31	Annual award nominations deadline

ASBMB endorses bill to make student loans more affordable

If passed, the Lowering Obstacles to Achievement Now Act would help decrease expenses for current and future borrowers. Read the society's endorsement at asbmb.org/advocacy/position-statements.

ASBMB Advocacy Training Program delegates leave their mark on policymaking

The 2022 delegates have impacted science policy at the local, state and federal levels. Read about their projects on page 20. Applications for the next cohort will be accepted starting in March.

SAVE THE DATE:

Transforming undergraduate education in the molecular life sciences

Join us July 27–30 in Boston for an interactive, education-focused meeting. Learn about engaging approaches to support students and faculty in biochemistry and molecular biology. Reconnect with peers, meet new colleagues and increase your network of education-minded professionals. Learn more at asbmb.org/meetings-events/transforming-undergraduate-education.

April 15: Applications for ASBMB grant-writing workshop due

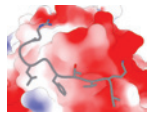
The ASBMB Interactive Mentoring Activities for Grantsmanship Enhancement grant-writing workshop is designed to help early-career scientists and senior postdoctoral fellows write winning proposals for federal research funding. Apply to attend the workshop June 8–11 in Washington, D.C., at asbmb.org/career-resources/image.

April 30: Annual awards nominations due

There's still plenty of time to nominate a colleague for an ASBMB award. Learn about the award categories and criteria at asbmb.org/career-resources/awards-grants-fellowships.

May 10: Abstracts due for motifs, modules and networks conference

This ASBMB conference on the assembly and organization of regulatory signaling systems will be held July 11–14 in Potomac, Maryland. The organizers are Wolfgang Peti of the University of Connecticut Health Center, Benjamin Turk of the Yale School of Medicine and Arminja Kettenbach of the Dartmouth Geisel School of Medicine. Learn more at asbmb.org/meetings-events/motifs-modules-networks.



June 1: Deadline for Sewer diversity scholarship applications

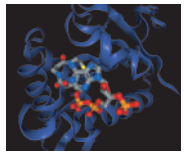
The ASBMB supports the advancement of diversity, equity and inclusion in science by offering the Marion B. Sewer Distinguished Scholarship for Undergraduates to students who show demonstrated interest in the fields of biochemistry and molecular biology and who enhance diversity in science. This award provides $2,000 of financial support toward undergraduate tuition costs for one academic year. For more information, visit asbmb.org/diversity/undergraduate-scholarship.

June 15: Deadline for regional meeting award applications

The ASBMB Student Chapters Regional Meeting Award supports small scientific meetings hosted by individual chapters or in collaboration with other schools or chapters. These meetings should bring students and faculty together, foster an exchange of ideas, and highlight research projects. Up to six regional meetings are funded annually. Learn more at asbmb.org/education/student-chapters/awards/regional-meeting.

June 20: Abstracts due for CoA and CoA derivatives conference

The ASBMB conference on CoA and CoA derivatives to be held Aug. 16–18 at the University of Wisconsin–Madison. The organizers are Luigi Puglielli at UW–Madison, Suzanne Jackowski at St. Jude Children's Research Hospital and James Ntambi at UW–Madison. Abstracts are due June 20. Learn more at asbmb.org/meetings-events/coa-2023.



CALL FOR SUBMISSIONS

The PRIDE issue

In the June/July issue of ASBMB Today, we'll take a look at what it means to be LGBTQ+ and working as a scientist. Share your story in an article, essay, photos — whatever best expresses your journey.

Email submissions to asbmbtoday@asbmb.org

Deadline: March 20

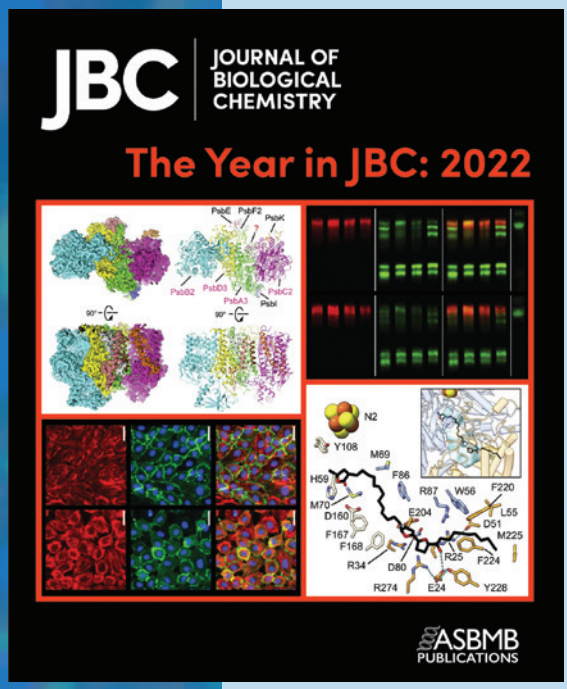
ASBMB
American Society for Biochemistry and Molecular Biology

VIRTUAL ISSUE

The year in JBC: 2022

The editors at the JBC are pleased to present this collection of research articles as a retrospective of "The year in JBC" for 2022. These studies report the recent progress in SARS-CoV-2 research; reveal structural details of a monomeric photosystem II core complex from a cyanobacterium acclimated to far-red light; model the CRL4A ligase complex to predict target protein ubiquitination; and much more. This small collection cannot fully capture the exceptional contributions from JBC's many authors, and these articles showcase some of the exciting work published this year.

jbc.org/best-of-2022



JBC JOURNAL OF BIOLOGICAL CHEMISTRY

Protein quality control strategies

By Aswathy N. Rai

Proteins keep our cells and bodies functioning normally. To do this job, each protein must fold into a unique structure. However, newly formed proteins sometimes misfold and aggregate, resulting in harmful or lost function.

Protein misfolding can cause human diseases such as cancer and cystic fibrosis and neurogenerative disorders such as Alzheimer's, Parkinson's and Huntington's diseases.

Per Widlund and his team at the University of Gothenburg study the cellular processing of misfolded proteins. "Proteins are major structural and functional components of cells," Widlund said. "Like the components of any well-used machine, parts need to be constantly replaced with new ones to prevent breakdown."

Proteostasis ensures that proteins are built correctly, delivered to cellular locations and recycled if they become too damaged to do their job properly. "Cells accomplish proteostasis with an intricate protein quality control network that ensures proteins achieve and maintain a functional state," Widlund said.

The two arms of the protein quality control network work together to prevent the toxic effects of misfolding. The spatial arm segregates misfolded protein aggregates into protective sites called inclusion bodies. The temporal arm ensures the accurate folding of new proteins, refolding of aberrant proteins and degradation of misfolded proteins by the ubiquitin-proteasome or vacuole-autophagy pathways.

"To combat protein misfolding diseases, we need to understand why the aggregates build up and how the failure to clear them is related to toxicity," Widlund said.

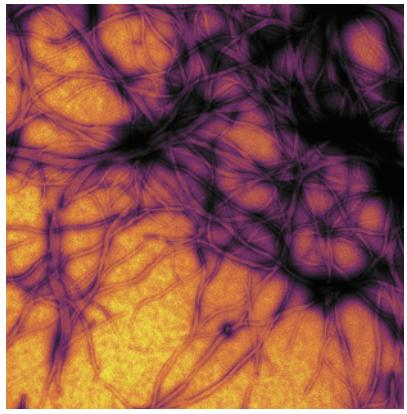
In a recent study published in the **Journal of Biological Chemistry**, Widlund and his team established a system, using yeast as a model, to study protein quality control mechanisms that clear misfolded proteins.

The new model system uses three temperature-sensitive nontoxic mutants of three proteins that misfold at 38 degrees Celsius with known differences in aggregate removal rates. The mutants, produced continuously in the cells, do not affect normal functioning or the lifespan of yeast cells, allowing the researchers to study the fundamental mechanisms of aggregation and clearance.

"We compared how three different misfolding proteins are processed and found that their ability to recruit protein quality control components and their removal varied," Widlund said. "Each misfolding protein's specific characteristics play a significant role in its processing, allowing certain proteins to evade protein quality control, potentially leading to toxicity and disease."

Using a combination of time-lapse microscopy, structured illumination, microscopy and electron microscopy as well as proteasome degradation and clearance assays, the team found that all the misfolded reporter proteins accumulated into aggregates in the same cellular compartments. However, their disaggregation efficiencies varied.

"We hypothesized that different misfolding proteins contained in the same aggregate would impact each other more," Widlund said. "We were surprised that one misfolding protein did not affect the removal of another, at least in young, healthy cells."



ROGER MOORE / NIAID

Recombinant proteins such as the prion protein shown here often are used to model how proteins misfold and sometimes polymerize in neurodegenerative disorders.

Of the three mutants studied, cells cleared misfolded glutamyl-tRNA synthetase less efficiently compared to the other two. And while all three mutants localized in the same cellular compartments, a small percentage of misfolded glutamyl-tRNA synthetase also accumulated in mitochondria. The cells most rapidly cleared misfolded delta 1-pyrroline-5-carboxylate reductase. The authors also report differences in the recruitment of proteasomes by these misfolded proteins.

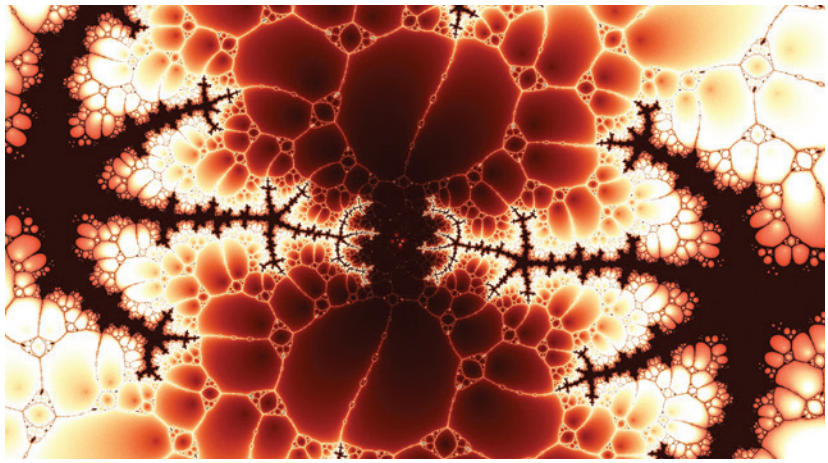
"The next step is to examine aged cells," Widlund said, "and see if this holds for other, more toxic, misfolding proteins."

DOI: 10.1016/j.jbc.2022.102476

Aswathy N. Rai (aswathy.rai@msstate.edu) is an assistant clinical professor and undergraduate coordinator at Mississippi State University's department of biochemistry, molecular biology, entomology and plant pathology. Follow her on Twitter: @AswathyRai

A key to cancer drug resistance

By Ken Farabaugh



PIXABAY

Pancreatic ductal adenocarcinoma, or PDAC, is a lethal cancer with a median five-year survival rate of only 8%. Surgery is not an option for most PDAC patients, because the cancer usually has reached an advanced stage and metastasized by the time it is diagnosed. Even the standard-of-care chemotherapy, gemcitabine, known as Gem, only extends a patient's life by about seven months, because drug resistance develops swiftly.

Qingxiang Lin is a research fellow at Massachusetts General Hospital and Harvard Medical School. "There are really very few options for PDAC patients whose cancers become drug resistant," he wrote in an e-mail. "This represents a very significant clinical problem for the nearly 50,000 patients whose lives are claimed yearly in the United States alone."

When he was a graduate student in Robert M. Straubinger's lab at the State University of New York at Buffalo, Lin and colleagues investigated key regulators of Gem resistance using proteomic technology. "Our straightforward overall hypothesis was global differential proteomic analysis of the highly Gem-resistant cell lines I developed would identify multiple cooperating mechanisms" of drug resistance, he wrote.

Dr. Lin is the lead author of a recent paper in **Molecular & Cellular Proteomics** about this work. Through his analysis, the researchers identified drug-induced dynamic changes in the levels of proteins associated with cancer cell metabolism, proliferation, migration and drug response mechanisms.

Among these proteins, they chose the most significantly changed for further analyses, including the ribonucleoside–diphosphate reductase large subunit, or RRM1, which plays a critical role in Gem metabolism, and the S100 calcium binding protein A4, or S100A4, which can be associated with cellular energy production. Lin's experiments showed that the decrease in S100A4 expression levels in Gem-resistant cells was consistent with reduced tumor cell proliferation, which could help protect these cancer cells from toxic drug effects, yet the increase in RRM1 levels enhanced Gem resistance. In addition, clinical data from human patients showed a correlation between lower RRM1 expression and better clinical outcomes.

"The picture painted by our data suggests that by altering multiple key proteins the mutant drug-resistant cells grow more slowly to avoid toxicity, reduce the amount of activated Gem within themselves, and increase their activity in repairing the DNA damage that the drug does," Lin wrote. "The time course protein-level responses of parental cells versus the Gem-resistant cell lines suggest that adaptive changes in cellular response systems that are related to cell proliferation, drug transport and metabolism, DNA repair and other functions, contribute to Gem resistance in PDAC."

This information led to multiple new hypotheses and findings at the protein level; the researchers have more work in progress to translate these findings into therapeutic strategies for human treatment.

"We have been developing a promising drug combination strategy to reverse drug resistance in extremely drug-resistant patient-derived tumors," Lin wrote. "We hope this drug combination can move to clinical investigation, and that PDAC patients can receive benefit from our work."

DOI: 10.1016/j.mcpro.2022.100409

Ken Farabaugh (kfarabaugh@asbmb.org) is the ASBMB's science editor.

A downside to liposome drug delivery?

By Ken Hallenbeck

Precisely targeting a drug to the right part of the body is always hard, but drug delivery is at its most challenging when the therapeutic is genetic material.

Unlike other classes of biologic drugs, DNA and RNA are not stable in circulation, so scientists have used lipid capsules called liposomes to envelop the therapeutic genes and shuttle them safely to the appropriate destination.

The human body treats engineered liposomes — and all drugs — like foreign objects. Upon injection, the immune system reacts to the circulating lipid capsules, and the white blood cells known as macrophages begin engulfing and clearing the perceived intruders.

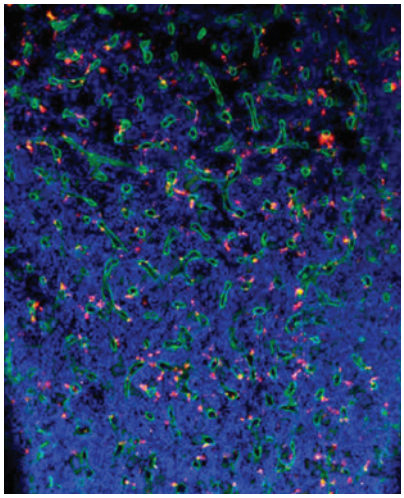
For many years, this phenomenon was not a problem, according to Yue Li, a researcher at Xuzhou Medical University in Jiangsu, China.

"In recent decades, countless nanoparticles have been designed for drug delivery, and there are over 20 liposomal products available on the market," Li said.

These medicines have been shown to be safe and effective by regulatory agencies such as the United States Food and Drug Administration.

However, in a study published in the **Journal of Lipid Research**, Li, along with co–first author Ran Yao and colleagues, showed that liposomes can have a negative impact on bone marrow macrophages.

JOURNAL OF LIPID RESEARCH



In this immunofluorescence image of a mouse bone section seven days after tail-vein injection, the liposomes (red) are distributed throughout the bone marrow cells (blue) and are associated preferentially with the vasculature (green).

These scientists knew that as macrophages encounter and engulf liposomes, they begin to accumulate lipid droplets. Researchers had put this to clever use delivering fluorescent labels into immune cells during lab experiments, but Li realized that the same phenomenon might be occurring when liposomes are administered as drugs. Indeed, previous work had shown it occurs in the liver.

To test the theory, Li and a team of researchers at the Xuzhou Medical University injected mice with liposomes and then collected macrophages from the mouse bone marrow for study. The result is stunning: Macrophages in the bone marrow underwent pro-inflammatory activation and showed signs of stress, such as lipid accumulation in the endoplasmic reticulum. This led to a decreased ability to create red blood cells and important immune cell types like monocytes.

What does this mean? Li said he thinks the finding "provides a novel consideration criteria for clinical drug trials." That is, patients who are immunocompromised or who have bone marrow infections might need to avoid liposome drug trials.

While this may be true, the finding must be replicated in human macrophages and tissue samples before researchers can be sure. The work also should be extended beyond liposomes to other classes of lipid nanoparticles.

It's not all bad news for liposomal drugs, either. For years, researchers have worked to engineer the surface of nanoparticles to escape immune detection. The original motivation was to increase effectiveness by keeping the drug in circulation longer. Now, those modifications may have a secondary benefit: sparing the hardworking bone marrow macrophages.

DOI:10.1016/j.jlr.2022.100273

Ken Hallenbeck (k.hallenbeck@gmail.com) earned a Ph.D. in pharmaceutical sciences from the University of California, San Francisco, and now is an early drug-discovery researcher. He serves on the board of directors of ReImagine Science and is the life sciences lead at TerraPrime. Follow him on Twitter: @kenkhallenback.

From the journals

By Ken Farabaugh, Andrea Pereyra & Swarnali Roy

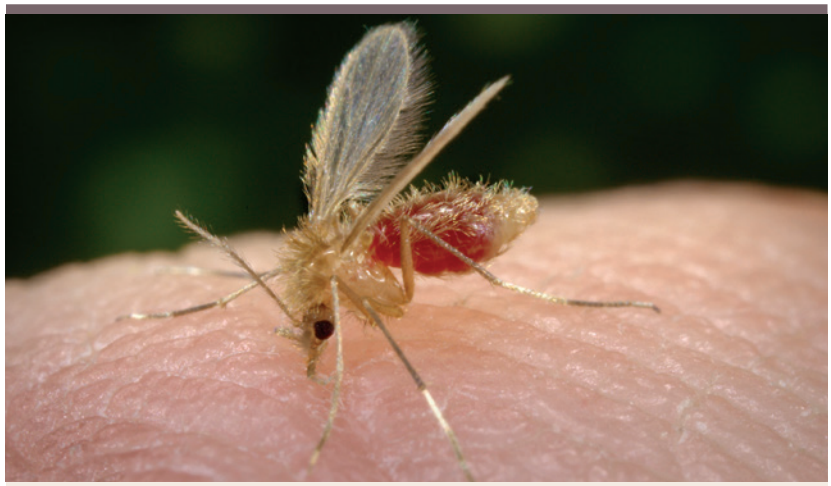
We offer summaries of papers recently published in the **Journal of Biological Chemistry**, **Journal of Lipid Research** and **Molecular & Cellular Proteomics**.

An insight for treating renal cancer

About 5% to 10% of all known cancer types are hereditary. These cancers, linked to gene mutations passed from parents to their offspring, are often difficult to treat.

Birt–Hogg–Dubé syndrome, or BHD, a rare autosomal dominant inherited disorder, often precedes development of renal cell carcinoma, or RCC. In 2002, researchers identified a germline mutation in the folliculin gene, or FLCN, as a factor for BHD development. Since this discovery, multiple research groups have tried to understand how FLCN functions in RCC.

In a recently published **Molecular & Cellular Proteomics** article, Iris Glykofridis and a team in the Netherlands delved into the phosphorylated kinase pathway to understand how FLCN suppresses renal tumorigenesis. They investigated the role of FLCN in the cellular signaling pathway via protein and receptor phosphorylation by analyzing phosphoproteomic profiles of human renal tubular epithelial cells with and without FLCN. They identified specific tyrosine phosphorylation sites with markedly higher levels of phosphorylation in major receptor tyrosine kinases like EGFR and significant dephosphorylation in transcription factor EB phosphoserines upon FLCN loss.



This Phlebotomus papatasi sandfly is in the process of ingesting its bloodmeal, which is visible through its distended transparent abdomen. Sandflies such as this spread the vector-borne parasitic disease leishmaniasis.

Hijacking chaperones for iron

Iron is a critical element for pathogen survival, growth and virulence. Many pathogens have developed strategies to obtain iron from hosts, while hosts have evolved to block iron availability to pathogens. Researchers recently have shown that poly(rC)-binding proteins, or PCBPs, act as chaperones to load iron into ferritin, an iron-binding protein, for sequestration; however, pathogenic manipulation of PCBPs remains relatively unexplored.

Leishmania donovani is a parasite that travels between sandfly vectors and vertebrate hosts. In the vertebrate host, Leishmania, which causes the potentially fatal neglected tropical disease visceral leishmaniasis, resides in macrophages and requires iron to maintain metabolic and defensive activities. In a recent article published in the **Journal of Biological Chemistry**, Sandhya Sen, Saswat Kumar Bal and colleagues at Jawaharlal Nehru University in New Delhi demonstrated that L. donovani is able to cleave PCBPs. Further experiments identified the protease responsible as the secreted zinc-metalloprotease GP63. The authors demonstrated that GP63-mediated cleavage of PCBPs prevents loading of iron onto ferritin and its subsequent sequestration. This hijacking of iron sequestration increases its availability and likely promotes growth and virulence of the pathogen.

This marks the first report of this novel strategy by pathogens to interfere with iron sequestration via ferritin by cleaving chaperone proteins to gain survival advantages within a host.

DOI: 10.1016/j.jbc.2022.102646

— Ken Farabaugh

Targeting sANPEP in brain disease

Neuroinflammation, a response to cellular injury in the brain or spinal cord, helps the immune system and the brain communicate by recruiting cytokines and chemokines and also plays a role in neurodegenerative conditions such as Parkinson's and Alzheimer's diseases, multiple sclerosis and amyotrophic lateral sclerosis.

Complex integral activity among cells in the central nervous system, or CNS, including neurons and glia cells, causes neuroinflammation. The macroglial cells known as astrocytes, the most abundant and diverse nonneuronal cells in the CNS, are major regulators of neuroinflammation. Microglia, an integrative part of the CNS system, are nonneuronal cells that regulate the innate immune response of the brain. The crosstalk between microglia and astrocytes supports neuronal function and survival after acute CNS injury or disease, and this communication is maintained via secreted growth factors, cytokines, chemokines and innate-immunity mediators.

A recent **Molecular & Cellular Proteomics** article by Jong-Heon Kim and a team from the Republic of Korea focuses on how the brain's renin–angiotensin system, or RAS, regulates the astrocyte–microglia crosstalk by analyzing the astrocyte secretome, which provides information about secreted proteins and their pathways.

The researchers identified a markedly elevated level of a soluble form of aminopeptidase N called sANPEP, a RAS component in the secretome, during neuroinflammation. They identified 322 proteins by proteomic analysis in astrocyte-conditioned medium following inflammatory stimulation. When they analyzed the proteins' functional distribution, they found sANPEP was one of the upregulated proteins in RAS that is related to inflammation-associated pathways in activated astrocytes. They also found a significantly higher sANPEP level in the plasma of mice genetically altered for neuroinflammation than in unaltered mice.

This work helps identify sANPEP as a biomarker in disorders such as Alzheimer's disease, because it is upregulated in bodily fluids and human astrocytes in a neuroinflammation model. Its enzymatic activity to promote microglial stimulation indicates therapeutic potential as a drug target.

DOI: 10.1016/j.mcpro.2022.100424

—Swarnali Roy

The researchers analyzed the phosphoproteomic data and showed that FLCN loss has a clear effect on the phosphorylation of kinases and substrates within multiple biological pathways and may be important for the onset of oncogenic transformation of renal cells. The authors hope that understanding the FLCN-dependent phosphorylation pathway can open a new window to help design novel candidates for targeted therapies.

DOI:10.1016/j.mcpro.2022.100263

A new cause of male infertility

Gene associated with retinoid interferon-induced mortality 19 (Grim-19) is best known as an essential component of respiratory complex I in mitochondria, regulating apoptosis and energy metabolism. However, mounting evidence suggests an additional role for Grim-19 in male reproduction.

In a recent study published in the **Journal of Biological Chemistry**, Hu Qu and colleagues at the Sixth Affiliated Hospital of Sun Yat-Sen University in Guangzhou, China, demonstrated that Grim-19 is expressed in Leydig cells (cells in the extracellular matrix–filled space adjacent to the seminiferous tubules that produce the male sex hormone testosterone) of mice from puberty onward and localized to mitochondria. Using mouse models deficient in Grim-19 expression, the authors showed that loss of Grim-19 led to reduced testosterone production and increased oxidative

stress and subsequently to germ cell apoptosis and male infertility, or azoospermia. The authors propose two mechanisms by which Grim-19 could affect fertility: inhibition of cellular signaling via the steroidogenic acute regulatory protein or exacerbation of the inhibitory role of the extracellular matrix on testosterone production via increased integrin activation.

These findings suggest that Grim-19 plays an important role in male sex hormone production and that its modulation could cause or be used to treat testosterone deficiency–related disorders or male infertility.
DOI: 10.1016/j.jbc.2022.102671

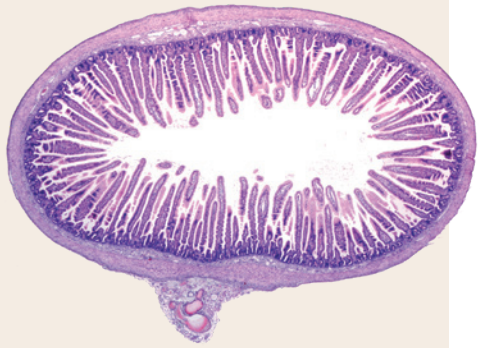
New treatment for a lipid imbalance

The abnormal imbalance of plasma lipids, or dyslipidemia, is a well-known risk factor for cardiovascular diseases. One such imbalance is an increase of circulating triglycerides, or TG, called hypertriglyceridemia, which affects between 14% and 38% of the world's population. Treatments include changes in diet and lifestyle or drugs such as statins and fibrates.

Rene Rodriguez–Gutierrez from the Autonomous University of Nuevo León, Mexico, and collaborators from the pharmaceutical industry are exploring other options. They recently conducted a clinical trial comparing the efficacy and safety of the drugs saroglitazar and fenofibrate in patients with severe dyslipidemia, and their findings were published in the **Journal of Lipid Research**. Both drugs act on the peroxisome proliferator-activated receptors, or PPARs, a group of proteins in the cellular nucleus that act as energy sensors, influencing lipid and glucose metabolism. While fenofibrate is a well-established PPAR alpha agonist for the management of dyslipidemias,

Let me in! Lipid flux in the small intestine.

The mammalian digestive tract consists of five compartments that collectively absorb nutrients, water and electrolytes, and excrete waste products. In the small intestine, food-derived amino acids, carbohydrates and lipids are transported from the intestinal lumen to the lymph and blood so they ultimately can reach the adipose tissue, heart and muscles for storage or energy production. The functional unit of the intestine is the enterocyte, a cell with two structurally and functionally different membrane regions: the apical domain facing the lumen and the basolateral domain interacting with the neighboring cells and with the lymphatic and blood vessels.



In this cross section of the small intestine, the villi — fingerlike structures extending from the intestine's wall into the lumen — are covered with a monolayer of enterocytes.

Past research has focused on the unidirectional path for dietary lipids from intestinal lumen to lymph via the enterocyte's apical brush border membrane. This path supplies triglycerides, cholesterol and phospholipids to the general circulation for uptake by peripheral tissues, while a small fraction remain inside the enterocyte. In a recent review in the **Journal of Lipid Research**, Joshua R. Cook and colleagues from Columbia University and the University of Pittsburgh describe details of intestinal lipid flux and highlight the dual track model via the basolateral membrane.

As the authors explain, scientific evidence dating to the 1950s suggests the basolateral track supplies the enterocyte with a second type of lipid reserves derived mainly from uptake of circulating free fatty acids and triglycerides and from newly synthesized lipids from circulating carbohydrates. Researchers know less about the fate and physiological relevance of these basolateral track lipids. The authors present evidence suggesting that intestinal fatty acids could undergo oxidation for energy production during fasting, could be fluxed to adjacent cells or could be used during synthesis of complex lipids.

Cook and colleagues also explore the crosstalk between the apical and basolateral tracks in the context of metabolism regulation. The authors hypothesize that these tracks work synergistically as an energy-sensing circuit, with the apical as what they call a "systemic fat output" and the basolateral track as a conduit for "systemic fat return" depending on whole-body energy status and needs.

Further research is needed to understand the implications of this integrated response in metabolic diseases such as obesity and diabetes.
DOI: 10.1016/j.jlr.2022.100278

— Andrea Pereyra

saroglitazar is a recently developed PPAR alpha and gamma dual agonist. Saroglitazar has been effective in lowering triglyceride levels and increasing insulin sensitivity in patients with moderate lipid imbalance, but researchers had not yet evaluatred its use on severe dyslipidemia.

Rodriguez–Gutierrez and colleagues treated 41 patients with moderate to severe hypertriglyceridemia with either saroglitazar or fenofibrate for 12 weeks and calculated the percent change in TG levels compared to baseline. They found that the dual PPARα and γ agonist saroglitazar induced a 55.3% mean reduction in TG levels compared to the 41.1% achieved by the PPARα agonist fenofibrate. Furthermore, 24% of the patients treated with saroglitazar had normal TG levels at the end of the 12 weeks compared to 12.2% of those receiving fenofibrate. Also, diabetic patients receiving saroglitazar showed a significant reduction in fasting insulin and C-peptide, suggesting additional benefits for insulin sensitivity. None of the patients reported serious adverse effects during the treatment.

The authors concluded that a 12-week course of saroglitazar was not inferior to fenofibrate in lowering TG levels in moderate to severe hypertriglyceridemia. Furthermore, they reported other benefits of saroglitazar over fenofibrate such as lesser indication of liver and kidney damage. Future studies could expand on the unique effects of dual PPARα and γ activation as treatment for lipid imbalance.

DOI: 10.1016/j.jlr.2022.100233

Novel regulation of a ribosomal factor

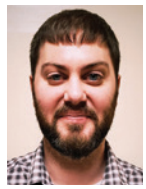
Human YVH1, or hYVH1, is a dual-specificity phosphatase that protects cells from environmental stress such as oxidative stress and heat shock, disassembles stress granules containing stalled ribosomes, and promotes biogenesis of the large ribosomal subunit. However, the mechanisms of hYVH1 action and regulation are unclear.

Ashley DaDalt and colleagues at the University of Windsor report in a recent publication in the **Journal of Biological Chemistry** that a phosphorylation event at Tyr179 on hYVH1 (mediated by the kinase Src) attenuated its localization to stress granules, promoted its translocation to the nucleus and enhanced its association with the 60S ribosomal subunit. Furthermore, the authors performed quantitative proteomics, the analysis of which revealed that Src and hYVH1 coexpression reduced the formation of stalled ribosomal intermediates via downregulation of three cofactors: nucleolin, Y-box binding protein 1 and interferon-related developmental regulator 1. These results were consistent with the hypothesis that phosphorylation of hYVH1 recycles the protein to the nucleus to maintain actively translating ribosomes, reflecting the translational fitness of the cell.

Taken together, these findings provide the first evidence that tyrosine phosphorylation regulates YVH1 activity and suggest that collaborative regulation of YVH1 and Src can maintain a cell's readiness to combat environmental stressors.

DOI: 10.1016/j.jbc.2022.102679

Ken Farabaugh (kfarabaugh@asbmb.org) is the ASBMB's science editor.



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Swarnali Roy (roys5@vcu.edu) is a postdoctoral researcher in the School of Pharmacy, Department of Medicinal Chemistry, Virginia Commonwealth University.

Leading with science

A Q&A with FDA chief scientist Namandjé Bumpus

By Laurel Oldach

> "At the FDA, we serve a public health mission and work within the context of regulatory science. We're also engaged with the broader international scientific community in thinking about how we can advance and validate technologies and what kind of unique perspective we can bring to stimulate discovery."

COURTESY OF NAMANDJÉ BUMPUS

Namandjé Bumpus has been chief scientist of the U.S. Food and Drug Administration since August.

When Namandjé Bumpus was at the Johns Hopkins University School of Medicine, as associate dean of basic research and later as head of the pharmacology department, her lab worked on how liver enzymes called cytochrome P450s metabolize drugs. Focusing on drugs used to treat HIV and hepatitis C, Bumpus used mass spectrometry to identify drug metabolites in patient samples, enzymology to determine how they are formed and pharmacogenetics to understand why patients vary in their response to the same molecule.

After more than a decade in academia, Bumpus stepped away from her lab on Aug. 1 of last year to become the chief scientist of the U.S. Food and Drug Administration.

On the day the National Academy of Medicine announced it had elected her as a member in recognition of her work on drug metabolism and pharmacogenetics, ASBMB Today spoke to Bumpus about the new job, her career, and what academic scientists may not know about the FDA. This interview has been condensed and edited.

Q. What does being chief scientist at the FDA entail?

It's broad; it's thinking strategically about our scientific mission. We have dozens of research labs here doing outstanding work in all areas of public health. I try to think about where we have intersections across the agency and how we can work together and amplify the message of science at FDA. I think people don't realize that we are scientists and have labs. We have scientists doing innovative research across the FDA.

The Office of the Chief Scientist has a range of components with diverse expertise and functions. For instance, a major part of my office is the National Center for Toxicological Research in Arkansas, where they perform original basic science research to investigate questions we need to answer to make some of our regulatory decisions; there are labs with a focus on drug safety and toxicology, artificial intelligence, and systems biology, among other areas. The scientific expertise and capabilities there are leading-edge, and the scientists contribute greatly to the FDA's public health mission. My office also handles memoranda of understanding with other institutions through our technology transfer staff if we're collaborating and transferring technology or inventions to make them more available.

We also have the Office of Scientific Integrity, which does many things that any scientific integrity office does but also some very FDA-specific things. For instance, this office coordinates for the Office of the Commissioner on hearing requests when matters arise in which the Food, Drug and Cosmetic Act or FDA regulations require an opportunity for a hearing.

The Office of the Chief Scientist also helps manage advisory committees through our Advisory Committee Oversight and Management Staff. FDA advisory committees provide advice to the FDA around certain regulatory decisions. One of my priorities is to determine whether we can optimize the advisory committee process. We also have an Office of Laboratory Safety.

The Office of Scientific and Professional Development leads FDA training initiatives, including certain research fellowship programs. And through our team in the Office of Regulatory Science and Innovation, we fund science intramurally and extramurally, including through our Centers of Excellence in Regulatory Science and Innovation program — a collaborative scientific partnership between the FDA and academic institutions. Our Office of Counterterrorism and Emerging Threats has deep expertise in policy and science around medical countermeasures and preparedness.

Q. How did you decide to apply?

What got me interested in this role was the opportunity to take the science that I'm really interested in, which is pharmacology, and apply it and have a bigger impact than I felt I could in my lab alone. I love having a research lab. I love training graduate students and postdocs and making interesting findings. But to be able to take that expertise and collaborate with people on so many different scientific questions all related to advancing public health is what really drew me. I am excited about the breadth of areas that I'm able to work in with regard to both science and policy.

I believe that with my background, coming from academia, I am

"What got me interested in this role was the opportunity to take the science that I'm really interested in, which is pharmacology, and apply it and have a bigger impact than I felt I could in my lab alone."

> "I think people don't realize that we are scientists and have labs. We have scientists doing innovative research across the FDA."

contributing a lot as far as the way we think about science and research at the FDA, and at the same time I'm learning and growing tremendously. For instance, I'm learning about policy and regulation and how science informs those areas.

Q. Tell me about some of the research that FDA labs are doing?

One area that my office is particularly excited about is microphysiological systems — people all over the world are working on organs on a chip. And several labs here are doing work in those areas, thinking about how we can validate them — how we can use the liver on a chip to predict drug toxicity, for example. We have collaborations across the agency, and we're starting to pull people together and talk about those data collectively. We're also working around AI and machine learning to see how we can move that forward to enhance public health.

At the FDA, we serve a public health mission and work within the context of regulatory science. We're also engaged with the broader international scientific community in thinking about how we can advance and validate technologies and what kind of unique perspective we can bring to stimulate discovery.

Q. What does regulatory science mean, exactly?

It's a science that's focused on the scientific and technical foundation that underlies public health and the products we regulate. It's the development of tools, standards and approaches that can be used to understand the safety, efficacy, quality and performance of FDA-regulated products. It's broad, and of course it applies to devices, biologics and food, among other things — not only drugs.

We're not necessarily doing discovery science. There is certainly discovery involved, and it's highly intellectual and innovative, but it's very much focused on regulatory questions: How can we predict toxicity from a drug or a chemical in food? Are there technologies that can do that? Are there in silico tools that can be used to simulate data so a new study doesn't need to be done? Those types of things underpin regulatory decisions.

Q. Do you still have trainees wrapping up at Johns Hopkins?

Yes. They have local advisers. The lab is now being led by a talented scientist, Ben Orsburn. We worked closely together for the past couple of years, and he is now taking the lab in innovative and interesting directions, such as work to advance single-cell proteomics. It's very exciting stuff.

This move was not an everyday thing, but I felt well supported by everyone in the laboratory, the department and at Hopkins that it was an opportunity I had to pursue. I also, of course, miss being a department chair and the amazing department family in pharmacology at Hopkins.

Q. So far, do you find scientific leadership in government different from in academia?

There's a lot of overlap; I certainly felt well prepared. A lot of it is about making decisions and thinking about the next studies to do and how best to utilize resources — all things we're trained to do in academia.

In academia, you work on teams, but they tend to be around a specific project or area of focus. Here, it's even more team oriented; we're a team on everything we work on. My office gets to interact with people in many product areas and learn from them and

try to provide scientific expertise and support. It's more of a collaborative focus because we're trying to move forward on one mission, and I really enjoy that.

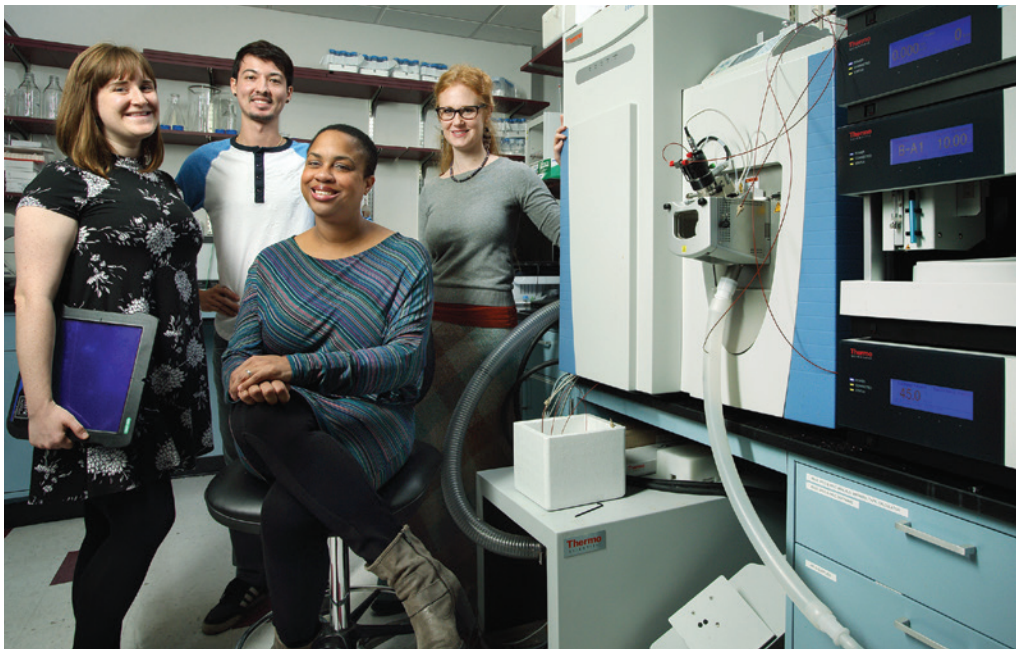
Q. What influences or mentors have contributed to you being ready to take on this role?

It's every step along the way. I always cite my grad school and postdoc advisors, Paul Hollenberg and Eric F. Johnson, respectively, for preparing me to be a scientist, because at the end of the day, I really lead with my science. I'm not just a leader or administrator; I'm a scientist. I want to look at data and talk about what experiments we should be doing and our strategy for moving the science forward. As many people know, I am deeply committed to equity and social justice; I've always told mentees that leading with science and focusing on your love of science gives you a strong platform to make a difference in the culture of science in addition to contributing through the discoveries you make.

My graduate advisor taught me how to be a scientist and told me I could do anything. Then, at Hopkins, lots of people were in my corner. My dean, Paul Rothman, appointed me to be a department chair, giving me a leadership opportunity that was a chance for me to grow my skills and be proven and tested and to mature as a leader so that I was able to step into this opportunity.

Each step, I've been lucky to have lots of supporters. Here, our commissioner, Robert Califf, also had a career as an academic, so we have a good understanding and communication. He values basic science as well as translational science. I feel I can really make an impact because I have support from that top level.

COURTESY OF NAMANDJÉ BUMPUS



During her 12 years at the Johns Hopkins University School of Medicine, Namandjé Bumpus worked on how liver enzymes called cytochrome P450s metabolize drugs. She recently left her lab to become chief scientist of the FDA.

Q. What else would you like us to know about the FDA?

People are surprised that we have research labs and by the breadth of techniques and approaches our people are using. We have a lot of expertise here and really outstanding scientists. It's a place people should consider for scientific research careers.

We have training opportunities for scientists at various career stages and a lot of people who are very excited about mentoring in and outside of the lab. It's a very collaborative environment, more so than people would expect. It's a great place to start a career and a great place to be as a scientist. I'm learning a lot, but I'm still using my scientific chops all the time.

Laurel Oldach (laurel.oldach@gmail.com) is a former science writer for the ASBMB. Follow her on Twitter: @LaurelOld.

Leaving their mark on policy

ASBMB Advocacy Training Program participants use new skills to improve their institutions, create new programs, draft policy recommendations and more.

By Mallory Smith

When Marvin "Cortez" Bowlin stood up during the advocacy town hall at the 2022 American Society for Biochemistry and Molecular Biology annual meeting in Philadelphia, he stole the show.

Bowlin passionately recounted how a peer grad student had been denied time off to attend her own father's funeral. Though it was clear that many in the audience of scientists from around the world were aghast, they weren't in a position to influence policies at Bowlin's university.

In that moment, Bowlin told ASBMB Today, he realized: "We have to be our own advocates. So, I better learn how to do that!"

Shortly after the meeting, Bowlin applied for the ASBMB Advocacy Training Program, a three-month externship run by the ASBMB public affairs department, to sharpen his advocacy skills and create the change he sought. He and nine other delegates completed the program over the summer.

Putting advocacy into action

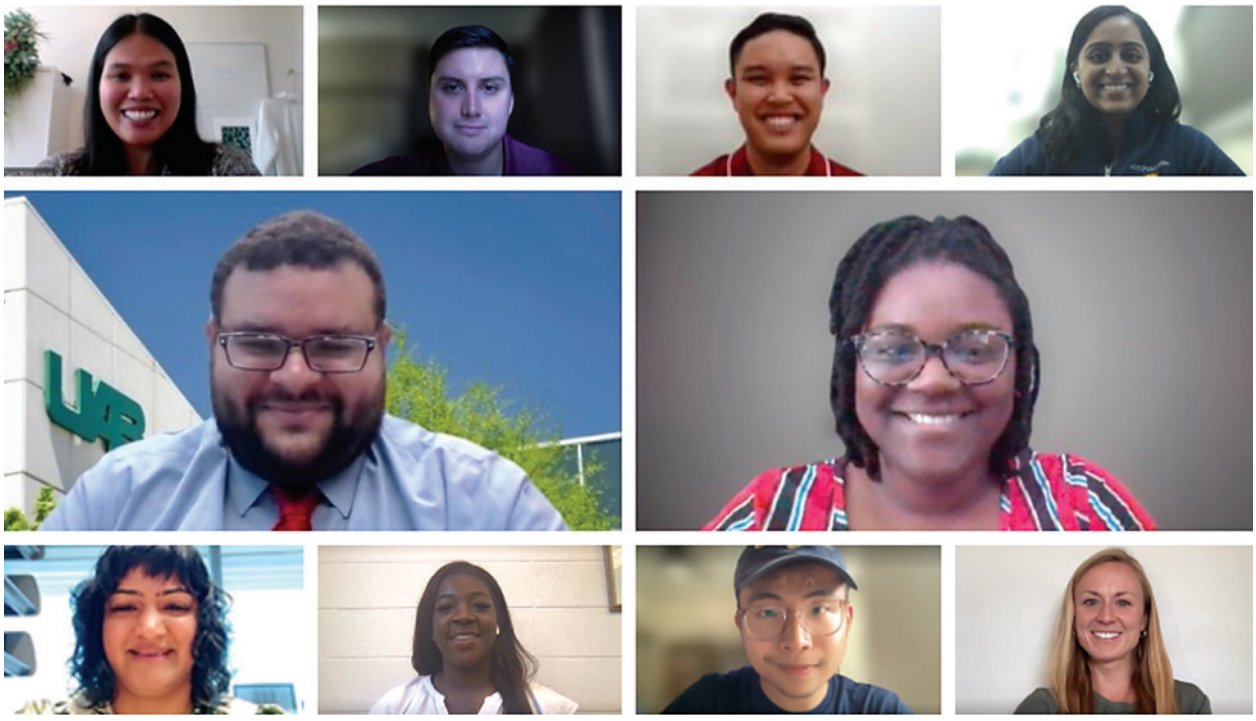
Starting in May, the participants attended 11 training sessions and completed accompanying assignments to learn the science policy landscape and develop their written and verbal communication skills. Their training led up to a virtual Capitol Hill day in August where the delegates met with their senators to advocate for programs and policies that will support the next generation of scientists. Specifically, they made the case to:

- Protect basic scientific research funding and keep the newly formed Advanced Research Projects Agency for Health budget separate from the National Institutes of Health's core budget.
- Fund the CHIPS and Science Act, which authorized millions of dollars to strengthen the scientific workforce and support diversity, equity and inclusion efforts. Lawmakers have yet to fund the higher education provisions from this act that passed in August.
- Support proposed increases for science, technology, engineering and mathematics training programs in the Senate Labor, Health and Human Services, Education, and Related Agencies subcommittee draft appropriations bill.

At first, the ATP delegates were nervous and not sure what to expect from their congressional meetings but quickly realized how fun and impactful they can be. One delegate, Cedric Lansangan, described Capitol Hill day as a "discomfort-inducing but consequently highly rewarding and stimulating activity."

Independent work

Each ATP participant chose a science policy issue on which to focus for the duration of the program. They were tasked with advocating for sound policy solutions at the local, state or federal level, and they were



The ASBMB ATP delegates captured screenshots during their virtual Capitol Hill day (with permission from congressional staff) which were assembled into a collage. From top left to bottom right: Nguyen, Feathers, Lansangan, Sriraman, Bowlin, Rand-Fleming, Arora, Evande, Li and Pitsch.

expected to complete an independent project, such as a policy brief, webinar or other outreach event.

Ankita Arora: Increasing racial and ethnic diversity in genomics research

Ankita Arora, a science writer at the consulting company Nucleus Genomics, advocated for diversity in genomic databases.

Arora, who just had completed a postdoctoral fellowship at the University of Colorado Anschutz Medical Campus, organized a webinar with leaders from the National Institutes of Health All of Us Research Program, the California Initiative to Advance Precision Medicine and the American Association for Cancer Research.

The webinar covered current strategies, recent improvements and the road ahead at both national and state levels to move toward a more diverse, equitable and inclusive precision medicine initiative.

Additionally, she published an opinion piece in The Colorado Sun advocating for establishing a statewide program for precision medicine grounded in diversity, equity and inclusion principles.

Roxanne Evande: Assessing the NSF GRFP peer-review process

Roxanne Evande, a Ph.D. candidate at the University of Delaware, investigated the peer-review process for the Graduate Research Fellowship Program at the National Science Foundation.

Evande cultivated a strong relationship with the former director of the program, Gisele Mueller–Parker, to gain insight and guidance. She created and distributed two surveys that assessed the experiences of applicants and reviewers. She compiled

her analysis into a policy brief calling for more transparency in peer review as well as in-person bias training for NSF reviewers.

Ryan Feathers: Helping students from low-resourced environments earn Ph.D.s

Ryan Feathers, a Ph.D. student at Cornell University, set out to provide resources to equip undergraduates from diverse backgrounds to pursue STEM Ph.D.s confidently.

Feathers established the Graduate School Admissions Information and Support for STEM Ph.D.s initiative, which can be found online at gain4stem.com. It offers guidance on admissions, funding and undergraduate research experiences.

It also supports incoming Ph.D. students via a mentorship program called the GAINS Buddies.

Lien Nguyen: Advocating for postdocs in Boston

By the time Lien Nguyen joined the ATP, she already was a postdoctoral leader at her institution, Brigham and Women's Hospital. She'd been advocating on behalf of postdocs for some time and decided to focus her ATP project on salary increases.

Nguyen put together an advocacy committee and developed communications to make people aware of it.

Her initial conversations with institutional leaders led to two new policies: (1) allow principal investigators the flexibility to pay postdocs higher salaries if they have available funds and (2) mandate that postdocs receive automatic increases per year according to the NIH's National Research Service Awards scale.

Today, Nguyen is working on surveys, identifying PI allies and hosting town halls with the hope of bringing salaries up to a minimum of $65,000 per year to match increases occurring in 2022 and 2023 at Harvard Medical School, a close affiliate of BWH.

Emily Pitsch: Promoting evidence-based policymaking and science literacy in Utah

Emily Pitsch, a fifth-year biochemistry Ph.D. student at the University of Utah, conceived of the Utah Science Policy Initiative, which has two major goals.

The first goal is to equip state legislators with scientific knowledge they need to make evidence-based decisions about bills. The second is to provide similar unbiased information to the public.

Pitsch has teamed up with Leah Murray of the Walker Institute of Politics and Public Service at Weber State University, who recently received funding for this sort of work from the Local Science Engagement Network.

Pitsch also secured funding from the Research!America Civic Engagement Microgrant Program to support the initiative.

Chelsea Rand–Fleming: Creating a local pipeline for U.S. veterans in STEM

Chelsea Rand–Fleming, a senior chemistry and biochemistry Ph.D. student at Auburn University, wanted to help U.S. veterans in her community pursue STEM careers.

She knew she needed the support of local educational and veteran community leaders, so she built relationships with professors, officials at veteran and military resource centers, and even the president of her university. She then identified employers eager to hire veterans for STEM positions.

Rand–Fleming plans to unveil a job board in the spring that will connect veterans to these employment opportunities. She is recruiting more students to join the effort and identifying more STEM employers.

Her long-term goal is to create a model — connecting veterans with resource centers, STEM education programs and full-time jobs — that can be duplicated in other communities.

Aishwarya Sriraman: Safeguarding against future chemical threats

Aishwarya Sriraman, an Oak Ridge Institute for Science and Education researcher at the U.S. Army Medical Research Institute of Chemical Defense, developed a policy brief with recommendations to improve the U.S. Strategic National Stockpile.

The stockpile is responsible for collecting and maintaining a repository of pharmaceutical medical countermeasures in the case of a public health emergency caused by a chemical, biological, radiological or nuclear threat.

Specifically, Sriraman identified gaps in the current medical countermeasures against chemical agents and noted the need for better drugs to combat certain chemical agents. In her brief, she called for an increase to the stockpile budget to ensure it can maintain existing medical countermeasures and integrate new ones.

Cedric Lansangan: Increasing student diversity on the physician–scientist pathway

Cedric Lansangan is a first-year Ph.D. student at Loma Linda University in Southern California. He came to the program with concerns about who makes it onto and all the way through the Ph.D.–M.D. pathway.

Broadly, Lansangan wanted to advocate for better organized and wider reaching outreach efforts to make M.D.—Ph.D. programs and careers more transparent and less intimidating. More specifically, he aimed to organize seminars at local or relevant national conferences. He submitted several conference proposals before beginning grad school this fall.

Lance Li: Analyzing the diversity, equity and inclusion of grants funded by NIH HRHR programs

Lance Li, a senior at Georgetown University, evaluated the NIH's High Risk, High Reward Program and its distribution of funding based on gender and institution classification.

Li found that HRHR funding primarily goes to research institutions that already have a lot of research funding. Nearly all the awards issued to minority-serving institutions went to large, well-resourced Asian American and Native

The ASBMB Advocacy Training program is a three-month externship (running from May to August) that provides hands-on science policy and advocacy training and experience.

Applications for the 2023 program will open in mid-March and close on April 21.

Scan here for more information:

American Pacific Islander–serving institutions in California and Washington. Notably, no historically Black colleges and universities were funded by the program.

Marvin "Cortez" Bowlin: Improving the graduate student environment at UAB

Marvin "Cortez" Bowlin, a graduate student at the University of Alabama at Birmingham, focused on raising graduate stipends at UAB.

While he didn't hold any official positions within the UAB student governing bodies, he leveraged his advocacy skills to become essentially a go-between.

First, he studied the disparate views of the student governing bodies and the administration. Then, thanks to his strong aptitude for driving consensus, he landed a seat at the negotiation table via a newly formed student advisory board.

Bowlin framed the issues faced by graduate students as opportunities for UAB to relieve students' burdens and allow them to dedicate more time and effort to research. This shift in messaging and delivery to the correct target audience led to significant and sustainable improvements for all the graduate students at UAB for years to come.

Ultimately, UAB agreed to a $3,000 increase to stipends and a yearly adjustment for inflation.

Additionally, Bowlin and others negotiated for improvements to transportation, more transparent campus safety reports and expansion of the institution's family assistance scholarship.

Bowlin said that the ATP helped him recognize that "you catch more flies with honey than you do vinegar."

Mallory Smith (msmith@asbmb.org) is an ASBMB science policy manager. Follow her on Twitter: @MalScienceGal.

Apply for the Marion B. Sewer Distinguished Scholarship for Undergraduates

Marion Sewer, an accomplished pharmacology professor, was deeply committed to service within the scientific community.

The Marion B. Sewer Distinguished Scholarship for Undergraduates offers financial support to students who demonstrate an interest in the fields of biochemistry and molecular biology and enhance the diversity of science. Students whose social, educational or economic background adds to the diversity of the biomedical workforce or who show commitment to enhancing academic success of underrepresented students are eligible.

Scholarship amount: $2,000 toward tuition for one academic year.

Requirements

To be considered for a scholarship, you must:

- Be a U.S. citizen, U.S. national or permanent resident at the time of application. Students with DACA status also are eligible. Foreign nationals who are in the U.S. on visas are not eligible.
- Be enrolled or accepted for enrollment as a full-time student at an accredited two- or four-year institution located in the U.S. or U.S. territories.
- Be an ASBMB member at the time of application. Undergraduates can join the ASBMB either directly or by joining an ASBMB Student Chapter at a participating institution.

Application deadline: June 1

Learn more and apply at **asbmb.org/undergraduate-scholarship**

ASBMB
American Society for Biochemistry and Molecular Biology

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Proteomics reveals new biological insights

By Steven Carr

The majority of investigations that reveal a deep mechanistic understanding of disease, genetic variation and drug mechanism of action require direct analysis of proteins, their modifications and their interaction partners.

Focused analyses of biological and clinical systems using mass spectrometry–based technologies detect, identify and quantify proteins and their modifications and interaction partners in cells and tissues under drug treatment or development or during disease perturbation. In this way, MS-based proteomics directly measures the impact and integrative consequences of genomic alterations. When these analyses are combined with specific chemistries, researchers gain insights into the mechanism of action of drugs, the identities of potential new therapeutic targets and new biological knowledge.

The three speakers selected by the editorial leadership of Molecular & Cellular Proteomics to present their work at Discover BMB are a mix of early-career and established investigators who are pushing the boundaries of mass spectrometry–based proteomics combined with elegant chemistries to provide new biological and clinical knowledge.

Katherine Donovan is a group leader and lead scientist at the Dana–Farber Cancer Institute. Her focus is on development and application of targeted proteome degradation and on deepening our understanding of the ubiquitin proteasome system for therapeutic purposes.

Jim Wells is a professor of pharmaceutical chemistry at the University of California, San Francisco. He focuses on understanding and modulating signaling processes in human cells through protein and small-molecule design. He is especially interested in the interprotein circuitry of pathways involved in cell death and inflammation and the intraprotein allosteric circuitry that governs how distant functional sites in one protein communicate.

Lan Huang is a professor of physiology and biophysics in the School of Medicine at the University of California, Irvine. Her research focuses on developing and employing novel mass spectrometry–based proteomic strategies for comprehensive analysis of macromolecular protein complexes to define their composition, heterogeneity, modification, interaction and structure.

Read more about these three scientists in the following pages.

Steven Carr (scarr@broadinstitute.org) is senior director of proteomics at the Broad Institute of the Massachusetts Institute of Technology and Harvard and an institute scientist. He is a deputy editor of Molecular & Cellular Proteomics.

Degrading the mighty proteome with small molecules

By Kanika Khanna

Katherine Donovan's research path hasn't followed a linear trajectory; she's zig-zagged from doing basic biochemical studies to proteomics-based translational research. In her words, she is now "designing small molecules to hijack the cell's waste disposal system and redirect it to disease-causing proteins."

But Donovan's movements have not been random, she said: "I've found that I gravitate toward collaborative interactions."

During her Ph.D. at the University of Canterbury in New Zealand, Donovan studied the adaptive evolution of pyruvate kinases in E. coli. Using biochemistry and structural biology techniques, she demonstrated how mutations in the protein make the bacterium better able to tolerate low-glucose conditions.

After joining Eric Fischer's lab at the Dana–Farber Cancer Institute in 2016, Donovan used proteomics to quantify changes in protein expression in mammalian cells when perturbed with drugs and small molecules. Her desire for collaboration motivated her to join Dana–Farber's new Center for Protein Degradation, or CPD, in November 2018. There she built and managed the proteomics operation and developed novel technologies to advance drug discovery for different targets.

Now a lead scientist in the Fischer lab, Donovan spearheads multiple projects in proteomics as well as serving as a proteomics advisor to the CPD. Many of her projects are focused on finding degradation therapeutics for proteins involved in diseases such as cancer and Alzheimer's.

Donovan's favorite part about research is the community she gets to interact with daily. "People are the biggest driver in my job," she said. "I am very lucky to have a fantastic proteomics team where everyone is super excited about science."

KATHERINE DONOVAN

DESIGNING DEGRADABLE MOLECULES

Cells rid themselves of misfolded proteins by a process in which the proteins are ubiquitinated by the E3 ligase complex and degraded by the 26S proteasome. This pathway can be hijacked by using small-molecule degraders to recruit E3 ligases artificially to proteins linked to diseases. This process, called targeted protein degradation, or TPD, offers several advantages over conventional inhibition strategies: proteins of interest can be eliminated completely, and TPD has the potential to target a large portion of the proteome that previously was considered undruggable.

Katherine Donovan and her team at the Dana–Farber Cancer Institute recently used a chemoproteomics pipeline to identify degradable kinases by designing the degrader molecules to be as promiscuous as possible. Mutations in kinases are at the root of many human diseases, and before this project, only 7% of the human kinome was reported as degradable, making kinases attractive candidates for TPD. The team prepared a library of 91 potential kinase degrader molecules and, using proteomics, found that they degraded about 200 distinct kinases.

The researchers released their data set as a public resource to advance the field of TPD.

"Our group saw how hard it was to design these molecules and how much time, effort and money was put in," Donovan said. "One of the ways in which we can advance the field and help other researchers is by making the data available to everyone. Science moves faster if you take a community approach."

Kanika Khanna (kkhanna@berkeley.edu) is a postdoctoral fellow at the University of California, Berkeley. She earned her Ph.D. at University of California, San Diego. Follow her on Twitter: @khannakanika111.

Exploring cell surface changes in cancer

By Chloe Kirk

Jim Wells' research has spanned biotech, academia and founding a company. He's determined that whatever he does, it doesn't feel like "punching the clock."

Focusing on how cell surfaces change in response to health and disease, Wells uses his seminal work in protein engineering to explore drug development targets through protein mutagenesis.

"It's important to me that my work ticks two critical boxes," he said. "One is that this lab would be a great place to grow as a scientist, and the second is the work has to be fun."

Raised in the San Francisco Bay Area, where he was inspired by enzymology researchers such as Daniel Koshland, Wells went to Washington State University for his Ph.D. to work under Ralph Yount who, he said, "taught me most of the things I know today, especially biochemistry and protein modification."

Eighteen months into his postdoc at Stanford, "I realized I really enjoyed gene structure and function, and this amazing new technology called site-directed mutagenesis was just published," Wells said. "I thought, 'wow, this could be really amazing to apply to proteins.'"

Recombinant DNA studies were at such an early stage that Wells knew he wasn't going to find an academic job to support this research. That's when a friend introduced him to a company at the forefront of applying recombinant DNA for commercial use: Genentech.

At Genentech, Wells and his group engineered the first gain-of-function enzymes, growth factors and antibodies by site-directed mutagenesis. "I thought I'd be there three years to learn the technologies," he said, "and ended up staying 16 years."

Wells went on to start his own company, Sunesis Pharmaceuticals, before he moved in 2005 to the University of California, San Francisco, where he is a professor of chemistry.

JIM WELLS

DEVELOPING ANTIBODIES FROM CANCER MARKERS

Jim Wells' work focuses on changing cell surface proteomics in changing cell health and diseases, most notably in cancers. He breaks his research into four projects: What's Up, What's Cut, All in the Neighborhood and Cell Portal.

The What's Up project is centered around new blooms of proteins that appear specifically in cancerous cells, and the lab has recently published a new tool to label these blooms of proteins.

What's Cut looks at the What's Up project with another level of resolution. Here, the team looks at posttranslational modifications, such as glycosylation or proteolysis, tagging those proteins to find out what targets are being modified, and then makes antibodies that can attack those targets; they published recently on targeting RAS-driven cancers.

The All in the Neighborhood project switches gears and studies how protein complexes change on a cell's surface during cancer.

The Cell Portal project examines how entire peptides change between normal and cancerous cells to engineer antibodies targeting cancerous peptide complexes, as the team recently reported in the Journal of the American Cancer Society.

Chloe Kirk (cck22@miami.edu) is working toward her Ph.D. in biochemistry and molecular biology at the University of Miami. Her interests are science research, communication and outreach. Follow her on Twitter: @chloeckirk

Uniting technology and discovery

By Laura McCormick

Growing up with two physics teachers as parents, Lan Huang naturally was drawn to science. In college, she majored in chemistry and later earned a Ph.D. in analytical chemistry, studying insulin secretion from single beta cells.

Huang moved to San Francisco to start her postdoctoral fellowship at the University of California in 1996, a move that coincided with the rise of biological mass spectrometry. She quickly fell in love with the new field of proteomics.

For several years, Huang worked at UCSF as a staff scientist in the mass spectrometry core facility, collaborating with numerous labs. In 2003, she opened her own lab at the University of California, Irvine, to develop new tools to study the ubiquitin proteasome system, holding a joint appointment until 2012, when she was appointed professor of physiology and biophysics in the university's medical school.

The proteasome — a large multiprotein complex — was the perfect challenge for Huang. As protein degradation is disrupted in numerous diseases, the ubiquitin-proteosome pathway serves as a promising pharmaceutical target. The proteasome regulates many essential cellular processes — highlighting its biological importance but complicating research studies because many proteins can interact with the complex at varying times.

Early in Huang's career, few labs used mass spectrometry to analyze protein complexes. Studying protein–protein interactions can be difficult; many complexes within the cell are dynamic, showing tight spatiotemporal regulation. As a result, the Huang lab focused on developing cross-linking strategies to stabilize protein–protein interactions, freezing a moment in time.

Huang's research program combines new methodology and biological discovery.

"You try to address some questions and you realize that there is some technology that needs to be developed," Huang said. "Then once you develop some new technology, you try to apply it. … It's a new push in both directions."

MAPPING PROTEIN INTERACTOMES

LAN HUANG

Lan Huang's laboratory continues to create new strategies to study protein–protein interactions through mass spectrometry, or MS.

Recently, her lab developed a set of photoreactive, MS-cleavable cross-linking reagents. Unlike traditional cross-linking approaches, these photoreactive reagents can target any amino acid. Furthermore, these reagents are MS-cleavable, allowing the cross-linked peptides to be separated during collision-induced dissociation to simplify sequencing and peptide identification, a big advantage when working with complex samples.

Huang's lab also created crosslinking reagents that are membrane permeable and enrichable, allowing researchers to cross-link protein complexes within cells. This achievement facilitates the identification of endogenous protein–protein interactions.

Ultimately, Huang hopes to use these tools to create detailed protein interaction networks in clinical samples. These advances also have implications for human health, accelerating the study of protein dysregulation during disease.

"Hopefully the information generated will help us to understand the molecular basis for disease development," Huang said, "and provide some hot spots to allow us to develop protein interaction–driven therapeutics."

Laura McCormick (lemccorm@email.unc.edu) is a graduate student in cell biology and physiology at the University of North Carolina at Chapel Hill. Follow her on Twitter: @le_mccorm.

Tabor award winners to speak at #DiscoverBMB

The Journal of Biological Chemistry is pleased to announce the winners of the 2023 JBC Herbert Tabor Early Career Investigator Awards.

Named for the late editor-in-chief of the JBC, these awards recognize early-career scientists for their standout first-author papers published in the past year.

The winners will give talks during a symposium on Sunday, March 26, at Discover BMB in Seattle.

Jenna Lentini, Regeneron
"Methyltransferase METTL8 is required for 3-methylcytosine modification in human mitochondrial tRNAs"

Ethan J.C. Walker, Broad Institute of MIT and Harvard
"Protein folding stabilities are a major determinant of oxidation rates for buried methionine residues"

Roshan Kumar, University of Michigan Medical School
"A redox cycle with complex II prioritizes sulfide quinone oxidoreductase-dependent H2S oxidation"

Anabel Gonzalez–Gil Alvarenga, Johns Hopkins School of Medicine
"Human brain sialoglycan ligand for CD33, a microglial inhibitory Siglec implicated in Alzheimer's disease"

Nishanth Kuganesan, University of Toledo
"Tumor suppressor p53 promotes ferroptosis in oxidative stress conditions independent of modulation of ferroptosis by p21, CDKs, RB and E2F"

Jodi Brewster, University of Wollongong
"Structures and kinetics of Thermotoga maritima MetY reveal new insights into the predominant sulfurylation enzyme of bacterial methionine biosynthesis"

Julianty Frost, University of Liverpool
"Von Hippel–Lindau small-molecule inhibitor binding increases stability and intracellular levels of VHL protein"

Look for profiles of these award recipients and links to their winning papers at asbmb.org/asbmb-today.

19 tips for giving an effective talk

By Adriana Norris

As scientists, we communicate our work in many ways. We publish peer-reviewed manuscripts, we write reviews and books to summarize the state of our fields, and we give oral presentations at seminars and conferences. Each of these formats presents unique challenges; however, all of them require intense editing and feedback from mentors and peers.

In this article, I'm sharing tips on how to prepare your talk, tips about your slides (design and structure), and tips on presentation. Discover BMB is less than a month away — it's time to get ready to present your science.

I am a fifth-year Ph.D. candidate at Vanderbilt University, and during my time in graduate school, I've learned many lessons about how to give an effective talk — often by giving an ineffective talk and receiving much-needed feedback. At first, I was uncomfortable hearing critiques, but I learned that the purpose of constructive criticism is to help me grow; when someone gives me feedback, it's because they care about my success.

By being receptive to constructive feedback, I learned that I tended to overexplain the technical aspects of my data without highlighting the broader impacts of the findings, I used brightly colored slides that were distracting, and I spoke too quickly. Thanks to this feedback, and after giving dozens of talks for different audiences in various settings, I learned to correct these issues.

Now when I give a talk, I often get feedback from the audience about how clear and engaging I was, so I want to share what I've learned about how to give an effective oral presentation.

The following list includes tips sourced from a tweet written by Tessa Davis (@TessaRDavis), a presentation coach who shares helpful advice, and from a YouTube video I created, "30 tips on how to give an effective talk," which is a culmination of the lessons I've learned about presenting during my time in graduate school.

I've learned that an effective oral presentation is clear, compelling and accessible and establishes a convincing argument supported by empirical data, all constrained by a time limit. As I mentioned at the outset, an effective presentation requires a lot of practice, feedback from trusted peers and editing.

Preparation

1. Create your presentation with your audience in mind. If you're talking to a room of M.D.s, you probably do not need to provide a lot of background about common diseases; however, if you're talking to structural biologists about physiology, spend more time on the background so they can follow along.

2. Write a script for the first slide or first few slides and memorize it. The beginning of a presentation is often the hardest part because you're nervous and just getting your footing. If you have a script for the first few slides, you know exactly what you are going to say. This helps you start the presentation with confidence and then ease into the unscripted portion.

3. Practice before you do the real thing. Practice your talk in front of trusted peers, ask for con-

structive feedback and use that feedback to edit your talk; then practice the edited talk again, keeping in mind your allotted amount of time. If possible, practice in the room where you will be giving the presentation.

4. Make sure you have seen your slides in the format you'll be presenting them in. I prefer to make my presentations in Google Slides, so I usually have to convert the slides into PowerPoint and save them on a flash drive to present at conferences. If you do something similar, make sure you open the presentation in whatever the final format is to make sure nothing has been shifted or messed up.

Design

5. *@TessaRDavis tweet:* **Use a decent font size.** Tiny fonts lead to unreadable text and a confused audience, so use a font size that can be seen in the back of the room (probably at least 30 points).

6. *@TessaRDavis tweet:* **Use high-quality images.** Don't use images that are pixelated and blurry or clip art with giant watermarks. Use images that are crisp and clear, without any distortions due to resizing.

7. *@TessaRDavis tweet:* **Avoid too many animations.** I only use animations to reveal the content on the slide in a stepwise manner, so as not to overwhelm the audience with slides that are jam-packed and hard to digest.

8. *@TessaRDavis tweet:* **Create a consistent look.** Use the same font and color style on every slide.

9. Make your talk as accessible as possible! Provide captions, transcripts, handouts and high-quality audio.

Structure

10. Make the title of each slide the main finding (the argument you are trying to make with the slide content). This will help your audience remember what argument you're trying to make so they can follow along more easily and reorient themselves if they get distracted.

11. Acknowledge the people who did the work. You can give acknowledgments throughout the presentation and end with an acknowledgments slide. It's important to highlight each individual's hard work as well as the team effort that went into the results you're showing.

12. Conclude with a summary and future directions. Try to relate the summary to the problem or gap in knowledge that you present in the beginning of your presentation; this makes your talk feel more like a complete story.

13. Remember: Quality vs. quantity. It's tempting to show off as much data as possible because you worked so hard to acquire it, but this can overwhelm an audience. Instead, strive to curate a story that is clear, compelling and linear. Obviously, you need to be truthful — don't hide data to create a false story — but strive to highlight the most compelling data to create an interesting narrative.

Presentation

14. Begin by highlighting the goal of your talk. Start by saying something like, "Today I hope to convince you that …"

15. Don't read text from your slides or stare directly at them instead of at the audience. Your slides are not your script; they are an accessory to buttress what you're saying.

16. Speak intentionally slowly. We often speak too quickly when we're nervous or excited. Speaking slowly can be challenging, but it will help you deliver your message to your audience more clearly. Practice this when you are preparing for your talk.

17. If you use a laser pointer, guide the audience's attention intentionally. Don't overuse your laser pointer and force your audience's eyes all around your screen. Practice using your laser pointer when you're preparing for your talk.

18. Have a confident stance and speak loudly and clearly. You can convey confidence with your body language. If you are able, stand up proudly and move around the room to help keep your audience's attention.

19. Stay within your time slot. Often, when giving an oral presentation, you are one of many speakers and will have a strict time limit. Practice your talk with a timer and make edits to stay within your slot. You don't want to go over time and cut into someone else's time; this can cause issues for both the speakers who come after you and the organizers of the event.

Adriana Norris (adriana.c.norris@vanderbilt.edu) is a fifth-year Ph.D. candidate at Vanderbilt University studying lipid biology and metabolism. She is a member of the ASBMB Science Outreach and Communication Committee and has a YouTube channel where she strives to make academia entertaining and accessible. Follow her on Twitter: @adricortee.

Must a female scientist be ambitious?

By Marina K. Holz

I recently was chatting with a colleague about a leadership position that opened up at her institution. "You should apply!" I urged her, sensing an opportunity. My friend was hesitant; she didn't think she was ready or qualified.

A few days later, we talked again. My friend looked at her professional accomplishments and compared them to those of people who typically hold this leadership position. Of course, she had the prerequisite experience to apply. She still didn't think she was ready, however, and thought she needed to participate in leadership training through her professional society. This is a known phenomenon — women think they need to be perfectly qualified for the positions they seek, whereas men are less picky about their own credentials for the job.

After I became a tenure-track professor, I started seeking out leadership positions at my institution because I wanted to create opportunities for students. For example, I established the first American Society for Biochemistry and Molecular Biology undergraduate Student Chapter on my campus. After I achieved tenure, I had to use my voice to advocate for the professional interests of my colleagues. I was elected to the university faculty council and eventually became the chair of my academic division. Currently, I am the dean of the graduate school at my institution and a member of the Women in Biochemistry and Molecular Biology Committee of the ASBMB, working to promote and support the careers of women.

When I started sitting at the leadership table, I noticed that there still are fewer women at that table than men. At my institution, I am the first female dean of my academic unit. Things are getting better, just not fast enough.

We still need to remove barriers that make science careers more challenging for women than men. Women now have equal access to undergraduate and graduate science education, but still there are fewer female than male assistant professors, and the disparity grows as you look up the career ladder. At senior leadership levels in the academy, men greatly outnumber women as department chairs, center directors, deans, provosts and presidents. One question we sometimes hear asked is whether women are just not as ambitious as men.

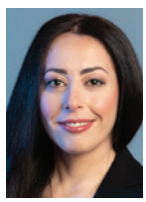
Looking around academic institutions and professional organizations, I see clearly that many women are ambitious and willing to pursue leadership opportunities. Women increasingly are elected as provosts and presidents of universities and chosen to lead professional and scientific societies. However, we also have to recognize that different women may have different ambitions and goals.

For many of my female colleagues, considering the careers of their spouses, the school choices of their children and proximity to extended family may eclipse any of the benefits of pursuing greater leadership opportunities or other forms of career advancement. We need to accept that women may have motivations beyond achievements in the workplace and that career achievements may be secondary to work–life integration.

Professional ambition comes with a price. Aggressively climbing the career ladder is difficult, and as the expression goes, it is lonely at the top. For example, when I became dean, I couldn't continue to be what I think of as a regular scientist and walk into my colleagues' offices to chat about an idea — apparently, some faculty members find it somewhat alarming when the dean enters their office unannounced.

Leadership requires constant decision making and risk taking, which can exact an emotional toll and affect your overall well-being. We need to encourage women who are ambitious, but we want to create networks and systems that will provide support and feedback and will identify women as successful when they achieve their own professional goals.

Marina K. Holz (mholz@nymc.edu) is the dean of the Graduate School of Biomedical Sciences and professor of cell biology and anatomy at New York Medical College and a member of the ASBMB's Women in Biochemistry and Molecular Biology Committee.



Parents in STEM demand change

By Mallory Smith

We all face this key scientist's dilemma: Can we be a parent, a caregiver, a partner, a friend AND a scientist?"

Monica Malta, an assistant professor at the University of Toronto, articulated this question during a LinkedIn chat hosted by the American Society for Biochemistry and Molecular Biology to discuss the systemic challenges faced by parents and caregivers working in science, technology, engineering and mathematics.

As a solo parent, Malta said, she almost left her academic career. After taking unpaid maternity leave, she didn't think she could return to her field. "But against all odds, I'm still here," she said. "Three kiddos after."

Malta described the uphill climb that she and many of her colleagues face: "Mothers in STEM face discrimination, drops in productivity and inequities in wages and promotion — all of which contribute to this huge drop in the full-time STEM workforce."

The career path from bachelor's degree to tenure-track faculty includes low pay, long hours and, often, frequent moves, so raising young children is difficult without financial or caregiving support.

As a result, mothers are almost twice as likely as fathers to leave academia when they're postdocs and three times less likely than women without children to obtain a tenure-track position.

Ahana Maitra is a postdoctoral fellow at Fiocruz Amazônia. "There is growing evidence … showing that systemic barriers related to motherhood are driving the major leak in the STEM pipeline," she said, "but this problem has been ignored forever."

Last year, Congress took a first step to help pregnant and caregiving parents in STEM. They passed a provision in the CHIPS and Science Act that directs the White House Office of Science and Technology to advise federal science agencies on implementing caregiving flexibility and support across all career stages.

Additionally, after letting it sit stagnant for a decade, lawmakers finally passed the Pregnant Workers Fairness Act in December as one of two amendments in the fiscal 2023 omnibus bill to help pregnant workers in the U.S. The amendments require employers to provide reasonable accommodations during pregnancy and childbirth as well as more time and space for breastfeeding.

Organizing and speaking out

Most research institutions and federal science agencies offer little support to help parents of young children navigate STEM careers, resulting in significant barriers to striking a successful balance. No standard policies or best practices ensure equitable and adequate support for parents at all career stages in academia. The support a parent receives varies depending on their circumstance, gender, employment status, institution, state and country.

A comparison of the 2017 and 2021 National Postdoctoral Association Institutional Policy Reports shows a more than 20% increase in the number of surveyed institutions offering paid maternity leave to postdoc employees. While this progress is encouraging, more than a third of institutions still lack paid maternity leave and have a reduced amount of support for postdocs who are not employees of their institution (those funded by training grants, research fellowships or other external funding sources).

In a letter to the National Institutes of Health in 2019, Postdoc Parents for Change asked for federal policy changes for postdocs including (1) at least eight weeks of paid parental leave and four additional weeks for birthing parents, (2) extended fellowships and grants to account for family leave, (3) transitional support back to work, and (4) assistance with affordable childcare.

The NIH later issued a one-year childbirth extension for K99/R00 awards and an incremental improvement that allows a $2,500 childcare cost allowance per budget period for National Research Service Award fellowship or training grants.

Maitra is a member of Mothers in Science, an international nonprofit founded in 2019 that has brought together thousands of STEM students and professionals around the world to raise awareness of systemic structural barriers that silently push mothers away from STEM career paths. Their fast-growing community has developed a wealth of resources, research and advocacy to support and elevate the needs of STEM parents.

Malta belongs to the grassroots organization 500 Women Scientists, which began its SciMom Journey campaign, also in 2019, to bring more visibility to mothers in science, share their stories and advocate for improved policymaking.

More than policymaking

Institutional policies are not the only things hurting STEM parents. Cultural stigma also can cause mothers and fathers to feel they can't be both an attentive parent and a successful scientist.

At the ASBMB LinkedIn chat, scientists railed against the idea that being a parent is a weakness or career barrier.

Maitra said she faced discrimination when she tried to gain access to career opportunities, such as conferences or important meetings or research projects. At times, she said, she was told bluntly that it was more important to take care of her kid first rather than dedicate herself to her career. "These experiences affected my chances to gain more visibility as a researcher," she said, "and I missed several chances for collaboration."

Malta urges institutional leaders and employers "to confront cultural beliefs that STEM professionals with caregiving responsibilities are less valuable, less committed to their careers and less productive than their colleagues without these responsibilities."

She also calls on leaders to listen to parents in STEM, especially those experiencing additional layers of discrimination, such as those directed toward racial, ethnic and LGBTQIA+ minorities, and work with them to brainstorm solutions and tailored strategies that work for them.

DETAILS

Read the full LinkedIn chat on asbmb.org.
If you have more ideas on how federal agencies and institutions can support parents in STEM, contact the public affairs team at publicaffairs@asbmb.org.

Unique challenges

There may not be a one-size-fits-all solution. Parents belonging to groups that historically have been marginalized in STEM are affected in unique and intersectional ways that stem from cultural and personal perceptions. A 2017 report from the Pregnant Scholar showed that white postdocs are more likely to have supportive advisors and to ask for and receive parental leave than postdocs of color.

Toni Mosley, a Black woman, a mother and a program manager for 500 Women Scientists' Fellowship for the Future, said she battled mental health challenges. "Black women are expected to do it all not only by society but by ourselves as well," she said. "When I found myself struggling to juggle my responsibilities, I realized I couldn't meet my own expectations. I didn't know how to ask for help, because I was afraid of looking weak, which caused my work and my mental health to suffer."

When Mosley finally reached out for support, she said, she received a simple piece of advice: "Never lose sight of your goals, but be realistic and forgiving." This empowered her to be flexible with some of her goals and timelines so she could begin to relax and enjoy being both a mom and a STEM professional.

Malta and the other scientists in the chat agreed that a supportive environment was key to their retention. In Malta's case, a lack of support pushed her to switch to an organization that was more welcoming.

And she continued her "scientist's dilemma" comments with a sobering admission: "Of course it is NOT easy to be a mother and continue working in STEM. ... I won't lie: It is hard."

Mallory Smith (msmith@asbmb.org) is an ASBMB science policy manager. Follow her on Twitter: @MalScienceGal.

Science meets soccer: It's all about passion

By Marcelo G. Kazanietz

As Argentina celebrated its third World Cup championship and the entire planet was thrilled by 35-year-old Lionel Messi's long-awaited historic conquest, I could not stop thinking that one billion people with diverse cultural backgrounds all were sitting in front of their screens to watch the final.

Throughout the game, our hearts raced — my smartwatch indicated over 130 beats per minute for over two hours. And as the penalty shootout ended, tears of joy or desolation rolled down our cheeks.

COURTESY MARCELO KAZANIETZ

Kazanietz raises the 1995 local league trophy.

I was born and raised in Argentina, so soccer (aka fútbol/football/futebol/calcio) runs through my veins. As a fan of Racing Club, a major Argentine team, I experienced the thrill of attending games each week throughout my youth. Still now, I watch every single game on my laptop — wearing my Racing Club jersey, of course — and I sometimes even fly to Buenos Aires to watch a final.

In my years as a postdoctoral fellow at the National Institutes of Health, Friday evening pick up soccer games outside our building were almost mandatory, with postdocs from all over the world (as well as lab chiefs) relieving stress after a long week of hard work. Running an electrophoresis gel? No worries: Just lower the voltage and you can play a longer game (and by the way, your Western blot bands will look sharper). For our NIH team, the joy of winning the county league in 1995 was comparable to having a paper accepted in a top-tier journal.

Passion — the energy coming from within in pursuit of your aspirations — is at the core of both sports and science.

As a postdoc, I would stay endless hours in the lab waiting for each scintillation vial to be read — and there were hundreds of vials sometimes. No way would I go home until the last vial was read and a graph was made. At times, reading the radioactivity counts could be as stressful as watching a World Cup match. I'd find myself loudly celebrating an exciting result as if I were in a soccer stadium after a last-minute goal in extra time: "Yes! Yes! Yes! There was 32P incorporation! My kinase is active!"

Forty-eight hours in the lab, mostly in the cold room, were not in vain.

The opposite was also sometimes true. I might leave the lab in total despair if the protein turned out to be dead. How could I have forgotten to add glycerol after the last purification step?

In science, passion gave me the resilience to overcome frustration and build a thick skin.

Nowadays, I often hear my fellow PIs talk about the struggle to recruit enthusiastic trainees who have a hunger for scientific inquiry. As one colleague asked, "Is passion in science evaporating in the young?"

While I hesitate to agree, I recognize that the landscape

COURTESY MARCELO KAZANIETZ

The tradition continues: Marcelo Kazanietz and his son Diego Kazanietz (named for the soccer legend, Maradona), before a final Argentine soccer league championship game in 2019 at the Racing Club Stadium in Buenos Aires.

COURTESY MARCELO KAZANIETZ

The 1995 NIH soccer team, with Marcelo Kazanietz standing third from right, after winning the MD local league championship.

of scientific careers has become exceedingly competitive. The rough path to get data published and the hurdles to gain grant funding are likely dissuading the upcoming generation of scientists in academia. I hear graduate students and postdocs say to each other, "I'm not sure I want to spend my life writing grants knowing that the odds to get them are so low."

I wouldn't argue with this statement. There's no right or wrong here. But as PIs, we should be committed to creating an environment that nurtures enthusiasm in our trainees, where they develop a backbone of motivation for their scientific undertakings.

I have seen many of my former trainees pursue successful careers and take leadership positions, largely driven by their pure enjoyment of science. Several former postdocs now run their own labs at academic institutions either in the US or abroad. A common denominator is their dedication to hard work, supplemented by an inner hankering to unearth the unknown and a craving for breakthroughs. Nearly 20 years after one of my postdocs left the lab as she became the new scientific director of her institute abroad, I received an emotional email, thanking me for instilling in her the passion for discovery. "Not at all," I replied. "Hard work and dedication pay off."

If we had a "P index," I'd predict it most likely positively correlates with success in science.

As in sports, success in science is not only about intrinsic talent or natural abilities. It requires genuine commitment, eagerness to learn, discipline, teamwork — and, truthfully, sometimes a bit of luck. Learning from errors and failed experiments — sound familiar? — together with dedicated troubleshooting as a systematic approach to problem solving, are key for overcoming any technical issues you encounter in the lab. Just like practicing penalty kicks, intensive training and endurance may lead you to the next round in your research.

TASNIM NEWS AGENCY

Lionel Messi

When Lionel Messi raised the World Cup trophy, that action capped years of hard work, sacrifice and perseverance, the fruit of a pure passion to pursue a dream. It embodied the ability of a team to thrive fearlessly through fierce competition.

My best advice: Work hard and play hard. Like Messi, you can become the hero of your scientific journey. It's all about passion.

Marcelo G. Kazanietz (marcelog@pennmedicine.upenn.edu) is a professor of pharmacology and translational therapeutics at the Perelman School of Medicine, University of Pennsylvania, and a member of the ASBMB Publications Committee.

Reducing barriers to research grant success

The IMAGE workshop returns

By Kirsten Block

After a four-year hiatus, the American Society for Biochemistry and Molecular Biology's Interactive Mentoring Activities for Grantsmanship Enhancement, or IMAGE, workshop will return in June 2023. To support this workshop over the next several years, the National Science Foundation has awarded more than $1 million to the ASBMB.

Why do we offer a workshop on grantsmanship?

While I haven't directly experienced many of the highs and lows of grant success and rejection, I've had an up-close view of trends in who is — and, importantly, who is not — funded. Before I worked for the ASBMB, I spent part of each year analyzing extramural funding at nearly 150 institutions across the U.S. I noticed that total dollars received might vary year over year, but generally (and unsurprisingly), the trends were consistent: The big-name institutions you would expect to see at the top of the list were continually successful, while less well-known schools rarely received much external research funding.

Drilling down to the level of principal investigator, I'd see some names every year with multiple awards, while others appeared only sporadically. I was delighted when I saw an early-career faculty member receive what appeared to be their first major research grant, but not all of them could maintain that funding. By and large, even for early-career researchers, their institution's overall funding predicted their continued success.

My project didn't look any further into the demographics of individual PIs, but a recent analysis by Mike Lauer and Deepshikha Roychowdhury at the NIH showed what many observe to be the case: Funding tends to go to white, non-Hispanic investigators and men.

However, good ideas — good research questions — can come from anywhere and anyone.

IMAGE then and now

The IMAGE workshop is designed for early-career faculty, those from historically excluded backgrounds and those at institutions with limited infrastructure to support grant development and submission. IMAGE offers information about behind-the-scenes grant review processes at the National Institutes of Health and the NSF, and each participant gets individual feedback on their grant application while it is in development.

To make the most of the IMAGE experience, participants must already have a one-page NSF-styled project summary or NIH-styled specific aims page that they are ready to present for feedback. Participants come away from this workshop not just with strategies to strengthen their research narratives but also with coaches and mentors to help them flesh out their proposals and follow through with submission.

The topics discussed and the relationships forged at IMAGE can serve a critical need for participants. Both the workshop itself and the built-in mentoring component are designed to address barriers these individuals often face in the pursuit of funding — whether seeking that first grant, resubmitting or undergoing renewal — by providing information about the process and guidance to navigate the extramural funding landscape. To remove an additional barrier, the new NSF award to the ASBMB includes travel support for many IMAGE participants.

With previous support from the NSF, the ASBMB hosted IMAGE workshops from 2013 to 2019; more

than 200 scientists participated in those seven years. Many of these researchers went on to receive funding, and according to research done by the ASBMB, those who applied for grants in the immediate term after the workshop were notably more successful in securing funding than comparable grant applicants who did not participate.

Those earlier IMAGE workshops were aimed at senior postdoctoral scientists and early-career faculty. Many of these past participants have now transitioned to their mid-career phase, which can be particularly challenging for some researchers, even those who experienced early success in applying for grants. That's why the new NSF award includes a focus on bringing some past participants back for refresher coaching and input. Early success doesn't always predict continued success, as I saw in my former project. The new IMAGE aims to support faculty not just at the beginning of their funded research but throughout their careers.

As I said, good ideas can come from anyone, anywhere. The upcoming IMAGE workshop will help scientists turn their good ideas into strong proposals and see those proposals through to submission, and it will move the funding odds a little more in their favor.

DETAILS

WHAT: ASBMB IMAGE workshop
WHEN: June 8-11, 2023
WHERE: Washington, DC
TO APPLY: asbmb.org/grantwriting
APPLICATION DEADLINE: April 15
QUESTIONS: education@asbmb.org

Kirsten Block (kblock@asbmb.org) is the ASBMB's director of education, professional development and outreach. Follow her on Twitter: @kfblock.

'I like to be in the lab'

By Martina G. Efeyini

Susan Abbatiello, a principal consultant scientist at Waters Corp., talked to ASBMB Today about her career path and lessons learned.

1 Before grad school, you worked at Genetics Institute (now Pfizer). Can you tell me about that?

Coming out of undergraduate, I felt very burned out. I looked for positions that were laboratory-based because I like to be in the lab, and I was offered a position at a company in Andover, Massachusetts, that made recombinant human proteins, which was a newer type of technology at the time. They gave me an entry-level position in a group that did method development. I worked there for five years.

2 Waters Corp. is a tech company specializing in scientific instruments. What do you do?

My project is called charge detection mass spectrometry. That technology has not quite yet become mainstream. Waters bought the intellectual property rights. It's different than any of the types of mass spectrometers I've worked on. It is able to measure large proteins, whereas conventional mass spectrometers that are time-of-flight or the Orbitrap weren't primarily designed for that.

3 What has been one of your favorite projects?

Around 2005, Thermo Fisher Scientific purchased a technology — FAIMS, which stands for high field asymmetric waveform ion mobility spectrometry. The instrument was really hard to use. It was the first commercial iteration.

Susan Abbatiello

CURRENT POSITION
Principal consultant scientist at Waters Corp.

CAREER PATH
Ph.D., analytical chemistry, University of Florida

FIRST JOB OUTSIDE OF ACADEMIA
Research associate at Genetics Institute (now Pfizer)

FAVORITE MOLECULE OR PROTEIN
"The first one that I worked on right out of undergrad: bone morphogenetic protein 2, or BMP-2. Its function is to induce bone growth."

A colleague and I began messing around with hardware modifications. We saw that not only could it limit the junk getting into your system, but you also could improve the signal-to-noise ratio of what you wanted to detect so your instrument stayed cleaner for longer and you got better signal. It's like a win-win-win.

I was in a product manager role. I wanted to make sure that anyone that would use it could use it intuitively. When that product launched, I was very happy; it was like a technology baby.

4 How can students interested in an industry role prepare?

Start as early as high school or undergrad. Try summer internships so they can work closely with people in the lab.

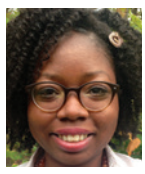
There are some skills I wish I had worked on earlier in my career. One is learning how to code, whether it's R or Python or just being able to write macros to do things more efficiently.

5 What advice do you give others interested in industry?

Finding a place where you can do what you do and be appreciated is a key and important aspect in a successful career. I've worked at a lot of different places, and at some I didn't feel appreciated. I moved around until I found a position where it seems to fit the best. I think it's important to not be afraid of that. We're not in the generation anymore where people are working 20 and 30 years at the same job.

(This interview has been condensed and edited. To read a longer version, go to asbmb.org/asbmbtoday.)

Martina G. Efeyini (mefeyini@gmail.com) is a science communicator and STEM education advocate, and a careers columnist for ASBMB Today. Follow her on Twitter: @mefeyini.



Discover BMB | 2023

American Society for Biochemistry and Molecular Biology

MARCH 25-28 | SEATTLE

Registration deadline: March 23

WORKSHOPS

- Open-source tools to explore protein–ligand interaction in the undergraduate classroom
- Enzyme Function Initiative
- Escaping traditional pedagogy
- Basics of the iCn3D program
- Outreach for all ages
- Building partnerships to bridge STEM outreach to the real world
- Developing scientific writing courses for STEM training
- Building science communication training into your classrooms, programs and grants
- Success in scientific publishing
- National Science Foundation funding opportunities
- Incorporating anti-racism, social justice and equity themes into biochemistry courses
- Anti-racist classroom practices
- CV workshop
- Building professional relationships
- How to engage in advocacy
- Advocacy town hall
- Lab management

SYMPOSIA

- Advances in organismal and cellular metabolism
- AI and ML in structural biology, drug design and systems biology
- Bias in, bias out in data science
- Biochemistry of elemental cycling
- Cell signaling — new tools and emerging concepts
- Education and professional development
- Frontiers in carbohydrate synthesis and recognition
- Lipid dynamics and signals in membrane and protein structure
- Organelles, mechanisms and phase properties of cellular quality contro
- Protein machines and disorder
- Regulation of RNA

INTEREST GROUPS

- Bile acids: Fantastic beasts or fantastic molecules?
- Biochemistry and climate change
- Building research and mentoring networks for women at predominantly undergraduate institutions
- Emerging topics and techniques: focus on protein acetylation and oxidation
- Empowering trainees: A roundtable with the IUBMB Trainee Initiative
- Engineering enzymes and microorganisms to replace petroleum products with renewable biofuels and biomaterials
- Molecular engineering
- Teaching Gen Z: Challenges and opportunities

SPECIAL EVENTS

MARCH 25

- Undergraduate Poster Competition
- Undergraduate speed networking
- Business meeting
- Welcome reception

MARCH 26

- Women scientists networking event
- Grad/postdoc travel awardee networking event

MARCH 27

- Yoga
- Wellness walk

MARCH 28

- Flash talk competition
- Community science day (for high school students)
- Networking reception at the Seattle Aquarium