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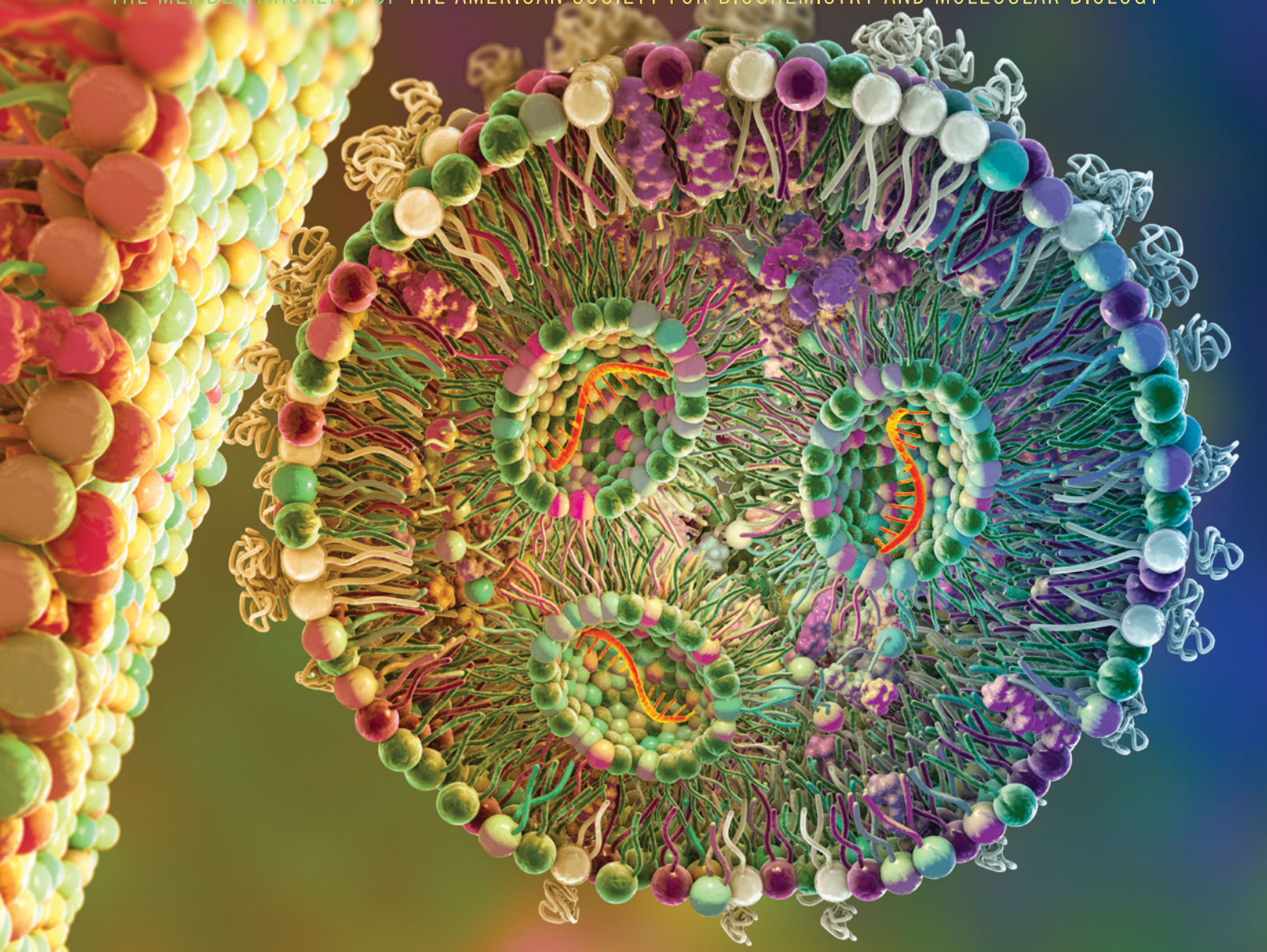
ASBMBTODAY

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



The perfect storm

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"Through the ASBMB, I've had the opportunity to interact with many scientists over the years, from all phases of their professional journeys. Writing about their work for ASBMB Today has immensely helped develop my science communication skills. I continuously apply this learning in my current role."

— Isha Dey

Cell biologist interested in understanding human physiology and cancer biology using 3D cell models

Scientist, Thermo Fisher Scientific

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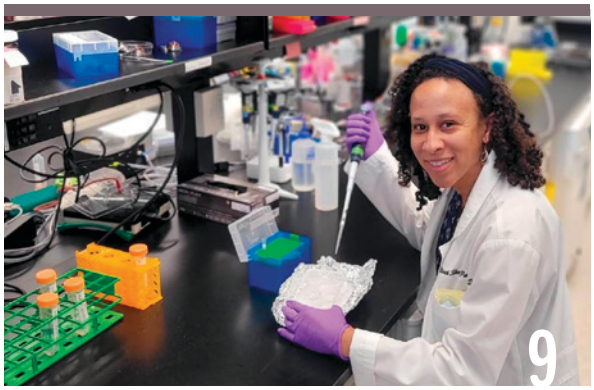

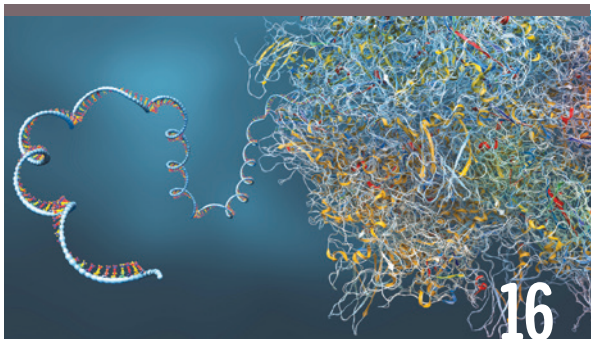

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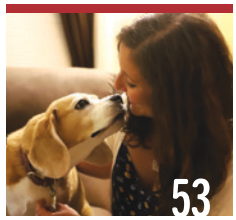

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Season's greetings

By Comfort Dorn

In my family, birthdays fall in clumps, and one of those clumps falls in early December. My son was born on Dec. 4 and my niece on Dec. 5. Six years ago, my granddaughter was born in the Netherlands. Because of the time difference, she arrived on Dec. 5 there, but it was still Dec. 4 here in the U.S. This has led to fierce debate about who gets to claim her as a birthday twin.

Western Christian countries also celebrate Dec. 5 as St. Nicholas Day. We pretty much ignore this holiday in the U.S., but as Sinterklaasdag it's a big deal in the Netherlands so, between one thing and another, my family has a head start in the business of December gift giving.

I struggle with gifts. I like to surprise people, but I want to be sure to give them something they'll like. This is pretty easy with small children but becomes more of a challenge as everyone ages.

In the back of my mind, I always think of the December issue of ASBMB Today as our Christmas gift to you, our wonderful members. And I want to give you something you'll like — and maybe even a little surprise.

In this issue, we have our annual gift guide, which is always fun to research and put together. We had a few discussions this year about Laboratory Barbie — she didn't make it into print, but you can see her on the website. Personally, I really love the DNA pencil holder.

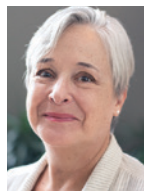
We also have a profile of Robert Haltiwanger, a Journal of Biological Chemistry associate editor who grew up, scientifically speaking, in the ASBMB family. And a really useful explainer of open science by one of our terrific contributing writers, Ankita Arora.

Of course, if you know me, you know my favorite part of ASBMB Today is the personal essays. This month, we have testimonials from folks who did one-on-one mentoring at Discover BMB, gathered by Paul A. Craig, and a heartwarming argument for taking your students to meetings, from Vahe Bandarian.

And because I like to save the best for last, we round out with Danielle Guarracino's essay, "The look of love." I won't say any more about it here.

Enjoy — and have a festive month.

Comfort Dorn (cdorn@asbmb.org) is the managing editor of ASBMB Today.



Lukeš named to EMBO

Julius Lukeš, of the Czech Republic, is among 60 new members of the European Molecular Biology Organization. EMBO, which promotes excellence in the life sciences in Europe and beyond, also named nine associate members.

Since 2006, Lukeš has been a professor on the science faculty at the University of South Bohemia in České Budějovice. He served as chair of the molecular biology department from 2003 to 2012. Since 2012, he has directed the Institute of Parasitology at the Biology Centre of the Czech Academy of Sciences.

LUKEŠ

At the heart of Lukeš' research are the cellular and molecular features of protists, especially the supergroup Discoba. He also investigates the evolution and diversity of parasitic and free-living protists, notably trypanosomes and diplonemids. He has co-authored about 400 scientific studies.

Lukeš' prior honors include the 2020 Prize of the President of the Czech Academy of Sciences for research excellence and the 2010 Prize of the Minister of Education for Excellence in Research.

Bishop appointed editor-in-chief

The American Association of Immunologists Council has selected Gail Bishop as the next editor-in-chief of the Journal of Immunology, also known as the JI, the association's flagship publication. She will serve a five-year term beginning Jan. 1.

Bishop is a professor of microbiology and immunology at the University of Iowa Carver College of Medicine and serves as director of the Center for Immunology and Immune-Based Diseases. Her research focuses on the molecular mechanisms of lymphocyte activation and tolerance. She is particularly interested in signaling interactions between innate and adaptive immune receptors.

BISHOP

Bishop has served as both an associate editor and section editor of the JI. In 2003, she received the UI Graduate Mentoring Award, and in 2009, she was awarded the Iowa Technology Association's "Woman of Innovation" award for academic research innovation and leadership. In 2015, she received both the Bonazinga Award for Excellence in Leukocyte Biology Research from the Society for Leukocyte Biology and State of Iowa Regents Award for Faculty Excellence. Bishop was named a distinguished fellow of the AAI in 2019 and a fellow of the American Association for the Advancement of Science in 2020.

"The challenges facing nonprofit scientific society journals today are considerable," Bishop said in an AAI press release. "However, The JI and I, as incoming editor-in-chief, are fortunate to have an exceptionally strong team to face these challenges."

Peters shares Faraday Horizon Prize

John W. Peters, who chairs the chemistry and biochemistry department at Oklahoma University, is a member of the team researching electron bifurcation that has won the Faraday Horizon Prize from the Royal Society of Chemistry.

The team draws researchers from Duke University, the University of Georgia, the University of Kentucky, Montana State University, Arizona State University, Washington State University and the National Renewable Energy Laboratory. The Royal Society cited these scientists for discovering the rules behind the division of electrons into high- and low-energy pools.

Electron bifurcation plays a key role in the metabolic pathways of plants and animals that produce energy within their cells. Horizon Prizes celebrate discoveries and innovations that push the boundaries of science, and the Royal Society noted electron bifurcation's potential for biological sources of renewable energy.

Peters joined the Oklahoma faculty in 2022 after serving as director and principal investigator of the Biological Electron Transfer and Catalysis Energy Frontiers Research Center at Washington State University and Montana State University, where he led much of the research. The U.S. Department of Energy supported this work.

PETERS

In 2020, Peters was a member of the team that won the Cozzarelli Prize from the National Academy of Sciences.

NAS elects new members

The National Academy of Sciences elected nearly 150 new members in May. Among them are American Society for Biochemistry and Molecular Biology members **Helen Berman, Russell DeBose–Boyd, Catherine Drennan, Anthony Kossiakoff, Andre Nussenzweig, Richard Roberts** and **Elizabeth Vierling.** The National Academy recognized these members for their distinguished and continued achievements in original scientific research.

Berman is a distinguished professor emerita of chemistry and chemical biology at Rutgers University. Her research has focused on the development of systems for making biological data freely available. She played a key role in founding the Protein Data Bank. In 2013, she won the ASBMB DeLano Award for Computational Biosciences for her efforts to create open-access data. She is a fellow of the American Academy of Arts and Sciences.

DeBose–Boyd is a distinguished chair in biomedical science and a professor of molecular genetics at the University of Texas Southwestern Medical Center. His research focuses on feedback mechanisms that control the synthesis of cholesterol. DeBose–Boyd has served as an associate editor of the Journal of Lipid Research since 2017. He is the ASBMB's interim treasurer and a member of the Finance Committee, and he was recently elected to the Nominating Committee. He is a mentor for the ASBMB Maximizing Opportunities for Scientific and Academic Independent Careers K99/R00 program and a member of the ASBMB Duel meeting board. He received the ASBMB's 2023 Avanti Award in Lipids.

Drennan is a professor of chemistry and biology at the Massachusetts Institute of Technology. Her lab uses X-ray crystallography and electron microscopy to understand how metalloenzymes catalyze chemical reactions such as the manipulation of organometallic bonds. She received the 2023 ASBMB William C. Rose Award for her research and commitment to training younger scientists. She won the Protein Society's Dorothy Crowfoot Hodgkin Award and was inducted into the American Academy of Arts and Sciences in 2020. Drennan is a member of the ASBMB Council, a past member of the Education and Professional Development Committee and a winner of the ASBMB–Schering–Plough Research Institute Award.

Kossiakoff is a professor of biochemistry and molecular biology at the University of Chicago. His lab studies the molecular events that lead to ligand–receptor activation and regulation using structural biology as well as protein engineering. In 2019, Kosiakoff won the Protein Society's Christian Anfinsen Award for methodological advances in the field of protein sciences. In 2012, he was elected a fellow of the American Association for Advancement of Science.

Nussenzweig is the branch chief of the Center for Cancer Research at the National Cancer Institute, National Institutes of Health. His research examines genome stability as well as DNA repair pathways and their roles in cancer prevention. Nussenzweig is a member of the European Molecular Biology Organization and the

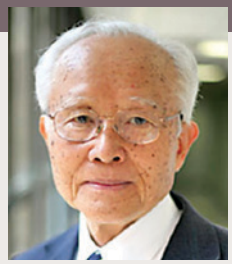
NAS elects new members CONTINUED

National Academy of Medicine. In addition, he was recently named a member of the American Academy of Arts & Sciences.

Roberts is the chief scientific officer of New England BioLabs Inc. His research focuses on enzyme discovery and uses bioinformatics and functional testing. Roberts won the Nobel Prize in physiology or medicine in 1993 for his contribution to the discovery of introns in eukaryotic DNA and the mechanism of gene-splicing. In 1994, Roberts received the Golden Plate Award from the American Academy of Achievement. In 1995, he was elected a fellow of the Royal Society and a member of the European Molecular Biology Organization. More recently, the Russian Academy of Sciences awarded him the Lomonosov Gold Medal.

Vierling is a distinguished professor of biochemistry and molecular biology at the University of Massachusetts, Amherst. Her lab focuses on molecular chaperones and cellular stress responses, including nitric oxide and mitochondrial metabolism in higher plants. Vierling was a member of the ASBMB 2022 Annual Meeting Program Planning Committee and helped organize a session on organelles and cellular homeostasis. She was appointed a fellow of the American Society of Plant Biologists in 2012 and the AAAS in 2002. She received a Guggenheim Fellowship in 2000 and an Alexander von Humboldt Senior Research Fellowship in 2007. She has participated in outreach events for students of all ages.

Tadashi Inagami



Tadashi Inagami, an emeritus biochemistry professor at Vanderbilt University known for pioneering research contributions to hypertension, heart failure and vascular disease, died on March 13 in Pittsburgh. He was 92.

Born in Kobe, Japan, on Feb. 20, 1931, Inagami earned a bachelor's degree in nutritional chemistry from Kyoto University and a Ph.D. in biophysical chemistry from Yale University through the Fulbright Foreign Student Program. He earned a second doctoral degree from Kyoto University in 1963. In 1966, Inagami became an assistant professor in biochemistry at Vanderbilt University School of Medicine, where he remained until his retirement in 2014.

Inagami was the first researcher to purify mouse renin and obtain its primary structure. He identified and cloned the angiotensin II type 1 receptor and angiotensin type 2 receptor, deepening understanding of angiotensin II signal transduction and its role in cardiovascular health. He also characterized the primary structure of the rat atrial natriuretic peptide hormone, which upregulates salt excretion and lowers blood volume, resulting in low blood pressure. He discovered that the angiotensin II signaling pathway leads to high cell proliferation in the heart, kidney and blood vessel walls. These findings contributed to the creation of medication to lower hypertension, such as angiotensin II type 1 receptor blockers, and treatments for heart failure and vascular and kidney disease.

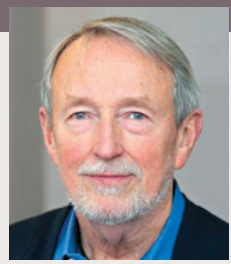
For 17 years, Inagami served as director of the interdisciplinary Specialized Center of Research in Hypertension at Vanderbilt. His many accolades included the American Heart Association/American Stroke Association Distinguished Scientist Award, the CIBA Award for Hypertension Research and the Japan Academy Prize. Vanderbilt honored him with the Earl Sutherland Prize for Achievement in Research in 1990.

After his retirement, Inagami and his wife moved to Pittsburgh, where he loved attending his grandchildren's baseball games and dance and violin recitals. He also enjoyed strolling through Squirrel Hill and Frick Park and exploring Japanese restaurants.

He is survived by his wife, Masako Inagami; daughters, Sanae Inagami and Mari Inagami; son-in-law, Ananth Krishnamurthy; and five grandchildren.

— Christi Thomas

Henry Bourne



Henry Bourne, a professor at the University of California, San Francisco, for four decades and a member of the American Society for Biochemistry and Molecular Biology for almost 30 years, died April 15 at the age of 83.

Bourne was born in 1940 in Danville, Virginia, to a surgeon father and a civil rights activist mother, according to a PNAS obituary. He attended Andover, where he was editor of the school paper, and then pursued degrees in history and literature at Harvard University. Before beginning his career in science and medicine, he worked as a journalist.

Bourne received his M.D. from Johns Hopkins University, graduating first in his class. After interning at Columbia University, he became a "Yellow Beret" (an alternative to serving in combat zones during the Vietnam War) at the National Institutes of Health, where he completed postdoctoral work. He pursued additional postdoctoral studies at UCSF. In 1969, he joined the faculty at UCSF and served as chair of the pharmacology department from 1984 to 1992. Bourne became a professor emeritus in 2005 and closed his laboratory in 2008.

Bourne was one of the first researchers to investigate signaling by trimeric G proteins. Specifically, he showed that G proteins are composed of a C-terminal Ras-like guanosine triphosphate-binding domain linked to a divergent N-terminal domain that is responsible for hydrolyzing GTP. In addition, his lab elucidated the pathological effects of G protein mutations in several rare human diseases, including a form of gigantism and a bone disorder. His later research focused on the cellular signals responsible for polarity and direction-finding of human leukocytes such as neutrophils.

Bourne earned many awards from organizations including the National Academy of Sciences and the American Association for the Advancement of Science.

He was an avid reader and began a book club at UCSF, according to a university obituary. After retiring, he wrote several books, including a personal memoir, a history of UCSF's biomedical research and a commentary on financing biomedical research.

Bourne is survived by two sons, Michael and Randy; a daughter, Margaret; and five grandchildren.

John DeMoss

John Alan "Jack" DeMoss, chair emeritus of the biochemistry and molecular biology department at the University of Texas Houston McGovern Medical School and a former member of the Journal of Biological Chemistry editorial board, died from complications of cancer on May 7. He was 93.

DeMoss was born in Indianapolis, Indiana, on April 10, 1930, to Ruby and Guy DeMoss. He earned his bachelor's degree in bacteriology in 1952 from Indiana University and his doctorate in microbiology from Case Western Reserve University in 1957. Following a two-year tenure as a National Institutes of Health postdoctoral fellow at the Yale University Medical School studying biochemical genetics, he started his first faculty position in 1959 as an assistant professor in the Yale Department of Microbiology.

In 1961, DeMoss moved across the country to become one of four founding professors of the biology department at the University of California, San Diego. Two years later, he undertook a similar adventure, traveling to Texas to become the founding chair of the biochemistry and molecular biology department at the UT Houston Medical School. He served as chair for 21 years, from 1971 until 1993, and continued as a professor, actively involved in research and teaching programs, until his retirement in 1999.

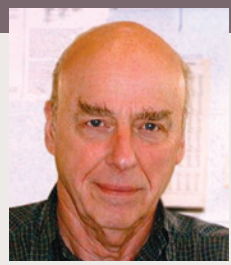
DeMoss had a long research career studying the structure and function of nitrate reductase in E. coli and various protein complexes involved in tryptophan synthesis in the mold Neurospora crassa.

Outside his lab and university, DeMoss also served on numerous National Institutes of Health grant review committees and advisory boards, as a member of the National Board of Medical Examiners for Biochemistry, as president of the Association of Medical School Departments of Biochemistry and as an editorial board member of the Journal of Bacteriology and the JBC. According to a UT Houston remembrance, his greatest legacy is his mentoring of early-career faculty while helping to found departments at two medical schools.

DeMoss is survived by his wife of 43 years, two sons, five grandchildren and five great-grandchildren.

— Nipuna Weerasinghe

Donald David Brown



Donald David Brown, a pioneer in molecular embryology and a member of the American Society for Biochemistry and Molecular Biology for almost 60 years, died in Baltimore County, Maryland, on May 31. He was 91.

Brown was born in Cincinnati, Ohio, on Dec. 30, 1931, to Albert Brown, an ophthalmologist and retina surgeon, and Louise Rauh. After graduating from Dartmouth College in three years, Brown earned his master's and medical degrees at the University of Chicago. He worked as a postdoctoral fellow with biochemist and future Nobel laureate Jacques Monod at the Pasteur Institute in Paris.

Brown joined the embryology department at the Carnegie Institution of Washington in Baltimore and worked there for the remainder of his career, becoming a department director in 1976 and retiring as an emeritus scientist in 2005.

The journal Science dubbed Brown the father of molecular embryology. Curious about embryonic development, he helped move the field from theoretical work to test-tube elucidation of the molecular changes in embryos. His discoveries, according to Carnegie, helped expand knowledge of genes and paved the way for early genetic engineering.

Eric D. Isaacs, Carnegie's president, paid tribute to Brown's research. "Don Brown's work transformed humanity's understanding of molecular biology, and every day his research informs new discoveries about the nature of life," Isaacs said in a Carnegie article.

Another Carnegie colleague spoke of Brown's emphasis on impactful research. "He told people, 'Life is too short to try to do all your ideas — do your best ones, the ones that could have the biggest effect in science,'" Allan Spradling told the Baltimore Sun.

Brown shared the 2012 Lasker–Koshland Special Achievement Award in Medical Science. The Society for Developmental Biology gave him its 2009 lifetime achievement award.

Brown is survived by his wife of 65 years, Linda Weil Brown; his children, Deborah Brown and husband David Isaac, Christopher Brown and wife Gina Brown, and Sharon Burris-Brown and husband Dave Burris–Brown; six grandchildren and five great-grandchildren.

Building through community

By Ankita Arora

When she was in high school in Columbus, Ohio, Olivia Miller fell in love with science, but before that, her grandmother's dementia sowed the seed.

"I had a very active role as a caregiver in her life," Miller said. "Seeing the medical aspect and learning more about how dementia worked sparked my interest in science. The further along I went in my studies, the more intrigued I became."

Miller was reluctant to attend the same school as her mother, Otterbein University in Westerville, Ohio. But a visit day changed her mind. The strong sense of community made her feel like she belonged there.

"What impressed the young 18-year-old me was that our program director gave me his business card and said, 'You contact me if you have any questions.' It was really welcoming," she said. "You could tell that they cared about their students deeply, which brought me to Otterbein."

During her freshman year, Miller started to attend weekly tea social hours organized by Otterbein's American Society for Biochemistry and Molecular Biology Student Chapter and never looked back. During her sophomore year, she led some chapter events and she became the chapter president during her junior and senior years.

As president, her biggest challenge was getting people to attend events, especially because the campus was just opening after the COVID-19 lockdown. She brainstormed with her professors and peers to develop new and more engaging events.

Olivia Miller was one of 20 student chapter members inducted into Chi Omega Lambda, the ASBMB's honor society, during Discover BMB in Seattle.

"We built off a three-pronged approach focusing on recreational, professional development and outreach events," she said. "Recreational events bring students together to have fun with an educational twist."

One recreational event was a do-it-yourself workshop on making soaps, where the attendees talked about the biochemical process of saponification. Professional development programs were the most popular, she said, with an event providing "résumé photos with white lab coats" topping the charts.

"My time as the chapter president has greatly helped me connect with my peers and develop my networking skills," she said. "I have also built a broader sense of community with other scientists. Being able to attend the ASBMB conference this year was an amazing opportunity. It's been very inspiring."

At Discover BMB, the society's meeting in Seattle, Miller was one of 20 student chapter members who were inducted into Chi Omega Lambda, the ASBMB's honor society, and her chapter, advised by John Tansey, received the 2023 ASBMB Outstanding Chapter Award.

Miller would advise this year's chapter president to take risks and engage with the scientific community. "We are a community," she said. "So, take advantage of that community to help build all of us up."

In addition to participating in the ASBMB student chapter, Miller was actively engaged in the Botanical Society of America student chapter at Otterbein. As part of the BSA club, she volunteered at the school's greenhouse (home to a grumpy old turtle) and attended weekly events such as nature walks and plant pressing tutorials.

"It's very interesting to engage with nonscience peers and see their perspective on classes and life in general," she said.

Miller recently graduated with a double major — a first major in biochemistry and molecular biology with a second major in biology — and minors in chemistry and psychology. She recently joined the biochemistry graduate program at Ohio State University, and she aspires to work in the biotech industry and contribute to the advancement of therapeutics.

Ankita Arora (ankita.arora@cuanschutz.edu)is an RNA-biologist-turned-freelance-science-writer. Her 12 years of experience in research and her storytelling skills help her distill science jargon into bite-size chunks that are fun to read.

From parasites to immune cells

By Jessica Desamero

As a postdoc at the National Heart, Lung and Blood Institute, Aleah Roberts studies the endocytosis of the B cell receptor into B cells.

When Aleah Roberts was in the 6th grade in Manassas, Virginia, a teacher assigned her to design a cake with the features of a plant cell. She's been interested in biology ever since.

At the University of Virginia, where Roberts earned her undergraduate degree in engineering science, she took a class on the biology of infectious diseases, and that's when she became fascinated with microorganisms and immunology.

During her postbaccalaureate studies at the University of Pennsylvania, Roberts started doing biomedical science research. She was interested in parasitic worms, so she looked for research opportunities in parasitology. In the first lab she joined, she studied schistosomes, parasitic flatworms that cause schistosomiasis, which the World Health Organization considers the second-most socioeconomically devastating parasitic disease. In her second lab, she studied the parasitic disease leishmaniasis, which is spread by sand flies and is common in some tropic and subtropic regions. These studies gave her experience in immunoparasitology, which she appreciated.

"It's a big group of immunoparasitologists at the vet school at UPenn, and I really liked it," she said.

Because of its large well-known Malaria Research Institute, Roberts decided to pursue graduate work at Johns Hopkins University. There, she studied the molecular parasitology of malaria parasites and earned her Ph.D. in molecular microbiology and immunology.

Now a postdoctoral fellow at the National Heart, Lung, and Blood Institute of the National Institutes of Health, Roberts studies the endocytosis of the B cell receptor into B cells.

"B cells are important because they are the cells in your body that really launch the adaptive immune response," she said. "They make antibodies … and to become activated to make an antibody, they first have to endocytose the antigen through the B cell receptor."

Scientists know how small B cell receptors are endocytosed, but they have not yet figured out how the cell takes up larger B cell receptor clusters and processes them to activate the cell. Roberts is studying this process. For her first project, she worked on identifying what physical plasma membrane structures and other unique structures are present at B cell receptor clusters, using an advanced microscopy technique. With this information, she was able to characterize endocytic mechanisms that may be involved. She then went on to study lymphoma cells, which also have large clusters, and found structural similarities.

Roberts has been a participant in the Maximizing Opportunities for Scientific and Academic Independent Careers program since July, and so far, one thing she loves is the mentoring by faculty members around the country. Her one-on-one mentor, whom she's met with multiple times, has been very supportive. Talking with other members of her cohort about their job searches and science in general also has been helpful.

"Having people outside of your lab look at plans and your experiments has been great because you get a different perspective," she said.

For her work in the future, Roberts hopes to branch out and merge her multiple research interests.

"I'm hoping to study immune cells and endocytosis of large antigens and link it to disease pathogenesis," she said, "not just in cancer but also in infectious diseases."

Jessica Desamero (jdesamero@gradcenter.cuny.edu) is a graduate student in the City University of New York's biochemistry Ph.D. program and volunteers with science outreach organizations.

How bacteria inhibit gene expression

By Meric Ozturk

Bacteria adapt to environmental changes by regulating their metabolism. The best way to do this is to change the gene expression. Proteins called transcription factors take care of this job and help organisms respond to change.

The transcription factor CarD is conserved among several bacterial lineages and reacts with other proteins to prevent or initiate gene expression. Although researchers know the initiating mechanism of CarD, they do not yet understand how it inhibits gene expression. Understanding the complete mechanism of CarD activity may help scientists develop new approaches to combat bacteria.

Dennis Zhu and Christina Stallings, researchers at the Washington University School of Medicine, study the inhibiting mechanism in Mycobacterium tuberculosis, or Mtb. They recently showed which factors affect CarD's activity in gene expression.

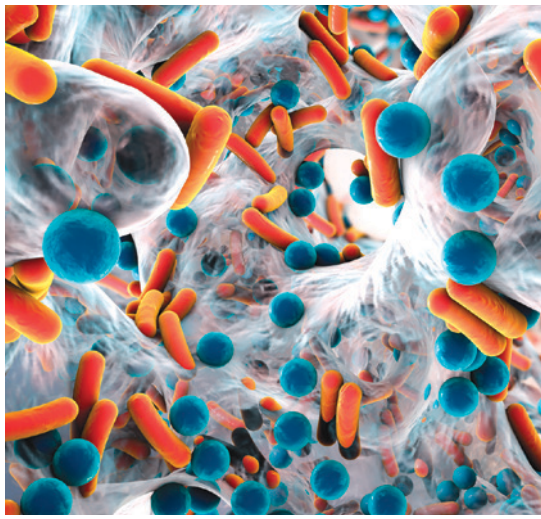
The RNA polymerase, or RNAP, enzyme binds to DNA to promote transcription. RNAP binds a promoter sequence to start transcription, and the RNAP–promoter interaction is called RNAP-promoter open complex, or RPo. Previous studies showed that CarD stabilizes RPo and initiates RNAP's activity. However, using RNA sequencing, Zhu and Stallings showed that altering the activity of CarD can cause downregulation and upregulation of some genes.

According to Zhu, their findings published in the **Journal of Biological Chemistry** are broadly applicable for other bacterial transcription factors as well.

"I believe what makes our study unique is that we approached it with a constrained hypothesis that the outcome of CarD regulation on mycobacterial transcription is dependent on RPo stability," Zhu said. "Other studies of RNAP-binding transcription factors have explored the natural promoter space of a bacterium and have performed similar promoter bashing to identify regulatory sequences."

Unlike previous studies, Zhu and Stalling observed the effect of CarD under different promoters. They showed that it has an inhibitory effect on promoters that already have highly stable RPo. This is the first demonstration of CarD's transcriptional repression activity, and they believe that this is how CarD inhibits some genes.

The researchers did all these experiments in the controlled conditions of a laboratory. However, a bacteria's natural environment is different. "The main limitation of studies like ours is the gap in understanding between the next-generation sequencing data sets that we gather from bacteria and the mechanistic details from our in test tube assays," Zhu said. "So many things are happening within the bacterium such as salt conditions, other proteins, chromosome architecture, translation, which we cannot fully capture in an in vitro transcription assay."



The next step for the group is creating a bridge between findings in the lab and more natural settings. CarD is a stress-response protein. That is, when bacteria feel environmental stress such as lack of nutrition or DNA damage, CarD is downregulated or upregulated, respectively.

Zhu and colleagues got bulk RNA sequencing data sets by exponentially growing Mycobacterium tuberculosis cells in a nutrient-rich media. "It would be interesting to explore how certain stress conditions, particularly nutrient starvation and DNA damage, affect CarD's ability to regulate," he said.

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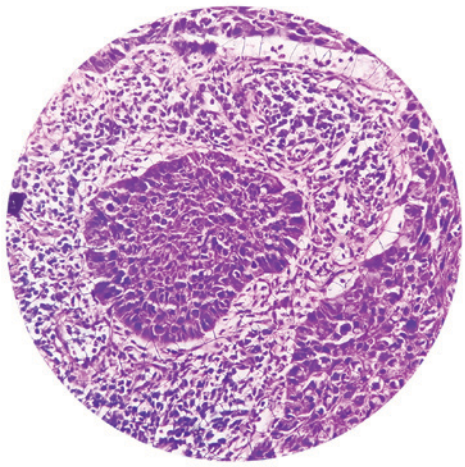
Meric Ozturk (ozturk@iastate.edu) is a third-year Ph.D. student in biochemistry at Iowa State University.

Exploring glycosylation patterns in oral cancer

By Nivedita Uday Hegdekar



MD SAIFUL ISLAM KHAN

Oral squamous cell carcinoma, or OSCC, a cancer that affects the mouth, is an aggressive disease with a dishearteningly low survival rate. Doctors usually estimate an OSCC prognosis based on the size of the tumor at diagnosis and whether the cancer has spread to lymph nodes and other areas.

This system isn't perfect, according to Carolina Moretto Carnielli, who studied the disease during her postdoctoral studies at the Brazilian Center for Research in Energy and Materials. "People with the same stage of OSCC can have different clinical manifestations and outcomes," she said. "We need to better understand what molecular changes are occurring as the disease changes."

To address this challenge, Carnielli turned to mass spectrometry–based glycomics and glycoproteomics to identify and characterize proteins and their glycosylation in tumor tissues from patients with distinct lymph node status, the main prognosis factor in oral cancer, offering insights into patient prognosis.

Glycosylation, a posttranslational modification involving the addition of glycan sugar molecules to proteins, plays a pivotal role in altering behaviors such as adhesion, migration and metastasis in oral cancer cells.

Carnielli's mentor, Adriana Franco Paes Leme, guided her postdoctoral research, including an internship in the laboratories of Morten Thaysen–Andersen and Rebeca Kawahara, researchers from Macquarie University in Sydney, Australia, and the Institute for Glyco-core Research, Nagoya University, Japan, who supervised the study. Carnielli and colleagues comprehensively characterized the glycoproteome in primary tumor tissues from OSCC patients, both with and without lymph node metastasis, by using an integrative multiomics approach that combined glycomics and glycoproteomics.

"Part of the goal was to characterize the glycan structures, their site-specific heterogeneity and their dynamics at different stages of the disease," Carnielli said.

While most of the tumor tissues had similar N-glycome profiles, suggesting a consistent pattern during cancer progression, Carnielli discovered that changes in the abundance of six specific sugar structures were associated with OSCC spreading to lymph nodes.

Recently published in **Molecular & Cellular Proteomics**, the team's study also shows previously uncharted associations between protein glycosylation in OSCC tumor tissues and critical clinical outcomes.

For example, Carnielli showed that a comparatively high abundance of two core-fucosylated and sialylated N-glycans and one N-glycopeptide from fibronectin were associated with low patient survival. On the other hand, a relatively low abundance of N-glycopeptides from afamin and CD59 was also associated with poor survival.

"This work also highlights the significance of using a multiomics technique such as integrated glycomics and glycoproteomics to comprehensively study these modification patterns in diseases," Carnielli said.

This research has far-reaching implications. When survival-associated N-glycans and glycopeptides in OSCC tumor tissues are identified, researchers understand that glycosylation makes a significant contribution to the disease progress, opening new possibilities to study associated mechanisms, tailoring personalized treatment strategies and predicting and monitoring disease outcome and progression.

"Some of these glycopeptides have the potential to serve as prognostic markers for OSCC outcome," Carnielli said; thus, offering hope for improved approaches for informing clinical intervention and treatment of this often-lethal cancer.

DOI: 10.1016/j.mcpro.2023.100586

Nivedita Uday Hegdekar (nivedita.hegdekar@gmail.com) is a recent Ph.D. graduate in biochemistry and molecular biology from the University of Maryland, Baltimore.

Why cognition declines in Type 2 diabetes patients

By Oluwadamilola "Dami" Oke

For years, scientists have observed a correlation between the progression of Type 2 diabetes and the onset of cognitive impairment. A new theory about the cause of this, largely based on animal, cell and human genetics studies, implicates the cytochrome P450-soluble epoxide hydrolase, or CYP450-sEH, pathway in both Type 2 diabetes and cognitive decline.

CYP450s are enzymes that break down polyunsaturated fatty acids into epoxides, metabolites that are believed to have anti-inflammatory and cell-signaling properties. However, the sEH enzyme breaks down these epoxides into diols — molecules believed to be harmful to the cell.

Once epoxides are broken into diols, they can interfere with other normal metabolic pathways and physiological functions. Both epoxides and diols belong to the group of lipid metabolites called oxylipins.

Researchers also have found that the implicated pathway is prevalent in patients with obesity, which made a team at the University of Toronto and Sunnybrook Research Institute curious about whether an association exists between the oxylipins derived from the CYP450-sEH pathway and the three conditions: Type 2 diabetes, cognitive impairment and obesity.

According to Natasha Anita, a Ph.D. candidate at Toronto and Sunnybrook and first author of the study, the researchers were motivated to investigate this association because they had previously found "that oxylipin levels in the blood differed between people with and without small vessel disease in the brain and that the diols were associated with poorer cognitive performance and neurodegeneration."

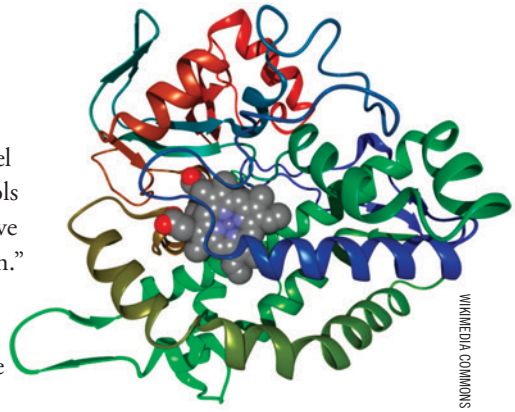
Knowing that diabetes increases the risk for small vessel complications and cognitive impairment, the team hypothesized that oxylipins would also be implicated in cognitive function in Type 2 diabetes patients. A report of their work was published recently in the **Journal of Lipid Research**.

Excluding individuals with Type 1 diabetes and neurological diagnoses, among other criteria, the researchers recruited 108 individuals with Type 2 diabetes; 51 were obese and 57 were not obese.

Using neuropsychological and verbal tests, the team assessed cognitive function, verbal fluency and mental agility. They also assessed learning and short-term and long-term memory.

In their JLR paper, the researchers wrote that their results largely agreed with the results of earlier studies in people without Type 2 diabetes. They found that increased levels of diols were associated with poorer cognitive performance.

"This is the first study to look at oxylipins in relation to cognition in Type 2 diabetes," Anita said. "Although diabetes is an established risk factor for Alzheimer's disease and dementia, currently there is no specific treatment for cognitive problems in this population."



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The cytochrome P450 enzyme breaks down polyunsaturated fatty acids into epoxides and could have a therapeutic role in treating cognitive decline.

The results from this study show the CYP450-sEH pathway to be a strong potential target for therapies.

"Our current work adds to the growing number of clinical studies examining the CYP450-sEH oxylipin pathway," Anita said. "We are hopeful that this indicates a new pharmacological target to prevent cognitive decline in this population."

Moving forward, Anita said the team is investigating "whether these oxylipins are associated with cognitive decline over time, and whether targeting this pathway will improve cognition in people with diabetes."

DOI: 10.1016/j.jlr.2023.100395

Oluwadamilola "Dami" Oke (okeo@gwu.edu) is a Ph.D. candidate of biomedical engineering at the George Washington University with an interest in communication and outreach for science advancement.

From the journals

By Renae Crossing, Ken Farabaugh and Andrea S. Pereyra

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

Lipid droplets go haywire in Huntington's

The full set of proteins in medium spiny neurons — brain cells vulnerable to Huntington's disease — has been published in the journal **Molecular & Cellular Proteomics**. The study confirms existing therapeutic targets and reveals new ones: particularly, the importance of proteins that process fats.

Huntington's disease causes neurons to break down, and it tends to get worse over time. To pinpoint cellular processes going awry, Kizito-Tshitoko Tshilenge and a collaborative team from the United States compared protein populations in brain cells impacted by the inherited disease with those of healthy cells.

First, scientists read between the lines: Diseased cells had more activity in the scaffolding between cells known as the extracellular matrix than healthy cells did. Moving to the nucleus, critical errors would accumulate because cells affected by Huntington's were less able to repair breaks affecting both sides of DNA: double-stranded breaks. And, the study showed, diseased cells took in more lipids and degraded fewer than their healthy counterparts. It turns out medium spiny neurons — like medium spicy noodles, perhaps — can be fatty.

Contributing to the disease were changes in the amounts of several key proteins. Apolipoprotein E, a protein that helps cells process lipid droplets: Cells with Huntington's disease had less of it. Minichromosome maintenance proteins, so named because they maintain DNA when it's damaged: There were fewer of them, too. And a family of proteins whose job it is to maintain brain health, septins: These proteins were dysregulated, as is the case in Alzheimer's disease and Parkinson's disease.

You want more names, don't you? The full list of proteins is available in the paper at mcponline.org.
DOI: 10.1016/j.mcpro.2023.100534

Phase separation promotes H3K4 methylation

Histone H3 lysine 4, or H3K4, methylation patterns make up part of the histone code that determines whether and how efficiently a given stretch of DNA can be transcribed. In humans, H3K4 methylation is, in part, regulated by the mixed-lineage leukemia, or MLL, family of proteins, with multiple methylation, in particular, being dependent on the MLL1 core complex. Scientists have previously shown that formation of the MLL1 core complex is highly concentration- and temperature-dependent; however, at normal human body temperature, formation is energetically disfavored, suggesting protein subunit concentration must overcome this thermodynamic barrier.

In a recent article in the **Journal of Biological Chemistry**, Kevin Namitz and colleagues at the State University of New York Upstate Medical University and Pennsylvania State University describe how phase separation could facilitate formation of the MLL1 complex at body temperature. Using enzyme kinetics and differential interference contrast and fluorescence microscopy techniques, they showed that hydrodynamic changes resulting from macromolecular crowding led to liquid–liquid phase-separated droplets of proteins with highly disordered regions, such as MLL1. Furthermore, these droplets displayed high enzymatic H3K4 methylation activity associated with a highly active oligomeric scaffold of the MLL1 core complex.

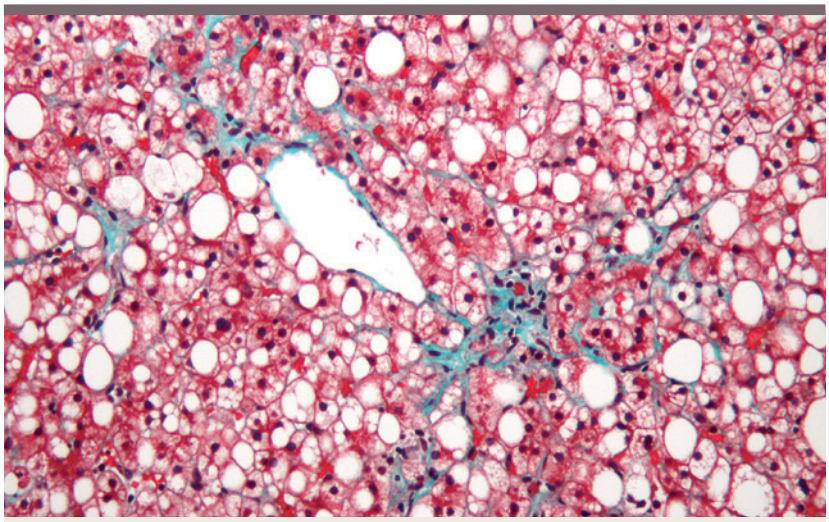
These findings suggest that phase separation is a principle effector of conformational changes that lower the K_M of the reaction and allow formation of the active MLL1 core complex scaffold at body temperatures. Future studies will be necessary to address how phase separation can promote H3K4 methylation activity.
DOI: 10.1016/j.jbc.2023.105204

'No eating after bedtime'

Do you enjoy late dinners and midnight snacks? You might want to reconsider. Studies have shown a positive correlation between night eating and obesity; that is, the later in the day you consume calories, the greater your chances of gaining weight.

Wenhao Ge, Qi Sun and colleagues at the Nanjing University of Science and Technology in China study the mechanism behind time-delayed eating patterns and body fat accumulation in mice. Their recent results were published in the **Journal of Lipid Research**.

The authors found that dietary oil



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In this micrograph of nonalcoholic fatty liver disease, the liver has prominent macrovesicular steatosis (white/clear round/oval spaces) and mild fibrosis (green). The hepatocytes stain red.

Leveraging TRIM38 in fatty liver disease progression

Nonalcoholic fatty liver disease, or NAFLD, affects more than a quarter of the world's adult population. Patients with NAFLD can be asymptomatic or present with insulin resistance, fatigue and abdominal pain. NAFL, or simple steatosis, can evolve into nonalcoholic steatohepatitis, or NASH, cirrhosis, and, in some cases, liver cancer. Yet, no established pharmacological therapy exists for NASH.

In a recent study published in the **Journal of Lipid Research**, Xinxin Yao, Ruixiang Dong and colleagues from Taikang Medical School in Wuhan University and other research centers in China explored the potential of tripartite motif 38 protein, TRIM38, as a therapeutic approach to treat NAFLD and NASH.

TRIM38 is part of a superfamily of proteins with regulatory functions over the immune system and the inflammatory response. Specifically, TRIM38 prevents the activation of nuclear factor kappa-light-chain-enhancer of activated B cells, better known as NF-κB, a mediator of inflammation in mammalian tissues that can play a role in the pathogenesis of NAFLD.

The authors found that TRIM38 was downregulated in liver samples from human patients with NAFLD and that deleting TRIM38 in mice worsened high-fat diet–induced hepatic steatosis, inflammation and fibrosis. To confirm the role of TRIM38 in liver disease, the researchers overexpressed the protein in cultured hepatocytes and then exposed them to high concentrations of lipids in the culture media.

The study showed that TRIM38 suppresses expression of inflammation-related and lipid anabolism genes. These findings position TRIM38 as a promising therapeutic ally to help alleviate NAFLD and prevent progression toward NASH.

DOI: 10.1016/j.jlr.2023.100382

— Andrea S. Pereyra

is preferentially incorporated into triglycerides and accumulated in adipocytes, or fat cells, when consumed at night rather than during the day.

In mammals, biologically determined rhythms, also known as the circadian clock, control feeding behavior and feeding-related processes in organs and tissues. This study found that the circadian protein Period 1, or Per1, directly contributes to night eating–associated obesity by modulating the activity of two key enzymes responsible for hepatic bile acid production.

In the gut, bile acids are necessary for correct emulsification and absorption of fat. Accordingly, mice lacking Per1 could not absorb fat during night feeding and were thus resistant to high-fat diet–induced obesity. When the researchers treated mice lacking Per1 with cholic acid, one of the most abundant acids in bile, intestinal fat absorption and accumulation in the adipose tissue were partially restored.

This study suggests that Per1 could be a potential target in treating obesity.

DOI: 10.1016/j.jlr.2023.100390

How stimulation impacts brain cells

A team of scientists has investigated how different parts of brain cells in rats respond to stimulation: in this case, water deprivation. The study contributes to research on brain plasticity by documenting which proteins are where and which proteins jump from standby into action.

Cells in the study hailed from the hypothalamus, a part of the brain behind hormones, heart rate and hunger. In a model system shared in the journal **Molecular & Cellular**

Proteomics, Soledad Bárez–López, André S. Mecawi and a team of scientists in Brazil and Bristol determined which proteins were active at the axon terminals (the parts of brain cells making contact with the nearby pituitary gland) versus those in the cell's skeleton (called the cytoskeleton and made of pure protein strings rather than bone).

The results reflected the expected functions of different cell regions: Cell bodies expanded their cytoskeleton, while the ends of cells concentrated signaling to nearby cells nearby. (Axon terminals are very social.)

What was unexpected: In stimulated cells, proteins that would go on to become hormones became hyperphosphorylated, ending up with more than one phosphate tag. Adding extra phosphate tags might be a key step in how cells get hormones to be ready for release. Think of it as a pep talk. (These are peptides we're talking about.)

Read the full paper online to find out which proteins came up most often in the research — including vasopressin, which controls how wide blood vessels are, and oxytocin, known as the love hormone.
DOI:10.1016/j.mcpro.2023.100544

Promoting axon regeneration

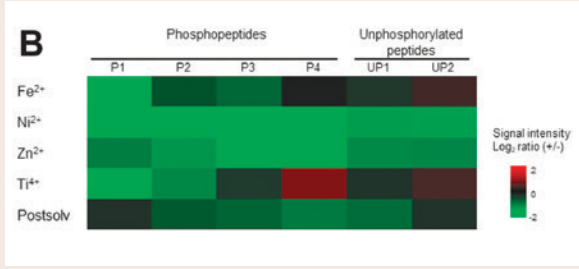
After neuron injury, the axon typically regenerates only slightly or not at all, leading to permanent neurological damage. Scientists have shown that an inhibitory protein, NogoA, contains two domains that prevent axon regeneration, and when researchers delete these domains in mice, leaving only the amino-terminal domain, regeneration and recovery from axon injury improve. However, when researchers also delete the amino-terminal domain, they do not see improved

Remove contaminating metal to study activated proteins

The bad news: Unwanted metal ions are knocking useful tags off proteins — tags that indicate that a protein is overactive in, say, cancer or metabolism. The good news: It's possible to filter that metal out.

Get rid of metals from the mobile phase if you're studying protein activation. That's the conclusion of new research published in the journal **Molecular & Cellular Proteomics**. Removing metal contamination with a simple device yielded at least 10 times more tagged protein fragments than a traditional setup.

Proteins active in health or disease often have a phosphate tag attached (or two, or three). Researchers may catalog these tagged proteins at scale using phosphoproteomics. The first step is separating proteins in a machine: high-performance liquid chromatography. But there's a catch: Metal in that equipment tends to contaminate samples, knocking tags off proteins — while at the same time, metal enables the lines and valves of the equipment to withstand high pressure. Some scientists have made metal-free components, but they don't work for trace samples, which require thinner parts. And, until this study, the removal of metal ions hadn't been tested for nanoscale samples, where narrow lines and extra contact time



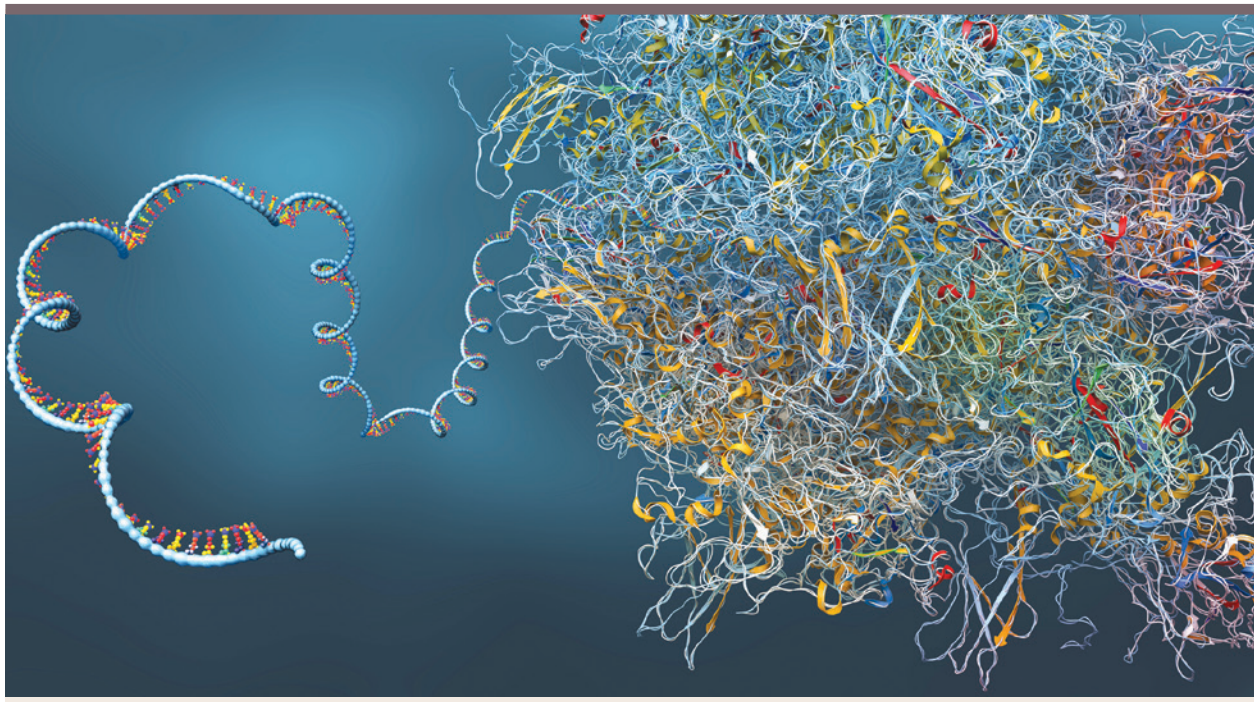
KOMORI ET AL. MCP

The signal intensity ratio of six synthetic peptides (horizontal) in the presence of various metal ions, with respect to the control. Red indicates positive signal intensity and green, negative.

mean even more metal ions in the mobile phase (that's the liquid protein samples are dissolved in).

Yumi Komori and a team of researchers at Kyoto University used a device to filter out metal ions from the mobile phase. Compared with unfiltered samples, they measured a 10-fold recovery of protein fragments attached to a single phosphate tag. For protein fragments with more than one tag, recovery increased 77 times versus controls. The team suggested that the technique may improve the recovery of samples not only at nanoscale but also at microscale.
How did the setup of their metal-removing device work? Find out in the full paper at mcponline.org.
DOI:10.1016/j.mcpro.2023.100535

— Renae Crossing



mRNA (left) being recruited to the ribosome (right) for translation.

Functionally clustered mRNAs are co-ordinately translated

A cell adapts its proteome to environmental conditions via the regulation of mRNA translation. Translation regulation in eukaryotes depends on not only mRNA abundance and degradation, but also a conserved set of 11 basal translation initiation factors, which bind both the mRNA (closed loop complex) or the ribosome (43S translation initiation complex) to position the ribosome at the mRNA start codon. However, results of recent studies showed that some mRNAs, instead of being translated or degraded, are stored in localized cytosolic condensates such as P-bodies and stress granules and did not bind classical translation initiation factors. Researchers are still debating over the mechanisms cells use to define which mRNAs will be translated and when.

In a recent paper in the **Journal of Biological Chemistry**, Christopher Kershaw, Michael Nelson and colleagues describe their continuing investigations while at the University of Manchester into patterns of mRNA interaction with translation initiation factors. Using RNA immunoprecipitation-sequencing, or RIP-seq, and gene ontology, they identified seven clusters of mRNAs based on interaction with the 43S translation initiation complex, the closed-loop complex and mRNA decay proteins.

While they noted that mRNAs stored in P-bodies bind translation repressors and mRNA decay proteins Pat1 and Lsm1, they also found that nearly half of the proteome is translated from two clusters of mRNAs despite these clusters displaying poor interaction with most translation initiation factors. Furthermore, RNAs that interacted with components of the closed loop complex had variable translation rates, raising questions about the role of this structure.

The authors conclude that their results support the RNA regulon model, which states that functionally related proteins are coordinately regulated as post-transcriptional operons. As interaction with translation initiation factors may not be the best predictor of high translation, it is likely that factors such as mRNA length may also play a role in defining the translation efficiency of mRNAs in normal or stress conditions.

DOI: 10.1016/j.jbc.2023.105195

— Ken Farabaugh

repair, raising the question of whether organisms naturally produce such an isolated amino-terminal fragment.

In their new study published in the **Journal of Biological Chemistry**, Yuichi Sekine and colleagues at Yale School of Medicine and Kyoto Pharmaceutical University investigated the production and role of the NogoA amino-terminal fragment in axon regeneration. They used Western blotting and a series of mutations to show that this fragment was produced in the forebrain by cleavage of full-length NogoA, and its levels increased after axons were severed in cortical neuron cell culture and in the spinal cord after trauma.

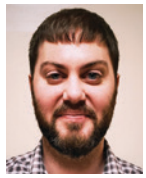
The researchers also found that when administered outside a cell, the NogoA fragment did not affect axonal regeneration, but when overexpressed within the cell it stimulated regeneration. Finally, to determine the mechanism involved, the authors used immunoprecipitation to determine interacting proteins and identified the NogoA fragment complexed with HSPA8, a heat shock protein. In further experiments, they showed that HSPA8 was also involved in axonal regeneration, perhaps via enhanced protein refolding.

These data identify a novel pathway by which NogoA cleavage and chaperone protein HSPA8 could mediate axonal regeneration. It remains to be seen whether this pathway can be therapeutically targeted for better regeneration in living organisms.

DOI: 10.1016/j.jbc.2023.105232

Renae Crossing (renaecrossing@gmail.com) is a writer and former teacher. She holds a first-class master's degree in life science from the Hong Kong University of Science and Technology and a first-class master's in teaching from the University of Melbourne.

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



Andrea S. Pereyra (pereyraa18@ecu.edu) is a postdoctoral scholar at the East Carolina Diabetes and Obesity Institute. She earned her M.D./Ph.D. at Universidad Nacional de La Plata in Buenos Aires, Argentina.

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14 Discover BMB late-breaking abstract submission site opens

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18 Discover BMB late-breaking abstract deadline

24 Lipid Research Division Seminar Series

31 Discover BMB early registration deadline

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Black History Month

3 ASBMB Honor Society application deadline

3 Outstanding Chapter Award deadline

12 Discover BMB housing deadline

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The perfect storm

The world has 2023 Nobel laureates Katalin Karikó, Drew Weissman and others to thank for laying a foundation for the COVID-19 vaccine decades before the pandemic

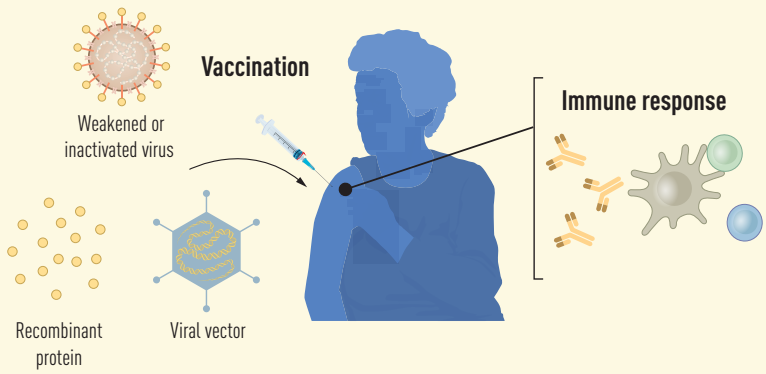
By Marissa Locke Rottinghaus

The SARS-CoV-2 pandemic surged around the globe like a vast hurricane, and just a year later some people may have thought the COVID-19 vaccine appeared out of nowhere.

But, hurricanes can take weeks to form in the sea and sky, spurred by multiple factors including angular momentum of the Earth's rotation, low atmospheric pressure, warm ocean temperatures and thunder.

Likewise, the complex technology behind the COVID-19 vaccines was in the works decades prior to their first authorized use in 2020. Katalin Karikó and Drew Weissman developed the foundations for the messenger RNA technology in the late 1990s and early 2000s. Robert Langer conceptualized the lipid nanoparticle carriers even earlier, the 1970s.

Laura Breda, a research assistant professor, and Osheiza Abdulmalik, a research associate, are now working with Weissman, Hamideh Parhiz, a research professor at the University of Pennsylvania School of Medicine, and Stefano Rivella, a professor of pediatrics at the UPenn School of Medicine, to develop a "one-shot" gene therapy cure for sickle cell disease and other hemoglobinopathies using technology similar to that used in the COVID-19 vaccine. Without Karikó and Weissman's seminal work, Breda and Abdulmalik said, none of their studies would be possible.



MATTIAS KARLÉN/ NOBEL COMMITTEE FOR PHYSIOLOGY OR MEDICINE

Parts of the viral genetic code, usually encoding proteins found on the virus surface, are used in vaccines to make proteins that stimulate the formation of virus-blocking antibodies. Alternatively, parts of the viral genetic code can be moved to a harmless carrier virus, a "vector." Before the COVID-19 pandemic, some of the methods for vaccine production used viral vectors, recombinant proteins and inactivated virus.

The foundation

Hungarian-born Katalin Karikó and American Drew Weissman won the 2023 Nobel Prize in physiology or medicine "for their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19."

Journal of Biological Chemistry Editor-in-Chief Alex Toker said their discovery "was instrumental in the design of mRNA vaccines and ultimately paved the way for the development of the COVID-19 vaccine therapies that saved millions of lives during the recent pandemic."

PEGGY PETERSON/UNIVERSITY OF PENNSYLVANIA

Katalin Karikó and Drew Weissman are the recipients of the 2023 Nobel Prize in physiology or medicine.

He added: "This underscores the importance of fundamental discoveries in basic mechanisms of cell and molecular biology and their transformative impact on human health."

Karikó and Weissman's work was all about demonstrating that an mRNA vaccine must find the "Goldilocks" zone when interacting with the human immune system. Too much recognition of an mRNA vaccine by the immune system could lead to hyperinflammation, elimination of the vaccine material and intense patient symptoms. At the other end of the spectrum, too little mRNA interaction with the immune system and the vaccine will go undetected, failing to induce the required immunity to protect a patient from future disease.

Karikó, a professor at the University of Szeged in Hungary and an adjunct professor at the UPenn School of Medicine, has devoted much of her career to understanding mRNA.

In its natural form in the human body, mRNA consists of four nucleosides: adenine, cytosine, guanine and uridine. Early attempts to use lab-produced mRNA as a vaccine were fraught with problems: It was unstable, difficult to deliver and led to excessive host inflammation.

LAURA BREDA

OSHEIZA ABDULMALIK

In the face of these challenges, Karikó teamed up with Weissman, a UPenn professor of vaccine research and immunologist. The two met at the university in the 1990s while using a photocopier, according to a UPenn press release.

Weissman was an expert on dendritic cells and the immune response to vaccines. The two observed that lab-made RNA activated the inflammatory immune response in dendritic cells, while mammalian RNA did not. The differentiating culprit was the chemical makeup of the nucleoside uridine.

In a 2004 JBC paper, Karikó, Weissman and colleagues detailed their finding that mRNA secondary structure activates the immune system to produce proinflammatory cytokines via binding to Toll-like receptor 3, a nucleotide-sensing TLR that is activated by double-stranded RNA, a sign of viral infection or necrotic tissue.

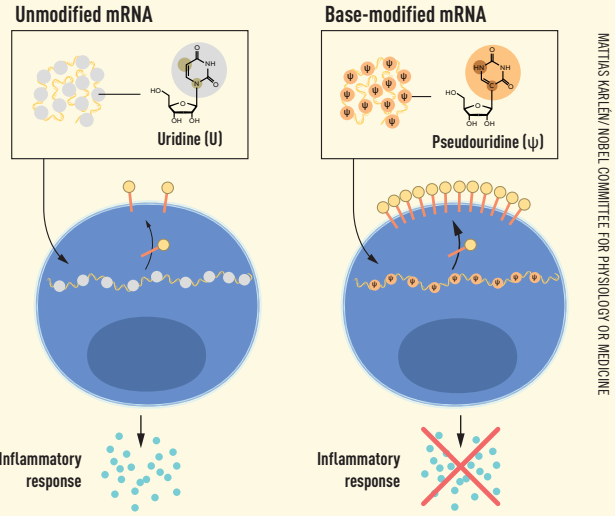
One year later, in a groundbreaking study, the team showed that uridine is recognized by human TLRs on dendritic cells, whereas pseudouridine, a post-transcriptional modified version of uridine, can subvert recognition. mRNA species containing pseudouridine alter the mRNA's interactions with RNA and proteins such as the enzymes that regulate protein production. Not only did the modified uridine suppress the inflammatory response, but it boosted mRNA-derived protein production as well.

"They were able to transform the in vitro transcribed mRNA into a more stable molecule capable of escaping immune response by just changing its structure," Breda said. "These changes made it more similar to one of the mRNA species in our body that essentially is not recognized by the immune system. This was not trivial, and it was so advantageous because it opened up

a door that no one thought was possible before."

The pair founded RNARx, a company focused on developing mRNA therapeutics for a wide range of diseases, in 2006. But they struggled to find investors, and the company eventually ran out of funding. In 2013, Karikó joined BioNTech as senior vice president and head of RNA protein replacement to further refine this vaccine technology. Helmut Jeggle, chairman of the BioNTech supervisory board, credits Karikó as one of the "pioneering scientists who significantly contributed to the establishment of mRNA as a new drug class."

Karikó and Weissman's efforts made possible the first approved mRNA vaccine, today known as the Pfizer-BioNTech COVID-19 vaccine. Karikó remained with the company until 2022.



MATTIAS KARLÉN/ NOBEL COMMITTEE FOR PHYSIOLOGY OR MEDICINE

mRNA contains four different bases, abbreviated A, U, G and C. Katalin Karikó and Drew Weissman discovered that base-modified mRNA can be used to block activation of inflammatory cytokines and increase protein production when mRNA is delivered to cells.

Wrapping it up

mRNA is inherently fragile and unstable. In cells, it is degraded within days. Karikó and Weissman worked to optimize mRNA stability, but without a delivery mechanism, the mRNA vaccine material, once injected into the body, would be rapidly destroyed without reaching its cellular destination.

mRNA won the Nobel Prize, but many, including Breda, believe the COVID-19 vaccine might not exist without its carrier: the lipid nanoparticle, or LNP, a tiny sphere of fat that remains stable inside the body. Like Karikó and Weissman's work on mRNA, the field of macromolecule delivery was born almost 50 years before the COVID-19 pandemic.

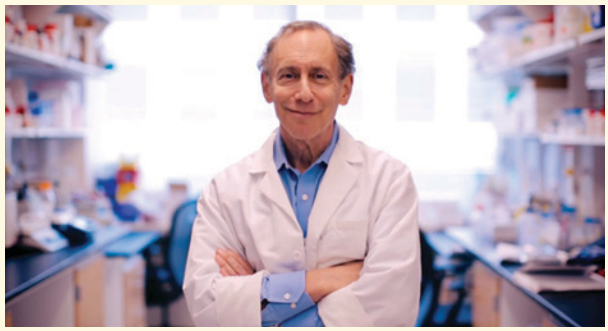
Robert Langer began laying the foundations for the COVID-19 vaccine at the bench in Judah Folkman's laboratory as a postdoctoral fellow. At the time, the scientific community believed it was impossible to encapsulate nucleic acids, Langer said. However, in 1976, Langer and Folkman did it using lipophilic polymers, a predecessor of today's LNPs.

Though the work was published in the journal Nature, Langer said that he was widely criticized.

"My first nine grants were rejected, and I could not get an assistant professor position in any chemical engineering department in the world," Langer said.

Eventually, Langer secured a position at the Massachusetts institute of Technology as an assistant professor of nutritional biochemistry. "Over time, our continued work and that of others changed people's thinking about what was possible," he said.

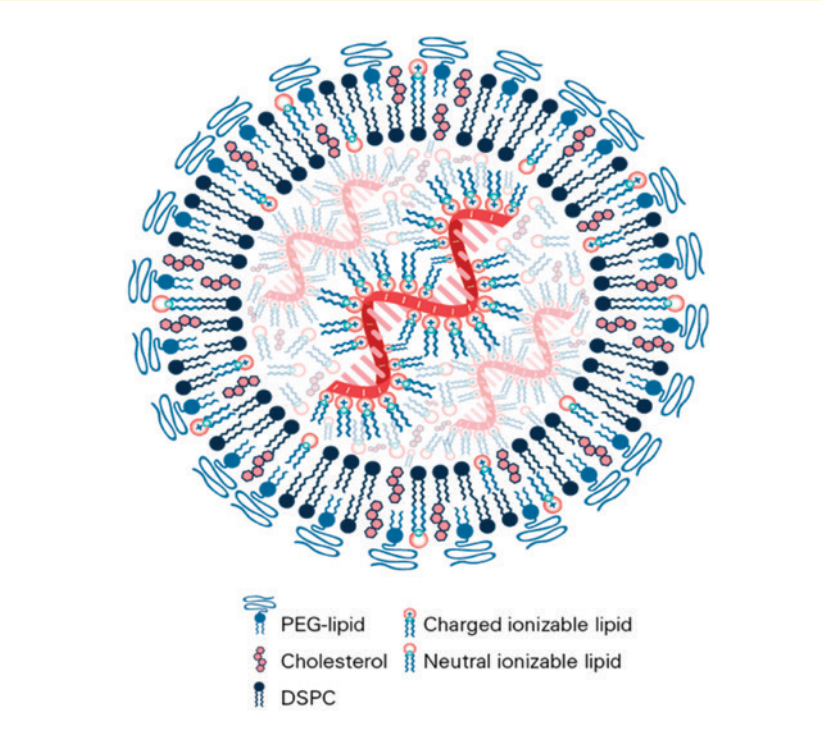
Indeed, Langer said one of the biggest advances in LNPs came with the development of lipid libraries,



MASSACHUSETTS INSTITUTE OF TECHNOLOGY/WIKIMEDIA COMMONS

Robert Langer is a co-founder of Moderna and a member of the American Society for Biochemistry and Molecular Biology.

MICHAEL D. BUSCHMANN ET AL. VIA WIKIMEDIA COMMONS



Example lipid nanoparticle structure. mRNA lipid nanoparticles contain low copy numbers of mRNA, and the mRNA is bound by the ionizable lipid that occupies the central core of the LNP. The polyethylene glycol lipid forms the surface of the lipid nanoparticle, along with a structural or helper lipid such as DSPC. Cholesterol and the ionizable lipid in charged and uncharged forms can be distributed throughout the LNP.

which allowed scientists to fine-tune the properties of the LNP and its cargo. Over time, LNPs became more diverse and decorated, like a patchwork quilt composed of various threads, shapes, colors and fabrics.

"The earliest of what some people call lipid nanoparticles would probably be considered liposomes," Langer said. "They were generally composed of lipid bilayers and had an aqueous interior. The current LNPs are more solid. They usually contain cholesterol, a structural lipid, a polyethylene glycol lipid and an ionizable lipid."

Similar to its mRNA cargo, the LNP had to not stimulate the immune system too much if it were to reach its final destination. Langer credits polyethylene glycol and ionizable lipids with circumventing immune recognition.

"Ionizable materials are important in that they are neutrally charged at a physiologic pH and positively charged at an acidic pH," Langer said. "So, they are less toxic than purely positively charged materials."

Ionizable lipids also allow the LNP to escape the cell endosome, once ingested, and avoid destruction in the lysosome, Langer said. After executing endosomal escape, the LNP delivers its vaccine payload to the cellular cytosol, where proteins such as the SARS-CoV-2 spike can be produced.

This and other work led Langer to co-found Moderna, where he played a key role in rolling out one of the first COVID-19 vaccines. Now a professor at the Massachusetts Institute of Technology, he has authored more than 1,500 scientific papers and is one of the most-cited engineers in history.

LNPs have had some great successes, but there is room for improvement, Langer said. He hopes future LNPs can be targeted to specific tissue and cell types and overcome anatomical roadblocks such as the blood–brain barrier. Weissman and colleagues Rivella, Parhiz, Breda and Abdulmalik have already published a study showing it is possible to target LNPs directly to hematopoietic stem cells to treat disorders such as sickle cell disease.

Beyond the nuts and bolts

Thomas Perlmann, secretary of the 2023 Nobel Committee for Physiology or Medicine, phoned each laureate before making the public announcement in Swedish and English. "They were very happy," Perlmann said.

He asked the scientists if they were surprised by the announcement because he suspected "they may not be, having received many prizes."

However, both Karikó and Weissman were surprised and overwhelmed by the news, Perlmann said.

This achievement was particularly overwhelming for Karikó, Perlmann said, because she never received a tenured position at UPenn or an R01 grant from the National Institutes of Health, which Perlmann described as a "clear sign that she struggled and didn't get recognition for the importance of her vision."

The number of graduate students in science, engineering and health has increased more than 23% since 2017, according to the National Center for Science and Engineering Statistics. However, the number of available tenure-track academic positions is declining. Therefore, more Ph.D. graduates in science and health are looking to fulfill their career aspirations outside of academia, similar to Karikó.

Ayantika Sen is a postdoctoral fellow at Stanford University who studies hyperinflammatory responses during SARS-CoV-2 infection. "Dr. Karikó's career spanned over decades, shuttling between the industry and academia, which sends an important message that impactful research can be conducted in both places; what matters is passion and collaboration with the right people," Sen said.

She added: "Accomplished researchers like Katalin Karikó and Jennifer Doudna have set great examples for new-generation female researchers like me, who aspire to gather the best of both worlds and make a long-lasting impact in the world with their research."

Ann Stock, American Society for Biochemistry and Molecular Biology president and a professor of biochemistry and molecular biology at Rutgers University, said she hopes the prize presentation will encourage current and future students to study biochemistry.

"The awarding of the Nobel prize to two biochemists for the application of pseudouridine to the development of mRNA therapies highlights the relevance of fundamental biochemistry and should be motivational for students, especially medical students, who sometimes lack enthusiasm for learning about the nucleoside and amino acid building blocks of nucleic acids and proteins," Stock said.

Sen said she was overjoyed to see the hard work of immigrant scientist Karikó highlighted on an international stage.

"On multiple occasions, she faced hardships in pursuing her passion and receiving support from her peers, but she kept going," Sen said. "I think young female researchers have a new role model to look up to and draw inspiration from."

Public skepticism

Vaccine skepticism has plagued public discourse and caused many people to pause or forgo getting immunized against SARS-CoV-2. Early in the COVID-19 pandemic, 31.6%

"Dr. Karikó's career spanned over decades, shuttling between the industry and academia, which sends an important message that impactful research can be conducted in both places; what matters is passion and collaboration with the right people."

AYANTIKA SEN

Randy Schekman, who received the 2013 Nobel Prize in physiology or medicine for his work on the machinery regulating vesicle traffic, said this prize is a “welcome antidote to the toxic nonsense spread by vaccine skeptics who use misinformation to sow confusion and doubt.”

of the U.S. population was unsure about receiving a vaccine, and 10.8% stated that they would refuse.

During a Q&A session after the announcement, a reporter asked the Nobel committee representatives if they considered the prize a “powerful strike back for the anti-vaccine movement.”

Olle Kämpe of the Karolinska Institutet, vice chair of the committee, noted that more than 13 billion people have gotten the vaccine and that, while the award would probably not sway those most resistant, "giving a Nobel Prize for this COVID-19 vaccine may make hesitant people take the vaccine and be sure it's very efficient and safe."

Randy Schekman, who received the 2013 Nobel Prize in physiology or medicine for his work on the machinery regulating vesicle traffic, said this prize is a “welcome antidote to the toxic nonsense spread by vaccine skeptics who use misinformation to sow confusion and doubt.”

Future of mRNA vaccines

Gunilla Karlsson–Hedestam, chair of the Nobel committee, emphasized how much this “flexible and fast” vaccine platform has and will continue to impact the general population and cited current research developments on influenza and therapeutic cancer mRNA vaccines.

As for the future of vaccine delivery, Langer said the possibilities are endless, including better lipid platforms, polymers, carbohydrates, micelles, exosomes and hybrids of many components.

Weissman and collaborators recently published a study showcasing a new method of LNP generation using microfluidic chips that will drive more precise and scalable production to meet the stringent manufacturing standards of the pharmaceutical industry.

Craig Martin is a professor of chemistry at the University of Massachusetts Chan Medical School who studies the structure and function in enzyme–nucleic acid interactions. “Karikó and Weissman have launched a field that is just now emerging,” Martin said. “mRNA vaccines are just the beginning. mRNA can deliver therapeutic proteins to cells and offers the promise of personalized cancer therapies. It is truly an exciting time for mRNA."

Scientists at UPenn and other institutions are now looking to adopt the COVID-19 vaccine technology to develop vaccines for other viruses, cancer and more.

Weissman and colleagues recently published a preprint showing that delivery of vascular endothelial growth factor A via nucleoside-modified mRNA encapsulated into LNPs may be a viable treatment option for individuals with acute and chronic liver disease. Likewise, Karikó and colleagues recently published a study showing that an mRNA–LNP vaccine can control human papillomavirus-associated tumors in mice.

“The Nobel recognized that it takes a lot of time and effort for the most rudimentary and basic scientific research to translate into clinical work,” Abdulmalik said. “This is the culmination of many, many years of committed and dedicated work of scientists. It basically took the perfect storm to make sure the technology was ready to fight the pandemic.”

Marissa Locke Rottinghaus (mlocke@asbmb.org) is ASBMB's science writer.

Meet Robert Haltiwanger

This JBC associate editor has a long history in glycobiology — and with the ASBMB

By Paula Amann

When Robert Haltiwanger came to Duke University as a Ph.D. student, he was not only stepping into the field of glycobiology, he was also entering a realm where the American Society for Biochemistry and Molecular Biology was a force to be reckoned with.

His principal investigator, Robert Hill, had served on the editorial board of the ASBMB's Journal of Biological Chemistry since 1965 and was elected president of the society in 1976.

"I was kind of raised in the society, and JBC was the prime target for most of our publications," Haltiwanger said. "I went to my first ASBMB meeting in 1982; it made me really want to be in the field."

Haltiwanger moved from one ASBMB glycobiology lab to another when he did his postdoc with Gerald Hart at the Johns Hopkins University School of Medicine. Hart was also an editorial board member for JBC at the time and "his lab also was deeply embedded in the society," Haltiwanger said.

So, when he launched his own research career at Stony Brook University in 1992, Haltiwanger was already an ASBMB member, and he began serving on the JBC editorial board in 1999. He became a full professor in 2004 and chaired the Stony Brook biochemistry and cell biology department from 2009 to 2015.

Haltiwanger accepted a new job as a professor at the University of Georgia in 2015. Hart joined him there in 2018, the same year Hart was elected ASBMB president. Two years later, Haltiwanger became co-director of the university's T32-funded doctoral glycoscience training program.

After giving talks at four ASBMB annual meetings, starting in 2001, Haltiwanger was named a co-chair of the society's 2020 meeting, set to take place in San Diego, but canceled by the COVID-19 pandemic. He ended up co-chairing the 2021 meeting, which was held virtually.

Haltiwanger became a JBC associate editor in 2022, and he was named an ASBMB fellow this year. He spoke with ASBMB Today about his research career and his history with the JBC. The interview has been edited for clarity and length.

ASBMB

Robert Haltiwanger, second from right, enjoys a presentation at Discover BMB, the 2023 ASBMB meeting in Seattle with, from left, Gerald Hart, a University of Georgia colleague and 2018–2020 ASBMB president; Tony Antalis, 2020–2022 ASBMB president; James Ntambi, ASBMB Council member; and Alex Toker, editor-in-chief of the Journal of Biological Chemistry.

What's your core interest in biochemical research these days?

Haltiwanger: My main area is glycobiology. The root "glyco" is related to the Greek word for "sweet." So in biology, my work is the study of the sweet life. It's an understudied field because the analysis of a glycoprotein is technically complicated.

Mass spectrometry has been instrumental in understanding the structures of glycans. The glycans are what we call the sugar portion, the

carbohydrate portion of a glycoprotein or glycolipid. These molecules tend to be on the cell surface: Every cell of your body has a sugar coat, called a glycocalyx.

People have known since the 1960s that there's a sugar coat on all the cells, but nobody really knew what it was doing, other than having a protective function. It's a physical barrier on the plasma membrane because the easiest way to kill a cell is to poke a hole in the plasma membrane and everything leaks out. Yet, the glycocalyx is made up of literally thousands of different carbohydrate structures, and hundreds of enzymes are responsible for synthesizing it. That suggests that there's probably more to it than just a protective barrier.

We're still discovering new carbohydrate modifications. Once you discover one, there's going to be an enzyme, called a glycosyltransferase, that generates that modification. If you identify the enzyme and you get the gene for it, you can knock it out in a fruit fly or a mouse and look for human diseases caused by mutations in those genes. That's what we do.

What did you learn while you were working at Duke University with Robert Hill?

Haltiwanger: The Hill lab worked on biochemical purifications of glycosyltransferases — and what are known as lectins, which are proteins that recognize specific carbohydrate structures. If there's some biological function to a cell surface carbohydrate, there has to be something that recognizes it. A whole bunch of lectins have been identified that recognize different carbohydrate structures.

I purified what is now known as the mannose receptor. It's involved in innate immunity. It recognizes surfaces of cells such as fungi, which are coated with mannose. A macrophage can recognize that, engulf it and then destroy it.

I was surrounded by people working on enzymes that make or recognize complex carbohydrates.

For your postdoc, you joined Gerald Hart's lab. What were they working on?

Haltiwanger: When I joined the lab, they had just discovered a novel form of glycosylation, called O-GlcNAc.

Most glycoproteins are on the cell surface. However, O-GlcNAc was found on proteins inside the cell nucleus and cytoplasm, which at the time was a heresy in the field, because everybody thought there were no sugars or glycoproteins inside the cell. It was a radical thing to propose.

For the first few years I was in the lab, I would go to scientific meetings, and we would present posters about nuclear and cytoplasmic glycosylation. People would come up and say, "Don't you know, there are no glycoproteins in the nucleus and the cytoplasm."

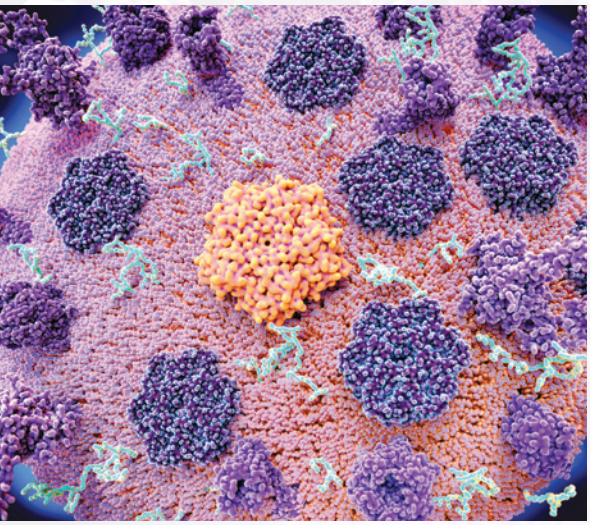
We had really good data, but that was the dogma: There are no sugars or glycoproteins in the nucleus and cytoplasm.

COURTESY OF ROBERT HALTIWANGER

Robert Haltiwanger went to his first ASBMB meeting in 1982. "I was kind of raised in the society," he said, "and JBC was the prime target for most of our publications."

COURTESY OF GERALD HART

In the early 1990s, Robert Haltiwanger was a postdoc in Jerry Hart's lab at the Johns Hopkins University School of Medicine. In this lab team photo, Hart is third from left, wearing a trench coat, and Haltiwanger is in the center of the back row wearing a green jacket.



Robert Haltiwanger has a long history of studying glycoprotiens which are found on the cell's surface as well as in the nucleus and cytoplasm.

So one lesson from that experience was 'don't follow the crowd.'

Haltiwanger: Dogmas only stand until there's data to refute them. That was definitely one of the things I took from my experience in Jerry's lab.

Jerry is just passionate about complex carbohydrates. It's really wonderful to be in the presence of somebody who was so excited about these molecules — anything that had a sugar on it. Since he moved to the University of Georgia, his lab is just down the hall from me.

Looking back on your years of work at Stony Brook, what is most relevant to you now?

Haltiwanger: When I started my independent lab, I was interested in understanding O-glycans. Over time, we've probably identified or helped identify a dozen different carbohydrate modifications and the enzymes involved in generating those modifications.

When you identify an enzyme, you have to biochemically characterize it. How does this enzyme work? What are the substrates that it uses? You have to identify the gene that encodes that enzyme, and then you can start studying its biology. When studying a gene, you can eliminate it in various cells or organisms and look for phenotypes. We've done a lot of that, and a lot of that has been collaborative work.

We've worked mostly in mammalian systems. Just last spring, we identified another novel sugar modification on proteins and the enzymes that add the sugar. We continue to identify novel structures and the enzymes that form them. There are structures that we still don't even know about. That's what drives my interest in glycobiology: finding new things.

What drew you to the University of Georgia?

Haltiwanger: There's a world-class center here called the Complex Carbohydrate Research Center. It's almost a 140,000-square-foot building. There are about 20 research groups in here, and everybody works on glycobiology. Nowhere else on the planet has that concentration of researchers in this field.

I've known most of the people here for a large part of my career because I go to the same meetings and see them. They had tried to recruit me a couple of times, in the early 2000s. My wife and I met in North Carolina, and we always thought we'd probably move south again. I was the chair of the biochemistry department at Stony Brook for my last eight or nine years there. I was ready to not be a chair anymore, so it was time for a transition.

What have you been working on lately?

Haltiwanger: Fibrillin is a structural protein in the extracellular matrix. People think Abraham Lincoln had Marfan syndrome, a common genetic disorder that's due to mutations in the fibrillins — fibrillin-1 in particular. It's a biologically important protein.

We demonstrated in a 2022 JBC paper that fibrillin is covered with glucose; it has probably 25 or 30 glucose monosaccharides added to it all over its structure. After we identified the glucose modifications, we identified the enzymes, POGLUT 2 and 3, and we identified the genes that encode them. We then generated knockout mice that lack POGLUT 2 and 3. These mice die shortly after birth if you knock out both of these enzymes, so we now know they are essential to life.

You had a first-author paper in JBC very early in your career. Talk about your involvement with academic publishing over the years.

Haltiwanger: I think I published four JBC papers as a graduate student, three of them as first author, on my lectin work. In Bob Hill's lab, that was where everyone published: JBC. Very few of his papers were published in other journals. JBC was where you would publish if you had a good story to tell. I have now published 40-some papers in JBC.

In the early 2000s, I was on the editorial board for five or six years and continued to publish in JBC. It was awesome.

I also have a major involvement in the Society for Glycobiology, which is smaller than the ASBMB. It publishes the journal Glycobiology, which Jerry Hart started in 1989. He was its first editor until about 2001. I became editor in 2011 for 10 years, until 2020.

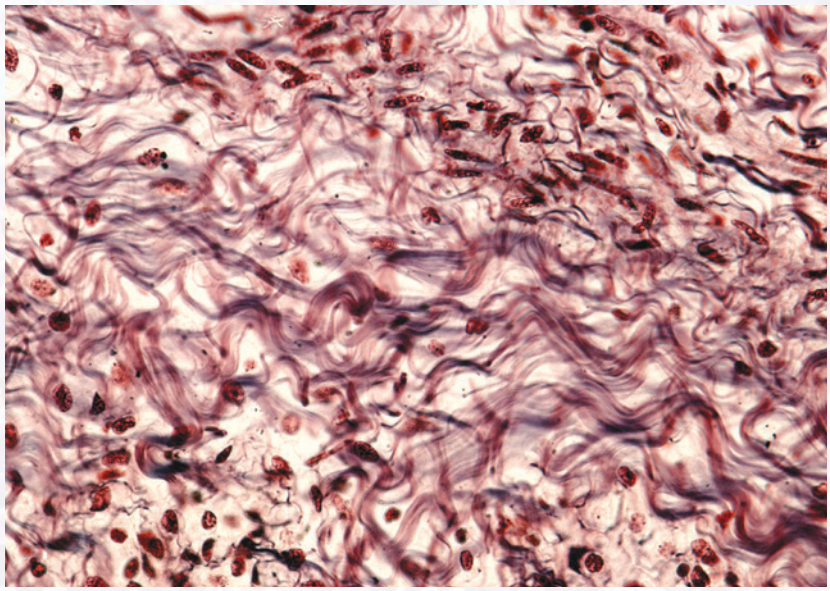
Jerry had been a JBC associate editor for about the same period, and he stepped down. He asked me: Would you be willing to take over? I agreed and came back to the JBC at the beginning of 2022 as an associate editor.

I'm very familiar with the journal. I've published most of my papers there. Even when I wasn't on the editorial board, I probably reviewed several papers every year for JBC. It's like my home.

How do you approach the editorial process?

Haltiwanger: My major responsibilities are glycobiology and extracellular matrices. To be honest, in those fields, and glycobiology in particular, most people have a very high opinion of JBC. It's where they send their best papers.

The thing I look for immediately is whether there's some mechanistic aspect of the work. Are they explaining biological mechanisms? Then I look at the manuscript to see what type of data they have, because, if they have X-ray crystallography, mass spectrometry, nuclear magnetic resonance or some specialized methodology, I need to make sure I assign it to an editorial board member who has that expertise and can evaluate it.



The Haltiwanger lab works on glycosylated protiens that make up the extracellular matrix and connective tissues such as fibrillin.

What do you do to recharge your batteries?

Haltiwanger: I like hiking and long walks in shaded areas. There's a botanical garden that has miles of hiking trails five minutes from the lab. I can go over there, and eat my lunch and then go for a walk for half an hour. It gets my mind off all of the questions that I was trying to wrestle with in the lab.

Paula Amann is a former ASBMB science writer.

Can science publishing be both open and equitable?

A White House memo has researchers, funders and publishers looking ahead

By Ankita Arora

> "The taxpayer who funded the research should have the right to see the outcome of that research without having to pay an additional fee to get access to those papers."
>
> — ALEX TOKER

The White House Office of Science and Technology Policy, or OSTP, issued a memorandum in August 2022 titled "Ensuring Free, Immediate, and Equitable Access to Federally Funded Research" that has gained widespread attention in the scientific community. The new policy guidance builds on a 2013 memorandum "Expanding Public Access to the Results of Federally Funded Research."

The 2022 memo requires federal agencies to make all taxpayer-funded publications and their supporting data openly accessible without an embargo period by the end of 2025. The previous memo allowed a one-year embargo. (See the table on the next page for other significant differences between the two.)

Why does it matter?

U.S. tax dollars fund groundbreaking scientific research. But to see the results, members of the public, who funded the research, must pay a subscription fee through a library or the journal. Individual subscription fees may vary between $10 and $40 per article. Some in the science community see this as akin to double taxation on knowledge. Among them is Alex Toker, editor-in-chief of the Journal of Biological Chemistry.

"It's just inherently and morally wrong," Toker said. "And that's what really started with the whole open-access movement. The taxpayer who funded the research should have the right to see the outcome of that research without having to pay an additional fee to get access to those papers."

The advantages of an immediate public access policy became apparent during the COVID-19 pandemic. The free-flowing exchange of research results led to increased translation of basic science discoveries into therapeutic interventions. Researchers were able to develop life-saving mRNA vaccines swiftly only because a Chinese laboratory immediately released the genomic sequence of the COVID-19 virus in early January 2020. This led many in the research community to ask why these benefits should not expand to all scientific endeavors.

Ashley Farley is a program officer of Knowledge and Research Services at the Bill & Melinda Gates Foundation. "When you talk about all lives having equal value and trying to ensure that everyone can lead a productive, healthy life, access to information and being able to build upon and share knowledge is critical to that success," she said.

The zero-embargo challenge

With the 12-month embargo in the 2013 OTSP memo, publishers could stick to the subscription model. Because there was no change, the memo did not call for additional

Topic	2013 Memo	2022 Memo
Embargo Period	Allowed a 12-month postpublication embargo period	Papers should be made freely available without any embargo
Agencies Covered	Agencies with research & development budgets over $100 million	All agencies with extramural R&D budgets
Publications Covered	Peer-reviewed papers	Peer-reviewed papers, peer-reviewed book chapters, editorials and peer-reviewed conference proceedings
Scientific Data	Research data associated with peer-reviewed publications should be stored and accessible to retrieve and analyze	Research data associated with peer-reviewed publications should be made freely available by default at the time of publication

funding for publication expenses. Authors could submit their work to a subscription-based journal that made author-accepted manuscripts, or AAMs, immediately available for free as "papers in press" but embargoed the final versions of record. In addition, some publishers permitted authors to share their AAMs in a public repository such as PubMed Central. This publishing model is known as green open access.

The zero-embargo period of the 2022 memo requires the publication model to transition to what's called gold open access. An article's final version of record is published online immediately, and the cost of publication is levied against the authors as article processing charges, or APCs. The ASBMB moved its three journals — the JBC, the Journal of Lipid Research and Molecular & Cellular Proteomics — to full open access in January 2021.

Scientific societies, funding agencies and commercial publishers are trying to figure out how to address the transition and rising costs. When asked how the change looked for the JBC, Toker said, "We are now in just the second year of that transition, which, I have to say, has gone very well, but it was not an easy transition by any means."

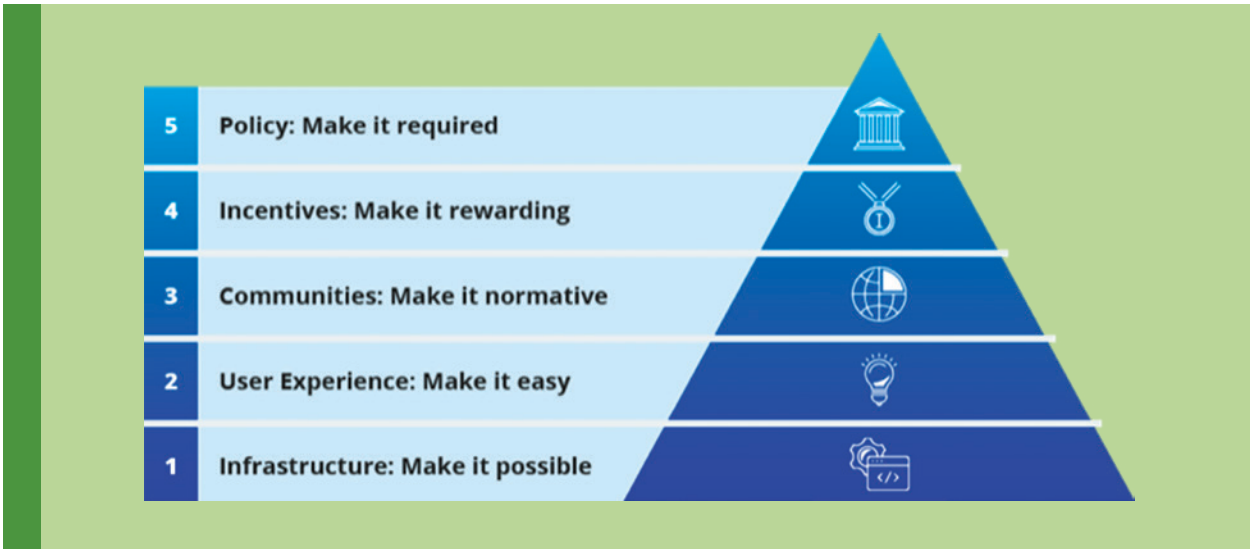
APCs for gold open access range from $2,500 to as high as $11,250 per paper. The OSTP memo does not include any provisions for additional government funding to offset publication costs. While federal agencies such as the National Science Foundation and the National Institutes of Health include publication costs in allowable grant expenses, members of the scientific community worry that this extra burden will decrease the funds available for research even as research costs increase.

Exorbitant APCs also might create a barrier to entry for researchers at underserved institutions or from developing countries who don't have access to additional funding to pay for APCs (Read the ASBMB's statement on the OSTP memo at asbmb.org/advocacy).

"There are individuals in countries around the world who simply do not have the resources to even do science," Toker said. "And when they can, they do not have the resources to pay for APCs. As editors,

"When you talk about all lives having equal value and trying to ensure that everyone can lead a productive, healthy life, access to information and being able to build upon and share knowledge is critical to that success."

— ASHLEY FARLEY



The Center for Open Science's intervention strategy incorporates five tiers.

as journals and as societies in particular, it is our obligation to make sure that we can do something to serve those individuals, those countries, where important science can and should be done."

So, how can the U.S. government and other funders ensure that equitable open access to readers doesn't lead to inequities in research participation?

Potential solutions

The Bill and Melinda Gates Foundation pays open-access fees from a central fund; they are not part of a researcher's grant budget. "But by no means is this going to be sustainable moving forward," Farley said. "We will address this in the next policy iteration and hopefully do so in a way that is equitable and achievable for any paper that we fund anywhere."

Most publishers allow researchers to apply for APCs waivers or grants. While these are often granted, the demand exceeds the availability. Production of the final record, copy editing, formatting and author marketing all cost money, and commercial publishers need to make a profit. No legal limit exists to what they can charge.

An alternative model would be an APC structure stratified according to the researcher's country, community or institution. COAlition S was started by the European Commission and the European Research Council in 2018 to make immediate open access feasible. The coalition is exploring whether incorporating a local purchasing power metric, a method to adjust costs to reflect what local markets can bear, into the APC model would enable equitable global participation.

The Center for Open Science, or COS, is a nonprofit whose mission is to move research toward more openness, rigor and transparency. COS employs an intervention strategy incorporating five tiers: technology to make open practices feasible, community building for easier participation, grassroots movement to normalize it, incentivizing it, and, the last lever at the policy level, mandating open science.

> "Currently, the reward system in academia is anchored to publishing papers in high-prestige journals, many of which have high APCs (article processing charges). But this is changing slowly."
>
> — HUAJIN WANG

Huajin Wang is the director of programs at COS. "The culture change layer to ensure equitable participation cannot be overlooked," Wang said. "Currently, the reward system in academia is anchored to publishing papers in high-prestige journals, many of which have high APCs. But this is changing slowly. Preprints (scientific paper that hasn't undergone the formal peer-review process) and free-sharing publishing platforms are becoming increasingly popular. This is going to gradually change the reward system."

Pushing forward

Farley would like to see a change in what science considers the finished product of research. "If I had a magic wand, I would really love to see a preprint-heavy policy," she said. "Slowly moving away from the version of record at the journal being the end-all-be-all to preprints being able to fulfill an open-access policy from a funders perspective will address the inequities in the fee structure."

The recent OSTP memo does not clearly specify what version of research papers it will apply to.

"Hopefully, through collective effort, we're soon going to evaluate the quality of the research more and more just based on the research itself," Wang said. "So it doesn't matter whether you publish a preprint online or publish in Nature or Science."

Wang sees the OSTP memo as pushing researchers toward this direction. "Now the perception of open access equals low prestige disappears," she said, "because everything is going to be open access."

OSTP also announced 2023 as the Year of Open Science to advance transparent and equitable science policies across the government. The announcement also released an official definition of open science: "The principle and practice of making research products and processes available to all, while respecting diverse cultures, maintaining security and privacy, and fostering collaborations, reproducibility, and equity."

"I think this is just the beginning," Toker said. "Honestly, I think we're undergoing a revolution in publishing. It started some time ago, but this is not the end."

> "Honestly, I think we're undergoing a revolution in publishing. It started some time ago, but this is not the end."
>
> — ALEX TOKER

Ankita Arora (ankita.arora@cuanschutz.edu)is an RNA-biologist-turned-freelance-science-writer. Her 12 years of experience in research and her storytelling skills help her distill science jargon into bite-size chunks that are fun to read.

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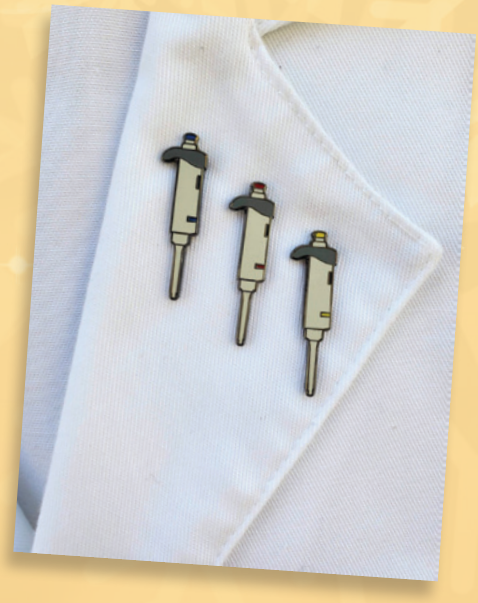

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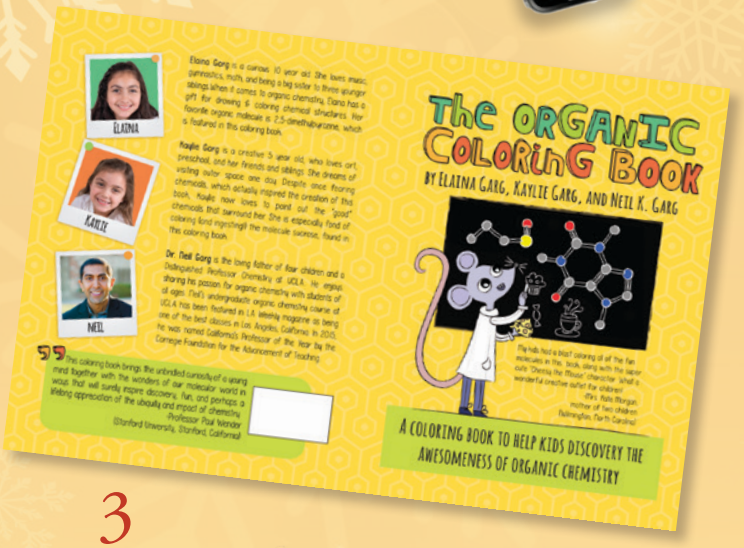
The ORGANIC ColoRinG Book
By Elaina Garg, Kaylie Garg, and Neil K. Garg
ELAINA
KAYLIE
NEIL
A COLORING BOOK TO HELP KIDS DISCOVERY THE AWESOMENESS OF ORGANIC CHEMISTRY

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CHAMPIONS
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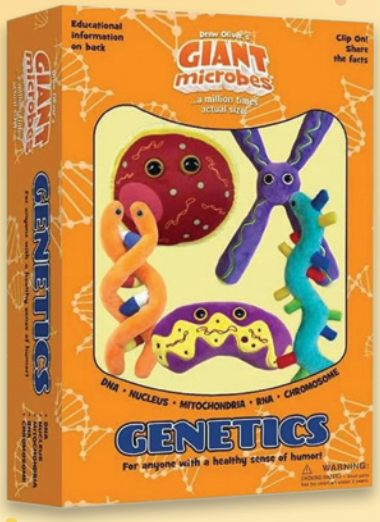
Educational information on back
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Clip On! Share the facts
GENETICS
DNA · NUCLEUS · MITOCHONDRIA · RNA · CHROMOSOME
GENETICS
For anyone with a healthy sense of humor!

2023 HOLIDAY GIFT GUIDE

ASBMB staff teamed up to bring you this year's holiday gift guide! We had a great time with our pre-holiday season research, and hope these suggestions will help you check some of your favorite scientists off this year's gift list.

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1. **Reusable Planners and Notebooks** by Rocketbook ($16–$60) **2.** **Enamel Pipette Pin** by Twisted Protein ($11.50) **3.** **The Organic Coloring Book** by Neil K Garg, Elaina Garg & Kaylie Garg ($5.38) **4.** **Custom Cartoon Biochemist Portraits** by CartoonPortrait ($30) **5.** **Team Mass Spec Apparel** $28.45–$46.88 **6.** **GIANTmicrobes Genetics-Themed Gift Box** by GIANTmicrobes ($25.95) **7.** **DNA Molecule Helix Pencil Holder** by 3D Print New York ($23.99 or 54.99) **8.** **Pocket Protector for Lab Coats** by Genius Lab Gear ($14.47) **9.** **Microbiology iPhone Case** by PhD In The House ($25) **10.** **Custom Lego Lab Sets** by ScienceGrit ($35-$55)

You can find direct links to each of these items (and more) at asbmb.org/asbmb-today.

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Interest group sessions for your #DiscoverBMB itinerary

Connect with colleagues with shared scientific and pedagogical concerns and curiosities in San Antonio

By Marissa Locke Rottinghaus

Interest group sessions at Discover BMB 2024 in San Antonio will bring together attendees with similar interests to share their recent findings, exchange ideas and establish connections.

The sessions will be held on the first day of the American Society for Biochemistry and Molecular Biology annual meeting, March 23, and feature speakers, discussion groups, breakouts and other types of networking activities.

The 2024 interest groups are described briefly below. Keep an eye on discoverbmb.asbmb.org for more details, including the speaker lineups.

Current understanding of DNA base excision repair pathway and its relevance to cancer

Organizers:
Zucai Suo, Florida State University College of Medicine
Patrick O'Brien, University of Michigan Medical School

Learn about the cutting-edge biochemistry, biophysics and cell biology techniques that will bolster your cancer biology studies. Speakers will discuss recent findings on the role of the DNA base excision repair pathway in cancer initiation and progression. Exchange ideas during roundtable discussions and casual networking.

O-GlcNAc regulation of cellular physiology and pathophysiology

Organizers:
Gerald W. Hart, University of Georgia
Lance Wells, University of Georgia

Dive into the world of O-GlcNAcylation of nuclear, cytoplasmic and mitochondrial proteins and the cellular stress response. Attendees will first get caught up to date with a short background talk on the roles of O-GlcNAc in survival/death signaling pathways and the regulation of autophagy. This will be followed by talks describing the latest on the mechanistic roles of O-GlcNAcylation in cancer and neurodegenerative diseases. Get your pressing questions answered during a short Q&A session as well as a panel discussion.

Membrane proteins

Organizers:
Francisco Barrera, University of Tennessee
Matthias Buck, Case Western Reserve University

Engage in discussion on proteins embedded in membranes. Speakers will discuss cryogenic electron microscopy structures of membrane receptors and transporters as well as single-molecule methods and molecular dynamics simulations. Make connections during an audience-driven Q&A session followed by an interactive, networking panel discussion.

International collaborations to promote global health Initiatives

Organizers:
James Mukasa Ntambi, University of Wisconsin–Madison
Edward Eisenstein, University of Maryland College Park

Join forces with researchers interested in providing sustainable agricultural, nutritional, health and educational interventions through service-learning and research to combat disease in developing nations. Speakers will cover how researchers can enhance their global engagement in areas such as epigenetics, genomics and proteomics. Network with researchers across biochemistry during a moderated Q&A session as well as a casual meetup.

RNA and gene regulation research at primarily undergraduate institutions

Organizers:

Megan E. Filbin, Metropolitan State University of Denver

Neena Grover, Colorado College

Meet RNA researchers at primarily undergraduate institutions and discuss approaches to make undergraduate research more accessible. Speakers will include members of the RNA@PUI Supergroup, who will share their undergraduate research projects. After the presentations, attendees can participate in an informal networking session to share ideas and establish collaborations.

Multifaceted mitochondria

Organizers:

Oleh Khalimonchuk, University of Nebraska-Lincoln

Laura L. Lackner, Northwestern University

Explore the diverse qualities of the mitochondria with scientists who study the powerhouse of the cell. Trainees and emerging investigator speakers will illustrate the intersection of basic mitochondrial biology and the molecular mechanisms of disease and aging. A short networking session will energize attendees and create synergy among researchers.

Signal transduction: an emergent behavior of biomolecular condensates

Organizers:

Josh Andersen, University of Utah

Carlos Castañeda, Syracuse University

Forge connections while discussing phase separation and cell signaling. Speakers will highlight how inhibition or activation of kinases and other enzymes, compartmentalization of enzymes and substrates/cofactors within the cell and posttranslational modifications regulate phase separation. Organizers will invite and help attendees to join a Slack community to keep in touch.

Emerging PTMs: AMPylationPlus Part II

Organizers:

Kim Orth, University of Texas Southwestern Medical Center

Anju Sreelatha, University of Texas Southwestern Medical Center

Shed light on AMPylation, a posttranslational modification that involves the addition of an adenosine monophosphate to protein substrates. Speakers will explore the biochemical mechanisms of enzymes that catalyze AMPylation, novel approaches to study AMPylation and the functional role of AMPylation in health and disease. Stick around and exchange ideas during a networking period.

Cryo-electron microscopy: from single particle to tomography

Organizers:

Elizabeth Wasmuth, University of Texas Health at San Antonio

John Jimah, Princeton University

Learn about cutting-edge advances in cryo-electron microscopy. Speakers will give an overview of the field and cover recent advances as well as developing methodologies for cryo-electron tomography and single-particle processing. Establish collaborations and get tips on your own cryo-EM work during a panel discussion and networking period.

Bridging cutting-edge innovation in mass spectrometry–driven proteomics between academic and industrial labs to elucidate novel biology in human disease

Organizers:

Mark R. Witmer, Bristol Myers Squibb

Cheng-Yu Chen, Bristol Myers Squibb

Join industry scientists and academic researchers for a discussion on how to strengthen the academic–industry interface. Speakers will discuss how researchers can use mass spectrometry–proteomic technology to expand capabilities and throughput for exploring new therapies. Talks from industry and academia experts will be followed by small group sessions to brainstorm new ideas.

TDP-43: from protein folding and structure to aggregation and importance as a biomarker

Organizers:
Fabrizio Chiti, University of Florence
Emanuele Buratti, International Centre for Genetic Engineering and Biotechnology

Get the latest insights on TDP-43 research, including a cryo-electron microscopy structure of TDP-43 isolated from patients. Speakers will discuss structural insights, the use of TDP-43 as a biomarker as well and the role of TDP-43 in neurodegenerative diseases. After short talks, attendees will have the opportunity to mingle, network and establish collaborations during a casual networking period.

Inter-organ communication in cellular and immune homeostasis

Organizers:
Narendra Kumar, Texas A&M University
Jayshree Mishra, Texas A&M University

Find out how organs communicate to maintain homeostasis. Speakers will explore the microbiota–gut–brain axis, gut–immune interactions, gut–liver axis, impact of DNA damage response on tissue crosstalk and signaling mediators of inter-organ communication. The short talks followed by panel discussions, Q&A and networking.

Nutrient sensing post-translational modifications: metabolism and disease

Organizers:
Lauren Ball, Medical University of South Carolina
Fangliang Zhang, University of Miami Miller School of Medicine

Explore how post-translational modifications contribute to health and disease. Speakers will cover the regulation of physiological and pathophysiological conditions by nutrient-sensing post-translational modifications as well as emerging techniques to detect post-translational modifications. After the talks, meet other investigators in the field during a networking period.

New advances in cardiovascular metabolic disease research

Organizers:
Mei-Zhen Cui, University of Texas Permian Basin
Yabing Chen, University of Alabama at Birmingham

Join your colleagues to learn about the latest discoveries in cardiovascular metabolic disease research. Speakers will showcase unique techniques and present on cardiometabolic vascular aneurysm, calcification, atherosclerosis, smooth muscle cell differentiation and signaling. Each talk will be followed up with a short, dynamic Q&A session.

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

Art, fashion, freebies and more are in store at #DiscoverBMB

This is the first article in a series about fun stuff to do and see in the exhibit hall in March in San Antonio

By ASBMB Today staff

After you've soaked up a ton of science during Discover BMB's thematic symposia, award lectures, interest groups and more, head on down to the exhibit hall floor for a nice change of pace.

The American Society for Biochemistry and Molecular Biology annual meeting always attracts vendors, who certainly will be showcasing their services and wares, but you'll also find lots of speakers sharing insights about careers, hands-on activities for the makers and creatives among you and plenty of prizes, freebies and keepsakes.

Here are just some of the fun things in store for you.

HEADSHOTS

Say 'cheese'!

Back by popular demand! Many of us are guilty of reusing the same old headshot year after year, which is why we're making it easy for you to get a new professional portrait taken during Discover BMB. Put on your nice clothes (at least from the waist up) and a happy face and take advantage of this helpful service.

BIOART

Molecular Motifs contest winners

"There is an art to science, and science in art the two are not enemies, but different aspects of the whole," biochemistry professor and science fiction writer Isaac Asimov once said. Get reminded of the beauty of biochemistry, and check out the winning submissions for the Molecular Motifs bioart contest.

BUTTON MAKING

Put a pin on it!

If being away from the lab causes a case of idle hands, get your craft and creativity on at our button-making station! After you're done, pin that button to your lanyard to show off your skills.

MARKETPLACE

Science swag and style

Every day can be casual Friday if you have the right graphic tee, amirite? Bring a little spending money to the ASBMB booth and snag a shirt commemorating the meeting — and maybe sporting a little attitude.

NETWORKING

Mingle at meetups

Bring your business cards because the meetups are back! Get together with people with shared scientific interests and other passions at these informal gatherings. As ASBMB President Ann Stock recently wrote, the exhibit hall is "a central hub for interactions." The meetups are at the core of that networking machinery, so take advantage of them.

PRODUCTS & SERVICES

Visit with vendors

You don't have to have purchasing authority to chat up the vendors exhibiting their goods and providing their product knowledge. They've reserved booths to not only showcase what they have to offer but also to learn more about what you need. So stop by and share your experiences and goals. You might be in for a sweet treat, too.

Science in San Antonio with Susan Weintraub

By Marissa Locke Rottinghaus

Susan Weintraub spent her childhood in Baltimore but has called San Antonio home since 1968. The professor of biochemistry and director of the Mass Spectrometry Core Laboratory at the University of Texas Health Science Center at San Antonio began there as a research assistant and worked her way up to the position she holds today.

Weintraub founded the mass spectrometry core at UTHSCSA, which provides comprehensive support for biological mass spectrometry, focusing on proteins and proteomics using state-of-the-art technologies. The core offers services including sample preparation, MS analysis, data processing and data interpretation. As director, Weintraub has helped hundreds of researchers learn about their biological systems of interest.

Weintraub has been a member of the American Society for Biochemistry and Molecular Biology for more than 20 years. ASBMB Today spoke with her to find out why San Antonio and the UT Health Science Center at San Antonio mean so much to her.

This interview has been edited for length, clarity and style.

COURTESY OF SUSAN WEINTRAUB

Susan Weintraub working in the Mass Spectrometry Core Laboratory at the University of Texas Health Science Center with a Thermo LTQ Orbitrap Velos Pro mass spectrometer.

Q: Tell me about your role at the UT Health Science Center at San Antonio.

Weintraub: My role is twofold: I'm a tenured professor in the biochemistry and structural biology department, and I direct the mass spectrometry core facility. The core is also a Cancer Center shared resource, and we provide state-of-the-art mass spectrometry services to a wide variety of biomedical researchers. Our first responsibility is to people at this institution, but we also analyze samples from outside institutions and companies.

Most of the work we do is on proteins. For example, a researcher may want to check that they produced the correct recombinant protein; we have several ways to tell easily if their sample is correct. We can also find out how it's been modified or if it fell apart during the preparation.

More often, researchers come to me with an underlying biomedical question. For example, a lab may be using a cell model and treating it with a drug of interest. We can use mass spectrometry to identify and quantify about 6,000 proteins in a very reproducible way. Then, I take that information and put it into a computational pathway analysis tool to identify which biochemical processes have been impacted by the chosen perturbation.

We've worked on samples related to cancer, neurodegeneration, aging, bacteriophages and Ebola and Marburg viruses as well as tuberculosis and SARS-CoV-2.

I typically meet the investigator by Zoom to discuss the project, feasibility and costs. The real key to this initial meeting is that they must have realistic expectations

before we proceed. Next, our lab staff gets involved, and they work on the practical aspects of receiving the samples and running them. I do a fair amount of the end data processing and assist with interpretation. I really enjoy getting to help with writing manuscripts, publications and presentations.

Q: How did you become director of the Mass Spectrometry Core Laboratory?

Weintraub: In 1968, my late husband joined the Air Force. We thought we were going to be stationed in Austin, but we were placed in San Antonio. I was lucky enough to find a master's program at Trinity University. After I finished my degree, I got a job at the UT Health Science Center, which had only been open one year at that point, doing neurochemistry research.

We were using gas chromatography, and in 1971 a Finnigan mass spectrometer showed up — the first commercial quadrupole instrument. Nobody expressed interest in using it. So I said, 'I'll do it!' It was an absolute dream job because I didn't have to secure any funding.

People started telling me that I needed to go back to school so, if something happened to my job, I wouldn't have to be only a lab tech. There was a Ph.D. program at the Health Science Center in San Antonio, but I couldn't research mass spectrometry because I was the resident expert. So, I worked on electron paramagnetic resonance because I liked instrumentation. After I finished, I did a brief postdoc working on lipids.

In 1979, UTHSCSA wanted to set up a mass spectrometry core, and I got the director position. The instrument was a Hewlett Packard 5982. The core was successfully supporting a number of investigators, but some key technical capabilities were lacking, so, in 1982, I applied for funding from the brand-new National Institutes of Health S10 shared instrumentation grant program to obtain an instrument with fast atom bombardment and capillary GC capabilities. Amazingly, I got funded. It was really exciting. Over the years, as needs have changed and instruments have progressed, I periodically submit other S10 proposals. I've been very lucky. I've had a total of nine S10 grants and had a chance to get funded in the 40th year of the program.

Q: What should #DiscoverBMB 2024 attendees see in San Antonio?

Weintraub: San Antonio is a historically and culturally fascinating city. Of course, everyone must see the Alamo. I'm sure many people will be shocked that it's right downtown. The city has really managed to keep it as authentic and noncommercial as possible. It's such a lovely place.

Market Square in San Antonio

The River Walk here is also downtown, and they've now extended it north and south. You can take the River Walk all the way to see the fabulous San Antonio Missions. Mission San Jose is the biggest and most tourist-ready of them. They are more than 300 years old and the only UNESCO World Heritage Site in Texas, so they are definitely worth seeing if you're looking for something historical.

In the other direction on the River Walk is an area with the historic Pearl Brewery. It was recently reenvisioned and configured into shops and restaurants. And there's a really neat place called Market Square west of downtown with a large number of shops and restaurants. It has a very authentic Mexican feel. You may even be able to barter with the vendors. There's a very famous Mexican restaurant there called Mi Tierra. Visitors have to try some Tex-Mex food when they are here.

For people who are into hiking and climbing, there's Enchanted Rock, a pink granite mountain north of San Antonio in Fredericksburg, Texas. It has an elevation of a whopping 1,825 feet, and it's just beautiful.

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

A pioneer in lethal pathogen research

Getting to know Jean Patterson of the Texas Biomedical Research Institute

By Nicole Lynn

The world has experienced multiple viral outbreaks over the past two decades, including severe acute respiratory syndrome, or SARS-CoV, Swine flu, Ebola, Zika and most recently SARS-CoV-2, or COVID-19. As travel, urbanization, and global land use increase, another outbreak is not just a possibility, it's a certainty.

Jean Patterson is an emeritus professor at the Texas Biomedical Research Institute, or Texas Biomed. She was the initial director and for a time chair of the institute's biosafety laboratory level 4, or BSL-4, task force. She has overseen research on countermeasures for highly infectious pathogens that can lead to sporadic but lethal outbreaks.

"As a virologist, I don't know if there's a viral epidemic I haven't worked on," Patterson said.

BSL-4 represents the highest research safety level. These laboratories typically require researchers to wear full-body, positive-pressure air-supplied suits. BSL-4 labs also use biosafety cabinets and multiple redundant safety measures to protect both the users and the outside environment from the pathogens within.

Patterson became interested in virology when she was a postdoctoral fellow at the University of Geneva, Switzerland, where she studied RNA-based viruses. There she adopted teaching methods that emphasized tight experimental controls, something she instills in her students to this day.

"If you do the proper controls, you learn something from every experiment," Patterson said. "You shouldn't waste an experiment by not learning something from it."

Simultaneously, Patterson stresses the importance of collaborative work, something she has engaged in throughout her career.

"Collaboration is harder than competition," said Patterson. "With competition, whoever gets there first wins, but when we learn how to collaborate well, now that's real art."

Early in her career, Patterson worked at Boston's Children's Hospital affiliated with Harvard Medical School, where she studied respiratory syncytial virus, or RSV, and later witnessed the outbreak of human immunodeficiency virus, or HIV. She performed research on ribavirin, an antiviral medication used to treat infections caused by the hepatitis C virus, or HCV, which can opportunistically infect the liver of individuals with HIV due to reduced immune capacity.

TEXAS BIOMEDICAL RESEARCH INSTITUTE

Jean Patterson stands next to positive pressure suits in the BSL-4 laboratory.

In 2000, Texas Biomed recruited Patterson for her viral expertise to oversee the inception of a high-containment laboratory, the first of its kind outside of the federal government.

Why build a BSL-4 in Texas? Long before Patterson's recruitment, building a "city of science," was the mission of Texas Biomed founder Thomas Baker Slick Jr., an inventor, entrepreneur and rancher. Slick's success in building three research organizations — Texas Biomed, the Southwest Research Institute and the Mind Science Foundation — at a time when San Antonio had no graduate education programs was monumental in mold-

TEXAS BIOMEDICAL RESEARCH INSTITUTE

The biosafety level-4 labs at the Texas Biomedical Research Institute contain some of the world's deadliest pathogens.

ing San Antonio into the research capital it is today.

"There is a strong military presence in San Antonio, and if there's one thing the military understand, it's risk," said Patterson. "They know nothing is ever 100% safe, and you can't pretend that it is."

Before planning construction for the new BSL-4 facility, Patterson and her team made many trips to labs at the Centers for Disease Control and Prevention, or CDC. Established in 1946 as the successor to the World War II Malaria Control in War Areas program, the CDC has since grown to study a wide array of diseases, environmental threats and health risks. Its BSL-4 is one of only two labs in the world that officially contain smallpox.

Patterson also consulted with labs at Fort Detrick, a biodefense research facility founded in 1943 that ran top secret U.S. biological weapon programs until 1969. During World War II, what was then known as Camp Detrick produced upwards of 500 bombs containing anthrax spores to fulfill an order from Winston Churchill. Detrick would later be at the center of the 2001 anthrax attack investigations, and widely recognized for its significant contributions to research involving cancer and infectious diseases like acquired immunodeficiency syndrome, or AIDS.

Based on what they learned from the BSL-4 labs at the CDC in Atlanta, and at Fort Detrick, in Frederick, Maryland, Patterson's team made plans for San Antonio.

"The facility was designed with simplicity in mind," said Patterson. "Local engineers and architects first drew it out on a napkin, saying, 'These are the principles, this is how it works.'"

At present, BSL-4 suit laboratories exist in about seven locations in the U.S., and one in Canada; there is also one BSL-4 glove box lab in Georgia. The exact number is often difficult to identify due to the semantics of BSL-4 classification. For example, whether suit laboratories but not glove boxes are included in the total lab number, or all facilities are collectively placed into one count.

Since the inception of Texas Biomed, federal agencies and pharmaceutical companies have used its BSL-4 for studies on select agents, pathogens and vaccine research. The advantage? Texas Biomed did not begin with a set mission and is unrestricted by long-term research goals. The research flexibility at Texas Biomed encourages government agencies and companies to work with them when they have to shift focus to meet agency or industry research goals.

When Patterson's BSL-4 lab opened in March 2000, her research initially focused on Lassa fever, a deadly zoonotic disease endemic to parts of West Africa. However, the anthrax attacks of 2001 triggered growth in U.S. bioweapons research, providing a foundation for later

San Antonio: Reverence for history and a fiesta vibe

At the intersection of historical landmarks, unique culinary delights and a dynamic culture, San Antonio offers an exciting and engaging environment for locals and tourists. A resident for over 20 years, Jean Patterson describes San Antonio as "A warm welcoming city and very friendly."

The city is home to a number of military installations, including Fort Sam Houston, Brooke Army Medical Center and two Air Force bases — Lackland and Randolph. All members of the Air Force, including reservists and the Air National Guard, begin their basic training in San Antonio, and it is home to many retired service members.

San Antonio lures visitors with its historical sites, such as the five Spanish colonial missions, including the Alamo. The city balances reverence and celebration.

One of the most popular attractions is the River Walk, a 15-mile stretch of parks, restaurants, entertainment and residences along the San Antonio River; it includes five miles of the downtown area that maintain a year-round fiesta vibe.

"The River Walk is really nice," Patterson said, "and it also lets you know how welcome you are to visit San Antonio."

investigations in Patterson's facility, including the development of multiple vaccines targeting Lassa fever and the Ebola virus.

Patterson collaborated with former student and postdoc Ricardo Carrion to develop and use the marmoset as a model for viral pathogenesis for infectious agents such as Ebola, Lassa fever, Zika, Marburg virus and Eastern equine encephalitis. Unlike other nonhuman primates, marmosets do not carry herpesvirus B, which is beneficial as infections in humans can prove fatal. They are less aggressive, and their small body size makes for easy handling; marmosets are also particularly useful for studying the effects of Zika during pregnancy as they twin and triplet throughout the year.

"Animals can do unexpected things," Patterson said. "The part that takes the most skill (in the BSL-4 setting) is working with the animals; having a high-quality veterinary staff gives us confidence to work with animals in these settings, which requires specialization."

Most recently, Patterson collaborated with Holger Schmidt of the University of California, Santa Cruz, on a new type of viral detection that combines microfluidics with photonics. Schmidt's group developed a sensitive chip-based assay that can detect RNA molecules using small fluid channels and light-guiding structures, making it unnecessary to amplify the gene product, which is often required for other detection methods.

"My collaborators are the real geniuses," Patterson said, describing her colleagues, former students and postdocs, as "compassionate and brilliant problem solvers."

With the aid of Patterson's group, these approaches have been validated in detecting Ebola, Zika and SARS-CoV-2, and are moving toward commercialization for second-generation diagnostics.

"It has been an enormous pleasure to work with Dr. Patterson and her colleagues at Texas Biomed over the years," Schmidt said. "I have very much enjoyed her professionalism, collaborative spirit and sense of humor."

Of all the viruses Patterson has worked with, one of her favorites is the Leishmania virus, a tropical double-stranded RNA virus she helped discover early in her career at Boston Children's Hospital. And certain viruses still elude her, including RSV.

"(The U.S.) had one of its first vaccine failures with RSV," she said, "and because it is such a prevalent and serious pathogen, it's always been the one in the back of my mind that you want to do something with, and find something that works."

There is hope, however; the CDC recommending as recently as September the first ever RSV vaccine, developed by Pfizer, for pregnant people to protect their newborns from severe infection.

Looking to the future of virology, pathogen research and vaccine development, Patterson is hopeful, particularly for broad-spectrum vaccines.

"We're never going to be able to predict the next outbreak or the severity of the next outbreak," she said. "I think the best way to go for public health is to develop vaccines that target across large viral families."

Nicole Lynn (nalynn@ucla.edu) is a Ph.D. candidate at UCLA and a volunteer writer for ASBMB Today.

Meeting mentoring — make it your new ritual

By Vahe Bandarian

We take comfort in rituals. Every morning I wake up, usually at 6 a.m. I make myself a cup of coffee and scan the tables of contents of journals for new papers. My morning ritual also includes scanning daily stories in the Chronicle of Higher Education. A couple of months ago, an article titled "We're not doing enough for grad students at conferences" by Benjamin L. Carp caught me off guard and sent me down memory lane, to 1992 and 1997.

Toward the end of the summer of 1992, I attended my first scientific meeting, the Plant Physiology conference in Pittsburgh. That summer I was racing to finish my undergraduate thesis, put the finishing touches on a paper, and prepare to start my graduate studies at the University of Wisconsin–Madison. My undergraduate adviser, Scott Grover, attended the meeting with me. At the poster session, he directed traffic to my poster. At that meeting, I met Ray Chollet and Randolph Wedding, whose papers I had read in the context of my research in Scott's lab on phosphoenolpyruvate carboxylate and plant C3/C4 biosynthesis.

In 1997, I attended the American Society for Biochemistry and Molecular Biology meeting in San Francisco — the first and only national meeting I attended as a graduate student. I was working in George Reed's lab at the Institute for Enzyme Research. Two students from Perry Frey's group at the institute also attended.

I remember the poster session vividly. Perry stood at the end of a row of posters, directing traffic to us while he also caught up with colleagues. I had many great interactions during the poster session. Ruma Banerjee was the first person at my poster. Ruma served as associate editor of JBC for many years and is now a PI of the ASBMB Maximizing Opportunities for Scientific and Academic Independent Careers grant, better known as MOSAIC, for which I serve on the steering committee. But the interaction I remember best was with JoAnne Stubbe, who was instrumental in establishing the intermediacy of protein and substrate radicals in enzymatic reactions.

COURTESY OF NOZOMI ANDO

JoAnne Stubbe, carrying her signature pad of paper, talks to a student during a poster session at a meeting at the Massachusetts Institute of Technology, where she is a professor emerita of chemistry.

JoAnne walked up to my poster, holding her signature pad of paper and pen. I was both terrified and thrilled. I had been working on electron paramagnetic resonance studies of a cobalamin-dependent enzyme, and I was familiar with all her work on ribonucleotide triphosphate reductase, another cobalamin-dependent enzyme. She wanted to hear about every experiment, asked questions, and all the while kept saying, "Your system is so nice, ours is too complicated."

I called George from a pay phone after the poster session, still riding on the energy from that interaction, filling him in on all the feedback.

> **"I rarely send a student to a conference I am not planning to attend. I think it is critical for me to introduce my co-workers to the field and to be there for support."**

The next day, JoAnne approached me at the poster session in the exhibit hall. She introduced me to Wolfgang Buckel, an expert in redox-mediated metabolic transformations, and told me to take him through my "beautiful" data. She had evidently been telling him all about the data.

"JoAnne, my poster session was yesterday," I said.

"But isn't it in your bag?" she asked. "You must not be excited about your science."

I let out a nervous chuckle, and the best I could do was describe the main findings. JoAnne seemed really disappointed.

I think back to these Plant Physiology and ASBMB meetings often. I have more years behind me than ahead of me in this field, and when I think about formative experiences, these two conferences stand out.

The common thread was that I had a mentor there to help me network. Scott and Perry both did a great job of introducing me to scientists in the field. And the scientists who came and engaged me at my poster gave me a chance to talk about my work and build self-confidence. Of course, for Scott and Perry to help me network was natural — they were my advisers. Perry was on my dissertation committee and a close collaborator with George Reed. JoAnne had no reason to be promoting my poster, other than the fact that she was just excited about science.

I learned over the years that my experience with JoAnne was not unique. Her ritual was to go around conferences with her yellow pad and pen and talk to everyone, ask questions, and generally engage young and old. Ten years after that ASBMB meeting, I watched her at an American Chemical Society meeting, talking to my student Reid McCarty at his poster and discussing his data. I chuckled as she asked detailed questions about his experiments — I had been there a decade earlier. I know it was as memorable for him as it was for me.

As a community, we need to consider the importance of networking for younger scientists. I rarely send a student to a conference I am not planning to attend. I think it is critical for me to introduce my co-workers to the field and to be there for support.

Today, while technology seems to connect us more than ever before, in many respects we are less connected with one another in a meaningful way. Conferences are a unique opportunity to engage and connect on a personal level. I am sure that most of us who mentor students and postdocs in the lab have had experiences like those I described above. We must consider attending conferences to pay back at least some of what we have built our careers on.

All this brings me back to why I am writing this article. Let's make it a collective ritual to attend conferences with our trainees. And when we're there, let's agree to spend at least a little time going from poster to poster with a pad and pen. Who knows? A young scientist we connect with may someday look back at the interaction as a defining moment in their professional growth.

Our impact as scientists is often measured by our h-indexes, but isn't it time to think about our responsibility to the field as more than the papers we publish, awards we receive, and grants we garner? Let's make networking and being present at Discover BMB a new ritual.

I'll be in San Antonio with paper and pen in hand. Will you join me?

Vahe Bandarian (vahe@chem.utah.edu) is a professor of chemistry and associate dean for student affairs at the University of Utah and chair of the ASBMB Meetings Committee.

One-on-one: A Discover BMB mentoring experiment

By Paul A. Craig

Six small white tents stood in a row along one wall of the exhibit hall at Discover BMB, the American Society for Biochemistry and Molecular Biology's 2023 meeting in Seattle. Inside these tents, each furnished with a table and two chairs, the society hosted its first in-conference one-on-one mentoring sessions. Over three afternoons, 38 mentors offered guidance in 103 appointments booked by 88 mentees.

How did it go? We asked the staff director who organized the sessions, the mentors and the mentees to weigh in on the methods and results.

Here's what they told us:

ASBMB

Chris Heinen (left), a professor at the University of Connecticut School of Medicine and a member of the ASBMB Education and Professional Development Committee, has a one-on-one mentoring session with Kyle Magro, a student in the Postbaccalaureate Research Education Program at the University of California, at Discover BMB 2023 in Seattle.

The organizer

Why and how we did it

When I was a trainee, I found it difficult to initiate broad, career-planning conversations with more experienced scientists outside my formal mentoring network. As someone who still, to this day, struggles to guide small talk into deeper conversations when at large meetings, I thought pop-up mentoring seemed like a perfect solution: It could give me the structure I need to be more intentional in making professional connections and a chance to learn from someone whose perspective was different from my usual network.

The ASBMB one-on-one mentoring stations were inspired by a National Postdoctoral Association pop-up program at the NPA's virtual meeting in 2021. I was invited to participate in what was described as a "one-time, no strings attached mentoring session" in which the topics were intentionally not discipline-specific so mentors and mentees could focus on other aspects of their careers and/or life.

I didn't serve as a mentor at that meeting, but the general concept stayed with me. When it came time to build out the career program at Discover BMB, I wanted to make this happen.

I had a lot of help from members of the Education and Professional Development Committee as we bounced ideas off one another, particularly about what topics would be broad enough to support a range of career stages and interests. We also recruited a number of those committee members to serve as mentors so they could review how the program went from personal experiences and recommend changes for future iterations.

These committee members were not the only mentors. When investigators registered for Discover BMB, a question in their registration form asked if they'd be interested in being a mentor to early-career scientists at the meeting. By the early-bird registration deadline, more than 250 people had indicated an interest. We needed dozens of mentors from a wide variety of organizations and career types and, because this was our first attempt, we knew were going to need feedback.

We asked the mentors to commit to one or more two-hour time blocks and to be flexible about topics. Mentees could sign up for 30-minute sessions, so mentors would host up to four sessions during each block.

Most often, mentees booked appointments on the spot and went directly into a mentoring session (or the next available session, often 10–15 minutes later). In a few cases, particularly with our industry scientists, we booked a day in advance.

— Kirsten Block, ASBMB director of education, professional development and outreach

A month or so after the meeting, we contacted mentors and mentees with a request for a brief testimonial. Here are the responses we received, ranging from personal experiences to specific career advice to tips on how to work the Discover BMB meeting.

The mentors

Forming relationships

During my one-on-one mentoring time slot, I talked to three scientists: a student from a primarily undergraduate institution, like my own, who wanted advice about applying to Ph.D. programs; a senior Ph.D. student planning to search for postdoctoral positions in the upcoming months who was concerned about their publication record and how to encourage their adviser to be more responsive about paper edits and planning; and a senior faculty member who was feeling a bit stuck and wanted a chance to discuss ideas about their career moving forward with someone not at their institution or close scientific circles. All three conversations were unique and engaging.

For the trainees, I was able to offer specific advice based on my own experiences, but with senior faculty members, I felt more like the mentee than the mentor. As someone who is potentially interested in administrative roles in the future, I had a lot of fun (for lack of a better description) discussing the pros and cons of moving into more administrative or education-focused roles. It was a unique and wonderful way to form relationships with other scientists in the larger ASBMB community.

— Jeanine Amacher, Western Washington University

Frustration and rewards

I was a mentor for about eight people at Discover BMB, ranging from a group of three high school students to those who had just completed their degrees (both undergraduate and graduate) to people who were considering midcareer changes.

One high school sophomore (who had presented a poster) worried that he would not be competitive with his peers when he applied to colleges. It was fun asking him how many of his peers had presented posters at national scientific conferences and seeing his eyes light up.

Some conversations were frustrating. One midcareer faculty member talked about career barriers in an academic department but resisted the idea that each of us must recognize that, if something is not working for us, we are the ones who must change. The conversation was not satisfying for either of us.

In another case, a postdoc was on the threshold of pursuing a career position but had just discovered a new and exciting aspect of his research. He needed just the slightest nudge to gain the courage to pursue this new line of research and left our one-on-one meeting with specific goals of people to meet, even while still at Discover BMB.

Perhaps most rewarding was my interaction with a student about to earn a BS in biology. We talked about what to do if you discover as you are completing your undergraduate degree that you really are not interested in the career you had been planning on since sixth grade — becoming a medical doctor. We talked about other career options, including research and science writing, but we also discussed what a good life looks like and how to get there from here. This led to life philosophy, books to read and how to balance perspectives with our friends and family, whether they are focused on their life paths or appear to be stuck in neutral. The two of us are reading some books together and plan to continue our discussions in the future. I'm not sure if this will be a long-term mentoring relationship, but that seems like a real possibility.

— Paul A. Craig, Rochester Institute of Technology

Connecting members

During Discover BMB 2023, I had four wonderful conversations with early-career scientists ranging

from undergraduates to postdocs. Some of them had a clear idea of what they wanted to do next, while others were considering their options. It was exciting to hear that they were all taking ownership of their careers. I particularly loved that they were actively trying to meet and seek advice from more senior scientists (beyond the advising center).

I serve on the ASBMB Membership Committee; connecting members and helping early-career scientists to build relationships with more senior scientists is a high priority for us. Personally, I especially enjoyed my meetings with undergrads — their excitement was inspiring. I sincerely hope the ASBMB will continue this valuable opportunity next year.

— Erica Gobrogge, Van Andel Institute

'The most difficult question'

I served as a one-on-one mentor at Discover BMB for an hour on Sunday and again on Monday, and I was busy talking to students and young professionals the whole time. It was exciting to hear their different stories and their optimism for the future.

The discussions all pertained to that most difficult question — what's next in my career/education journey? Though I was happy to give them my thoughts and advice, my sense is that many of these young scientists already knew the answers to their questions but benefitted from the reassurance of talking through things with somebody else. While some may have outstanding mentorship at their home institutions, there is value in hearing different opinions, particularly from someone who doesn't know you and is starting with a blank slate about your situation.

I found this to be an enjoyable experience. I mean ... come on ... one of the joys of getting older is feeling like you can tell younger people what they should do! I look forward to participating again, and I'd like to see an expansion, including sessions that target young faculty.

— Chris Heinen, University of Connecticut School of Medicine

A chance to reflect

Serving as an ASBMB career mentor was a positive and enriching experience. The organizers did a fantastic job of pairing mentees and mentors. I had the opportunity to interact with a diverse range of students.

ASBMB

Alberto A. Rascón (left), an associate professor at Arizona State University and a member of the ASBMB Maximizing Access Committee, has a one-on-one mentoring session with Ashley Terrell, a research assistant at the University of Oregon, at Discover BMB 2023 in Seattle.

During the mentoring sessions, I talked with enthusiastic high school and graduate students, shared my experiences and pointed out failures I learned the hard way. The mutually beneficial experience allowed me to reflect on my academic journey while guiding aspiring scientists and educators in a nonprescriptive informal setting.

— Aswathy Rai, Mississippi State University

A range of topics

I participated in the mentoring sessions after being a grad school exhibitor during the undergraduate poster session. At that event, students could speak with representatives from several schools, but the venue did not allow for in-depth conversations where students could ask for advice or get more detailed information. Several people I talked to in the mentoring session had either spoken with me the day before or a friend suggested talking with me.

Advice on graduate school is widely available online or in other forums, but speaking with someone one-on-one who has experience and is knowledgeable about the topic can be very helpful. Topics in the mentoring conversations ranged from the pros and cons of taking

time off before entering grad school (what I call an opportunity year) to what to expect during a typical qualifying exam.

I applaud the ASBMB student members for seeking advice and meeting new people in their network.

— Stuart Ravnik, University of Texas Southwestern Graduate School of Biomedical Sciences

Questions and suggestions

Students in molecular biosciences are looking for advice as they ponder the next steps in their career path. Common questions posed during the one-on-one sessions:

- Should I do a Ph.D.?
- Do I need to do a postdoc if I'm not interested in a faculty position?
- How do I transition from academia to industry?
- What skills are employers looking for?

Some of my suggestions:

- Complete the Science Careers Individual Development Plan.
- Create a schedule of informational interviews to find out more about different careers.
- Consider your values, interests, strengths and personality.
- Write draft versions of a cover letter and a one-page résumé using challenge/action/results statements for a position of interest.
- Practice your three-minute elevator pitch; start with a compelling grabber statement that people will remember.

Don't just stand by your poster and hang out with friends at a meeting. Attend workshops and sessions, and then reach out to the presenters to build your professional network.

— Reinhart Reithmeier, University of Toronto

'Important, exciting and fun'

I would describe the mentoring conversations at Discover BMB as important, exciting and fun. I met with several undergraduate students who were interested in going to graduate school to earn a Ph.D. They had questions about what graduate school is like and what they need to do to be competitive for Ph.D. programs. These conversations are important as students consider their academic and professional careers. The decision to earn a Ph.D. will shape the rest of their lives. The conversations were exciting because these students are the next generation of the BMB workforce; they are our field's future researchers, educators and leaders.

And these conversations were fun both for the students and for me, I believe. It's fun to meet students from around the country and to hear about their journey into science. It's fun to help them think about their next academic steps and envision what they can do with their education and training. It's fun for students to dream about their future and for me to dream with them.

Mentoring allows me to help students achieve their goals. I enjoy encouraging them and opening their minds to opportunities and possibilities. Mentoring at Discover BMB is a great opportunity to have such an impact on students beyond my university.

— Nathan Vanderford, University of Kentucky

Sharing a nonlinear path

I signed up to advise students seeking industry careers and opportunities during the one-on-one mentoring sessions at Discover BMB. In my appointed two hours, I talked with three or four graduate students, both master's and Ph.D., who mostly were interested in understanding how industry careers differed from academic careers, finding the right industry employer and position, and whether industry would be a good fit for their futures after graduate school.

I enjoyed sharing my industry experience along with my transition to entrepreneurship during these one-on-one mentoring sessions. My career path to industry as a biochemist working in exercise science and sports physiology research was not part of my original plan, nor did I know it was possible with my skills in immunology. During the mentoring sessions, I chose to highlight the importance of having transferrable skills that can be used across STEM fields.

When I was in graduate school, I never considered entrepreneurship or starting a nonprofit organization focused on STEM education and self-awareness for young girls. Hence, I'm always willing to share my nonlinear experience, lessons learned, and valuable insights with students who are considering industry

careers and trying something different.

Kudos to ASBMB for providing this much-needed opportunity for students and members seeking to transition and learn more about industry careers.

— Shyretha Brown, Building Bridges Inc.

Insightful industry questions

I've spent my entire career in industry. At Discover BMB in Seattle, I had the opportunity to speak for 20 minutes to a group about my 30-plus–year career path, from my undergraduate days to my current role in big pharma. In a Q&A after this session, and then in a two-hour one-on-one mentoring session, I was kept busy answering thoughtful questions on how to prepare for a job in an industry setting. From these conversations, it's clear that many young scientists hunger to learn more about career opportunities across industry, whether in small or large companies, and they appreciate perspectives from scientists who have industry knowledge and experiences.

The four students I spoke with during the mentoring were well prepared and had insightful questions. They asked me about application and interviewing process as well as what qualities and experiences would make them standout candidates for industry. I emphasized that, in addition to excellent technical skills and research experience, strong communication, critical thinking and people skills — especially being collaborative — are essential qualities we focus on when hiring.

This time was mutually beneficial — as I shared my perspectives on internships, interviewing and networking, the students shared their enthusiasm and energy with me. These sessions are an excellent opportunity for industry professionals to participate in Discover BMB and make meaningful connections with the next generation of scientists. As a member of the ASBMB Membership Committee, I can see the value of these interactions between our members — students and professionals.

I have many years of experience, but members with only a few years in industry can provide valuable insights to students and postdocs, all the more so because they were in the trainee's shoes only a few years earlier.

— Mark R. Witmer Bristol Myers Squibb

ASBMB

Rupsa Jana (left), an undergraduate at Northeastern University, meets with Audrey Lamb, a professor and chair of chemistry at the University of Texas at San Antonio and a member of the ASBMB Council, in a one-on-one mentoring session at Discover BMB 2023 in Seattle.

Mentees

'We keep in touch'

I decided to sign up for a one-on-one mentoring session because I was unsure about my career direction and wanted to gain some insight from an accomplished scientist. My mentor was incredibly helpful and recommended two amazing books for me to read, "So Good They Can't Ignore You" by Cal Newport and "You Majored in What?" by Katherine Brooks.

In addition, I was very interested in learning Python and had signed up to take a Python course. Coincidentally, my mentor was leading a crash course in Python scripting for biochemistry and molecular biology that I was able to attend.

We now keep in touch via email and still have occasional Zoom meetings to discuss the books and future career directions. I highly recommend doing a one-on-one mentoring session.

— Caitlin Haren

A weight lifted

The mentoring I received in Seattle was more helpful than I expected. I had not planned on participating and was just hanging around the mentoring

BY THE NUMBERS

Mentors

1 postdoc
7 early-career faculty
21 established faculty
4 administrators
4 industry scientists
1 emeritus faculty

Mentees

5 high school students
1 high school teacher
34 undergraduates
3 postbaccalaureates
35 Ph.D. students
1 M.D. student
4 postdoctoral fellows
2 early-career faculty
3 mid- to late-career faculty

area, looking at posters before my next event. Then I thought, "Why not at least get some information about this, because isn't the whole point of being here to make the most out of every opportunity?"

I walked over to the desk and asked about the mentoring and how it worked and was told it was by appointment. My schedule had an open slot later on, and so it began. I came back later that day, and when I met with my person in those little pop-up tent rooms, it went from awkward to not awkward very quickly.

My mentor was from Wellesley College, which was perfect for me as I am in a small, private liberal arts college as well, though not nearly as renowned. We talked for a long time about my big-picture aspirations, as well as my experience and goals. Ultimately, I received very useful actionable steps for my resume and postbac transition into grad school. This has been a stressful concern for all the usual reasons, so to say I am grateful for the guidance I received that day is an understatement.

My short, ad hoc mentoring was the most direct, pointed, and deliberate advice I have received. I could feel the weight of uncertainty lift from my shoulders, finally. This may sound hyperbolic, but that is not my intent. For everyone who is weighing these decisions and has weighed them, I trust you will understand.

I am grateful to my mentor for a moment and to the ASBMB for making this possible.

— Phinn Markson

Judgment-free zone

As a faculty member, I have never experienced a mentor–mentee discussion at my institution, so I took advantage of one-on-one mentoring sessions in Seattle. I met with three different faculty–administrator mentors; we exchanged information and worked together toward achieving my professional goals. This provided me with a platform to discuss my career issues, the challenges that I had to deal with in my profession and how to navigate through them.

I was comfortable talking to each mentor about career issues, something we generally don't do in a professional setting, thinking that we will be judged. One mentor was very straightforward, told me the hard truth about academics and suggested some approaches to consider. He also asked me to read some books, which will guide me through this process. I learned about undergraduate research institutions and some funding opportunities I had never heard of.

Though I had only 30 minutes with each mentor, I learned a lot within that short time. The mentors advised, shared knowledge, talked about their own experiences and helped me produce a plan for moving forward.

— Jayshree Mishra, Texas A&M University

Conclusion

Overall, the one-on-one mentoring seemed to be a very positive experience for everyone involved.

The ASBMB will offer one-on-one mentoring again at Discover BMB in San Antonio, and the Education and Professional Development Committee is already planning some enhancements based on their experiences and the feedback of others.

If you are interested in being a mentor, please be sure to identify this interest on your meeting registration.

If you are interested in speaking with a mentor at the meeting, make sure to stop by our career center in San Antonio and sign up for a session or two.

Paul A. Craig (paul.craig@rit.edu) is a professor at the Rochester Institute of Technology, where he teaches general chemistry and biochemistry, and he is PI of the Biochemistry Authentic Scientific Inquiry Lab, a team of faculty from more than 10 campuses.

The look of love

That feeling you get when you gaze into your dog's eyes? It's biochemistry.

By Danielle Guarracino

Before I leave the house, I say goodbye to my dog. Sometimes, tongue in cheek, I'll ask her to watch the house and protect it (she's usually half asleep in her doggie bed). Other times, I'll tell her I won't be long, especially if she gives me puppy-dog eyes when I start to leave.

Tobie is an 8-year-old beagle who has been in our family since she was 7 weeks old. Sometimes, she seems more like our oldest child than a pet. We often joke that she plans to throw a rager, inviting all the neighborhood dogs over, in our absence.

In the years before I had to rush out the door with my daughter for school drop-off, we had a ritual: Tobie would sit on my lap and lick my face before we parted. It left me feeling good about the day to come, especially knowing my best friend would be there when I came home, eager to see me. On some level, I believe it also eased her anxiety about being left alone in the house for hours.

Over the years, I've casually read, heard and witnessed the bond between canines and humans, particularly between a pet and its owner. Researchers have studied communication strategies, the evolution of personalities, and even what dogs think when interacting with their specifically bonded humans. Domesticated dogs all originate from wolves and, through millennia, have adapted to human behavior.

While humans continue to define and study the evolution of dogs, we focus less on the convergent evolution of humans to bond with dogs. A 2015 article in the journal Science by Miho Nagasawa and colleagues began to unpack the inference that when dogs are domesticated, they adopt human "social cognitive systems involved in social attachment."

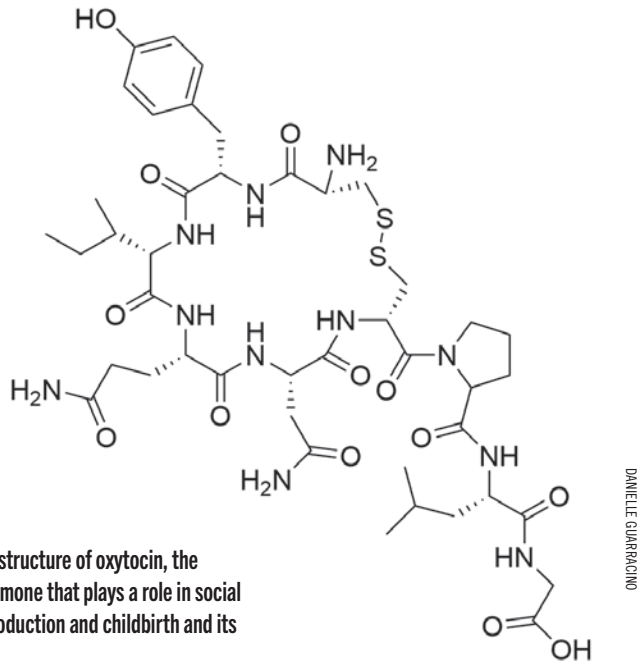
In other words, dogs, more than any other animal (including our closer genetic relations, such as chimpanzees) have an integrated form of social communication with humans that taps into bonding strategies and has led to the human–canine relationships that many of us know and love.

The love hormone

Much of this study, and similar work, hinges on tracking and understanding the role of the so-called "love hormone," oxytocin, or OT. As defined by Christian Gruber and colleagues in a 2010 article in Current Pharmaceutical Design, OT is an endocrine hormone comprising nine amino acids in a macrocyclic arrangement, is produced in the hypothalamus and travels along neuronal axons

The anterior cingulate cortex, the area of the brain that is receptive to oxytocin, is also ignited when a person looks at a picture of their dog. And maybe when you look at this picture of Tobie.

ARIEL BAUTISTA



DANIELLE GUARRACINO

The chemical structure of oxytocin, the endocrine hormone that plays a role in social bonding, reproduction and childbirth and its aftermath.

for release at terminals in the brain and spinal column. It is essential for smooth muscle contraction in mammary glands and the uterus, neurotransmission in the central nervous system that affects human behavior and cell-signaling functions in the ovaries and testes.

Oxytocin binds to its G-protein coupled receptor, which is mediated by proteins involved in many second messenger systems. These receptors, expressed in mammary glands and the uterus, are involved in pregnancy and nursing, but researchers, as explained in a 2018 article in BMC Psychiatry by Catherine Maud and colleagues, also have found expression in association with the central nervous system, which leads to the social and behavioral ramifications of oxytocin binding.

In humans, OT regulates a system of attachment, particularly that between a birth parent and an infant. This is often described as a loop, where the parental gaze stimulates oxytocin release in the infant, which, in turn, increases social attachment, which then loops back to the parent, and so on.

In the studies described in the 2015 Science article, scientists sought to understand the interspecies attachment between humans and dogs by relating it to the hormone OT. Some equate the possible oxytocin-mediated positive loop between dogs and humans with that between a parent and infant. Our dogs are like our children — or at least our biochemistry thinks so.

The studies

To test this hypothesis, the researchers performed two studies, which they elaborated on in later work. First, they examined urinary oxytocin concentrations in dogs and owners during mutual gazing and other interactions for up to 30 minutes. They then compared this with the same interactions with hand-raised wolves to determine if the oxytocin loop was a product of dog–human co-evolution. Second, they administered oxytocin to dogs directly through an aerosol spray to study their subsequent gazing behaviors as well as the urinary oxytocin concentrations excreted by the owners as a result.

Interactions in these studies included dog-to-human gazing, humans talking to dogs and humans touching dogs. The greatest changes in oxytocin production, as well as the highest collected urinary concentrations, were for the gazing groups.

When the researchers compared the dog experiments with those done with domesticated wolves, the wolf-to-owner gaze did not correlate with any appreciable change in oxytocin levels. This provided more evidence that dog-to-owner gazing is a form of communication that co-evolved as dogs were domesticated from wolves, and this is manifested by the positive response, as seen by the oxytocin release, in both the owner and dog.

Further studies examined sex differences in dogs; a dose of oxytocin significantly increased dog-to-owner gazing to female dogs but much less in male dogs. Urinary collections of oxytocin showed higher increases in concentration in owners of female dogs treated with the peptide hormone, as well. This pointed to heightened gazing between female dogs and owners and consequent stimulation of oxytocin release in the owners. Providing humans with administered oxytocin also shows sex-based differences, attesting to the possibility that females are more sensitive to oxytocin's effects or that the alternative, vasopressin receptor, is activated in males. No sex differences were noted in measures of natural oxytocin production measured, only when the hormone was administered.

ARJEL BAUTISTA

The author and her beagle, Tobie, demonstrate the mutual loving gaze that may trigger an oxytocin-mediated positive loop.

The bonding loop

For a human baby, mutual gazing with a parent is a healthy part of bonding. In fact, according to Jun Shinozaki and colleagues' 2007 article in the journal Neuroreport, when humans are shown pictures of family members, magnetic resonance imaging shows activated areas of the brain (specifically the anterior cingulate cortex) that are receptive to oxytocin. These same areas are ignited when humans are presented with pictures of their dogs. So, humans may feel affection in similar ways for their dogs and their human family members.

When dogs were domesticated, it seems their neural systems that use gaze as part of communication evolved to activate the human oxytocin release associated with bonding among family members, especially between a parent and child. The proposed interspecies oxytocin-mediated positive loop related to dog-human bonding reinforces the relationship between dogs and humans.

After my husband and I discussed these findings, he decided to "stare down" Tobie in an effort to initiate chemical reactions and behavioral feelings. Tobie seemed surprised and didn't maintain the gaze for very long, but biochemically I knew they both were probably surging with the love hormone.

In more organic instances, loving gazes between humans and their pets are certainly cherished. When Tobie sits in my lap on a bad day, licks tears when I'm sad or jumps up on me when I'm celebrating, I think she truly understands me. Dogs truly have keyed into our emotions and evolved realistic communication methods that feed back from us to them in a harmonious loop. Since Tobie first imprinted into our lives and hearts, I've never doubted that she was my first baby.

Gaze lovingly into your dog's eyes today, and see if it doesn't make you feel a bit more content.

Danielle Guarracino (guarracd@tcnj.edu) is a professor of chemistry at the College of New Jersey and a member of the ASBMB Today editorial advisory board.

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