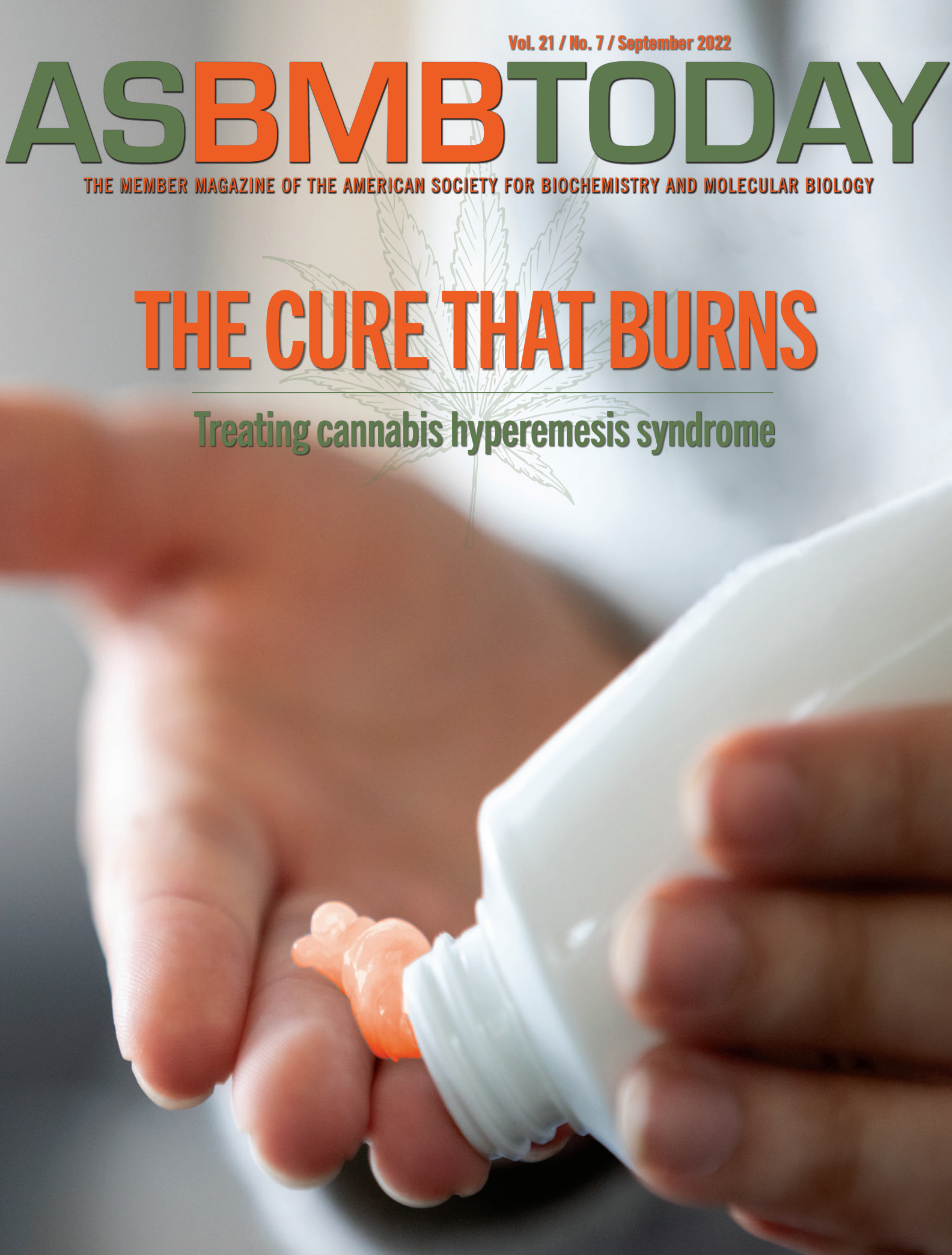
Vol. 21 / No. 7 / September 2022

ASBMB TODAY

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

THE CURE THAT BURNS

Treating cannabis hyperemesis syndrome



ASBMB
American Society for Biochemistry and Molecular Biology

Calling all ASBMB members!

It's time to renew your membership for 2023.

Together we'll continue to advance science, connect researchers around the world and build a bright future for biochemists and molecular biologists everywhere.

Not a current member of ASBMB but would like to join? Find where you fit in at

asbmb.org/membership

Connect with your colleagues

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- Publish your work in ASBMB's open-access journals. Regular and industry members receive $500 off article processing costs.
- Share your experiences in our member magazine, ASBMB Today.
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- Access new member-only content about the latest in science, career development, education, advocacy and more.
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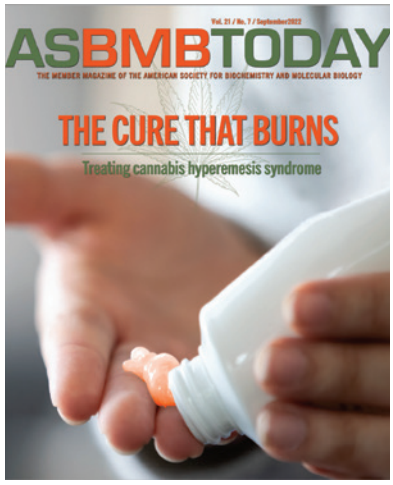

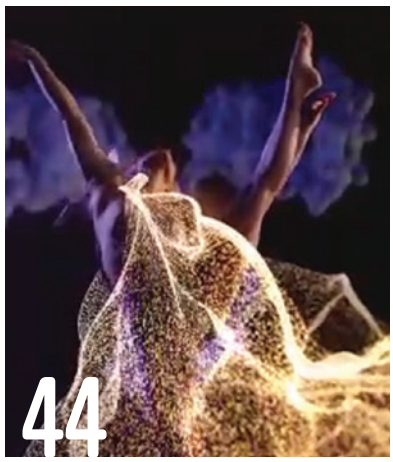

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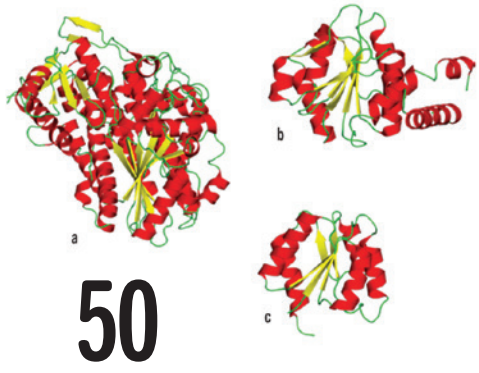

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www.asbmb.org/asbmbtoday
PRINT ISSN 2372-0409

Thank you, postdocs

By Ann Stock

This month, from Sept. 19 to 23, we will celebrate National Postdoc Appreciation Week — an observance established in 2009 by the National Postdoctoral Association to recognize the contributions of postdocs, who are a powerful force in the academic research enterprise.

I look back fondly on my postdoc as the best years of my scientific career. I was immersed in exciting research that I had chosen in a lab headed by a fantastic mentor and powered by incredible lab mates, many of whom remain in touch after more than 30 years. I was able to capitalize on the experimental skills I had honed as a grad student, learn new techniques and focus on research without the distractions of funding, budgeting and personnel management. It was indeed a special time.

Before slipping too far into rosy retrospection, I must admit that the freedoms and opportunities that make these years so enjoyable also can create challenges and anxiety. Postdoctoral training has no specific requirements or quantitative metrics of success. It lacks the matriculation date and structured social network created by a graduate class. There is neither a clearly defined end point nor a single path forward. In positions that fall between student status and permanent employment, postdocs often face uncertainties and inequities.

Fortunately, postdoctoral fellows need not face these challenges in isolation. The American Society for Biochemistry and Molecular Biology offers many activities to engage our community of postdocs. And each year, we celebrate National Postdoc Appreciation Week on our social media channels with the hashtag #ASBMBLovesPostdocs!

Here's how you can get involved:

- **Coffee breaks**: Join us each day on Twitter at 1:30 p.m. Eastern Sept. 19–23. We'll tweet a prompt to start a conversation about science, and folks who respond will have the chance to win a cup of coffee on us!
- **Twitter chat**: We'll host a chat about postdoc life. Stay tuned for an announcement about the date and this year's panelists.
- **Recognize a postdoc**: Know one who's doing great work? Send one or more of the following to asbmbtoday@asbmb.org by Sept. 14:
  - A thank-you note of no more than 50 words and a photo.
  - A video under one minute of yourself thanking a postdoc. (Feel free to film it on your cell phone.)

We'll share your photos and videos on Twitter using the hashtag.

In closing, to all our current postdocs:

We look forward to celebrating with you! We appreciate you not only this week but every week. Revel in our gratitude for all you do, and take a moment to reflect on the freedom and opportunities you have now. A research career is a continuum — as you look toward your next destination, don't forget to enjoy the journey!

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

Protein Society announces 2022 awards

The Protein Society recently announced its list of 2022 award winners. The awards were conferred at the society's annual meeting in July. Among those recognized were American Society for Biochemistry and Molecular Biology members Squire Booker, Daniel Herschlag and Nozomi Ando.

Squire Booker received the Hans Neurath Award, which recognizes individuals who have recently made a "contribution of exceptional merit to basic protein research." Booker, a professor at Penn State University, studies biosynthetic enzymes that use S-adenosylmethionine and iron–sulfur clusters as radical catalysts. The Protein Society award announcement noted his lab's recent development of a new way around a challenge in studying radical SAM enzymes with cobalamin cofactors, which produce important antibiotics. Of particular interest, the lab showed a mechanism by which an enzyme can extend a fully saturated hydrocarbon chain one carbon at a time.

BOOKER

Booker is a Howard Hughes Medical Institute investigator and a member of the ASBMB's nominating and finance committees. In the past, he has led the Maximizing Access Committee (formerly the Minority Affairs Committee) and served on the meetings and program planning committees as well as the editorial board of the Journal of Biological Chemistry.

Daniel Herschlag received the Stein and Moore Award, which recognizes "eminent leaders in protein science who have made sustained high-impact research contributions to the field." Herschlag, an enzymologist, pioneered the concept of catalytic promiscuity, which has become important both for understanding proteins' evolutionary history and for accomplishing directed evolution. He, his lab and his collaborators are responsible for the RNA chaperone hypothesis, for demonstrating that RNA binding proteins play ubiquitous roles in gene expression, and for developing a microfluidic platform for the parallel biochemical characterization of thousands of enzymes.

HERSCHLAG

In 2010, Herschlag received the ASBMB William C. Rose Award, which recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists.

Nozomi Ando was one of two recipients of the Protein Science Young Investigator Award, which recognizes scientists in the first eight years of their independent careers. Ando is an associate professor at Cornell University, where she works on new methods for using diffuse scattering data from X-ray diffraction images of protein crystals to obtain information about movement within proteins. The lab has found that there are two types of correlated motion in protein crystals: those within a single protein and those that connect two or more individual protein units. The finding has implications for our understanding of how allostery works.

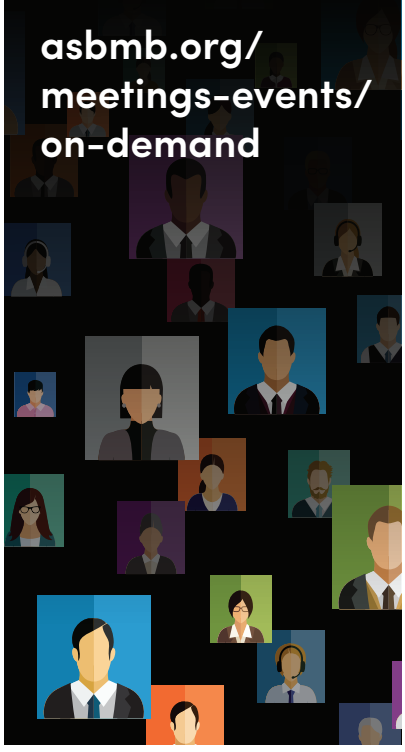
ANDO

ACS announces 2022 awards

In late March, the American Chemical Society announced its awards for 2022. Among the honorees were American Society for Biochemistry and Molecular Biology members Karen Allen, Benjamin Cravatt, Kimberly Jackson and Carlito Lebrilla.

Karen Allen, a professor and chair of the chemistry department at Boston University, won the 2022 Abeles and Jencks Award for the Chemistry of Biological Processes. Allen's lab studies the structure, function and mechanisms of phosphatases, phosphoglycosyltransferases and decarboxylases, working to understand both reaction mechanisms and enzyme evolution. Allen is a co-organizer of the 2023 ASBMB annual meeting, Discover BMB. She is the inaugural recipient of this award, which was named for the late enzymologists William Jencks and Robert Abeles, who taught and studied mechanistic enzymology at Brandeis University. Given by the ACS division of biological

ALLEN



chemistry, the award celebrates "outstanding contributions to the understanding of the chemistry of biological processes."

CRAVATT

Benjamin Cravatt, a professor of chemistry and chair of chemical biology at Scripps Research, received the Alfred Bader Award for outstanding contributions in bioinorganic or bio-organic chemistry. Cravatt's lab developed a technique to use chemical probes that bind to and tag enzymes' active sites, enabling researchers to read out enzyme activity at proteome scale. They have used the technique to study endocannabinoid signaling, cancer and neurological disorders. Researchers in the lab also have extended their methods to map small molecule–protein interactions globally and discover chemical probes for historically undruggable proteins. Cravatt was also one of three recipients of the 2022 Wolf Prize in chemistry, and he won the ASBMB–Merck Award in 2014. The late Alfred Bader, a Canadian chemist, businessman and philanthropist, and his family established this award in 1986.

JACKSON

Kimberly Jackson, a professor and chair of the department of chemistry and biochemistry at Spelman College, received the ACS Award for Encouraging Disadvantaged Students into Careers in the Chemical Sciences. Jackson is director of the food studies program at Spelman, a historically black college. Her lab studies potential therapeutic molecules for advanced prostate cancer, and many of the undergraduates who trained with her have gone on to earn Ph.D.s or medical degrees. The award includes a prize of $10,000, which Jackson directed to an Atlanta-based nonprofit called PinkSTEM that aims to empower girls to succeed in science, technology, engineering and mathematics.

LEBRILLA

Carlito Lebrilla, a distinguished professor and former chair of the chemistry department at the University of California, Davis, received the Frank H. Field and Joe L. Franklin Award for Outstanding Achievement in Mass Spectrometry. Known for his glycoproteomics work, Lebrilla studies disease biomarkers in cancer and Alzheimer's disease as well as bioactive compounds in breast milk and how milk glycoproteins affect infant microbiomes. Lebrilla is a member of the editorial advisory board of Molecular & Cellular Proteomics. This ACS award, sponsored by the Waters Corporation, is named for two noted mass spectrometrists; Field worked in developing chemical ionization, and Franklin studied the chemistry of ion molecules.

Goldwater scholars announced

The Barry Goldwater Scholarship and Excellence in Education Foundation has announced its 2022 class of scholars. The award, given to second- and third-year undergraduates, supports more than 400 students majoring in science, engineering and math.

Nine ASBMB Student Chapter members are among this year's honorees:

Ryan Osselborn, a junior at Lake Forest College in the Chicago suburbs, plans to pursue a Ph.D. in biomedical sciences after college and hopes to find new diagnostic biomarkers for neurodegenerative diseases such as Parkinson's.

Kade Townsend, a junior currently studying the evolution of antibiotic resistance in Pseudomonas aeruginosa at the University of Kansas, is interested in bacterial genetics research, especially in human pathogens, and plans to earn a Ph.D. in microbiology after college.

Ari Zlota, a biochemistry major at Northeastern University in Boston, is interested in medicine and plans to apply for M.D./Ph.D. programs in immunology. He wants to study the role of the immune system in wound healing to develop regenerative medicines.

Yena Woo, an Emory University junior, studies the fibrinolytic cascade in brain recovery after ischemia and wants to run a lab developing therapies for neurodegenerative diseases after earning an M.D./Ph.D.

Giona Kleinberg, a junior at Northeastern University with a biochemistry–bioengineering major, is interested in translational research in developmental neurobiology and hopes to earn an M.D.–Ph.D. and run his own lab.

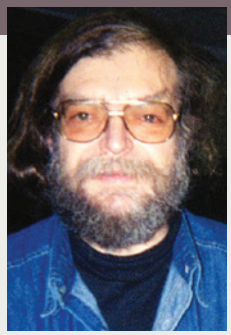
Taylor McGee is a junior at Hampden–Sydney College in Virginia. He is interested in viral research (particularly HIV), computational biology and bioinformatics. He intends to develop antiviral drugs and teach after earning his Ph.D.

Gretchen Fujimura is a student at Oregon State University. She has used biophysical approaches to study rabies. She intends to earn an M.D./Ph.D. in immunology, focusing on virology and biochemistry, and to conduct clinical trials on vaccines.

Raegen Esenwein is a student at Duquesne University, where she has studied the role of a topoisomerase in viral infections for several years. She is also pursuing minors in mathematics, biochemistry, and women's and gender studies. She plans to earn a Ph.D. in molecular biology and biochemistry.

Sarah Fahlberg is a junior at the University of Wisconsin–Madison who plans to pursue a Ph.D. in computational biology and develop computational tools that can be used to model protein structure and function. She hopes eventually to lead a lab.

Nadrian Seeman



Nadrian "Ned" Seeman, a nanotechnologist who built the first self-assembling DNA structures and a member of the ASBMB since 1986, died Nov. 16, 2021, in New York City. He was 75.

Born Dec. 16, 1945, in Chicago, Seeman earned an undergraduate degree in medicine at the University of Chicago and a Ph.D. in crystallography and biochemistry at the University of Pittsburgh. He did postdoctoral training at Columbia University and with Alexander Rich at the Massachusetts Institute of Technology. He worked as a crystallographer in the biology department at the State University of New York at Albany before joining the faculty at New York University, where he remained for the rest of his career as a professor of chemistry.

Inspired by the crisscrossed structure of the Holliday junction, which forms during DNA recombination, Seeman began to develop DNA sequences that would self-assemble, based on their sequence, into predictable structures. In 1991 he reported the first DNA cube, and in 2009 a crystalline DNA nanostructure. Although Seeman's research puzzled his colleagues initially, the approach has matured into a field known as DNA nanotechnology, and DNA structures are used today to construct nanorobots and drug delivery vehicles and in numerous research contexts.

Among Seeman's many honors and awards were the Kavli Prize in nanoscience, the Feynman Prize in Nanotechnology, the Einstein professorship of the Chinese Academy of Sciences, the Jagadish Chandra Bose Triennial Gold Medal, the American Chemical Society's Nichols Medal and the Benjamin Franklin Medal in chemistry. He was the founding president of the International Society for Nanoscale Science, Computation and Engineering; a fellow of the American Academy of Arts and Sciences and the Royal Society of Chemistry; and a member of the Norwegian Academy of Science and Letters.

He is survived by his wife, Barbara Lipski, and longtime co-worker Ruojie Sha.

John Edmond

John Edmond, an emeritus professor of biological chemistry at the David Geffen School of Medicine at the University of California, Los Angeles, died Feb. 18 at age 85. He had been a member of the American Society for Biochemistry and Molecular Biology since 1974.

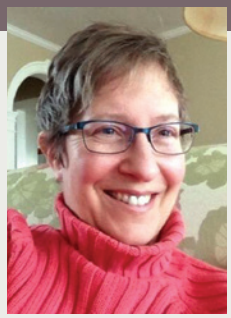
Edmond was born Jan. 21, 1937, in the village of Fintry in central Scotland. He went to Glasgow to earn his undergraduate degree and Ph.D. in chemistry and spent some time as an assistant lecturer at the University of Glasgow. He studied lipids in a basic research lab at Shell Oil in England for several years before being recruited in 1968 to join the biological chemistry department at UCLA.

Edmond remained active in research for more than 30 years, studying developmental neurobiochemistry. He was interested in the need for nutrients to fuel rapid brain growth in newborns; his lab studied neonatal rats and cultured neurons and astrocytes to understand these nutritional demands. Later in his career, he studied the effects of carbon monoxide on the developing brain, demonstrating that even at levels that were recognized as safe at the time, the gas could damage neurons permanently and cause hearing loss.

"No task was too small to recruit his help," colleagues in his department recalled in an article they wrote about Edmond in March. His commitment to service encompassed years he spent volunteering in many capacities on the university's academic senate, including as chair, along with National Institutes of Health study sections and the editorial board of the Journal of Neuroscience Research.

Edmond is survived by his wife, Lorna; two children; and four grandchildren.

Patti Taranto Erickson



Patti Taranto Erickson, a professor of molecular and cellular biology at Salisbury University and the faculty adviser of Salisbury's American Society for Biochemistry and Molecular Biology Student Chapter, died Dec. 24 at home in Salisbury, Maryland. She was 54 and had been fighting breast cancer for 16 months.

Born Nov. 13, 1967, in New Jersey, to Alfred and Patricia Taranto, Erickson moved with her family to Shelby, North Carolina, in 1975. She attended a public residential high school for high-achieving students and then went to Virginia Tech, where she earned an honors degree in biochemistry. She interned for a year at the Max Planck Institute for Biochemistry in Germany before earning a Ph.D. in plant biology from the University of California, Berkeley, in 1998.

Erickson worked as a bioeducation scientist in California, until she and her husband moved to Maryland. For several years, she was a stay-at-home mother and ran Patti's Handmade Chocolates. She joined the Salisbury faculty in 2008.

In her lab, Erickson investigated responses to oxidative stress, including whether nordihydroguaiaretic acid, a lipid-soluble compound with antioxidant properties, protects the creosote bush from environmental stresses or inhibits germination of competing plants. The lab also used RNA interference to knock down target genes in Caenorhabditis elegans and to test for altered oxidative stress responses.

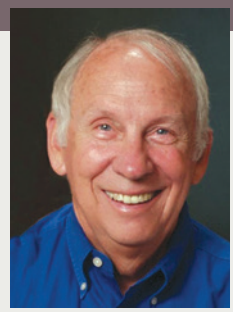
Erickson often mentored SU students in collaboration with colleagues at George Washington University and the J. Craig Venter Institute, where she did genomics research during a sabbatical year. She took groups to national scientific conferences where, according to an obituary, she excelled in getting her students to meet and take selfies with Nobel laureates.

As SU chapter adviser, Erickson used a Student Chapters Outreach Grant to bring elementary school students to the university, where they did experiments and toured the science facilities, and she also helped chapter members organize science activities for children at local libraries.

Erickson's parents created a scholarship fund at Salisbury to support students who are dedicated to the pursuit and application of knowledge in the biological sciences.

She is survived by her husband, Les Erickson, and son, Spencer, as well as her parents, a brother, and a sister.

Ronald C. Reitz



Ronald Charles Reitz, an emeritus professor at the University of Nevada who studied cancer as a part of his research, died Dec. 20 at the age of 82 after a yearlong battle with cancer. He had been a member of ASBMB since 1976.

Reitz was born on Feb. 27, 1939, in Dallas and grew up in the small Texas city of Pittsburg. During high school, he achieved Eagle Scout, the highest rank in the Boy Scouts of America. He went to Texas A&M University to obtain his undergraduate degree in chemistry and then, in 1962, headed to Tulane University in New Orleans, where he received his Ph.D. in biochemistry in 1966 under the tutelage of James G. Hamilton.

In New Orleans, Reitz met his wife, Jeanne Geiger, a mathematics educator. After they married, he moved to the University of Michigan as a postdoctoral fellow in biological chemistry under the mentorship of William E.M. Lands, a nutritional biochemist and a pioneer in fatty acid research.

In 1969, Reitz was hired as an assistant professor of biochemistry at the University of North Carolina. He moved to Reno in 1975 to be a full-time professor at the University of Nevada, and he held that position till 2001, saying, "It was the best decision I ever made," according to an obituary in the Reno Gazette Journal. He was also a visiting research professor at Nagoya City University, Japan, and the Max Planck Institute for Biophysical Chemistry, Germany.

During his 30 years as a professor of biochemistry, Reitz carried out a detailed study to understand the mechanism of hydrocarbon biosynthesis from aldehyde in selected insect species. He also studied the effects of different phospholipids and fatty acids on tumor growth and their efficacy as antitumor agents. He had expertise in enzymology, lipid metabolism and metabolic diseases. Over the course of his career, he published his work in 70 peer-reviewed journals with 2,274 citations.

Reitz is remembered by family and friends as kind and soft-spoken and by students for the wisdom and guidance that helped them flourish. He loved to spend weekends doing outdoor activities such as camping, hiking and golfing.

He is survived by his wife, Jeanne Geiger Reitz; his two children, Brett Reitz and Erica Reitz Yahn; his brother, Robert, and sister, Sharon; and his four grandchildren.

— Swarnali Roy

James Bryant Howard (1942–2022)

By Douglas C. Rees

James Bryant Howard, professor emeritus of biochemistry at the University of Minnesota School of Medicine, died unexpectedly on Feb. 13 in Cochiti Lake, New Mexico. He was 79.

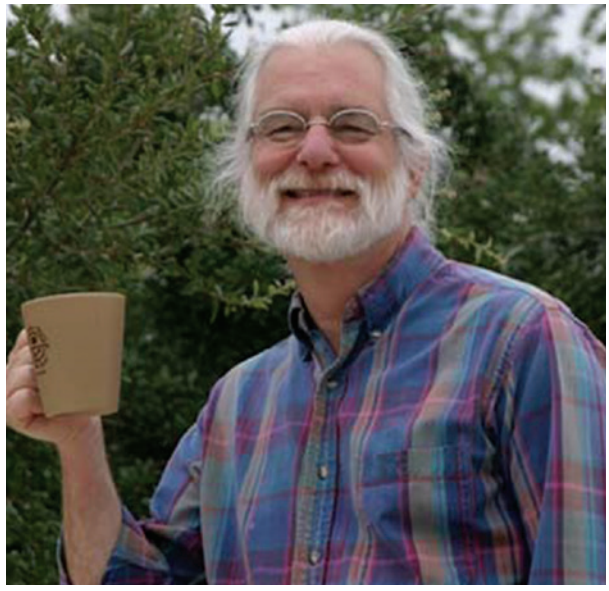
Howard had been a member of the American Society for Biochemistry and Molecular Biology for more than 40 years, and he served on the Journal of Biological Chemistry editorial board from 1986 to 1991.

Born April 25, 1942, in Indianapolis, Howard completed his Bachelor of Arts in chemistry at DePauw University in 1964 before heading west to graduate school at the University of California, Los Angeles. He received his Ph.D. in biological chemistry at UCLA in 1968 as one of Alex Glazer's first graduate students. Howard often said that the exciting environment for biochemistry at UCLA catalyzed his lifelong passion for protein chemistry, structure and function.

After a postdoctoral position with Fred Carpenter at UC Berkeley, Howard joined the biochemistry faculty at the University of Minnesota School of Medicine in 1971, where he remained until becoming emeritus in 2002. Among his notable research accomplishments were his identification of the modified histidine in EF-2 that is the target of ADP-ribosylation by diphtheria toxin (with James Bodley); discovery of the alkylamine-sensitive thioester linkage in the active site of the alpha2-macroglobulin; and a broad series of studies on the nitrogenase proteins, including determining the Azotobacter vinelandii nitrogenase iron protein sequence, identifying the [4Fe-4S] cluster ligands, and characterizing cluster chelation and interconversion reactions.

A great believer in the importance of sabbaticals, Howard arranged to visit the Massachusetts Institute of Technology, Harvard, UC Davis and the National Institutes of Health through this mechanism. I first met him while he was on sabbatical with William Lipscomb at Harvard in 1980 – 81 to crystallize the nitrogenase iron protein. He convinced me of the significance of a structural approach to the study of nitrogenase that, beginning with my postdoc, started a 40-plus year collaboration.

Over the past two decades — until COVID-19 — this collaboration included annual visits by Jim Howard and his wife, Claralyn, to Pasadena, where I work at the California Institute of Technology. Beyond nitrogenase,



Howard had a strong interest in geobiology and interacted extensively with the Caltech community in this area. After he became emeritus, the Howards moved to New Mexico, and his research interests included isolation and characterization of nitrogen-fixing autotrophs in his home lab from the year-round seeps in the surrounding mesas.

Howard was a true natural philosopher; he loved designing experiments, going over results, attending seminars and discussing what it meant to prove a result. His curiosity was infectious. He focused on the details of experimental design and enjoyed discussing with students and postdocs how to quantitate protein concentration accurately, the temperature dependence of pH and the importance of ionic strength effects — topics that typically are considered trivial but can have disastrous consequences if overlooked. A natural skeptic, Howard had a high bar for being convinced, and there was no bigger satisfaction than getting with him to that point. Beyond science, he read extensively and loved jazz and art, cycling and sailing, and the outdoors. He was a keen student of academia and the bigger issues of life and society.

Our thoughts go to Claralyn Howard; their daughter, Cathy, and her husband, Tony Grundhauser; granddaughters Emma and Lucy; and Jim's sister Aleta Howard at this difficult time.

Douglas C. Rees (dcrees@caltech.edu) is a professor of chemistry and a Howard Hughes Medical Institute investigator at the California Institute of Technology.

ASBMB names 2023 award winners

They will give lectures at Discover BMB in March in Seattle

By ASBMB Today Staff

The American Society for Biochemistry and Molecular Biology announced today the winners of its annual awards. Colleagues and other leaders in the field nominated the winners for making significant contributions to biochemistry and molecular biology and to the training of emerging scientists.

The recipients will give talks about their work at the society's 2023 annual meeting, Discover BMB, slated for March 25–28 in Seattle.

In addition to cash prizes ranging from $500 to $35,000, each ASBMB award consists of a plaque and transportation expenses to the ASBMB annual meeting.

ASBMB Award for Exemplary Contributions to Education

Recognizes an individual who encourages effective teaching and learning of biochemistry and molecular biology.

Regina Stevens–Truss is a professor at Kalamazoo College who has served in numerous leadership positions at the ASBMB. She has been a member of the society's Education and Professional Development Committee and Minority Affairs Committee (now Maximizing Access Committee). She is a past member of the steering committee that created the concept-driven teaching strategies that laid the foundation for ASBMB's certification exam. She was the principal investigator in 2012 on a National Science Foundation grant that supported a STEM K–12 outreach initiative by the society called Hands-on Outreach to Promote Engagement in Science (HOPES for short).

ASBMB–Merck Award

Recognizes outstanding contributions to research in biochemistry and molecular biology.

Squire J. Booker is an Evan Pugh professor of chemistry and of biochemistry and molecular biology and the Eberly Family distinguished chair in science at The Pennsylvania State University. He is also an investigator of the Howard Hughes Medical Institute. His lab studies catalytic mechanisms of redox enzymes involved in natural product biosynthesis and human health. He is deputy editor of ACS Bio & Med Chem Au, an open-access journal of the American Chemical Society, and an executive associate editor of the ACS journal Biochemistry. He became an inaugural fellow of the ASBMB in 2021. He also won this year's Ruth Kirschstein Diversity in Science Award. (See below.)

Avanti Award in Lipids

Recognizes outstanding research contributions in the area of lipids.

Russell DeBose–Boyd is the Beatrice and Miguel Elias distinguished chair in biomedical science and professor of molecular genetics at the University of Texas Southwestern Medical Center at Dallas. DeBose–Boyd's lab studies regulatory mechanisms governing feedback regulation of HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis. He is an associate editor for the Journal of Lipid Research and an editorial board member for the Journal of Biological Chemistry, both ASBMB journals. Read our Q&A with DeBose–Boyd.

Bert & Natalie Vallee Award in Biomedical Science

Awarded to an established scientist for outstanding accomplishments in basic biomedical research.

Erica Ollmann Saphire is a professor and the president and chief executive officer of the La Jolla Institute for Immunology. Saphire's lab has solved structures of key proteins of the Ebola, Marburg, rabies and Lassa viruses, explained how they remodel these structures as they drive themselves into cells, how their proteins suppress immune function and where human antibodies can defeat these viruses. She used this information to galvanize two international consortia of former competitors to advance antibody therapeutics together. Saphire is a two-time ASBMB award winner. In 2015, she won the ASBMB Young Investigator Award.

Delano Award for Computational Biosciences

Given to a scientist for the most accessible and innovative development or application of computer technology to enhance research in the life sciences at the molecular level.

Eytan Ruppin is a computational biologist and chief of the Cancer and Data Science Laboratory in the Center for Cancer Research at the National Cancer Institute. His lab develops computational approaches for the integration of multiomics data to better understand the pathogenesis and treatment of cancer. His research is focused on basic and translational studies aimed at broadening the scope of precision oncology to the realm of the tumor transcriptomics.

Earl and Thressa Stadtman Young Scholar Award

Awarded to a scientist with 10 years or less of post-postdoctoral experience.

Scott Dixon is an associate professor in the biology department at Stanford University. His lab studies cell death and lipid metabolism using small molecule screening, biochemical analysis of protein function, and model organism genetics. Dixon is a member of the program planning committee for Discover BMB, the society's annual meeting.

Herbert Tabor Research Award

Given for excellence in biological chemistry and molecular biology and contributions to the community of scientists.

Ajit Varki is a physician-scientist and distinguished professor at the UC San Diego School of Medicine. His lab studies roles of sialic acids in biology, evolution and disease, with a particular emphasis on uniquely human features. Of his nearly 500 publications, one-sixth are in the Journal of Biological Chemistry. He is also recognized for creating the first major open-access research journal, the Journal of Clinical Investigation (1996), and first major open-access textbook, "Essentials of Glycobiology" (2008). He's an elected member of both the American Academy of Arts & Sciences and the National Academy of Medicine and winner of the Rosalind Kornfeld Award for Lifetime Achievement in Glycobiology (2020).

Mildred Cohn Award in Biological Chemistry

Recognizes and honors scientists at all stages of their careers who have made substantial advances in understanding biological chemistry using innovative physical approaches.

Anne Kenworthy is a professor of molecular physiology and biological physics at the University of Virginia and the assistant director of its Center for Membrane and Cell Physiology. Her lab studies membrane nanodomains, such as lipid rafts and caveolae, to learn how they assemble and function in health and disease. Together with collaborators at the University of Michigan and Vanderbilt University, her group also recently provided the first glimpse into molecular architecture of an essential building block of caveolae — oligomeric complexes formed by the membrane protein caveolin-1.

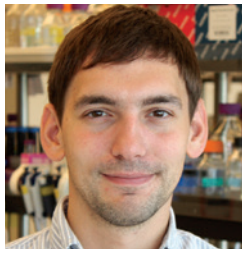
Ruth Kirschstein Diversity in Science Award

Honors an outstanding scientist who has shown a strong commitment to the encouragement of scientists from historically marginalized groups.

This is the second award this year for **Squire J. Booker,** a professor and distinguished chair at The Pennsylvania State University. (See the ASBMB–Merck Award above.) Booker is a past chair of the ASBMB's Minority Affairs Committee and established the ASBMB grant-writing workshop, which is now known as the Interactive Mentoring Activities for Grantsmanship Enhancement workshop. He also co-organized the 2016 ASBMB annual meeting. He now serves on the Finance and Nominating committees.

Walter A. Shaw Young Investigator Award in Lipid Research

Recognizes outstanding research contributions in the area of lipids by a young investigator.



Itay Budin is an assistant professor of chemistry and biochemistry at the University of California San Diego. His laboratory approaches ranging from membrane biophysics to synthetic biology to investigate lipid function. Current areas of focus in his lab include the inner mitochondrial membrane and lipid adaptation for life in extreme conditions. In 2017, Budin received a Journal of Biological Chemistry/Herbert Tabor Young Investigator Award.

William C. Rose Award

Recognizes outstanding contributions to biochemical and molecular biological research and a demonstrated commitment to the training of younger scientists.

Catherine Drennan is a professor at the Massachusetts Institute of Technology and a Howard Hughes Medical Institute investigator. Drennan's lab studies the structural biology of metalloenzymes. Her team's targets have included multiple enzymes that depend on metal cofactors, such as ribonucleotide reductase, an early enzyme in DNA biosynthesis. She is a former member of the ASBMB Education and Professional Development Committee. As a postdoctoral fellow, she started the undergraduate poster competition at the ASBMB's annual meeting. Her pedagogical work includes research into best practices for active lectures and the development of resources that help undergraduates appreciate the value of chemical principles in biology and medicine. She was a member of the ASBMB's inaugural class of fellows in 2021.

ASBMB Early-Career Leadership Award

Recognizes individuals with a strong commitment to advancing the careers of women in biochemistry and molecular biology along with demonstrated excellence in research and/or service.

Gira Bhabha is an assistant professor at the NYU Grossman School of Medicine, where she began her independent career in 2017. The Bhabha lab works closely with the lab of Damian Ekiert; since their inception, the two labs have functioned synergistically as a single group. The Bhabha/Ekiert

labs study structural mechanisms and cell biology of microbes and their interactions with hosts, using integrative approaches including X-ray crystallography, cryo-electron microscopy, cryo-electron tomography, optical microscopy, biochemistry, microbiology and cell biology techniques.

ASBMB Mid-Career Leadership Award

Recognizes individuals with a strong commitment to advancing the careers of women in biochemistry and molecular biology along with demonstrated excellence in research and/or service.

Kerry-Anne Rye is a professor at the University of New South Wales in Sydney and co-editor-in-chief of ASBMB's Journal of Lipid Research. Before taking the helm at JLR in 2020, she was an associate editor since 2008. She has been a research professor since 2013 at UNSW, where she serves as the deputy head of the School of Medical Sciences and studies atherosclerosis and diabetes. Rye was a member of the inaugural class of ASBMB fellows in 2021.

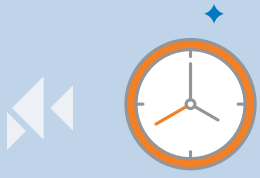
Alice and C.C. Wang Award in Molecular Parasitology

Recognizes established investigators who are making seminal contributions to the field of molecular parasitology.

Dyann Wirth is a professor at Harvard University's T.H. Chan School of Public Health and the Broad Institute. Her lab studies the Plasmodium genus, members of which commonly infect humans with malaria. Her team is working on methods for molecular genetic manipulation of protozoan parasites to analyze genes important for their virulence and resistance to drugs.

Keith Matthews is a professor at the University of Edinburgh. His laboratory studies African trypanosomes, parasites spread by the tsetse fly, and the changes they undergo in the fly using targeted reverse genetic approaches, global RNA and protein analysis and other strategies.

Upcoming ASBMB events and deadlines



SEPTEMBER

8	Discover BMB abstract and travel award submission site opens
15	ASBMB accreditation applications due
19	Discover BMB registration site opens
28–Oct. 2	**Epigenetic and genome stability conference**
29–Oct. 2	**Transcriptional regulation and RNA Pol II conference**

OCTOBER

1	Student Chapter Outreach Grant fall deadline
15	Discover BMB early-decision abstract submission deadline

NOVEMBER

1	Discover BMB early-decision abstract notification sent to authors
2	**ASBMB Virtual Career Expo**
30	Discover BMB on-time abstract and travel award application submission deadline

2022 ASBMB election results

Members of the American Society for Biochemistry and Molecular Biology have elected several new leaders. Three members of the Council were re-elected. There's a new secretary. And both the Nominating Committee and the Publications Committee have new members.

Council

The ASBMB Council serves as an advisory board to the president and the executive director for setting priorities and strategic directions, overseeing resource allocations, and ensuring that all activities align with the mission of the society. Councilors are elected for three-year terms and can be re-elected or reappointed to serve one additional term. Three incumbents were re-elected to the Council.

Suzanne Barbour is a professor and dean of the Graduate School at the University of North Carolina at Chapel Hill. She wrote in her candidate statement: "I am particularly intrigued by an opportunity that was discussed at a recent Council meeting: pursuing philanthropic support for the ASBMB. My experience as a dean, working with alumni, friends and prospective donors, will be helpful for this effort." Barbour is a former member of the Minority Affairs Committee (now the Maximizing Access Committee), has organized annual meeting symposia and was honored as a member of the first class of ASBMB fellows in 2021.

Joan Broderick is a professor and department head at Montana State University. In 2022, she was elected to the National Academy of Sciences. Before coming to Montana State in 2005, she was on the faculty of a small liberal arts college and a research-intensive state university. "This range of experiences has given me a broad perspective on science education and academic research — and the intersection of the two," she wrote.

Matthew Gentry is a professor at the University of Kentucky. He has served on the society's Membership Committee, Public Affairs Advisory Committee and Journal of Biological Chemistry editorial board. For this term on the Council, he has prioritized sharing with members "how to utilize their passions to serve on an ASBMB committee," recruiting the society's next executive director, serving as a resource and adviser to President Ann Stock, and spreading the word about how the ASBMB can help biochemists at all career stages.

Nominating Committee

The Nominating Committee nominates regular members of the society to stand for election for president, the Council, the Publications Committee and the Nominating Committee. Committee members are elected for three-year terms and can be re-elected or reappointed to serve one additional term. ASBMB members elected two new committee members this year.

Juan L. Mendoza is an assistant professor at the University of Chicago. He twice has co-chaired the Enzyme Interest Group at the ASBMB annual meeting and is an active advocate for diversity and inclusion. "I am passionate about making education in STEM accessible to everyone and inspiring future generations of scientists. For me, this includes active participation in community outreach and societies such as the ASBMB," he wrote.

Jeremy Thorner is a distinguished professor emeritus at the University of California, Berkeley. He won the ASBMB's Herb Tabor Research Award in 2019. "The many activities of ASBMB are best achieved by ensuring gender equity and diversity in its advisory bodies and leadership, as well as in its general membership," he wrote. "To thrive, our organization needs to be inclusive, and to hear from and recruit diverse voices. Hence, the most important function of the Nominating Committee is to make certain we draw on the rich pool of our membership and secure the participation of individuals from all quarters of the biochemical sciences."

Secretary

The secretary is responsible for reviewing the minutes of the society, serving on the Nominating Committee and the audit task force, and completing other duties as assigned by the Council, which may include certifying Council resolutions to support the operations of the society. The secretary is a voting member of Council and participates in the governance of the society. The secretary serves a three-year term.

George Carman is a distinguished professor at Rutgers University and director of the Rutgers Center for Lipid Research. He won the ASBMB's Avanti Award in Lipids in 2012, has been an associate editor for the society's Journal of Lipid Research and Journal of Biological Chemistry, and has served on the Council and several committees. He co-directs the society's Lipid Research Division. "The ASBMB has been a large part of my professional life since I joined the society in 1980," he wrote. "Throughout my career, I have profited from formal and informal mentors, and I am obliged to pay forward my knowledge and experiences to early-career scientists including undergraduate and graduate students, and postdoctoral associates." Carman was a member of the society's inaugural class of fellows in 2021.

Publications Committee

The Publications Committee oversees the society's scholarly publishing activities, advises the Council on policy and ethical issues that may arise, and advises journal editors about editorial matters, including the approval of associate editor appointments. Committee members are elected for five-year terms and can be re-elected or reappointed to serve one additional term. ASBMB members elected four new committee members.

Walid Houry is a professor at the University of Toronto. He's been a member of the Journal of Biological Chemistry editorial board since 2017. During his term on the committee, he intends to advocate for "innovative article review and publication formats." He wrote: "I find this to be especially important given the new and different article reviewing and publishing approaches being used by other journals."

Marcelo Kazanietz is a professor at the University of Pennsylvania. He has been an editorial board member for the Journal of Biological Chemistry and several other peer-reviewed publications. "I understand emerging challenges to keep disseminating our scientific discoveries in a highly competitive environment. I aim to support efforts toward facilitating communication between editors, authors and readers, with the ultimate goal of promoting high-impact science while affirming strong ethical publishing values," he wrote.

Daniel Leahy is a professor at University of Texas at Austin. He served on the ASBMB Council from 2012 to 2015, has helped organize meeting themes and other society events, and is a member of the society's 2022 class of fellows. "Chief among the jewels in the ASBMB crown are its publications, which are run by scientists for scientists, and I am delighted at the opportunity to help continue the ASBMB's tradition of excellent publications as modes of scientific communication continue to evolve," he wrote.

Anne-Frances Miller is a distinguished professor at the University of Kentucky. She has been a member of the Journal of Biological Chemistry editorial board and a member of the Publications Committee before. "I understand that publications are central to both the professional conduct of science and also its social fabric," she wrote. "I am a big admirer of how ASBMB's publications have spanned both spheres via the several journals the society produces. ASBMB Today nurtures networks of people and interest and keeps the science fun, engaging us all beyond the boundaries of our own specializations and keeping the best of our humanity connected to the best of our science. Meanwhile, ASBMB's established research journals provide critical channels for sharing high-quality scientific progress, complete with the assurances of expert peer review."

2022 PROLAB winners named

By Angela Hopp

Ten early-career scientists will receive grants this year from the Promoting Research Opportunities for Latin American Biochemists program, which will allow them to advance their research by working in the labs of collaborators abroad.

Since 2012, the American Society for Biochemistry and Molecular Biology, the Pan-American Society for Biochemistry and Molecular Biology, and the International Union for Biochemistry and Molecular Biology have given 93 biochemists these travel awards. The program supports travel and other expenses related to temporarily relocating to the U.S., Canada and Spain.

This year's PROLAB travel grants are going to Ph.D. students and postdoctoral fellows from Argentina, Brazil and Uruguay.

The 2022 recipients are:

Delfina L. Borús

Project title: Gene expression regulation by FABP1 in enterocytes

Delfina L. Borús is pursuing a doctoral degree in biological sciences at the National University of La Plata in Argentina. Her thesis work focuses on the transcriptomic role of fatty acid binding protein 1, and she'll be working in the lab of Judith Storch at Rutgers University. Borús' adviser is Natalia Scaglia in the lab of Betina Córsico, which has collaborated with the Storch lab for more than two decades. "This trip is an amazing opportunity for my doctoral thesis work as Dr. Storch has a distinctive knockout mouse model. I'll be able to learn cutting-edge techniques along with helping me improve my skills at the lab," Borús said. "This is going to be for sure a life-changing experience."

Karina Flores Montero

Project title: Analysis of cysteine string protein beta (CSPβ) binding to membrane by biophysical tools

Karina Flores Montero is working on her doctorate at the Histology and Embryology Institute of Mendoza at National University of Cuyo in Argentina. She is pursuing a thesis about the assembly of complexes of SNAREs in sperm under the direction of adviser M. Celeste Ruete. Flores Montero will work in the lab of Josep Rizo at the University of Texas Southwestern Medical Center at Dallas. The Rizo lab has extensive experience with biophysical techniques and membrane-reconstitution approaches. "For me, this award means a great opportunity to grow in my academic career, since I will work in one of the most renowned laboratories in my area of research. Also, this training will allow the quality and impact of my research to be greatly improved," Flores Montero said.

Sabrina A. Foscaldi

Project title: Rhizobium leguminosarum's biological response to light — Transcriptomic analysis induced by bacteriophytochrome

Sabrina A. Foscaldi is a postdoctoral fellow in the lab of Fernando Goldbaum at the Leloir Institute Foundation in Argentina. During the first part of her postdoc, Foscaldi worked on a project focused on the structure of a bacteriophytochrome photoreceptor from the phytopathogen Xanthomonas campestris. She's now working on a related photoreceptor in Rhizobium leguminosarum, a symbiotic bacterium that fixes atmospheric nitrogen. Foscaldi will visit California State University, Fullerton, to work in the lab of María Soledad Ramirez, which studies molecular mechanisms of antibiotic resistance in prokaryotes and has expertise in bacterial transcriptomic analysis. "The visit will contribute to my research on the bacteriophytochrome-mediated signaling pathway of Rhizobium leguminosarum. Through this grant, we expect to detect differentially expressed genes from light- and bacteriophytochrome-dependent transcriptomic analysis through RNA sequencing —RNA-Seq," Foscaldi said. "This travel grant will allow me to learn about this technology and is a valuable support to my research and professional growth. I'm very grateful for this opportunity."

Joaquin Garat

Project title: Optimization of single-cell Ribo-Seq approaches to study protein synthesis regulation in Alzheimer's disease models

Joaquin Garat is a Ph.D. student studying ribosomal protein coding gene expression in the nervous system at the Instituto de Investigaciones Biológicas Clemente Estable. Garat is in the lab of Jose Sotelo, which has been collaborating with George Bloom at the University of Virginia for several years on a study of Alzheimer's disease's effects on protein synthesis. Garat will extend that work in the Bloom lab. "This opportunity will allow me to work with excellent investigators and to use transgenic animal models that are not available in my country," Garat said. "During my stay, we plan to work on single-cell Ribo-seq protocols in collaboration with Guillermo Eastman, a postdoc at Bloom's lab, that will allow the study of translation regulation heterogeneity between different cell types in health and disease."

Geovana S. Garcia

Project title: The biochemical basis of the growth induced by the xenotopic expression of the mitochondrial alternative oxidase in Drosophila larva

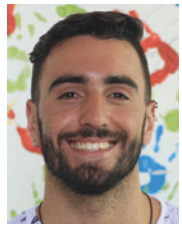
Geovana S. Garcia is a Ph.D. candidate at São Paulo State University's Jaboticabal campus in Brazil. She's working on a thesis about mitochondrial alternative oxidase expression in Drosophila in the lab of Marcos T. Oliveira, with whom Garcia first began working as an undergrad. Garcia will be hosted by Jason Tennessen's lab at Indiana University Bloomington. The lab uses the fruit fly to study metabolism, physiology and development. "My research proposal aims to evaluate how the xenotopic expression of mitochondrial alternative oxidase — AOX, an enzyme with therapeutic potential — modulates larval growth in a metabolic level," Garcia said. "In Tennessen's lab, I will have technology available to quantify key metabolites and hormones in diverse larvae expressing AOX, aggregating our understanding of larval growth and metabolic basis of tumors. I will have the opportunity to work in the same building as Bloomington Drosophila Stock Center, one of the largest providers of stocks for fly research in the world. My academic career will be incredibly impacted by this opportunity."

Bruno Hernández Cravero

Project title: Role of unsaturated fatty acids in alpha-synuclein aggregation in Caenorhabditis elegans

Bruno Hernández Cravero is pursuing a doctorate in the lab of Diego de Mendoza at the Institute of Molecular Biology of Rosario in Argentina. He will visit Luisa Cochella's laboratory at the Johns Hopkins School of Medicine, where he plans to establish mutant and transgenic strains of C. elegans to study polyunsaturated fatty acids' role in alpha-synuclein aggregation. "Parkinson's disease is a neurodegenerative disease of humans. Leveraging the easy genetic manipulation of C. elegans and the expertise at Cochella's lab, I'm going to use CRISPR–Cas9 technique to build a worm that mimics Parkinson's disease," H. Cravero said. "CRISPR–Cas9 technique has been highly developed, and its applications are extremely varied. I am very grateful to the ASBMB for giving me this award, as I am very happy and excited to learn this technique and then be able to apply it."

Horacio Martín Pallarés



Project title: Zika virus infection modulates translation of cellular antiviral factors

Horacio Martín Pallarés is a Ph.D. student at the Leloir Institute Foundation in Argentina. He's studying the mechanisms of Zika virus replication and viral immune system evasion processes in the lab of Andrea Gamarnik. Zika virus belongs to the Flaviviridae family, which includes a large number of emerging and re-emerging human pathogens that cause fever and encephalitis, such as West Nile virus, Japanese encephalitis virus and dengue virus. A Zika outbreak in the Americas and its suspected link to microcephaly put this virus at the forefront of an international research effort to understand its replication strategies and pathogenesis. Pallarés will spend time in the lab of Ariel Bazzini at the Stowers Institute for Medical Research. While in Kansas City, Missouri, he plans to use ribosome profiling and RNA sequencing to study how Zika virus regulates host gene expression. "I'm very excited about the PROLAB travel award. This is an invaluable opportunity for me! It will be crucial for my thesis project, and it will allow me to acquire

new skills in techniques that are poorly developed in Argentina," Pallarés said.

Haydé Saracho

Project title: Genetic and biochemical characterization of new defense systems in the genus Acinetobacter

Haydé Saracho is a Ph.D. student at Planta Piloto de Procesos Industriales Microbiológicos in Argentina. Her thesis is focused on identifying and characterizing plasmids using data of next-generation sequencing. Her thesis director and co-director are Daniel German Kurth and Julian Rafael Dib, respectively. Saracho will spend time in the lab of Mario F. Feldman at Washington University School of Medicine in St. Louis. The Feldman lab studies the Gram-negative bacterium Acinetobacter baumannii, which causes a variety of infections and has been classified by the World Health Organization as a top priority for therapeutics. In light of the emergence of drug- and phage-resistant strains, Saracho will work on characterizing new defense systems in sequenced genomes of the organism. "I want to express my gratitude to the program, which will allow me to travel to the laboratory of an experienced team to experimentally validate my predictions about the defense systems against phages of bacteria of the genus Acinetobacter. This could be the beginning of a longer collaboration between our laboratories," Saracho said. "The experience acquired will be essential to implement these techniques in our own laboratory. I believe that this award will be a milestone in my career and will improve my options for the future."

Juliana Topalian

Project title: Bacterial degradation of lignocellulose and fermentation of pentoses for cost-effective production of bioproducts

Juliana Topalian is working on her doctorate at the University of Buenos Aires in Argentina. She's studying how aerobic soil bacterial enzymes alter the structure of polysaccharides in lignocellulosic biomass — with an eye toward exploitation for various applications. Her thesis advisers are Eleonora Campos and Martin Blasco. Topalian will join the University of Georgia's Complex Carbohydrate Research Center to work in the lab of Breeanna Urbanowicz, which is focused on understanding the molecular pathways used by plants to synthesize complex polysaccharides. "I am grateful for this opportunity that will allow me to advance in my research, learn new techniques and gain experience in using equipment not available in my home lab. This will help me to expand our knowledge on structural polysaccharides and their degradation by lignocellulosic bacteria and strengthen the international collaboration between both laboratories," Topalian said. "I also believe this will be an extraordinary experience to grow not only professionally but also personally."

Harmonie Vallese Maurizi

Project title: Role of pigment epithelium-derived factor in the crosstalk between neurons and glial cells in the retina

Harmonie Vallese Maurizi is a Ph.D. student at the Universidad Nacional del Sur in Argentina. Her thesis is focused on apoptosis and neuronal regeneration. Her thesis director and co-director are Lorena German and Luis Politi, respectively. Vallese Maurizi will spend time at the National Eye Institute in Bethesda, Maryland. She'll be working with S. Patricia Becerra, who leads the agency's Section on Protein Structure and Function and whose group studies pigment epithelium-derived factor, or PEDF, in the retina. "Scientific research is very difficult in our country, due to the sparse funding resulting from the bad economic situation. Receiving this grant is an excellent opportunity to push forward my research career," Vallese Maurizi said. "I am so happy and grateful for having been selected for this award! It is a great contribution to my academic growth; it will allow me to get extensive hands-on training in new top-notch techniques in a highly qualified research laboratory — one of the most recognized on PEDF research."

Angela Hopp (ahopp@asbmb.org) is executive editor of ASBMB Today and communications director for the ASBMB. Follow her on Twitter: @angelahopp.

Springing from research to med school

By Inayah Entzminger

COURTESY OF ZOE FRIAS

Zoe Frias recently graduated from Arizona State University.

Zoe Frias fell in love with science in high school. She was not interested in any one subject, she said, until she started taking biology and chemistry classes.

"It was the first time where I truly felt like I was enjoying what I was learning in school," she said.

Frias recently graduated from Arizona State University, where she majored in biochemistry and biological sciences and served as co-president of the ASU American Society for Biochemistry and Molecular Biology Student Chapter. She has ambitions to become a physician, using her undergraduate research experience and scientific knowledge in a professional journey that includes medical school.

As an undergrad, Frias was eager to get involved in research. Her undergraduate honors thesis was based on her work in an environmental biotechnology lab that uses hollow-fiber membranes for carbon dioxide delivery to algae for biofuel production.

Despite her success with this research, Frias wants to move on. She has taken the Medical College Admission Test and applied to medical school. "I can't imagine myself going into any other field," she said. "It combines all the things I enjoy about science while also best serving the needs of others."

Frias joined the ASU ASBMB Student Chapter because she was looking for ways to get involved on campus. It fit with her interests not only because of her major but also because the chapter provided a way to hear about research opportunities and meet students with similar interests.

However, she said the organization of the Student Chapter had some drawbacks. The chapter is located at the ASU West campus, and Frias is enrolled at the Tempe campus, about 25 miles away. In-person club activities require travel by car, which not every student can afford in money or time. In her leadership role, Frias worked to transition the club to a campuswide organization.

"One positive of the pandemic was making club activities be online, especially with Zoom meetings," she said.

During the COVID-19 pandemic, the chapter was able to invite guest speakers such as researchers and faculty members, hold meetings and celebrate holidays with student members — all without requiring that anyone travel to a distant campus.

In anticipation of returning to in-person activities, Frias led the effort to spread the word about the ASBMB Student Chapter at ASU. Chapter leaders send announcements through the ASU Honors College newsletter email and invite professors to share information about the chapter with their students.

Before she graduated, Frias wanted to leave the Student Chapter strong with new members and catering to a variety of interests.

"We want to know what our club members are looking for so we can plan our activities accordingly," she said. "The most important thing in a club is knowing what your members want."

Inayah Entzminger (ientzminger@gradcenter.cuny.edu) is a doctoral student at the City University of New York Graduate Center, researching the positive RNA strand barley yellow dwarf virus.

Start or renew an ASBMB Student Chapter

The ASBMB Student Chapters program is a national network of more than 100 chapters representing more than 2,000 undergraduate students and faculty members dedicated to the advancement of research, education and science outreach.

Learn more at: asbmb.org/education/student-chapters

ASBMB
American Society for Biochemistry and Molecular Biology

CALL FOR SUBMISSIONS

The wellness issue — January 2023

2022 has been a wild ride. What have you done to stay on balance?

Have you started a new practice to care for your body, mind or spirit? Do you have newfound appreciation for longtime healthy habits?

Whatever you do for wellness, we want to read about it.

Need more information? Email questions to asbmbtoday@asbmb.org

To send us your submission, go to asbmb.org/asbmbtoday and click 'Submit' at the top of the page.

DEADLINE: SEPT. 20

ASBMBTODAY

Understanding protein dynamics to design better drugs

By Ankita Arora

COURTESY OF DENISE OKAFOR

Denise Okafor is an assistant professor at Pennsylvania State University.

When she was a child, C. Denise Okafor was fond of science. She decided she wanted to be a doctor, because that was the only science career she knew. In her third undergraduate year, as she went from class to class to fulfill her pre-med requirements, a few teachers suggested she consider applying to the Research Experiences for Undergraduates, or REU, program. And that changed the course of her life.

Okafor learned what scientific research meant and how it's used to answer questions about the world we live in. Her teachers explained that she would go to a bigger research school for 10 weeks in the summer and do meaningful work on ongoing research projects.

"I didn't know what research was," Okafor said. "But it sounded like a great adventure."

Now an assistant professor of biochemistry and molecular biology at Pennsylvania State University and recipient of a National Science Foundation Faculty Early Career Development, or CAREER, award, Okafor said her professors were instrumental in helping her figure out the right path to follow — first by exposing her to available opportunities and then by encouraging her to apply to graduate school.

The winding road to a Ph.D.

As an REU fellow, Okafor worked on a computational project. She enjoyed the process of learning — the process of setting up the system for simulating, modeling and then analyzing results. After this experience, she knew she wanted to do computational work during her Ph.D.

"It was almost like a challenge to myself — I think it will be fun to try, so let's try it," she said.

Okafor pursued graduate studies at Georgia Institute of Technology doing computational research in a supportive environment, but even after two attempts, she was unable to pass her qualifying exams. She couldn't convince her committee that she had the potential to complete her degree.

"Graduate school was tough for me," Okafor said. "I had a lot of doubts, lot of questions whether if this is the right path for me, can I really be successful?"

She didn't advance to candidacy and ended up writing a master's thesis. But supportive professors encouraged her to pursue a doctoral degree even after failing the candidacy exam, and she found a different group for her Ph.D. work.

She advises students in a similar situation to find someone to talk to, someone who is experienced but doesn't have anything to lose or gain from the student's decision.

"Find the mentors early, cultivate those relationships, and go to them for an outside perspective," she said.

Okafor switched to an experimental lab, where her research was focused on the biochemistry of RNA — investigating RNA folding and function as mediated by divalent cations.

Understanding protein dynamics

Okafor's goal when she started her postdoctoral training was to teach at a primarily undergraduate institution. With that in mind, she applied to a teaching postdoc program funded by the National Institutes of Health

called the Institutional Research and Academic Career Development Awards.

The program is a partnership among research-intensive institutions and teaching-focused institutions that provides training to postdocs from historically marginalized groups with an aim to develop both research and teaching skills through workshops and teaching assignments. As a part of the program, Okafor taught at Morehouse and Spelman colleges, two historically Black colleges in Atlanta.

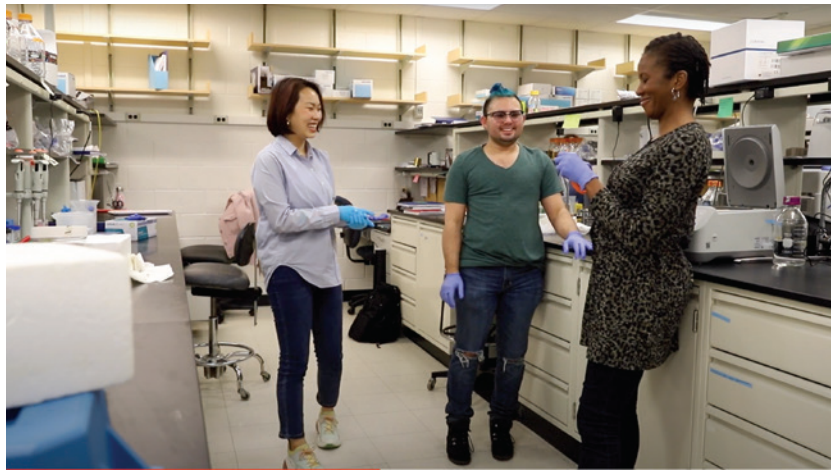
She joined Eric Ortlund's lab at Emory University, where she studied how gene expression is regulated by nuclear receptors — sensors that detect a ligand, a small binding molecule, and relay that message to DNA. While working on the project, she realized she enjoyed using molecular dynamics simulations to understand the properties of various ligands and how these ligands influence biological function.

"I saw the combination of computational and experimental investigations as an underutilized technique and wanted to jump into the unique field and pursue a research career," Okafor said.

In 2020, Okafor started her lab at Penn State to continue research in the field of nuclear receptors, focusing on the farnesoid X receptor, or FXR. This multidomain protein has a DNA-binding domain, which allows for turning on the gene, as well as a ligand-binding domain.

"We want to understand when a ligand binds to the ligand-binding domain how that affects the DNA-binding domain," Okafor said. "How are their functions linked to each other? And we want to decipher the mechanisms by which those are interacting."

The CAREER award provides five years of funding to support this project. Additionally, Okafor wants to host high school teachers in her lab over the summer so they can learn how to run a simulation of a protein, analyze it and make videos showing the protein's trajectory that their students will be able to understand.



COURTESY OF DENISE OKAFOR

Denise Okafor, right, chats with two members of her lab at Penn State. The group focuses on the famesoid X receptor.

"I want to introduce the idea of proteins as dynamic molecules that are constantly in motion into the high school curriculum in a very accessible way," Okafor said. "This gives them an early exposure to learning about the proteins the way they exist physiologically."

The path forward

"I'm here because I had really good mentoring and had some people advocating for me," Okafor said. "So, I'm very passionate about doing the same for others and paying it forward."

She advises trainees to seek peer-to-peer mentoring and form communities.

"If you don't see a community that you want, then you should start it because chances are very high that someone else is feeling like you," she said. "You're just a mass email away from getting it started."

Okafor is excited about starting a project on understanding Black women's health. Black women face many health disparities, especially related to fertility. One example is uterine fibroids. The progesterone receptor, one of the nuclear receptors, plays an important part in fibroid pathology.

"I'm very interested in working on the progesterone receptor and applying everything we learn from our work now to alleviate the symptoms," she said.

Ultimately, Okafor wants to apply her research on nuclear receptors to designing drugs with fewer side effects. Because these receptors are targets in diseases such as diabetes and various cancers, understanding how to design ligands that target them appropriately could have huge therapeutic impact.

"Most of the side effects are result of unintended genes being turned on," Okafor said, and she wants to understand how drugs can be made in a selective way to drive only desired outcomes.

Ankita Arora (ankita.arora@cuanschutz.edu) is a postdoctoral research fellow at the University of Colorado Anschutz Medical Campus. Follow her on Twitter: @arorankita.

ASBMB journals' metrics improve

Clarivate released a 2022 update to its Journal Citation Reports in late June. All three ASBMB journals — the Journal of Biological Chemistry, the Journal of Lipid Research, and Molecular & Cellular Proteomics — saw significant gains in their metrics, including impact factor and CiteScore.

	Impact Factor	CiteScore	Total Citations	Average time to first decision
JBC	5.486 (up from 5.157)	8.8 (up from 7.7)	392,757	17 days
JLR	6.676 (up from 5.922)	11.0 (up from 8.9)	29,128	10 days
MCP	7.381 (up from 5.911)	11.6 (up from 9.2)	21,766	34 days

ASBMB Today wins gold

ROSENCRANS

An essay published in ASBMB Today recently won a first-place EXCEL award from Association Media and Publishing in the category of editorial/opinion piece in a magazine.

The editors invited Robert Rosencrans, an M.D.–Ph.D. student in the Medical Scientist Training Program at the University of Alabama at Birmingham, to submit the essay, "Putting body weight in context," based on a Twitter thread, for the June/July 2021 Reimaging Issue of ASBMB Today.

"I didn't expect to start seeing the intersections of fatphobia with environmental racism or police violence," he wrote. "But once you start seeing the redundant harms larger people are exposed to, it's hard to stop."

The AMP EXCEL Awards, now in their 41st year, recognize excellence and leadership in media, publishing, marketing and communications for both nonprofit and for-profit associations. In previous years, ASBMB Today contributors honored for essays have included Kayunta Johnson–Winters, who won silver for "Being Black in the ivory tower" in 2021; TL Jordan, who won bronze for "What I wish people understood about being a trans scientist" in 2020; Byron Rubin, who won bronze for "Up the creek without a sequence?" in 2019; and Jennifer Dubois, who won gold for "Disappointed by cancer" in 2018.

Call for virtual scientific event proposals

The ASBMB provides members with a virtual platform to share scientific research and accomplishments and to discuss emerging topics and technologies with the BMB community. The society will manage the technical aspects, market the event to tens of thousands of contacts and present the digital event live to a remote audience. Additional tools such as polling, Q&A, breakout rooms and post-event Twitter chats may be used to facilitate maximum engagement.

Seminars are typically one to two hours long. A workshop or conference might be longer and even span several days.

Prospective organizers may submit proposals at any time. Decisions usually are made within four to six weeks.

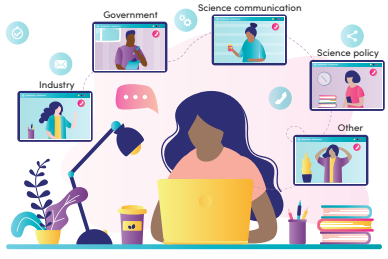
Propose an event at asbmb.org/meetings-events/propose-event/virtual-scientific-events.

Sept. 15 — ASBMB accreditation applications due

Since 2013, more than 100 bachelor's degree programs in BMB and related disciplines across 39 states have received accreditation from the American Society for Biochemistry and Molecular Biology. Accreditation provides a national, independent tool for evaluating program outcomes. By earning ASBMB accreditation, programs demonstrate a commitment to the highest standards of quality and innovation in BMB education. Applications for the next round of accreditation are due Sept. 15. Learn more at asbmb.org/education/accreditation.

Nov. 2 — The ASBMB Virtual Career Expo: Anything but Academia

The ASBMB Virtual Career Expo: Anything but Academia will highlight the diversity of career paths available to people with training in the biological sciences. No matter your career stage, you're invited to attend and explore career options and connect with knowledgeable professionals in different fields. Mark your calendars for 11 a.m. to 5 p.m. Eastern on Nov. 2. Learn more at asbmb.org/meetings.



Oct. 14 — Science outreach/ communication grant applications due

The ASBMB Science Outreach and Communication Committee offers five $1,000 grants to support public-engagement activities by society members. These activities may be conducted in person or in a hybrid or fully virtual format. All members are eligible to apply. Applications will be accepted from Aug. 17 through Oct. 14. Learn more at asbmb.org/soc-grant.

ASBMB gives $10K to internship program

The American Society for Biochemistry and Molecular Biology has contributed $10,000 to the National Institutes of Neurological Disorders and Stroke's Health Disparities in Tribal Communities Summer Internship Program, which provides brain and nervous system research experience and career development opportunities for undergraduate and graduate students. The 8- to 10-week program takes place on the NIH campus and exposes Native American and other traditionally underrepresented students to topics related to health disparities research in tribal communities.

The ASBMB's contribution to the Foundation for the National Institutes of Health will fund housing for program participants, helping remove an obstacle to participation and allowing them to gain research experience that will help in their future careers. This donation demonstrates the society's commitment to diversity, equity, accessibility and inclusion.

Staffing updates

Ken Farabaugh has been promoted to the position of science editor. Farabaugh has served as the ASBMB's developmental editor for the past year, and many of our authors may be familiar with his suggestions to achieve clarity in published research articles and Journal of Biological Chemistry Editor's Pick highlights. Prior to this, he worked as a freelance science editor on many successful manuscript submissions and grant applications. Farabaugh earned his bachelor's degree in molecular biology from Kenyon College and his Ph.D. in pharmacology from Case Western Reserve University in Cleveland, Ohio.

Deborah Martin joined the ASBMB as an accounting assistant in April. She holds a bachelor's degree from the University of the District of Columbia and has more than 10 years of experience in the field. She has held various accounts payable and receivable roles with several for-profit and nonprofit companies in the D.C. metro area.

Brittany Rhodes joined the ASBMB as an administrative assistant in April. She contributes to projects in the accounting, publications and communications departments. Rhodes earned her bachelor's degree in biology in 2020 from Northern Illinois University, where she focused on veterinary science. After graduation, she worked as a veterinary assistant/receptionist in Illinois.

ASBMB letter to the NIH Center for Scientific Review

The ASBMB public affairs staff wrote to the National Institutes of Health's Center for Scientific Review advisory council in April to comment on changes CSR is making to improve fellowship review. The society recommended that CSR eliminate grades as indicators of qualifications, allow an optional statement of special circumstances by applicants, and encourage a statement of qualifications that extends beyond grades and publications. Read this letter and others at asbmb.org/advocacy/letters.

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Gene level: $5,000

Single-conference sponsorship.

Benefits include your logo on the event webpage, printed program, thank-you slide and social media posts. Plus a banner ad in an event email and a full-page company ad in the printed program.

Codon level: $2,000

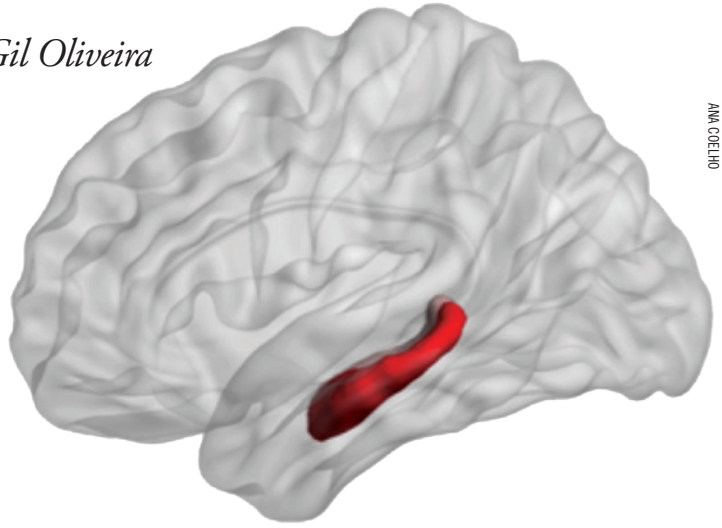
Single-conference sponsorship.

Benefits include your logo on the event program, webpage, slide and social media.

At every level, add-ons for follow-up emails, social media posts, poster prizes, conference bag inserts and travel awards are available.

Hippocampal lipids linked to brain disorders

By Luísa Santa–Marinha & Tiago Gil Oliveira



ANA COELHO

The hippocampus (shown in red) can be organized along its longitudinal axis, segregating two poles: the posterior and anterior (in humans) or the dorsal and ventral (in rodents).

The hippocampus is a fundamental brain region for memory processes, and its function is impaired early in the onset of neurodegenerative disorders such as Alzheimer's disease, or AD.

Most studies addressing the hippocampus have considered it as a whole structure, but it also can be divided into subregions along its longitudinal axis, segregating dorsal and ventral poles. For instance, the dorsal hippocampus, or DH, contributes differentially to specific dimensions of spatial memory, while the ventral hippocampus, or VH, is proposed to be implicated predominantly in behaviors linked to emotions.

Lipids are major brain constituents, so we performed mass spectrometry lipidomic analysis of hippocampal subregions along the longitudinal axis. Within the lipidomic signatures we uncovered, we observed that the DH presents increased levels of phosphatidic acid and decreased levels of phosphatidylcholine compared to the VH, potentially implicating the phospholipase D, or PLD, pathway in DH–VH axis regulation.

Although six PLDs are found in mammals, only PLD1 and PLD2 have reported canonical PLD activity, which is based on the hydrolysis of phosphatidylcholine in the presence of water to free choline and phosphatidic acid, a known second messenger signaling lipid. Using mice that were genetically altered to lack Pld1 and Pld2 genes, we gathered data to support the hypothesis that PLD1 and PLD2 are the only contributors to PLD activity in the mouse forebrain.

PLD1 ablation significantly decreased the hippocampal levels of phosphatidic acid, affecting predominantly the DH lipidome, but upon PLD2 ablation, only minor lipid changes occurred, including increased PLD products suggesting PLD1 upregulation.

Since PLD1 was the main PLD activity source, we then focused predominantly on characterizing the effects of PLD1 ablation and showed that the mice lacking Pld1 presented specific deficits in novel object recognition and social interaction, disruption in dendritic arborization, and altered synaptic plasticity in the DH. Overall, we determined that PLD1 ablation impairs hippocampal functioning, predominantly affecting the DH, which, due to its allocated functions, is predicted to be particularly affected in Alzheimer's disease.

We previously had observed that PLD2 ablation is protective in mice genetically altered to have Alzheimer's. Future studies should address cross-regulation mechanisms between PLD1 and PLD2 and how these can be used to develop therapeutic strategies to treat or prevent hippocampal dysfunction and memory deficits.

Luísa Santa–Marinha (id7078@alunos.uminho.pt) recently earned a Ph.D. in medicine and is now a postdoctoral researcher at the Life and Health Sciences Research Institute in the School of Medicine, University of Minho, and a psychiatry resident at Centro Hospitalar Vila Nova de Gaia/Espinho in Vila Nova de Gaia, Portugal. Follow her on Twitter: @LuisaSMarinha.

Tiago Gil Oliveira (tiago@med.uminho.pt) is an assistant professor at the Life and Health Sciences Research Institute in the School of Medicine, University of Minho, and a neuroradiologist at Hospital de Braga, both in Braga, Portugal. Follow him on Twitter: @TGO_lab.

A membrane ATPase without transporter activity

Guido Guidotti's laboratory and the search for CD39

By Laurel Oldach

NANCY KLECKNER

Guidotti teaching his Biochemistry of Membranes course at Harvard in 2020 just before the pandemic.

Had he been a trifle less modest, Guido Guidotti's name might have appeared on many more of the textbook membrane protein discoveries of the 20th century. Trainees in his lab at Harvard University unraveled the stoichiometry of the sodium-potassium ATPase; discovered that it, and a glucose transporter, are responsive to insulin; and explored cell signaling responses to other hormones, such as vasopressin. But Guidotti was loath to claim credit for research from his lab if he had not conducted experiments himself.

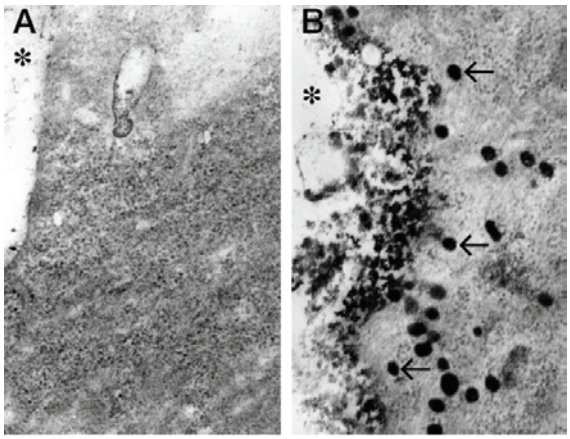
"There are many papers from Guido's lab where Guido's name is not in the author list," said former student Ting-Fang Wang, who is now a professor at Academia Sinica in Taiwan. It was only after a grant reviewer objected to his use of papers on which his name didn't appear as evidence of past progress that Guidotti began to sign all of the work published from his lab.

That's how Guidotti came to be the senior author on Wang's 1996 **Journal of Biological Chemistry** article, "CD39 is an ecto-(Ca^{2+},Mg^{2+})-apyrase." Guidotti and Wang combined clues from the literature with a detailed biochemical investigation of CD39 to demonstrate that the protein catalyzes the removal of a pyrophosphate group from ATP and that it exerts this activity outside of the cell rather than in the cytoplasm. Subsequent studies have found important roles for CD39 as a regulator of purinergic signaling in blood clotting, neuronal synapses, cancer and immunity.

Long road to CD39

Wang worked on a protein that had frustrated trainees for nearly a decade. Trainees in the lab, beginning with Sue-Hwa Lin, were working with a purified membrane protein that they initially expected might transport calcium out of cells to maintain a low intracellular concentration. Much like known calcium pumps, this enzyme cleaved ATP, and its activity increased when calcium or magnesium were present. But it was challenging to work with. It was embedded in the membrane, but all attempts to solubilize it led to activity loss. Several people had tried to clone the gene, according to Wang, but found that when they overexpressed what they thought was the right gene, it lacked activity. Despite these challenges, over time it became clear that there was no calcium transport activity. Instead, the protein simply converted ATP to AMP, cleaving a pyrophosphate group.

Guidotti was an avid late-night reader of scientific journals, according to his wife, molecular biologist Nancy Kleckner. Aware from his reading that potatoes seemed to have an ATPase similar to the mystery membrane protein the lab



KOZIAK ET AL. JBC 2000

In electron micrographs from a 2000 study of CD39 that Guidotti's group published in the Journal of Biological Chemistry, CD39 transfected into cells appears at membranes stained with a CD39 antibody (right) or for ATPase activity (left).

was investigating, Guidotti asked his student Mas Handa to purify the potato enzyme. After peeling many potatoes, Handa obtained an active enzyme and a partial peptide sequence. BLASTing the latter, they found that it was homologous to human CD39, a membrane protein expressed in B cells.

There was significant circumstantial evidence to suggest that CD39 was an extracellular ATPase when Wang picked up the project. Aware thanks to his immunologist wife that infection can induce CD39 expression, he incubated B cells infected with Epstein–Barr virus with radiolabeled ATP and observed much greater pyrophosphate cleavage than in uninfected cells. This was another clue that CD39 could be the enzyme they were looking for.

Because attempts to purify the protein had destroyed its enzymatic activity, Wang and Guidotti compared the ATPase activity in intact and lysed cells. The activities were the same, indicating that the active site was not sequestered in the cytoplasm but rather outward-facing. It also was unaffected by inhibitors of other well-characterized membrane ATPases, such as ion pumps.

Using degenerate primers matching the potato apyrase enzyme and a cDNA library from B cells, Wang isolated the CD39 gene. This enabled him to study transfected cells that, unlike EBV-infected B cells, differed only in the expression of CD39. This enabled a molecular demonstration that CD39 can cleave ATP, producing AMP. In a follow-up study, Wang, Guidotti and Yvonne Ou reported that interactions between the protein's transmembrane domains could enable formation of a tetramer with greater enzyme activity.

CD39 and purinergic signaling

Not long after the first JBC paper was published, Wang said, a Harvard lawyer called the lab to ask whether he wished to pursue a patent on CD39. Unsure of how to answer, he called Guidotti from his office next door to pick up the phone. "Without any doubt, he said, 'This is Harvard. This is a place for educating students and training young scientists. This is not a place for making money,'" Wang recalled.

Wang called that answer absolutely characteristic. Guidotti always refused to self-promote, he said, but "People respected him; people knew that's what he did. But in the real world, it's very hard for other people to copy this model."

The lawyer was correct to recognize the potential value of knowledge about CD39. Subsequent studies have shown that by regulating the extracellular balance between ATP and AMP — and providing a rate-limiting substrate for another enzyme to convert AMP to extracellular adenosine — the enzyme affects many physiological systems.

Another group found shortly afterward that CD39 embedded in vascular cells is important in blood clotting; ATP can be released during cell lysis, and CD39 determines whether ADP, which promotes platelet aggregation, can accumulate, or whether the ATP instead is metabolized to adenosine, which inhibits aggregation.

Meanwhile, Guidotti's lab also continued to study the activity of CD39 and the purines it regulates. They found CD39 expressed in neurons and astrocytes, where later studies indicate that the balance between extracellular ATP and adenosine is important for sleep–wake cycles.

Finally, in the immune system, extracellular ATP is interpreted as an inflammatory danger signal, while extracellular adenosine promotes immunosuppression. By converting ATP to AMP, which later is cleaved to adenosine, CD39 can modulate inflammation and the activity of cytotoxic cells. Today, several antibodies that allosterically inhibit CD39 are in late stages of clinical development for treatment of different cancers. Because extracellular ATP acts on numerous immune cells, boosting their activity, reducing CD39 activity can help enhance immune surveillance and clearance of tumor cells. There is also preclinical evidence that the inhibitors act synergistically with other types of immunotherapy, such as PD-1 inhibitors.

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter: @LaurelOld.

Partial agonist drug design for cannabinoid receptors

By Justin R. Lovett

G protein–coupled receptors, or GPCRs, are essential to signal transduction. The human genome encodes hundreds of GPCRs, which have been associated with diseases such as diabetes and cardiovascular abnormalities. Consequently, many GPCRs are drug targets.

Cannabinoid receptors are GPCRs expressed in our central and peripheral nervous systems as well as our immune system. Drugs targeting cannabinoid receptors 1 and 2, known as CB_1 and CB_2, initially showed great promise for the treatment of pain, obesity and inflammation but were removed from the market after they were shown to have adverse effects on patients. Researchers found that full agonists, which maximally activate the receptors when bound, were especially harmful. Therefore, many have turned their attention to the potential of partial agonists, which produce a smaller effect.

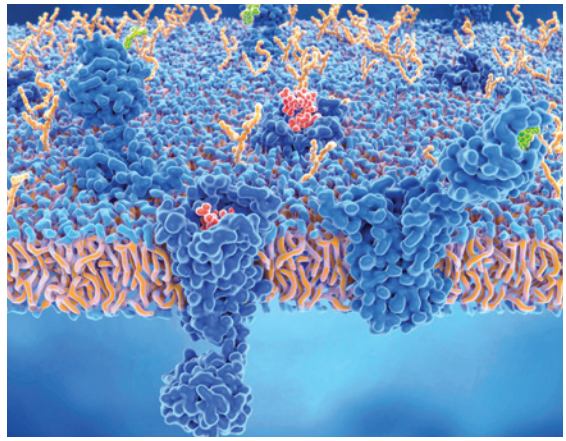
Delta-9-tetrahydrocannabinol, or Δ^9-THC, is the euphoric psychoactive compound in marijuana. Researchers have found that it acts as a partial agonist of CB_1 and has positive effects in the treatment of Parkinson's and other neurodegenerative diseases. However, the Food and Drug Administration still bans the sale of most THC products.

Soumajit Dutta, a Ph.D. candidate at the University of Illinois at Urbana–Champaign, uses molecular dynamic, or MD, simulations to study ligand interactions with CB_1 in hopes of understanding how full and partial agonists interact with the receptor. This could enable selective drug development targeting cannabinoid receptors. Combining his interests in computation and in mechanisms of allosteric modulation, Dutta and his team used computational analysis to understand why THC only partly activates CB_1. They recently published this research in the **Journal of Biological Chemistry**.

Using ligand and protein structures from the literature, Dutta performed unbiased molecular dynamics simulation with analysis by Markov state modeling to simulate the binding of THC to CB_1 in two poses, one that resembles agonist binding and one that resembles antagonist binding.

Full agonists of CB_1 "overstimulate the receptor, leading to negative side effects such as seizures or loss of motor function," Dutta said, because a full agonist fills the large binding pocket, overexciting the receptor. On the other hand, THC is small and does not occupy much space in the binding pocket, allowing mobility within the pocket in order to activate the receptor without overstimulating.

An essential component in the activation of the CB_1 receptor is called the toggle switch, a tryptophan residue located in the binding pocket. Dutta made the novel finding that Δ^9-THC had less interaction with the toggle switch residue within the active site pocket than a full agonist, which could explain why it works as only a partial agonist.



The opioid and cannabinoid receptors are involved in pain sensation, mood, appetite and memory. Agonists are potent analgesics: endorphin (red) and tetrahydrocannabinol (green).

This research provided essential information about the mechanism of Δ^9-THC binding to CB_1 and CB_2 so that drug developers can begin to design scaffolds to target CB_1 specifically. They hope such molecules will alleviate the negative side effects seen in early agonist cannabinoid receptor drugs. Meanwhile, Dutta plans to build on his research by looking at additional ligands in the database that also act as partial agonists on cannabinoid receptors.

Justin R. Lovett (justin.r.lovett@gmail.com) is a graduate student at Stephen F. Austin State University in Bidisha Sengupta's laboratory focusing on research in biophysical chemistry.

A target to prevent kidney injury by chemotherapy

By Aswathy N. Rai

Cis-diamminedichloroplatinum II, commonly known as cisplatin, is a chemotherapeutic agent used to treat various cancers. However, cisplatin-induced acute kidney injury, or AKI, can result from the uptake, metabolism and accumulation of cisplatin by proximal tubular epithelial cells in the kidney. The accumulation leads to apoptosis, vascular damage, necrosis, oxidative and endoplasmic reticulum stress, and inflammation.

Leah Siskind at the University of Louisville has been researching mechanisms to protect the kidney from off-target harmful effects of chemotherapeutics such as cisplatin. Her long-term research goal is to extend the life span of patients while preserving their quality of life.

"Many people don't realize that the side effects of chemotherapy are not limited to hair loss, diarrhea and nausea," Siskind said. "Kidney injury is one of the significant dose-limiting side effects of cisplatin. Therefore, we cannot use cisplatin at the dose we should use it at because it is so bad for the kidney. And even when we use cisplatin at the safe levels, 30% of all patients develop nephrotoxicity."

Ceramide, sphingosine and sphingosine 1-phosphate, or S1P, are bioactive sphingolipids responsible for various forms of cell death and destruction. Ceramidases, or CDases, are enzymes that maintain the dynamic balance in concentrations of ceramide and sphingosine in the cell. Ceramidases cleave the fatty acid from ceramide to produce sphingosine, which is metabolized to S1P or salvaged to form ceramide again.

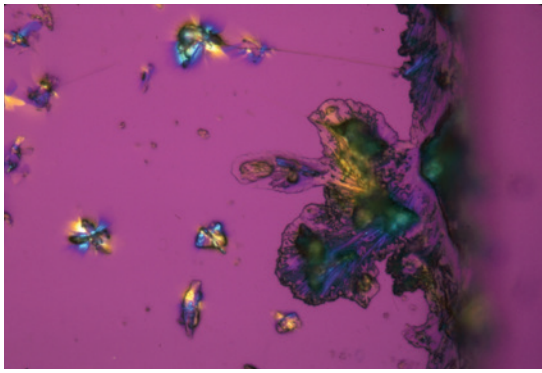
CDases fall into three broad categories — acidic, neutral and alkaline — based on the optimal pH for catalytic activity. Neutral ceramidases, or nCDases, function at a neutral pH, convert ceramide to sphingosine, and regulate the delicate balance between cell death and autophagy.

In a recent article in the **Journal of Lipid Research**, Siskind and a team of researchers reported that genetically altering mice to remove nCDase protected against cisplatin-induced AKI by reducing the recruitment of inflammatory cells, apoptosis, endoplasmic reticulum stress and increase in autophagy.

Nephrotoxic injury from acute tubular necrosis causes AKI. When the nCDase–/– mice were treated with cisplatin, mRNA levels in several inflammatory cytokines were reduced and the kidney tissue showed less damage from tubular necrosis, loss of brush border and tubular cast formation than in unaltered mice.

In AKI, loss of renal function is associated with increased blood urea nitrogen and serum creatinine. The levels of these chemicals were reduced significantly in cisplatin-treated nCDase–/– mice compared to cisplatin-treated mice with normal nCDase levels.

Using TUNEL staining, the authors showed that cisplatin-treated nCDase–/– mice were protected from apoptosis and cellular proliferation compared to mice with normal nCDase levels.



LARRY OSTBY/WIKIMEDIA COMMONS

Cisplatin, a platinum compound used as a chemotherapy drug, can have severe side effects.

"Neutral ceramidase is a great target because it seems to be very protective for kidneys when inhibited or knocked out," Siskind said.

Previous studies from collaborator Yusuf Hannun's lab, which elucidated the crystal structure for neutral ceramidase, showed that inhibiting nCDase can slow or stop progression of certain cancers, she added.

"The next step is to find a good inhibitor, but it's been elusive."

Siskind and her collaborators will continue their work to identify mechanisms that protect the kidneys from chemotherapeutics and to find promising inhibitors of nCDase.

DOI: 10.1016/j.jlr.2022.100179

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

Move over, DNA. The future is protein.

How and why the proteomics field is expanding its dimensions

By Renae Crossing

In the coming decades, efforts to understand disease will be propelled by building 3D maps of protein arrangements in cells over time, a team of scientists says.

A workshop about the study of proteins on a large scale — proteomics — yielded a perspective piece that is part vision, part plan, recently published in the journal **Molecular & Cellular Proteomics**.

DNA is like a game plan, explains Neil Kelleher, a researcher at Northwestern University who was involved in the study, and RNA is like the team huddle; it's what the cell decides to do with the circumstances on the day.

It's time to watch the game itself. "This is the decade," Kelleher said.

Watching the game

"Traditionally, we study one protein or pathway at a time," the authors write, because "the cell is otherwise too complex."

That's like watching one player over time and whom they pass to.

Proteins take multiple forms in a cell after they come off the bench. An electric link between fans and footballers inspires the play that decides a championship. A comment or word from a coach flicks a switch. In the cell, such switches can be as simple as a few atoms added (phosphorus and a trio of oxygens are a popular one). Altered by their circumstances, proteins are like people.

Mapping their shapes over time will be game-changing.

"This could impact all diseases," said Kristin Burnum–Johnson of Pacific Northwest National Laboratory, first author of the paper.

How will this happen?

Bottoms up, touchdowns

Scientists will tackle this from two directions: bottom-up and top-down. They start with clinical tissue samples, Burnum–Johnson explained.

"For bottom-up approaches, you extract proteins from tissue regions and break them into identifiable peptides (shorter strings of proteins)."

Bottom-up strategies, combined with RNA and metabolite data, will reveal the lineup and top-down strategies — those sweet, sweet action shots.

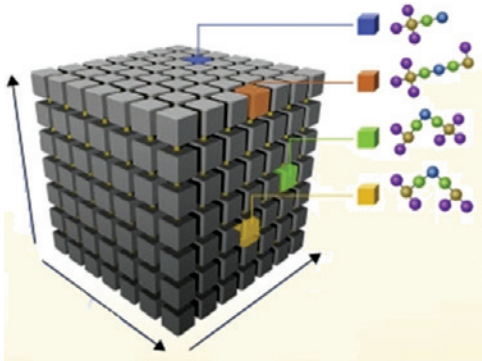
Kelleher knows about this. The top-down approach, revealing the specific forms proteins take (which RNA sequencing can't tell you), has become so sensitive that his research recently found 30,000 precise forms of proteins in blood and bone marrow alone. That's almost 10 times more than in previous studies. There are thousands more cell types for postgame analysis.

Single-minded

Researchers will continue pushing for higher resolution. They'll need to integrate data, which is not a simple challenge. They'll need to think beyond stadium walls; the extracellular matrix is rich. Like football and cells alike, consortiums and partnerships will drive the process. The National Institutes of Health wants research gaps to be identified, and private investment is supporting the sequencing of single molecules. These combined efforts remind Kelleher of the Human Genome Project.

The central dogma of biology is DNA to RNA to protein. It's only natural that scientific research follows the path that is familiar. It's protein's turn.

DOI: 10.1016/j.mcpro.2022.100254



NEIL KELLEHER ET AL./MCP

Maps will show how proteins take different forms over space and time, from milliseconds to years. It's postgame analysis for cells

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. Follow her on Twitter: @renaecrossing.

From the journals

By Isabel Casas, Laura McCormick & Meric Ozturk

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

Potential Alzheimer's target treatments

Alzheimer's disease is the most prevalent form of dementia. It affects millions of people over the age of 65 in the United States alone. It is characterized by extracellular plaques in the brain consisting of neurotoxic amyloid beta-peptides — Aβ — and intraneuronal hyperphosphorylated Tau protein aggregates.

While the production of Aβ from amyloid precursor protein, or APP, could be diminished by enhancing alpha-processing, the physical interactions between APP and α-secretases remain to be understood.

Lisa Hitschler and Thorsten Lang at the University of Bonn in Germany recently used super-resolution light microscopy to examine the abundance and association of APP and α-secretases ADAM10 and ADAM17 in cell-free plasma membranes.

They found that both secretases localize closely to APP. However, only ADAM10 co-aggregated with APP. They also identified the transmembrane domain in APP required for association with α-secretases.

The researchers propose that the APP transmembrane domain interacts either directly or indirectly with ADAM10 but not with ADAM17. They suggest this interaction could help in the development of therapies based upon promoting APP cleavage by α-secretases.

They reported their study in the **Journal of Biological Chemistry.** *DOI: 10.1016/j.jbc.2022.101911*

Pasteurization and enzymes in human milk

The unique nutritional composition of human milk protects infants from disease by stimulating immune function, establishing the gut microbiome and acting against microbes to reduce infection. However, human milk from a biological parent is not always available. In such cases, experts advise that donated human milk is the best option in the first six months. Before it is fed to an infant, donor milk should be pasteurized to kill bacteria and viruses. Pasteurization has a minimal effect on the nutritional composition of milk; however, exposure to high heat for 30 to 45 minutes may harm some enzymes that are important for lipid digestion.

Triacylglycerols make up 98% of lipid content and provide about 55% of the total energy intake of an infant fed human milk. Digestion of triacylglycerols and subsequent absorption of free fatty acids are essential for brain and nervous system development. However, if pasteurization harms enzymes that play a role in lipid digestion, donor milk is not the best option. Syaza Abu Bakar at the Monash Institute of Pharmaceutical Sciences and a group of researchers in Australia investigated differences in lipid digestion, comparing nonpasteurized and pasteurized human milk, in their recent study published in the **Journal of Lipid Research**.

Bile salt-stimulated lipase, or BSSL, is an important enzyme for lipid digestion. The researchers observed that nonpasteurized milk has more free fatty acids than pasteurized milk, meaning that pasteurization of milk impairs digestion. Lab experiments showed that adding bile salts to the milk, however, helps to achieve almost complete digestion, suggesting that BSSL is removed in pasteurization. The researchers concluded that, for healthy infant growth, the activities of enzymes such as BSSL should be protected and preserved during pasteurization. *DOI: 10.1016/j.jlr.2022.100183*

Structure of a deadly virulence factor

Enterococcus faecalis is a nosocomial pathogen that lives in the human gastrointestinal tract and is responsible for a wide range of infections that can be life threatening. The E. faecalis N-acetylglucosaminidase AtlA plays a predominant role in cell separation.

In a zebrafish model, atlA mutants are less virulent due to a limited dissemination of bacterial chains in the host organism and a more efficient uptake by phagocytes that clear the infection. Other pathogens — including Listeria monocytogenes and Salmonella typhimurium — have structural homologs to AtlA, making it attractive to researchers interested in designing new inhibitors to bacterial pathogenesis.

In a recent paper in the **Journal of Biological Chemistry**, co–first

authors Véronique Roig–Zamboni and Sarah Barelier, along with their colleagues in France, reported a 1.6 Å crystal structure of the E. faecalis AtlA catalytic domain. The team revealed a closed conformation of a conserved beta-hairpin and a complex network of hydrogen bonds that bring two catalytic residues to the ideal distance for an inverting mechanism. The authors suggest that this structure will inform rational drug design targeting this enterococcal virulence factor and even orthologs in other pathogens.
DOI: 10.1016/j.jbc.2022.101915

Mapping the cell

The cytoplasm is a densely packed yet well-organized space. A multitude of biochemical reactions occur simultaneously, each localized to a specific domain, such as inside the nucleus, on the mitochondrial surface or at the plasma membrane. As a result, the localization of RNA and proteins — as well as the intracellular trafficking to their final destination — must be tightly regulated. Disruption of this spatial organization can be problematic, as numerous diseases are characterized by mislocalized proteins.

Although researchers can gain a wealth of knowledge from global transcriptomic and proteomic data sets, the story is incomplete

A new way to accelerate wound healing

Wound healing is a dynamic process. First the body stimulates clotting factors to reduce blood loss. Then inflammation is initiated to protect wounded tissue from pathogens. After foreign agents are removed, tissue cells proliferate and new epithelial layers form. Many different molecules signal each other in every step of healing, which requires a balance between pro-inflammatory and anti-inflammatory processes. When the signaling cascades and inflammatory balance are impaired, a wound cannot heal.

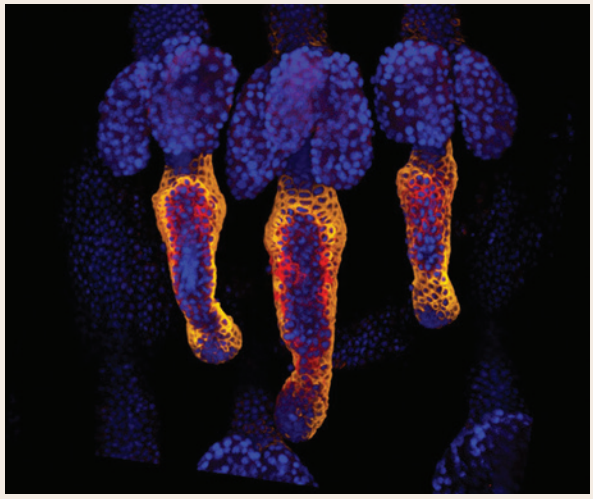
Eicosanoids are signaling lipid molecules that play a role in mammalian wound response and impairment of that response; they include prostaglandins, thromboxanes and leukotrienes. An imbalance between anti-inflammatory eicosanoids, such as prostaglandins, and proinflammatory eicosanoids, such as epoxyeicosatrienoic acids, causes wound healing problems. Thus, researchers study different ways of regulating eicosanoid expression to develop more efficient healing.

Eicosanoids are synthesized by activity of phospholipase A2, or PLA2, which is activated by ceramide-1-phosphate, or C1P — a key regulator of cell growth and survival that plays a crucial role in cell division and DNA synthesis. C1P is regulated by ceramide kinase, or CERK, enzymes, and previous studies have shown that downregulation of CERK blocks PLA2 activation, which causes eicosanoids to be depleted in response to inflammation.

Kenneth D. Maus at the University of South Florida, Tampa, and a team of researchers from the University of Virginia School of Medicine and elsewhere in the U.S. targeted the CERK enzyme by generating small-molecule inhibitors and by genetic manipulation to observe its effect on wound healing. Their article about this work was published recently in the **Journal of Lipid Research**.

The group developed a small-molecule inhibitor against CERK, and they genetically modified mice to have ablated CERK synthesis. They showed that CERK inhibition or ablation accelerates the transition from inflammation to proliferation in wounds. These results suggest that inhibition of CERK enhances wound healing and maturation of the tissue, and they provide preclinical data to explore future human clinical application.
DOI: 10.1016/j.jlr.2022.100187

— Meric Ozturk



YARON FUCHS & SAMARA BROWN/ROCKEFELLER UNIVERSITY

This confocal microscopy image from a mouse shows a tail wound in the process of healing.

Working from the outside in

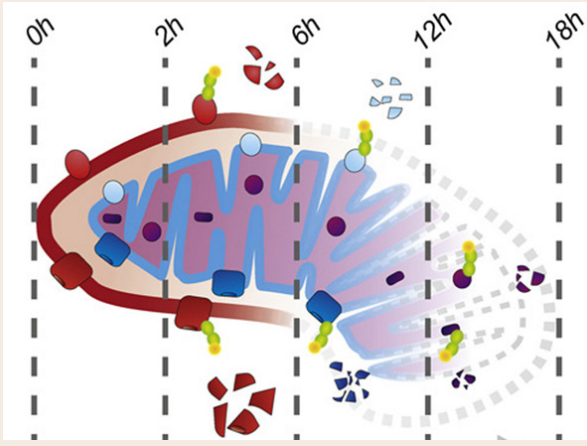
As cells adjust to the stresses of life, mitochondria also must adapt. Over time, mitochondria get damaged and then recycled by a specialized autophagy process called mitophagy.

During mitophagy, proteins are marked for degradation through ubiquitination. Phosphorylation works in tandem with ubiquitination, as each modification can provide positive or negative feedback for the other. In particular, mitophagy requires the E3 ubiquitin ligase parkin and the serine/threonine-protein kinase PINK1. Researchers have identified mutations in both enzymes in Parkinson's disease, so understanding their function is critical.

Despite an abundance of literature, scientists still have key questions about the process of mitophagy. Some researchers have demonstrated that autophagosomes consume mitochondria all at once during mitophagy, although others suggest individual sections within the mitochondria can be broken down piece by piece.

In a recent paper published in the journal **Molecular & Cellular Proteomics**, Katharina I. Zittlau and colleagues at the University of Tübingen describe using a three-tiered proteomic approach to examine parkin-dependent mitophagy in HeLa cells. After inducing mitophagy, the team quantified total protein levels over 18 hours to evaluate mitochondrial protein degradation in the presence or absence of functional parkin. They also measured changes in protein ubiquitination and phosphorylation.

Their data support an outside–in breakdown of mitochondria during mitophagy, showing evidence



KATHARINA ZITTLAU ET AL.

Mitochondria are broken down from the outside in during mitophagy. Shown over time from left to right are changes in the outer membrane and its proteins (red), inner membrane and its proteins (blue), matrix proteins (purple) and ubiquitin with distal phosphorylation (green/yellow).

for the ubiquitination and degradation of proteins in the outer mitochondrial compartments first, with the inner compartments following later. Using a vast data set, the researchers also identified examples in which a phosphorylation event blocked or enhanced ubiquitination during mitophagy. In particular, they showed that dephosphorylation of voltage-dependent anion-selective channel protein 2 is required for its parkin-dependent ubiquitination and ultimate degradation.

This study provides detailed information that enhances our knowledge of mitophagy as well as the specific contribution of parkin to each stage of the process.
DOI: 10.1016/j.mcpro.2021.100191

—Laura McCormick

without spatial information. Local enrichment or depletion of macromolecules — often masked in whole-cell omics — regulates these biological pathways and, ultimately, cell function.

Josie A. Christopher and a team from the University of Cambridge recently published a comprehensive review of methods used to study the subcellular localization of proteins and RNA in the journal **Molecular & Cellular Proteomics**. The authors provide a detailed overview of techniques such as microscopy-based assays, imaging mass cytometry, and coupling proteomics/transcriptomics with biochemical fractionations or proximity labeling. The advantages and limitations of each are discussed to help readers select the best methods for their own projects.

The techniques highlighted in this review will be crucial in answering basic questions about cellular organization as well as leading the way for translational research and new diagnostic approaches.
DOI: 10.1016/j.mcpro.2021.100186

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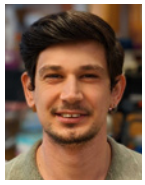


Secrets of spider silk proteins

Spider silk is remarkable stuff.

Orb-weaving spiders can produce up to seven types of silk for different purposes, and the silk's mechanical properties — including tensile strength and elasticity — are like nothing humankind has created. That's why there's a lot of interest among researchers in both using the material and learning from it.

Spiders synthesize silk in a dedicated gland. The polymer building blocks — known as spidroins — can be made of thousands of amino acid residues with highly repetitive regions, including flanking N- and C- terminal globular domains, which regulate silk formation.

The N-terminal domain of these spider silk proteins is essential for storage and silk assembly. Researchers have scrutinized the N-terminal domains of the major and minor ampullate spidroins (MaSp and MiSp, respectively) and found them to be monomeric at neutral pH. However, at lower pHs, they dimerize to connect spidroins in a fiber.

In a recent **Journal of Biological Chemistry** article, Médoune Sarr and colleagues at the Karolinska Institute and colleagues from the Latvian Institute of Organic Chemistry reported the structure of the N-terminal domain of flagelliform spidroin both in solution and in crystal forms.

The authors show that it is structurally similar to the N-terminal domain of the MaSp and that protonation events affecting interaction involve specific amino acid residues different from those in MaSp NT. The authors conclude that the overall mechanism of pH-dependent dimerization is conserved, although it can be mediated by different pathways in different silk types.
DOI: 10.1016/j.jbc.2022.101913

— **Isabel Casas**

THE CURE THAT BURNS

Treating cannabis hyperemesis syndrome

By Laurel Oldach

At a remote U.S. Army outpost in Afghanistan sometime in 2019, a defense contractor began to vomit uncontrollably.

Medics gave him intravenous fluids and a drug for nausea. It didn't help. Unable to get the man's symptoms under control, the doctors had him medically evacuated to Bagram Air Base, which housed the most sophisticated military hospital in the country.

There, Rory Stuart, a lieutenant colonel in the U.S. Air Force and an emergency physician at the University of California, Davis, worked the patient up. The man kept vomiting and retching while Stuart's team conducted tests that proved inconclusive. His vital signs were normal. Scans and samples of his blood and urine showed no appendicitis, no kidney stones: just intestinal inflammation and kidney problems possibly caused by severe dehydration. Figuring the patient might have a particularly nasty viral infection, Stuart admitted him to the hospital for observation and more fluids.

A few hours later, Stuart received a call from a colleague who supervised the inpatient unit. Stuart recalls his colleague saying, "'He's freaking the other patients out, he's making the nurses mad, and it's just so weird: He won't get out of the shower.'"

Suddenly it all made sense. "I was like, 'Oh, God, are you kidding me?' Because I had dealt with these patients back home," Stuart said.

He asked the nurses to collect a second urine sample. Unlike the first sample, this one was high in sugar and had the wrong specific gravity. It also, lab technicians observed, smelled an awful lot like the apple juice the patient had been served at lunch.

By testing the original urine sample again, the technicians found exactly what Stuart was expecting: a high level of tetrahydrocannabinol, or THC, in the patient's system.

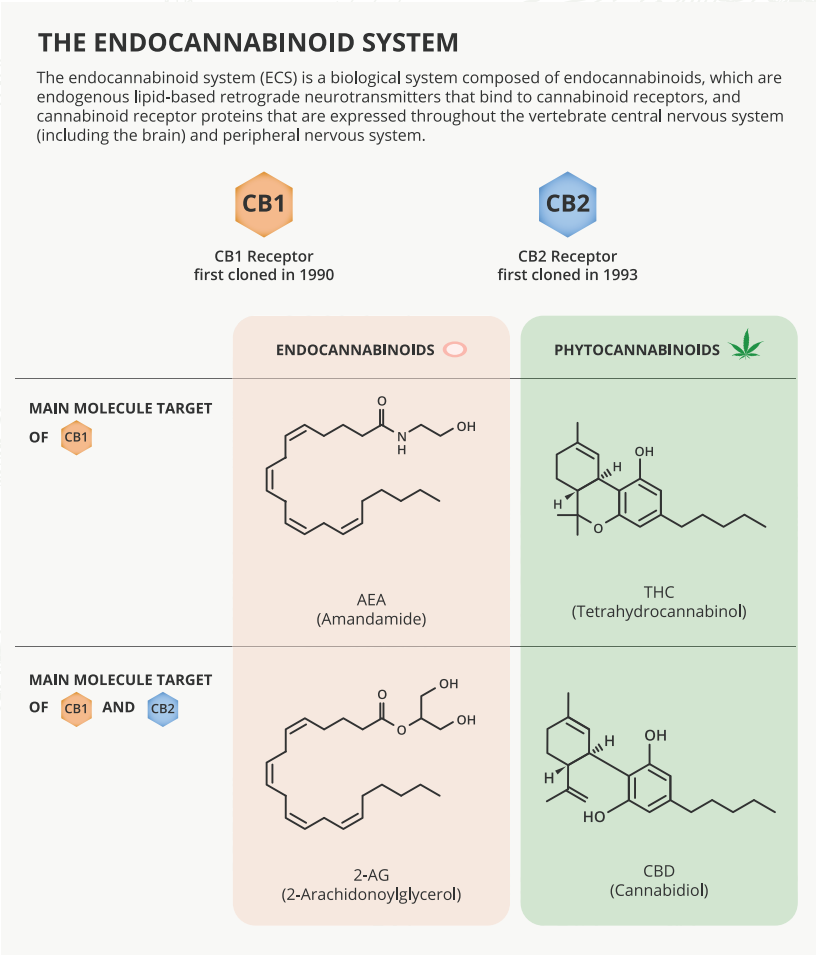
The experience, which Stuart and a UC Davis colleague wrote up in the journal Military Medicine, was an unusually colorful instance of cannabis hyperemesis syndrome. The ailment afflicts a small subset of heavy cannabis users, causing relentless vomiting after exposure to the drug — the opposite of what most users expect. Relief from hot showers — and from a topical cream containing a chili pepper molecule — hints at a fascinating molecular crosstalk that physicians still do not understand.

Relief from hot showers — and from a topical cream containing a chili pepper molecule — hints at a fascinating molecular crosstalk that physicians still do not understand.

A paradoxical diagnosis

Just about everyone knows that cannabis can prevent nausea and vomiting, especially among cancer patients undergoing chemotherapy. So cannabis hyperemesis syndrome, or CHS, is counterintuitive.

One study found that, on average, patients visit a doctor's office or



emergency room three to five times before they receive a diagnosis of CHS. "These patients experience the worst of medicine," said Jeff LaPoint, an emergency toxicologist. Often in terrible pain, they go through many scans to rule out emergencies, such as appendicitis or ectopic pregnancy, and more slowly developing illnesses that require medical interventions. Before the vomiting starts, people often have weeks of stomach pain or nausea — both of which, like vomiting, could have any number of causes that must be ruled out. One Reddit user, interviewed by text for this story, said they knew more than one person who had had their gallbladder removed in a fruitless effort at resolving their illness.

Perhaps that's why, by the time a doctor tells a patient that cannabis is the cause of their misery, patients rarely accept that explanation. No, they'll explain: They're using the weed to relieve the nausea. Stuart, the air force physician, said, "You rarely win that argument." Yet a core diagnostic criterion for CHS is that when people stop using the drug, their symptoms resolve.

The particulars of pot and puking

Vomiting depends on a part of the hypothalamus called the nucleus tractus solitarius, which integrates many inputs. It connects to parts of the brain and peripheral nervous system that sense movement and position, chemicals circulating in the blood, and the status of the stomach and gut. It also takes input from the cortex, where higher-order thinking takes place.

According to Vincenzo Di Marzo, a biochemist who studies endocannabinoid and cannabinoid signaling at Quebec's Université Laval, most of the neurons in the vomiting center and its chemical-sensing trigger zone express the cannabinoid receptor CB_1R. The most abundant G protein–coupled receptor in the brain, it responds to signaling molecules called endocannabinoids.

When CB_1R at the presynaptic terminal of a neuron is activated, it makes that neuron less likely to fire at that synapse. CB_1R also is expressed in the peripheral nervous system in the vagus nerve and enteric nerves that connect the brain with the gut.

The most abundant compound in marijuana, THC, causes a user to get high by binding to CB_1R. In animal models, that interaction also can make vomiting less likely.

A second cannabinoid receptor, called the CB_2 receptor, also binds to THC and endocannabinoids. CB^2R is expressed mostly in immune cells,

but researchers led by University of Alberta scientist Keith Sharkey reported in 2005 that this second set of cannabinoid receptors does appear in neurons in the vomiting center, and stimulating them also reduces vomiting.

Why, then, does a frequent high dose of cannabis cause vomiting?

"Sometimes, drugs produce exactly the opposite effect of what you'd expect," Di Marzo said.

Because CHS mostly arises among people who have used cannabis at least once a week, often for years, and because cannabinoids tend to accumulate in tissues, there is reason to surmise that the syndrome results from desensitization of cannabinoid receptors, especially CB_1R. Desensitization through phosphorylation, arrestin binding or internalization is a common biochemical response to restore homeostasis after chronic receptor activation.

Ethan Russo, a neurologist and co-founder of a cannabis-focused biotechnology company called Credo Science, said that any CB_1R agonist can cause cannabis hyperemesis syndrome. For example, people using synthetic cannabinoids, which activate CB_1R very strongly, can become ill even without taking THC.

Di Marzo said that if baseline activity from CB_1 receptors is necessary to keep the vomiting center quiet, then desensitizing those receptors could be a trigger for CHS symptoms.

In recent years, marijuana products have become much higher in THC than they used to be. Experts suspect that change, combined with increasing state legalization nationwide, has spurred an increase in CHS cases since the condition was identified in 2004.

"It's like if we were drinking Newcastles for 4,000 years, and then one day we decriminalized that and said, 'Here's Everclear; it's the same thing,'" said Jeff LaPoint, the director of the medical toxicology division at Kaiser Permanente in San Diego.

A predilection for hot showers

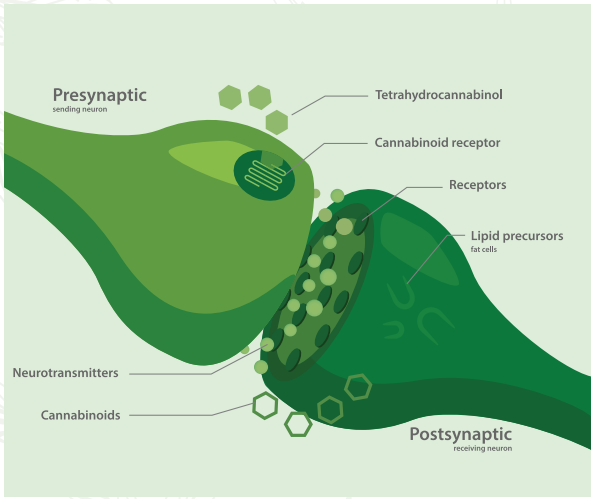
The defense contractor in Afghanistan responded very typically to the treatments his doctors tried. First, he showed no response at all to the first drug to treat nausea and vomiting, or antiemetic, that the doctors tried, an emergency department workhorse called ondansetron.

Michael Mullins, an emergency toxicologist at Washington University in St. Louis, said, "We'll often give it in the waiting room, because it's so safe."

Bundles of neurons relaying messages from different sources to the vomiting center use different neurotransmitters and neuromodulators to communicate. Therefore, many antiemetic drugs can work in some instances but not others. According to U.K. pharmacologist Gareth Sanger, who helped to develop the drug, ondansetron works by blocking a group of serotonin-gated ion channels found in the vagus nerve, which connects the stomach to the brain.

Although patients get no relief with a first-line anti-nausea drug, many experiencing CHS find that a hot shower can help ease their symptoms. The first case series that described the syndrome noted compulsive bathing as one of its patients' signature characteristics. Physicians say that they don't see the same degree of devotion to hygiene among other patients in gastrointestinal distress.

As a medical fellow in New York, LaPoint treated some of the first people to arrive in city hospitals with synthetic cannabinoid poisoning. He also happened to have been writing



A schematic illustration shows how cannabinoid receptors fit into synapses. When activated by a drug or an endocannabinoid signaling molecule, the cannabinoid receptor acts like a dimmer switch, reducing the chances that the synapse will fire.

Many people who suffer from cannabis hyperemesis syndrome find on their own that hot baths and showers provide temporary relief.

> "It was a breakthrough to have an over-the-counter medication that someone could take home and be functional."
>
> JEFF LAPOINT

a textbook chapter on cannabinoids. The juxtaposition got him thinking. Because hot baths work so well — but are an impractical treatment for emergency room patients — LaPoint said that many in his field were trying to figure out easier ways to help CHS patients warm up.

LaPoint wondered, while mulling it all over, whether TRPV1, one of the body's best-known heat-sensing receptors, might be involved in the relief that hot bathing can bring. Not long after TRPV1 was discovered — a finding that earned the 2021 Nobel Prize in Physiology or Medicine — scientists had shown that TRPV1 is also part of the endocannabinoid system. The receptor binds to the endocannabinoid anandamide and to a number of botanical cannabinoids, although not THC.

LaPoint still remembers the first patient he tested the idea with. She was an 18-year-old who used cannabis concentrates known as dabs. She had been in and out of the hospital around five times in the past week. She arrived in such pain that her screams preceded her down the hall. LaPoint found a woman security guard and sent the patient to the doctors' shower to get the pain under control. The remedy worked, but as the patient waited for her ride to arrive, her pain came back.

LaPoint suggested an off-label application of capsaicin cream. The cream, which uses a molecule from chili peppers to provoke a sensation of heat by activating TRPV1, was safe and widely used for arthritis pain.

"Look, no one has ever done this before," he recalled telling her. "I wouldn't ask you about this when you're screaming in pain — but now you're just mildly uncomfortable."

The patient was game — and the cream, applied to her abdomen, seemed to help. It was a breakthrough, LaPoint said, "to have an over-the-counter medication that someone could take home and be functional."

LaPoint reported at the 2014 North American Congress of Clinical Toxicology that applying capsaicin cream to the bellies of seven patients with CHS resolved their symptoms within half an hour.

Presented with a remedy for these patients, who were otherwise difficult to help, other emergency toxicologists tried it too. Mullins at WUSTL and colleagues published a retrospective case series in 2017 showing that almost all of 13 patients who had received serotonin antagonists to no effect improved after using topical capsaicin. But some colleagues found the concept dubious, critiquing the lack of a plausible mechanism of action.

A team at the University of Virginia currently is conducting a clinical trial comparing the effects of capsaicin to a placebo. The investigators expect to complete the study this year.

Capsaicin is by no means the only treatment toxicologists have tried out for CHS patients. The medical literature has a long list of case reports that describe testing an antiemetic in one or a few patients with CHS.

When capsaicin isn't available — like at military hospitals, which rarely see arthritis patients — physicians can instead use a dopamine antagonist such as droperidol or haloperidol. That's how Rory Stuart treated his patient in Afghanistan. Within two days of starting IV fluids and haloperidol, the man left the hospital.

Dopamine antagonists have their drawbacks — they can sedate a person, making it unsafe to send them home from the ER by car, and they carry a risk of cardiac side effects. Still, Mullins called droperidol "one of my favorite drugs in the whole wide world, because it almost never fails for nausea and vomiting."

Between capsaicin and droperidol, some emergency physicians see the CHS problem as solved. Still, questions linger around the disease's pathophysiology and its unusual treatments.

Many cannabinoids, many receptors

Assuming capsaicin works as well in a placebo-controlled trial as emergency toxicologists think it will, one question is why activity of its target, TRPV1, is important.

TRPV1 is expressed both in the vomiting center in the hypothalamus and in the vagus nerve, and its ligands tend to reduce vomiting in animal models. In fact, capsaicin has been used to block vomiting that's a side effect of chemotherapy. But according to Di Marzo, researchers don't know whether its activation or desensitization is driving a reduction in vomiting.

In a review article on CHS in the journal Clinical Toxicology, researchers ticked through numerous reasons that activating TRPV1 might be effective: Perhaps it diverts blood flow to the skin to cool down, reducing pain in the gut. Perhaps its activation blocks the transport or release of neuropeptides from pain-receptive nerve fibers to the hypothalamus. Perhaps the pain from capsaicin simply overrides pain sensed in the gut.

The endocannabinoid system is notoriously difficult to study because its many receptors overlap in function. Cannabis complicates matters further, with a cornucopia of closely related molecules, each of which affects several receptors. THC and CBD may be the best known and the most abundant active compounds in a cannabis leaf, but they are two among many, including cannabigerol, cannabidiolic acid and dozens more. Several of those secondary cannabinoids, Di Marzo's lab has shown, are also TRPV1 ligands, although none seems to open the channel as strongly as capsaicin does. Different strains of cannabis and different preparation methods can alter the cannabinoid profile of a dose of smoke, edibles, oil or dab.

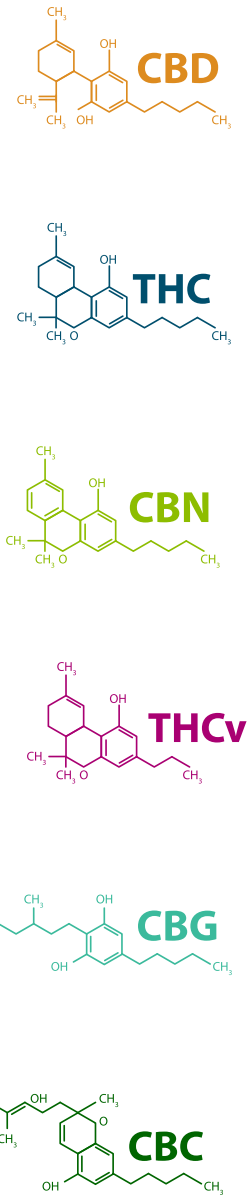
According to University of Pennsylvania structural biologist Vera Moiseenkova–Bell, cell signaling may be disrupted at several points by the presence of a high concentration of cannabinoids. Cannabinoids are hydrophobic. They're at home embedded in the plasma membrane, where they can slip into binding pockets buried in the transmembrane domains of many receptors.

As membrane-spanning protein structures have become easier to study thanks to new biophysical methods, researchers have been able to zero in on how cannabinoid–receptor interactions work — and even have begun to probe how cannabinoids alter receptors' interactions with other ligands.

Working with the ion channel TRPV2, Moiseenkova–Bell and her lab recently published a structural study that showed exactly where CBD and the channel's canonical ligand, 2-ABP, bind. The lab also found that when they both bind at the same time, they produce a stronger response than either alone.

Whether CBD could boost capsaicin activation on TRPV1 in the same way is not known, Moiseenkova–Bell said — but such drug–drug interactions are possible.

To sort out which cannabinoids are important in the development of CHS, Rachel Wightman, an emergency physician and medical toxicologist at Brown University, is conducting a mixed-methods study. It's the only study of CHS that the



Cannabis plants produce many natural products in the cannabinoid family; these are a few of the most common. While closely related, the cannabinoids may exert different biochemical effects.

While the medical literature is clear that the only way to stop experiencing CHS is to stop using cannabis, LaPoint said, he often counsels patients to use a lower-THC formulation — advice they may be more likely to follow.

National Institutes of Health currently is funding.

Wightman's research team is recruiting patients who arrive at the hospital with presumed CHS. They draw blood for metabolomic testing to compare the presence of cannabis metabolites when patients have symptoms to when they do not.

They also are looking to understand the patterns of the disease and cannabis use practices through surveys and interviews. How often do episodes of severe vomiting arise? How do patients feel about the care they receive and the recommendation that they stop using?

Another salient question is what differentiates people who develop CHS from peers who use a similar amount of the drug but never become nauseated.

After running a small genetic study comparing 28 people who were experiencing CHS to a dozen who never had it, Ethan Russo and colleagues at CReDO Science identified a group of genetic variants that appear enriched among people with CHS.

They found single-nucleotide polymorphisms in genes that code for enzymes that break down cannabinoids and farther afield, including two genes involved in dopamine signaling, a lipid transporter protein and a noncoding region of the genome close to the TRPV1 gene.

The study identified correlations only, leaving further causal explanation up to future research. Russo's company has begun to sell a genetic test based on those findings, but the Food and Drug Administration has not evaluated its ability to screen for a predisposition to CHS.

Impractical for the clinic?

While capsaicin may be effective, it also can be painful.

LaPoint said that he sometimes sees patients who write on intake forms that they have a capsaicin allergy — either to avoid a burning belly or in hopes of securing stronger painkillers.

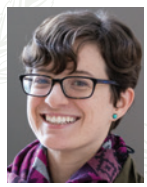
"I've come across patients who are like, 'Oh my God, I hate that capsaicin. Whoever thought of that, I'd like to get ahold of them,'" LaPoint said. "I'm like, 'Bro, it was my fault.' … They usually laugh."

Because his hospital in San Diego — "craft beer, craft weed" — sees so many patients with CHS, LaPoint said, he spends some time educating fellow physicians in how to help: "Don't miss a serious surgical emergency. Don't blow this off as 'just cannabis hyperemesis.' Don't keep scanning them; and don't get them started on opioids. Other than that, there's a lot of room for style."

While the medical literature is clear that the only way to stop experiencing CHS is to stop using cannabis, LaPoint said, he often counsels patients to use a lower-THC formulation — advice they may be more likely to follow.

When Stuart last saw the defense contractor in Afghanistan, he was in good shape, recovering from days spent vomiting with no ill effects that seemed likely to last. Stuart never did hear what became of the man, who admitted in a roundabout hypothetical fashion to having used the synthetic cannabinoid "spice" to elude drug testing. Stuart said it's likely, though, that the man's employer sent him back to the U.S.

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter: @LaurelOld.



The mechanism of the monkeypox antiviral

The molecule targets a multilayered quirk in the poxvirus life cycle

By Laurel Oldach

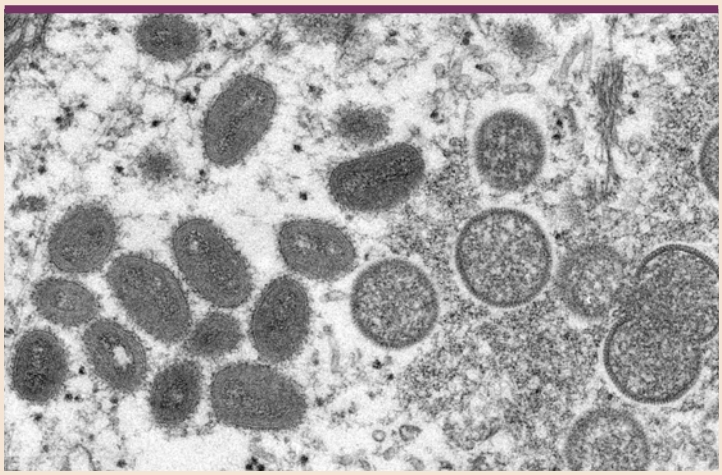
Since the World Health Organization announced in May that a traveler in the U.K. had tested positive for monkeypox, cases have been reported in at least 65 countries where the virus usually is not found. In late July, the WHO declared monkeypox a global emergency.

At the offices of SIGA Technologies, a health security company in the U.S. that produces an antiviral molecule recently approved in some countries to treat monkeypox, chief scientific officer Dennis Hruby said his team has been working "frantically" to respond to the outbreak.

Monkeypox is not a new virus. Nigeria, which has an ongoing outbreak, has reported over 500 suspected cases since 2017, and in the Democratic Republic of Congo, the WHO estimated over 2,700 people were infected with a more severe strain in 2021 alone.

However, the sudden detection of the virus in scores of countries where it is not endemic, among patients with no obvious connections to one another and no history of travel to places currently fighting outbreaks, suggests that there may be a transmission chain — either between people or from an animal reservoir — that health authorities don't know about.

It's too soon to say whether that is true in this outbreak. But, Hruby said, governments are acting fast to contain the virus.



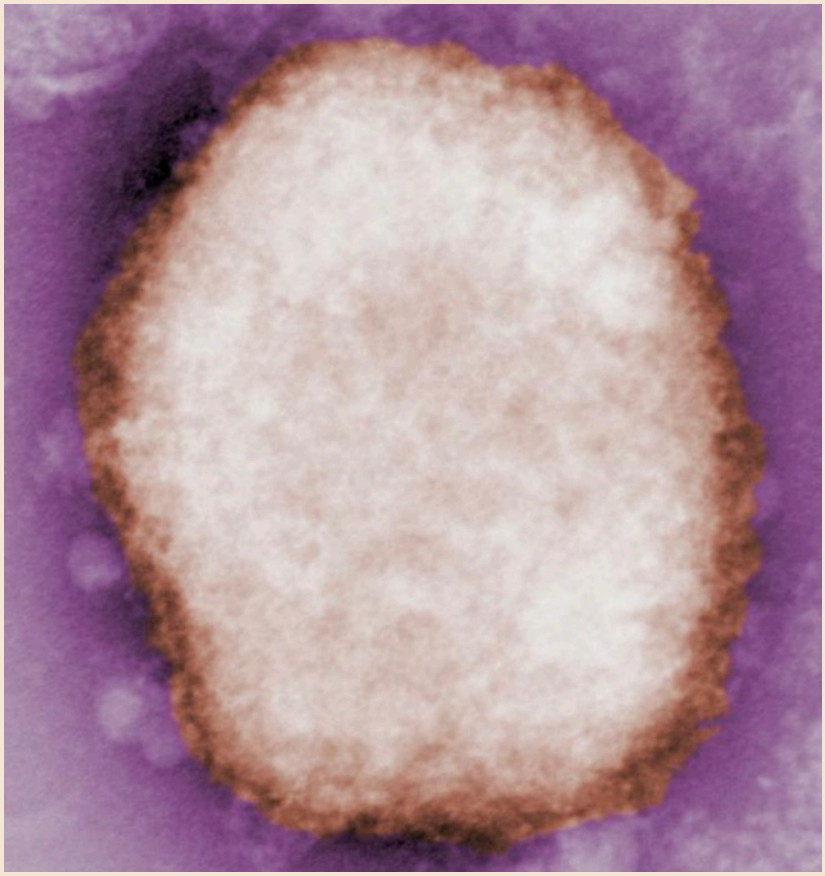
CYNTHIA S. GOLDSMITH, RUSSELL REGNERY/CDC

This electron microscopic image shows monkeypox virions obtained from a clinical sample of human skin associated with a 2003 outbreak. On the left are mature, oval-shaped virus particles, and on the right are the crescents, and spherical particles of immature virions.

"We've already been having conversations with a number of governments about stockpiling drug for smallpox," Hruby said. But the outbreak has ignited much more customer interest. (See "Monkeypox treatment options," page 43.)

SIGA Technologies makes one of two small molecules approved by the Food and Drug Administration, and recently approved in Europe, to treat smallpox. (Global rights to the other FDA-approved drug, a nucleotide analog optimized to block poxvirus polymerases, were bought recently by Emergent Biosolutions.)

SIGA's flagship drug, identified through a high-throughput screen in 2005, has a somewhat unusual mechanism of action. Called tecovirimat, it targets a viral structural protein called the F13 homolog, alias p37, that enables a strange quirk of poxvirus biology. Exactly how the protein works remains a bit of a mystery.



CHARLES D. HUMPHREY, TIARA MOREHEAD & RUSSELL REGNERY/CDC

This negative-stain transmission electron micrographic image shows a mulberry-type monkeypox virus particle that was found in human vesicular fluid. The surface of these M-type virions are covered with short, whorled filaments, while C-type, or capsular-type virions, are penetrated by stain and are seen as a sharply defined, dense core, surrounded by laminated zones of differing densities.

A virus in a double wrapper

Poxviruses — there are dozens, including smallpox, monkeypox, rabbitpox and the recently identified Alaskapox — have an unusual life cycle. Although they are DNA viruses, they avoid the host cell's nucleus completely, conducting all of their genome replication, transcription, translation and new virus assembly in the host cell cytoplasm.

They also make two forms of infectious progeny thanks to a curious cellular escape strategy. A mature, infectious pox virion, produced in a zone of the cytoplasm called the virus factory, has a viral protein capsid wrapped in a membrane stolen from its host. But before it leaves the cell, it accumulates two more layers of membrane packaging and then sheds one of them by fusion with the cellular membrane. That leaves the extracellular virus wrapped in a double layer of membrane.

Not every virion makes it through this process. University of Rochester virologist Brian Ward, who studies poxvirus replication, estimates that between 5% and 10% of intracellular mature virions eventually escape the cell in double-enveloped form. Infected cells generally don't burst open, so the majority of the viral progeny they generate stay bound up inside — infectious but sequestered.

In variola, the virus that causes smallpox, "a maximum of 10% of the virions that are made are enough to cause that disease," Ward said. "If you had 20% — twice as many — it would be devastating.

"I think to some extent, the virus does want to limit how much of the virus gets out, to control its pathogenicity."

Researchers know relatively little about how the second and third membranes, which seem to derive from the cell's trans-Golgi network, become wrapped around the virus. There are two mechanistic possibilities, Ward said, but little experimental support for either. One thing scientists do know is that the F13 homolog protein is crucial for the wrapping process. (The F13 protein is found in vaccinia virus. Researchers working on other viruses agreed to call its homologs in other poxviruses "F13 homologs" when it became clear that developing a new system of protein nomenclature for every species of poxvirus was much too confusing.)

Anchored to the membrane by palmitoylation and perhaps by some phospholipase-related domains, F13 homologs are found between the inner and outer membrane layers of the extracellular virus.

Hruby studied F13 as an academic virologist, he said, before launching his biotech career. "If you'd asked

me if (the gene that makes p37) was going to be a target for an antiviral, I would have not thought that was possible," he said. "One of the advantages of blind high-throughput screening is you come out with hits that hit targets you never would have predicted."

A small molecule that blocks viral escape

In 2005, Hruby and colleagues at SIGA published the results of a screen of more than 350,000 small molecules they had licensed from another company. After some tweaks and optimization, one of them, known as ST-246 and subsequently as tecovirimat, proved to be effective in halting the replication of cowpox virus, one of many less dangerous relatives of smallpox.

Virologists use cells grown in a monolayer and then stained with crystal violet to measure the disruptive potency of a virus. Just one cowpox virion per 100 cells can destroy a smooth blue lawn of cells almost completely, leaving only a few hardy tufts behind. In lower concentrations, the virus forms plaques that dapple the lawn with groups of dead cells. But in cells treated with ST-246, the screen showed, the highest dose of virus formed no plaques at all, a clue that the molecule blocks viral infection.

Further studies using a different virus showed that ST-246 didn't stop virions from assembling within the cell; treated and untreated cells contained about the same quantity of intracellular mature virions after infection. Instead, the molecule dramatically reduced the virus's escape into the culture media. That gave the SIGA researchers the idea that ST-246 could alter a virus's wrapping in its second and third membranes.

By growing many rounds of the cowpox virus in cells with a low concentration of the molecule and then mapping the mutations that lent resistance, they identified the F13 homolog as tecovirimat's target. Later biochemical studies showed that the drug disrupted the interaction between F13 and two cellular proteins involved in trafficking, Rab9 and TIP47.

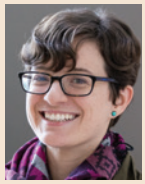
Without a clear understanding of the steps in viral wrapping, it is difficult to determine exactly why breaking up the Rab9-TIP47-F13 interaction is so effective.

It's plausible that, after treatment, the F13 homolog fails to localize properly for envelopment, Ward said. "But there's no real hard evidence for that. What we do know is that the drug works fantastically. They have saved people's lives with this drug."

Ward recalled, for example, the 2008 case of a 2-year-old boy who became seriously ill with vaccinia contracted after his father, a soldier, was vaccinated against smallpox. After more than a week in the hospital in worsening health, the child received both tecovirimat and a nucleotide analog and began to recover.

Presented with Ward's assessment that the drug's mechanism is uncertain, Hruby pushed back. "I think we know how the drug works. It keeps F13 from going to the membrane, and by doing that, it keeps the virus from budding." Still, he conceded, there are open questions for basic researchers to tackle. "What we don't know is down at the molecular level. … We know the region of the protein where it interacts, but the exact biochemical mechanism, no, we don't."

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter: @LaurelOld.



Monkeypox treatment options

The close relationship between monkeypox and its deadlier cousin smallpox is a big part of why a stockpile of effective drugs to treat monkeypox exists — for citizens of wealthier nations.

In the wake of the Sept. 11, 2001, terrorist attacks, the U.S. invested heavily in defense against bioterrorism. That included developing treatments for the virus that causes smallpox, which was eradicated in the 1980s but still exists in a few freezers around the world.

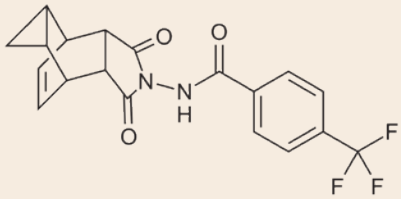
SIGA Technologies was one of the beneficiaries of that investment. Over the years, their funding has come from the National Institute of Allergy and Infectious Disease, which contributed slightly over $35 million to SIGA's smallpox antiviral program from 2003 to 2010, and the Biomedical Advanced Research and Development Authority, or BARDA, biosecurity program, which agreed to contribute up to $435 million at the clinical testing stage.

In 2018, SIGA researchers reported in the New England Journal of Medicine that tecovirimat, which is branded as TPOXX, was safe for healthy humans to ingest.

It was impossible to test the drug in humans with smallpox; there are none. However, the company reported that it prevented death among rabbits and monkeys infected with an otherwise lethal dose of rabbitpox or monkeypox viruses. Shortly thereafter, the FDA approved the drug to treat smallpox, and the U.S. and Canadian governments began to accumulate stockpiles.

SIGA declined to disclose the price it charges per 14-day course of treatment. The company has an agreement with Oxford University and the local Ministry of Health to provide the drug free of charge to patients with monkeypox in the Central African Republic, and Hruby said that they intend to conduct clinical trials in other countries where the virus is endemic.

"Of course," he added, "we didn't anticipate having a pandemic to test the drug."



EDGAR181/WIKIMEDIA COMMONS

Tecovirimat also goes by the brand name TPOXX.

‘With advances in mass spectrometry, we can explore terra incognita’

A conversation with Molecular & Cellular Proteomics associate editor Albert Heck

By Laurel Oldach

COURTESY OF ALBERT HECK

ALBERT HECK

Albert Heck is a professor at Utrecht University, where he runs a lab of more than 50 researchers developing novel techniques for mass spectrometry. Like many proteomics scientists, Heck is motivated both by his love of the technique and by his conviction that researchers learn more about a cell’s behavior from its proteins than its DNA or RNA. He met with ASBMB Today by Zoom to talk about his work and his first year as an associate editor of the journal Molecular & Cellular Proteomics.

This interview has been condensed and edited.

Q. You recently told the Analytical Scientist that you’re a mass spectrometrist at heart. Why? What about analytical instrumentation appeals to you?

New inventions follow new technologies. I don’t know who said it first, but it’s stuck in my mind. As mass spectrometry has developed, we can study questions that we couldn’t study 20 years ago. That makes it so exciting. I feel that we can explore terra incognita — parts of life that we were blind to.

I’m really a technology nerd. That’s very different from researchers that work their whole life on mitochondria, or on one protein, and become super experts. I admire them, but I like to come in from the sides with my new technologies, allowing me to explore almost every question in the life sciences.

Q. Your background is in physical chemistry and reaction dynamics. How did you get into biochemistry?

I did my Ph.D. in mass spectrometry at the University of Amsterdam in the Netherlands, studying really fundamental ion–molecule reactions in the gas phase. At that time, the limitation was still that you could only analyze what you could easily bring into the gas phase. We didn’t have methods like electrospray and MALDI (matrix-assisted laser desorption/ionization). So for biological mass spectrometry, there was not that much yet to explore.

I did a postdoc at Stanford with Dick Zare and David Chandler (Sandia), working on reaction dynamics of some of the most fundamental chemical reactions: H + D2 → HD + H. When I was thinking of going back to Europe in 1996, the University of Warwick had a call for someone who knew how to work with a totally new innovative mass spectrometer. They knew me from my thesis work, and they invited me to set up this new facility with this very expensive FT-ICR mass spectrometer. That was like giving me, as a very eager kid, the keys of a Ferrari.

But then they said to me, "But you have to study biomolecules." And — this is true — I said, "Bio-whats?"

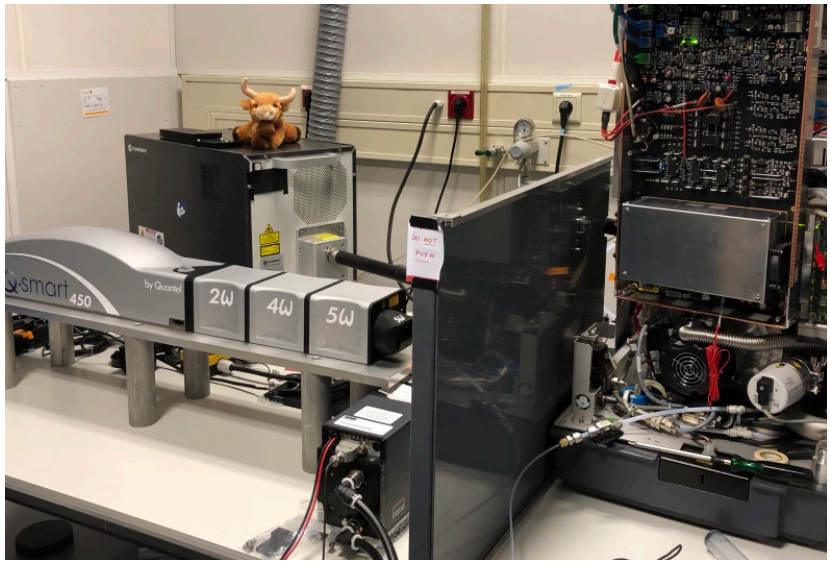
It was getting the keys of a Ferrari, but maybe not on the circuit that I initially wanted to drive. I decided to go for it, and that brought me into the field of biomolecular mass spectrometry. My background in biology was close to zero. Of course, I had had biochemistry courses, but I had really drifted more to the physical and theoretical chemistry side. With hindsight, if they hadn't given me the key to the Ferrari, I would probably not have gone in that direction. And with hindsight, I'm very happy that this occurred, because now I find biomolecules and proteins by far the most exciting things to study. But indeed, so much for career planning.

Q. When you were first setting up your lab with this mandate to investigate biomolecules, how did you decide what to work on?

When electrospray was developed, which opened the field of biomolecular mass spectrometry, I was intrigued by whether proteins and peptides in a mass spectrometer could be kept more in their physiological states. Analyzing protein ions in a vacuum is quite different from the cellular environment, but you could claim that it's a postmortem analysis of your protein. I started my own lab in 1998 at Utrecht University in the Netherlands, asking: Can we do native analysis of how these proteins act in their natural environment, using mass spectrometry? That has been a key question in in all the years that I've been active. And I don't say that I developed it, but I was one of the early pioneers of this area that's now called native mass spectrometry, and I'm very pleased to see that this research area has grown so much, especially in the recent past.

Q. How is sample handling different in native mass spectrometry than in a conventional liquid chromatography–mass spectrometry approach?

If you think about the environment of a cell, there are a few important features: The pH is around 6-7, there are salts, there is a dense environment of other molecules. If you think about the mass spectrometer, there's a vacuum, there's no water, the protein itself becomes highly charged. In LC–MS, running solvents are used containing organic (solvents), and typically a pH of around two. Under these conditions, a protein gets totally unfolded or even crashes out of solution. For mass analysis, the unfolding is not too bad, because it also allows the protein to become highly charged, allowing you to measure its mass quite accurately. But what we tried is to keep the pH around neutral. This is less compatible with LC–MS, but we found ways to get these proteins still in their folded states into the mass spectrometer. A noncovalent



COURTESY OF ALBERT HECK

Asked about the toy cow on this mass spectrometer in his lab, Albert Heck wrote, "Each instrument in our lab has a mascot, which we hope saves it from serious trouble and downtime."

heterodimer will fall apart in an LC–MS column, but with native mass spectrometry, it will stay a complex whose mass can be determined. Even with much larger protein complexes like proteasomes, ribosomes or whole intact viruses, we have shown we can bring them directly into the mass spectrometer and mass analyze them.

The bigger the ions you measure, the more your mass spectrometer has to have a mass range that can handle these ions. We analyze protein complexes and viruses that are sometimes in weight over one million Da. For comparison, peptides have typically masses of a few hundreds of Da. It's a completely different order. Therefore, we also worked a lot on making mass spectrometers better for analyzing these sorts of ions.

For instance, we are working on viruses used biotherapeutically as gene delivery vectors. We can now use mass spectrometry to determine if a virus is properly loaded and therefore usable as a biotherapeutic.

The first wave of gene delivery applications went quite badly a few years back. But now, almost every biopharma company that takes itself seriously is working on gene delivery using adeno-associated viruses or other viruses as their platform. It's going to be big business again. For everything that biopharma makes, the analytical chemistry and proteomics fields have to be ahead, because these products cannot go to the patients without proper quality control. With these biopharmaceutical products becoming more and more complex, the analytical technologies to measure them also need to keep up, and that keeps us very busy.

If you had asked me this 10 years ago, at that time I thought these measurements were far beyond our reach. That's also so nice about mass spectrometry. You get the question, "Where do you think the field will be in five years?" And I always give the same answer: "If you had asked me five years ago, my answer would have been totally wrong and overtaken by non-expected new developments."

Albert Heck recently wrapped up a collaboration with animators and dancers to produce a video dramatizing his lab's research, which he hopes will convey wonder about the natural world and perhaps inspire some viewers to read more. "I think most scientists that work on antibodies, they don't realize that this is two words, 'anti' and 'body.' For someone in art, they have no idea what an antibody is. But they know what anti is and they know what body is," he said. "It's a great pleasure to work with these people because they give you also new insights and also make links that you never made."

Q. You've worked closely with instrument manufacturers to develop new instruments and techniques. Are those interactions with industry scientists different from collaborating with fellow academics?

It's for sure different but also alike. I always say, "Don't underestimate the personal click." In academic collaborations, you work with people you like, with whom you share interests; I think my most successful industrial collaborations are also with people that I like, who hopefully like me as well, and with whom I share interests.

Through these collaborations, I start to think more as they think. They have to convince their financial or marketing people that what they do will be profitable. When we developed an instrument with ThermoFisher, I was mostly thinking about viruses. But at some point, I thought it could also analyze better the antibodies that biopharma companies were making. By showing that it really works, my collaborators in industry had much more room to do what they wanted to do.

We also collaborate with medical doctors. They always ask, "Yeah, but what does it mean for my patient?" Someone like me normally doesn't ask that question. But if you work with people who do, you also start to think about it. I enjoy collaborating with all these different people, because it makes you also think about other fields that you may want to contribute to.

Q. Say more about your work with physicians?

This is a typical example of what I really enjoy. For me, the story started five years ago, when I heard some lectures about immunology and started to read. Textbooks say every human can make a billion times a billion different antibodies. I started to ask people that I thought knew more about immunology than I did, "OK, but how many are actually ending up in your blood?" And the only answer I got was "Ja, you can make billion times billion different antibodies." But how many are there in the blood? You can make a calculation and conclude already that this cannot be a billion times a billion different ones; it needs to be less. But you still get a staggering number. I asked this question because I wanted to see if I could separate and measure them all; if there are a billion times a billion, mass spectrometry is very powerful, but that can never be done.

Q. Give it another five years?

Yeah, I should never say never in this field. But at some point, I said to some of my people in the lab, "People say it cannot be done, but let's just do it." To make a long story short, we saw that at any moment there are maybe 1,000 different antibodies that are so abundant that they make up 99% of all the antibodies in your blood. This is such a different number.

First of all, this changes the textbook in immunology. Then you're going to ask, Why are these there, and why are all the other possibilities not there? None of us has identical antibodies; everyone has their own repertoire. We want to know how these repertoires adapt when you get vaccinated and how that changes from directly after vaccination to months later. COVID-19 vaccination is now hot, but actually with every pathogen that can attack you, these hundreds to thousands of antibodies that you make will determine if you get very sick or if you can survive. We hope to find out which antibodies are helping people to survive. We aren't there yet, but with these mass spectrometry–based methods that we've developed, we are able to monitor antibodies using just a few droplets of blood. This, again, is something that I had never dreamed of five years ago.

And now, which I find equally exciting, I'm contributing to immunology in areas where immunologists were stuck for 20 years. They sequenced all the B cells and found that you indeed have a zillion B cells in your body that all can make an antibody. But that's the same as all sequencing: It still doesn't mean that

"We hope to find out which antibodies are helping people to survive. We aren't there yet, but with these mass spectrometry–based methods that we've developed, we are able to monitor antibodies using just a few droplets of blood. This, again, is something that I had never dreamed of five years ago."

ALBERT HECK

you know which proteins are really expressed in the cell.

Q. How did you first become involved with Molecular & Cellular Proteomics?

When Molecular & Cellular Proteomics was started, I considered it a recognition of the field — a platform where I could meet my buddies and where we could also really contribute with publications that helped the field. It became one of the prime journals for me from the start.

One thing that I have gotten more convinced about is that we should cherish our societies and our society journals. Most of these journals don't have the same drive for profits that we see with bigger publishers.

And MCP has really been leading in quality control in publishing in proteomics. In a technical field like proteomics, this is very important. I think several people have some reservations with the journal because there is such strict data quality control. I sometimes also don't like it, because it takes you a few hours to fulfill all these rules. On the other hand, we had a joke for years that if you had good proteomics data, you could publish in MCP, and if you didn't have such good data, you could maybe go for Cell. That was true 10 years ago, but what you have seen is that these top journals also adopted more and more the MCP templated guidelines. I think MCP has played a major role in setting standards, and the journal should be applauded. Along with being my home for publishing, that role in maturing the proteomics field helped me to say yes, I also want to do my part in supporting the society and the journal.

Laurel Oldach (loldach@asbmb.org) is a science writer for the ASBMB. Follow her on Twitter: @LaurelOld.

What we're asking for — on your behalf

Recent advocacy activities focus on sustained funding for curiosity-driven science, safe and equitable work environments, and support for next-generation researchers

By Sarina Neote

The American Society for Biochemistry and Molecular Biology's Public Affairs Advisory Committee and staff advocate for robust funding and policies that provide flexibility to scientists, ensure the sustainability of the American research enterprise, and support scientists from all backgrounds at all institutions.

Here's what we've been up to. (You can read all of our position statements and letters at asbmb.org/advocacy.)

Our NIH budget recommendations

Sustained increases to the National Institutes of Health's budget are essential. We provided written testimony at a hearing about the federal budget for fiscal year 2023 by the U.S. House Committee on Labor, Health and Human Services, Education, and Related Agencies. We requested:

1. $49.05 billion for the NIH base budget.
2. $3.25 billion for the National Institute for General Medicines within the NIH.
3. $430.5 million for the NIH to direct specifically to the Institutional Development Awards program.

Virtual Capitol Hill Day: A real success

Members of the PAAC and others met with lawmakers May 11. Participants urged them to:

- Separate funding for the Advanced Research Projects Agency for Health from funding for the NIH.
- Pass pro-science provisions in the competitiveness bills moving through Congress.
- Support a "Dear Colleague" letter (a document used by members of Congress to encourage their colleagues to support specific issues) to increase funding for STEM training programs at the Department of Energy, the National Science Foundation and the NIGMS.

Twenty-six participants located in 19 states had 59 meetings.

Compelling the NIH to deal with harassment

We sent a letter on May 25 to U.S. Sens. Patty Murray, D-Wash., and Roy Blunt, R-Miss., and Reps. Rosa DeLauro, D-Conn., and Tom Cole, R-Okla., requesting that language be included in appropriations legislation requiring the NIH to create a strategic plan and timeline to address workplace toxicity and harassment at the agency's intramural campus.

What we want in the U.S. competition bill

The America COMPETES Act of 2022, passed by the U.S. House in February, would bolster U.S. competitiveness in scientific research and development. The Senate passed its own version of the COMPETES Act — the United States Innovation and Competition Act of 2021 — several months later. Now Congress must establish a conference committee to negotiate the differences and come up with a single unified bill.

We're asking policymakers to ensure that provisions in both of the bills are included in the final version, such as those that focus on attracting and retaining international talent, addressing systemic barriers faced by the next generation of scientists, and combatting sexual harassment in science, technology, engineering and mathematics.

Sarina Neote (sneote@asbmb.org) is the ASBMB's director of public affairs.

‘How life began merits a preceding discussion of what life actually is’

By Jeanine Amacher

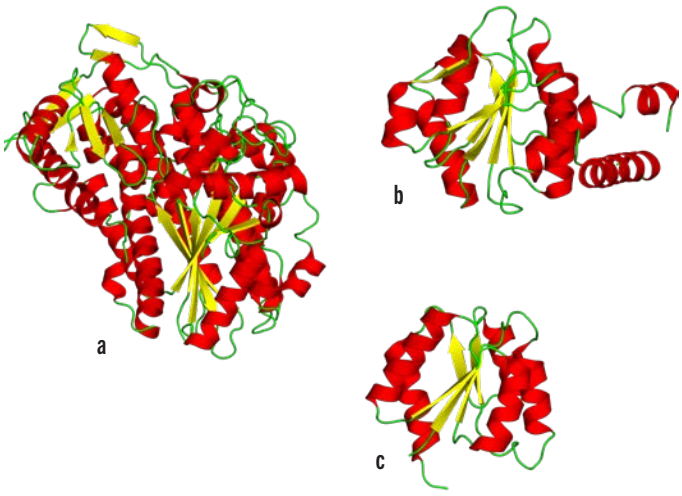
The origin of life has perplexed and fascinated scientists for the better part of a century. Nir Ben–Tal and Amit Kessel’s new book, “From Molecules to Life: The Origin of Life on Earth,” uses biochemistry and evolution to describe hypotheses of life’s origins and the last universal common ancestor, an anaerobic prokaryote.

According to Ben–Tal and Kessel, life likely began on Earth around 3.5 to 3.8 billion years ago with a combination of RNA–peptide–lipid–metal molecules. They said the two key operational capabilities to life are informational (encoding and transmitting genetic information) and metabolic (accelerating chemical processes and utilizing nutrients).

“From Molecules to Life” focuses specifically on the biological macromolecules that are critical to life as we understand it, such as nucleic acids, proteins and lipids. The chapter on protein evolution describes the nine most ancient folds of protein domains, including the idea that most gene families formed from 2.85 to 3.3 billion years ago and new protein families formed mainly from existing genes after that time.

The book describes hypotheses and experiments that show how amino acids and simple molecules related to the cell can arise spontaneously, given the right conditions. Amino acids and similar molecules are found on meteorites, suggesting this chemistry also occurs on other planets.

This interview has been edited.



What motivated you to write this book?

Kessel: As biologists, we were mainly motivated by the need to bring more biology into the story. Most origin-of-life textbooks focus on the chemical evolution step of life’s emergence — the organic chemistry that spontaneously turned simple compounds into biomolecules like proteins, RNA and peptides on primordial Earth. The nature of these biomolecules and how they evolved into functionally efficient forms capable of forming biochemical networks is usually ignored.

Today, it is possible to track some of these processes thanks to the ample biological data obtained in recent years on proteins and on the genes coding for them. This has allowed scientists to use a top-down approach to analyze the sequences and structures of contemporary proteins in order to trace their evolution back to early peptides and peptide–RNA complexes, which are similar to those created by the chemical evolution step.

Ben–Tal: Several years ago, I gave a talk about our discovery of protein segments that are extensively reused in the protein world, suggesting that they might be evolutionary descendants of ancient functional peptides.

The talk was meant mostly for undergraduate bioinformatics students, and I felt that I should briefly introduce them to the origin of life in order to give a broader context of our own research. The very enthusiastic response to this talk is what made us think about writing a book that integrates protein evolution with the preceding step of chemical evolution. Obviously, the book is based for the most part on studies by other scientists, including many who are no longer with us, and our own research adds just a tiny bit.

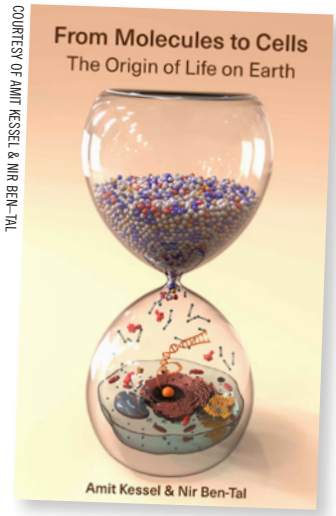
We also felt that the discussion of how life began merits a preceding discussion of what life actually is. To this end, we included a chapter that describes the basic features that are common to all living organisms on Earth. We then used these features to compare the general definitions of life used widely today, such as that used by NASA, with a

narrower yet more accurate definition that refers to life as we know it on our planet.

Did "From Molecules to Cells" stem from your interest in protein evolution?

Ben–Tal: In our lab, we exploit evolutionary data, on the one hand, to highlight key aspects of a protein of interest, as in ConSurf, and, on the other hand, to infer from detailed mechanistic studies about one protein into homologues. In general, the ample sequence and structure data enables investigation of proteins as families.

In recent years, we discovered numerous protein fragments, which we call "themes," that are extensively reused by proteins. This discovery, followed by the finding that some of these themes are involved in ancient protein functions like the binding of nucleotide cofactors, suggested that they may be descendants of peptides that preceded proteins.



COURTESY OF AMIT KESSEL & NIR BEN–TAL

"From Molecules to Life: The Origin of Life on Earth" by Amit Kessel and Nir Ben–Tal is available in a Kindle edition from Amazon.

The book is our effort to bridge the gap between what is known from the bottom-up chemical evolution approach and what we are beginning to reveal from peptide/protein evolution.

Elaborate a bit on what you call the world hypotheses, including the RNA world, the peptide/amyloid world, the lipid world and the virus world.

Kessel: The world theories came up when scientists looked for a molecule that could serve as a progenitor of life. Such a molecule would have to be simple enough to form spontaneously under primordial Earth conditions, yet sufficiently sophisticated to act in both informational and operational capacities. That is, to be able to hold genetic information, pass it on to the next generations,

About the authors

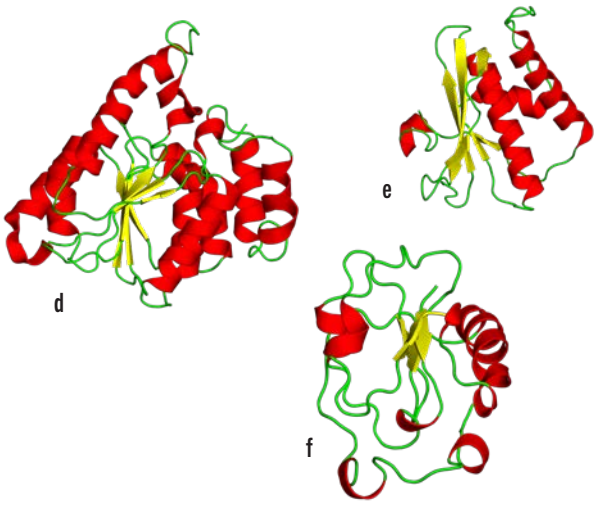
Nir Ben–Tal is a professor of biochemistry and molecular biology and heads the Ben–Tal Lab of Computational Structural Biology at Tel Aviv University. He received his Ph.D. from the Technion–Israel Institute of Technology and conducted postdoctoral research at Columbia University. He is an author on more than 150 publications and has trained more than 50 graduate students and postdoctoral fellows. His lab created the ConSurf server; the 2010 and 2016 papers describing this resource have been cited over 3,000 times. He is senior editor of the journal Protein Science and a member of the editorial boards of the scientific journals PLoS Computational Biology, eLIFE and the Journal of Biological Chemistry.

Amit Kessel is a research associate at Tel Aviv University, where he works as a computational biologist and a lecturer. He received a Ph.D. from Tel Aviv University and conducted postdoctoral research at Columbia University. His website provides a summary of the new book, describes his other work, and provides general resources for scientists, students and interested members of the general public. Follow him on Twitter: @KesselAmit.

Ribbon illustrations on pages 50, 52 and 53 represent the nine most ancient protein folds as suggested by Gustavo Caetano–Anollés, a professor of bioinformatics at the University of Illinois at Urbana-Champaign, and co-workers.

a. **The P-loop fold of nucleoside triphosphate hydrolases.**
b. **NAD(P)-binding Rossmann fold.**
c. **Flavodoxinlike fold.**
d. **S-adenosyl-L-methionine-dependent methyltransferase fold.**
e. **Ribonuclease H-like fold.**
f. **Ferredoxinlike fold.**
g. **OB fold.**
h. **TIM beta/alpha barrel fold.**
i. **DNA/RNA-binding 3-helical bundle fold.**

Illustrations courtesy of Amit Kessel & Nir Ben–Tal.



promote biochemical processes and evolve.

In all the living organisms we know, the informational role is carried out by DNA and the operational role is carried out by proteins and RNA, and they are all coupled via the gene expression system. This could not be the case in the first protocells, because such complex systems did not exist. So the same molecule needed to function in both informational and operational roles.

DNA and proteins were excluded because DNA cannot catalyze processes and proteins are too complex to form spontaneously. Walter Gilbert proposed his RNA world theory when he and others realized that RNA molecules, already known to store genetic information, catalyze chemical reactions in contemporary organisms.

Other researchers later proposed similar world theories for peptides (isolated or in the form of stable amyloid structures) and for lipids, which were also found to be catalytically active and form spontaneously. These theories were spiced with proposed hybrid molecules such as the 'peptide nucleic acid,' which has stable peptide backbone and nucleotide side chains that can form base pairs.

Ben–Tel: Although the RNA world seems to be the most plausible theory, it is burdened by certain aspects of RNA molecules, such as their unstable nature and very limited catalytic activity. Moreover, to evolve, RNA molecules would have to self-replicate by template-based synthesis. Such a process has been demonstrated only for short or otherwise simple RNA molecules, which cannot act as catalytic entities.

While these problems remain unresolved, some of them could be mitigated if the RNA molecules formed molecular complexes with peptides, metals and lipid molecules (isolated or as assemblies). Binding any of these entities would stabilize the RNA molecule by suppressing internal dynamics and masking charges.

And each of these entities could contribute its unique advantages: Peptides and metals could mediate substrate binding and increase the catalytic efficiency of the RNA, whereas peptides and lipids could increase the catalytic scope of the RNA. In our view, such multichemical entities' synergy was crucial for completing the emergence-of-life process.

What do you envision when you think of Earth at the time of the last universal common ancestor?

Kessel: Life is believed to have appeared during the early Archaean eon. At this time, Earth has already cooled down, the molten rock on its surface solidified and water vapor condensed into oceans. It's difficult to know exactly how the planet looked back then, because very little geological evidence is left.

We envision this Earth as covered largely by water, with considerable volcanic and hydrothermal activity. This is in line with the widely accepted view of life's emergence on the planet; the process is thought to have occurred in hydrothermal microenvironments, which could provide all that was required for the chemical evolution stage — starting materials, an energy source (heat) and even mineral catalysts. Most of these microenvironments were probably hydrothermal vents on the oceans' floors, whereas others were on land, such as hot springs and geysers. The latter two were probably more important for the chemical evolution stage, since the air–water–land interfaces they contained promoted polymerization reactions. The process was affected by the atmosphere, which contained mainly nitrogen and carbon dioxide but also several greenhouse gasses. The latter kept the planet relatively warm despite the faint sun.

Building off this idea, briefly discuss how life arose on this planet.

Ben–Tal: We assume the process included the gradual formation of increasingly complex organic molecules from simple compounds like methane, ammonia, hydrogen cyanide and hydrogen sulfide via spontaneous chemical reactions. This ultimately led to the formation of biomolecular building blocks that polymerized to form functional peptides and RNA molecules.

The first clue that such a process was possible came from the Miller–Urey experiment in 1953, which demonstrated the spontaneous formation of amino acids in a closed system containing only methane, ammonia, hydrogen and water vapor subjected to electric sparks. Indeed, amino acids are extremely easy to form and can be found also inside meteorites.

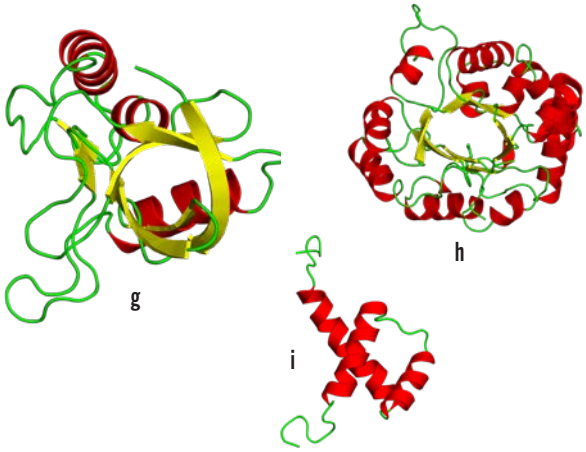
Kessel: Some of these peptides and RNA molecules are thought to have been sufficiently complex to carry out simple life processes, and when they became trapped inside lipid vesicles along with their substrates, they formed the first protocells. Continued evolution of the latter into real cells was accompanied by morphological and functional changes as well as the development of a DNA genome, a protein translation system and a protein-catalyzed metabolism.

What about life on other planets?

Kessel: Could such a process happen on other planets as well? I don't see why not. There are a lot of planets out there and, given a set of starting materials, an energy source and liquid water, we have no reason to believe that complex molecules could not form as they did on Earth and form simple living organisms.

In our solar system, a few candidates are proposed. For example, Mars is relatively close to the sun for biological organisms that may live there to harness solar energy, and it also contains subsurface liquid water. Still, these organisms would have to cope with the strong radiation on the planet's surface.

Europa and Enceladus, moons of Jupiter and Saturn, respectively, are very far from the sun, and their surfaces are completely icy. However, below their surfaces, there are high-temperature activities that might promote life the same way hydrothermal vents are thought to have done on primordial Earth.



How do you think proteins evolved into the complex molecular machines we see in extant organisms?

Kessel: This is one of the toughest questions to answer; while there is ample evidence about the major mechanisms of protein evolution — which involve replication, fission, divergence and recombination of domains and smaller parts — it is very difficult to know exactly how a certain protein or molecular machine evolved. This is because we rarely have enough representatives of the intermediate states of the process, especially when it is very old.

Ben–Tal: The ribosomal complex is one case where information obtained from numerous phylogenetic studies was used to suggest an almost complete evolutionary process, although these studies focused on the RNA components of the complex. The process started from catalytic RNAs capable of randomly attaching amino acids, continued in a separate development of a decoding center that bound amino acid–carrying tRNA, and culminated in the assembly of the two parts into a genetically guided protein-synthesizing machine.

Some phylogenetic studies try to date the evolutionary processes of proteins by assigning the appearance of domains and folds to known evolutionary and geological events, such as the emergence of eukaryotes and multicellular organisms and the oxidation of the atmosphere. This yielded the proposed time frame for the appearance of the first protein gene families. Such time calibrations of processes are generally inaccurate and should be taken with caution.

Kessel: Still, even a qualitative investigation of protein evolutionary processes yields very interesting findings. For example, the stepwise evolution of different protein functions, starting with redox catalysis and nucleotide/iron–sulfur binding, followed by respiration, photosynthesis and signaling. It is also interesting to see how the first protein folds that appeared match these ancient functions, such as nucleotide binding by the Rossmann, P-loop and flavodoxin folds.

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What is better for your career than a publication? A preprint.

By Ken Hallenbeck

Publication in a peer-reviewed journal is the goal of almost all academic research, because authorship is accepted by the scientific community as a career accomplishment. This is a challenge for early-career researchers, or ECRs, because the modern peer-review process can take months to years from initial submission to final acceptance.

ECRs can be stuck trying to leverage a completed project into a career advance without final publication acceptance. Often, ECRs record not-yet-published manuscripts as "in preparation," "under review" or "accepted," but that doesn't help a hiring committee examine the work itself. One way to circumvent this problem is by preprinting.

Preprinting is the practice of uploading a completed manuscript to a public server. Currently, over 50 preprint servers cover a wide range of disciplines, and conversations about the practice have reached the mainstream media. The overall growth in preprinted manuscripts is accelerating.

So should you join the preprinting revolution?

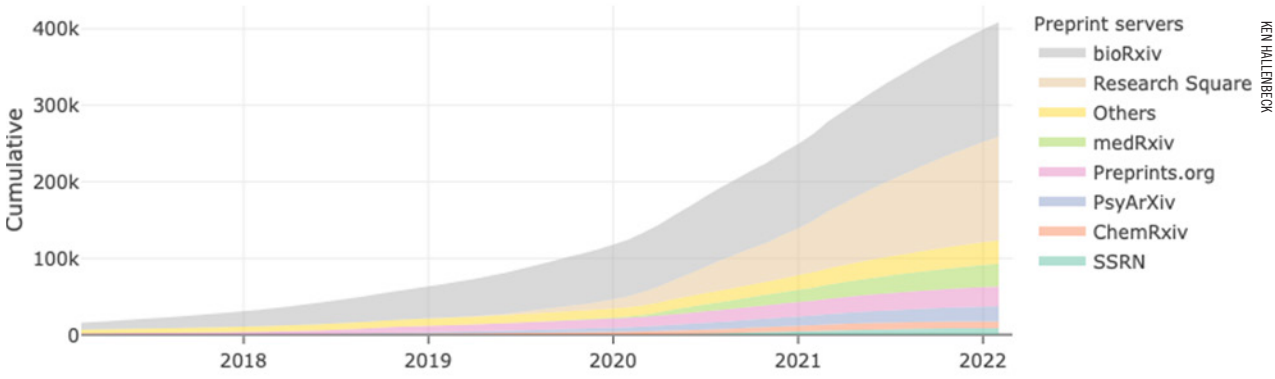
Preprinting pros and cons

Depositing a paper outside of an academic journal allows an author to start promoting the work immediately. A first or co-first author on the job market can link directly to the manuscript in their CV and during interviews. In addition, studies show preprints that go on to publication in a peer-reviewed journal have increased readership and are cited more often. Preprinting not only speeds up the initial sharing process but also adds value in the long term.

One reason for this increased readership is that preprints have no access barriers. Preprint servers are free to use and free to access, expanding the readership reach of an article and enabling open science. Anyone can read, comment on and cite preprints, and that gives preprinted work a wider audience.

Given the accessibility of preprints, authors often are concerned about the risk of scooping — a competing research group will see the preprint and rush to publish their results in a journal before the preprint authors have an opportunity to do so themselves. However, I have seen no evidence that data published in preprints is scooped more often than data withheld until journal publication.

In fact, the opposite is true. Researchers have used their preprints to initiate collaborations with other groups in the field or to coordinate simultaneous publication of their work, thereby avoiding concerns about priority claims. As a recent example, Josh Hardy, an adjunct research associate at Monash University, saw a preprint from another group and got in touch



KEN HALLENBECK

The number of papers printed on preprint servers has jumped in the last two years.

with the preprint authors. The two groups coordinated the journal publication of their respective papers, which ended up appearing in the same journal.

Preprinting practicalities

All authors must be on board to preprint a manuscript, and the conversations should happen early in the drafting process so there is time to address concerns. There are a variety of resources that may assuage their concerns, such as the ASAPBio FAQ.

There are a few important things to consider once you have the go-ahead to preprint.

- **Journal:** If you plan to submit the manuscript to a journal, familiarize yourself with the journal's editorial policies about preprints. Some journals specify the preprint servers that they accept for preprint deposition.
- **License:** It is also important to think about the license you will apply to the preprint. There are several options — from no license (meaning you do not give default permission to reuse the work) to a range of Creative Commons licenses that designate the type of uses allowed.
- **Format:** In general, preprint servers are format agnostic, meaning they accept a single file of your manuscript in any format (for example, a single PDF file in the formatting style of the journal of your choice!) and then authorship information. However, some journals work with preprint servers to allow for direct submission of your manuscript to a journal after posting to the preprint server. You may only need to click one button for preprint and journal submission!

Many researchers are still wary of preprinting; perhaps you or a co-author have unaddressed concerns. A more detailed guide on preprints, their history and the current status of adoption is available as a preprint (of course!): "A Guide to Preprinting for Early Career Researchers." I also suggest you keep an eye on the latest preprints coming out in your research field. New results are preprinted every day, and you might just find your next collaborator!

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

'We're all a bunch of weirdos doing our stuff'

By Martina G. Efeyini

Charles Sanders talked to ASBMB Today about his experience working on biopharmaceutical products at XBiotech, where he started as a research associate in March, and Grifols, where he worked for more than three years after earning his bachelor's in biochemistry. This interview has been condensed and edited.

1 What made you decide to focus on products?

Both Grifols and XBiotech manufacture medicine, and I enjoy pharmaceuticals. I just really enjoy helping people. I've been wanting to make medicines for a long time. I feel like it's a good contribution to the world.

2 Grifols is one of the largest producers of plasma medicines in the world. Tell me about your work there as a testing technologist.

It was an entry-level position. … We would take the plasma that got sent to us. We would screen it using different biochemical assays, like the ELISA. We had something called the C8000 that would test for total protein concentration and concentration of alanine aminotransferase as a test for donor liver health. We also tested for syphilis and rabies — all kinds of fun stuff.

Charles Sanders

CURRENT POSITION
Research associate II at XBiotech

CAREER PATH
Bachelor's in biochemistry, Texas State University

FIRST JOB OUTSIDE OF ACADEMIA
Testing technologist at Grifols

FAVORITE MOLECULE OR PROTEIN
"I actually do have a favorite one because I love its name. It's polytetrafluoroethylene. I just like the way it rolls off."

3 Tell me about your new role at XBiotech as a research associate.

I'm still in the training phase. … I've been doing mostly gel runs and western blots. Basically, doing protein analysis, checking for different proteins, and seeing if antibodies will bind to them, because we're looking for specific things.

There's different departments: There's cell lines — they do all the cloning. There's biochemistry, there's animal models — all kinds of teams — but I'm specifically in the in vitro testing.

I feel at home. We're all a bunch of weirdos doing our stuff.

4 How did you wind up at XBiotech?

I think the three years of experience I got at Grifols really helped me, and I think that's what got me drafted to this position. I did undergrad research, and the scientist who leads my team recognized my principal investigator's name. And then he saw what I'd been doing at Grifols.

He said that, because of COVID-19, most people were doing their master's degrees online, but they don't have any actual research experience. So I outranked a lot of master's students because I have real-world experience... I think it was all worth it.

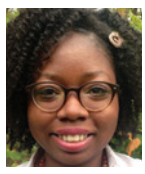
5 What advice do you have for students interested in industry?

Do it if you want to experience the world. I think you should explore the world and learn how the Food and Drug Administration works and good manufacturing practices.

If you want to stay in academia, you can do that. But I actually think academia is more stressful. I felt like, if I just stayed in academia, I'd be losing potential to learn about the world.

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

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



CLASSIFIEDS

Postdoctoral Fellowship — Molecular Mechanisms and Translational Oncology
Cleveland Clinic

Do you have a background in molecular, biochemical or chemical mechanisms, cancer, medicinal or analytical chemistry? Are you interested in translational medicine and taking your mechanistic findings rapidly to the bedside in a vibrant clinical research program? If so, a postdoctoral fellowship position supported by the National Institutes of Health and the Prostate Cancer Foundation is available in the laboratory of Dr. Nima Sharifi at the Cleveland Clinic. This position is ideal for an individual with a strong interest in rapid translation of basic mechanistic discoveries to the bedside as this is a principal goal of the Sharifi Laboratory. The position will provide a unique and multidisciplinary exposure to tumor metabolism, molecular oncology, drug development, and clinical trials.

https://careers.asbmb.org/job/postdoctoral-fellowship-molecular-mechanisms-and-translational-oncology/63887081/

Postdoctoral Position
University of California, Davis

A postdoctoral position is available in Dr. Cecilia Giulivi's laboratory at the University of California Davis.The successful candidate will work on multidisciplinary research projects combining biochemistry, molecular biology, genetics, combined omics (lipidomics, proteomics, and metabolomics), imaging, epidemiology, toxicology, and psychiatry. Trainee will be mentored at developing an independent research program to provide the foundation for future research careers.

https://careers.asbmb.org/jobs/view/postdoctoral-position/63752089/

Principal Investigators in Cellular, Systems and Developmental Biology
Lunenfeld-Tanenbaum Research Institute

The Lunenfeld-Tanenbaum Research Institute of Sinai Health, a University of Toronto affiliated biomedical research center, is recruiting emerging leaders in the area of Cellular, Systems and Developmental Biology. They are seeking applicants who will develop innovative, outstanding and independent programs in Cellular, Systems and Developmental Biology. Research approaches include, but are not limited to, the application of functional genomics, proteomics, metabolomics, epigenomics, single-cell analytics, and tissue engineering to investigate complex systems from the molecular to organism level including humans and/or model animal systems. Topic areas encompass reproductive, developmental, and regenerative biology, cellular physiology, and network and systems biology.

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Postdoctoral Position
University of Pittsburgh School of Medicine

The Chu Laboratory is seeking creative, collaborative and independently motivated post-doctoral researchers to study the role of secretory/degradative pathways and synaptic pathobiology in primary neuron, mouse and/or iPSC models of familial dementias. Join an active team of researchers working on FTLD-tau, valosin-containing protein and PINK1, with opportunities to study Golgi/retromer & lysosomal biology or mitochondria.

https://careers.asbmb.org/job/post-doctoral-position-to-study-organelle-homeostasis-and-synaptic-biology-in-familial-neurodegeneration/63787800/

To see a full list of jobs, please visit careers.asbmb.org

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